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Analysis of the stress-deformed state of the femur with gunshot fracture with various methods of its fixation

I. A. Lurin [1,2], O. A. Burianov [3], Y. O. Yarmoliuk [3,4], B. V. Matviichuk [3,5]

[1] National Academy of Medical Sciences of Ukraine, Kyiv

[2] SSI «Center for Innovative health Technologies» of the State Administration of Affairs, Kyiv, Ukraine

[3] Bogomolets National Medical University, Kyiv. Ukraine

[4] National Military Medical Clinical Center «Main Military Clinical hospital», Kyiv. Ukraine

[5] Military Medical Clinical Medical treatment and Rehabilitation Center, Irpin`, Ukraine

The standard method for stabilizing diaphyseal gunshot fractures of the femur (GFF) is external fixation using a rod apparatus (ex-fix). Objective. To perform a comparative analysis of the biomechanical effectiveness between conventional ex-fix fixation and a modified «ex-fix + intramedullary spacer» design by assessing the stress-strain state of the femur with a midshaft gunshot fracture. Methods. A finite element model of a midshaft femoral gunshot fracture was developed. Two fixation scenarios were simulated: standard rod-based ex-fix, and a combined system using an intramedullary spacer and an ex-fix rod apparatus. Displacement, stress, strain and safety factor were chosen as the effects studied. Results. Conventional fixation resulted in significant stress concentrations at the fracture site (62.4 MPa) and high deformation levels (215.9), exceeding the strength threshold of cortical bone. This may lead to fragment instability and femoral axis misalignment. Rod exit points showed deformation (121,1), contributing to loosening, inflammation in adjacent soft tissues, and overall instability of the fixation system. In contrast, the addition of an intramedullary spacer redistributed stress more evenly, reduced the mechanical load on bone tissue, and improved structural integrity. The combined «spacer + ex-fix» configuration demonstrated superior performance in minimizing deformation and fragment displacement. Conclusions. Finite element modeling confirmed that the «bone + ex-fix + spacer» system outperforms the traditional «bone + ex-fix» configuration in key parameters: displacement, stress, deformation, and safety margin.

Стандартним методом фіксації в разі діафізарних вогнепальних переломів стегнової кістки (ВПСК) є стрижневий апарат зовнішньої фіксації (АЗФ). Мета. Провести порівняльний аналіз фіксації стегнової кістки стрижневим АЗФ і модифікованою конструкцією «стрижневий АЗФ + інтрамедулярний спейсер» шляхом дослідження напружено-деформованого стану стегнової кістки в разі вогнепального перелому в середній третині. Методи. Побудовано скінченно-елементну модель ВПСК у середній третині. Фіксацію здійснювали двома способами: стрижневим АЗФ і комбінацією інтрамедулярного спейсера та стрижневого АЗФ. Досліджуваними показниками було обрано переміщення, напруження, деформацію та запас міцності. Результати. Виявлено, що класична фіксація кісткових уламків за ВПСК у середній третині за допомогою стрижневого АЗФ спричиняє значне напруження в зоні перелому (62,4 МПа) та деформацію (215,9), які перевищують межу міцності кісткової тканини. Це може призводити до нестабільності уламків і порушення осі сегмента кінцівки. Деформація кістки в місцях виходу стрижнів (еквівалент 121,1) викликає їхнє розхитування, що спричиняє запальні процеси в навколишніх м'яких тканинах і загальну нестабільність фіксаційної системи. Запровадження внутрішнього фіксатора в комбінації з АЗФ забезпечує рівномірніший розподіл напружень у моделі, знижує навантаження на кістку та збільшує запас її міцності. Ефективнішим рішенням, згідно з критеріями мінімізації деформації та переміщення уламків, виявилась система фіксації типу «інтрамедулярний спейсер + стрижневий АЗФ». Висновки. За результатами комп'ютерного моделювання виявлено, що система «кістка + АЗФ + спейсер» має перевагу над системою «кістка + АЗФ» за досліджуваними показниками: переміщення, напруження, деформація та запас міцності. Ключові слова. Вогнепальний перелом стегнової кістки, напружено-деформований стан, моделювання.

Keywords. Gunshot femoral fracture; stress-strain state; simulation

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Introduction

In modern combat operations, limb injuries account for up to 62.6 % of surgical casualties. Of these, lower limb injuries occur in 58 % of cases, and upper limb injuries in 42 % [1–3]. The proportion of thigh injuries in the structure of combat trauma ranges from 13.6–28.3 %, of which 16.2–22.3 % are diagnosed with a femur fracture [4–6]. Diaphyseal gunshot fractures of the femur (GFF) account for 81.4 % of such injuries and are accompanied by primary bone defects in 79.3 % of cases [7–9].

The standard fixation method for diaphyseal GFF is an external fixation rod (EFR), consisting of a beam and six Schantz rods — three proximal and three distal to the fracture zone [10–12]. Despite its prevalence, this design has a number of significant drawbacks: instability in prolonged use due to microdeformations of the bone in the areas of rod passage [13, 14]; functional limitations, complicating the rehabilitation process; the likelihood of bone deformations due to uneven load distribution; psycho-emotional discomfort of patients [15, 16].

These issues reduce the effectiveness of treatment and require the development of more stable, biomechanically sound methods for fragment fixation that also do not complicate access to the wound area.

Objective: to conduct a comparative analysis of femoral fixation with an external fixation rod device and a modified design "external fixation rod device + intramedullary spacer" by studying the stress-strain state of the femur in a gunshot fracture in the middle third.

Material and methods

A finite element model of the femur was constructed, a multifragment (7 intermediate parts) gunshot fracture in the middle third was simulated (Fig. 1). The intermediate bone fragments had partial contact with each other, with the proximal and distal fragments of the femur. In the diaphyseal part, the minimum bone diameter was 3.3 cm, the width of the bone-medullary canal was 1.5 cm. In the zones of the transition of the diaphysis to the metaphysis, the diameters increased according to anatomical features.

Two methods of fixation were analyzed: rod EFR, a combination of an intramedullary spacer and rod EFR.

The intramedullary spacer consists of a 0.5 cm thick frame made of surgical steel (AISA 316), covered with bone cement (polymethyl methacrylate). The total thickness of the spacer is 1.0 cm. A metal loop is placed at its proximal end, which allows implantation and removal of the fixator (Fig. 7, 10). The proximal end of the spacer is located in the area of the greater trochanter of the femur; the distal end is 2.0 cm above the articular surface. External fixation rods with a diameter of 0.5 cm are inserted into the metaphyseal areas of the bone, bicortically, in the areas of expansion of the bone-medullary canal, past the trajectory of the spacer.

During modeling, the material was considered homogeneous and isotropic. Its mechanical characteristics were selected according to technical literature [17–20]. The following physical and mechanical parameters were used for the analysis: E — modulus of elasticity (Young's modulus), v — Poisson's ratio (Table 1).

An example of an anatomical femur was obtained by converting a computer tomogram into a solid-state model using the IntelliSpace Portal software. The 3D model was imported into the Solidworks 19 software. The mathematical mesh was created using the triangulation method. The stress-strain state of the models was calculated using the SimSolid software.

The finite element method was used to analyze the stress-strain state of biomechanical models. The boundary conditions were set using the Structural linear function: the distal articular surface of the femur was rigidly fixed (immoveable function); sliding fixation was applied in the area 1.0 cm distal to the articular surface. A force of 400 N was statically applied to the proximal end of the femur using the Force/Displacement function (Fig. 2). A triangular mesh with Gaussian points was automatically created. The studied effects were displacement, stress, deformation, and safety margin. A system of linear equations of equilibrium of finite elements was solved to determine the components of displacement in each node. The obtained results were then used to calculate the components of equivalent deformation, which is a generalized value, taking into account its various types, i. e. shear, compression, tension.

The magnitudes of stresses were compared at control points, namely: the zone of gunshot fracture and the area of entry of the external fixation rods into the bone, under the conditions of two variants of femur fixation.

The maximum level of stresses in different parts of the femur and fixators, the magnitude of equivalent deformation and displacement of bone fragments at control points, the safety margin of bone tissue and elements of the fixation system were studied.

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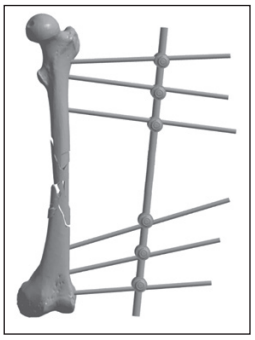

Fig. 1. Model of femur with gunshot fracture, fixed with an EFR

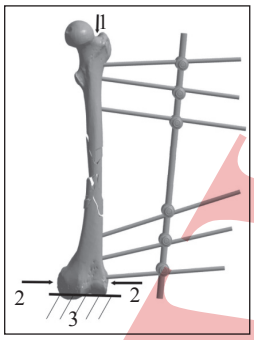

Fig. 2. Points and directions of force application to the femur model fixed with an EFR: 1 — point of force application of 400 N; sliding (2) and rigid (3) fixation of the bone

Table 1

Physical and mechanical properties of the materials used

Material	Young's modulus, E, MPa	Poisson's ratio, v	Safety margin, Rna, MPa
Cortical bone layer	17 600	0.30	170
Cancellous bone layer	500	0.28	10
Surgical steel AISI 316	200 000	0.30	505
Bone cement	1,82	0.18	70

To assess the safety margin of fixing metal elements, the formula (during stressing according to von Mises) (1) was used:

$$K_S = R^n_a/\sigma_a, \quad (1)$$

where K_s is the safety margin; R_{na} is the normal strength limit of the material; σ_a is the stress in the material from normal loads.

Since bone tissue behaves as a biomaterial with plastic characteristics, the shear strength was studied according to formula (2):

$$\tau_{SS}=F/A, \quad (2)$$

where τ_{ss} — shear strength; F — force at which the specimen fails; A — cross-sectional area of the specimen.

According to the technical literature, the threshold value of Ks and τss is 1.0. In the case of indicators less than 1.0, the material begins to fail [18–20].

Results

At the first stage of the study, the stress-strain state of the femur model with a gunshot multifragment fracture in the middle third with an EFR under the action of an applied force was studied. When a force of 400 N is applied to the femur fixed with an EFR, a displacement of bone fragments of 10.5–11.7 mm occurs in the fracture zone (Fig. 3).

The next step was to study the stresses in the femur and the fixing elements (Fig. 4).

According to the image, the stress is distributed throughout the femur, ranging from 9.4 to 62.4 MPa. The highest stress is observed in the fracture zone, at 62.4 MPa.

The deformation that occurs in the femur when a force is applied was studied (Fig. 5).

The maximum deformation concentrated in the fracture zone is 215.9. At the exit points of the external fixation rods in the femur, the equivalent deformation is 121.1.

The margin of safety of the femoral bone tissue in a gunshot fracture in the middle third is shown in Fig. 6.

When applying force, the value of the margin of safety of the bone tissue in the gunshot fracture zone is below 1.0, which can lead to its further destruction.

The study has shown that when using the EFR for fixation of bone fragments in the case of applied force, excessive stress occurs in the bone tissue and fixing elements, which leads to bone deformation and a decrease in the margin of safety of the tissue. At the same time, the EFR does not allow to fully ensure stability during loading.

In the case of using the femoral fixation system "EFR + intramedullary spacer" (Fig. 7), with an applied force of 400 N, fragments move within it (Fig. 8).

In the areas of the femur fixed by the "EFR + intramedullary spacer" system, the move ranges from 0.32 to 1.38 mm.

The stress that occurs in the femur fixed by the "EFR + spacer" system is shown in Fig. 9. It is distributed evenly throughout the bone and is 12.6–13.1 MPa.

When a force of 400 N is applied, the maximum stress occurs at two points of the spacer in the zone

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of the gunshot fracture. According to the infographic, it is 26.5 and 20.4 MPa (Fig. 10). It is noteworthy that the femur is unloaded. The maximum stress that occurs in the zone of the fracture is 13.1 MPa.

The deformation of the femur, fixed with an EFR and an intramedullary spacer, is shown in Fig. 11.

The deformation of the femur under the conditions of its gunshot fracture, fixation of bone fragments by the "EFR + intramedullary spacer" system, according to the infographic, is insignificant, 38.5 for the bone, 124.1 for the spacer.

When calculating the safety margin of the spacer, the following data were obtained: maximum stress 26.5 MPa, Kz = 19.1, i. e. the safety margin is sufficient.

The results of the analysis of the safety margin of bone tissue fixed by the "EFR + spacer" system are shown in Fig. 12.

The safety margin of the bone is in the range from 1.20 to 1.28. It follows that the main load falls on the intramedullary spacer.

A comparison between femoral bone fragment fixation using an EFR alone and the combined approach of "EFR + intramedullary spacer" yields the following conclusions. In the first variant, the main load falls on the femur; the EFR partially stabilizes the fragments, as evidenced by the displacement and stress indicators. In the second, the intramedullary spacer is an internal frame, strengthens the bone tissue and prevents deformation and instability under the influence of applied force.

The computer analysis has shown that the system "femur + EFR + spacer" outperforms "femur + EFR" in terms of displacement, stress, deformation, and safety margin (Table 2).

Discussion

During the treatment of wounded with diaphyseal gunshot fractures of the femur, the fragments are initially fixed with a rod external fixation device, which may contain two or three rods proximally and distally from the injury zone, as well as one or two beams. According to modern studies, the amount of movement of bone fragments during fixation with EFRs is affected by the distance both from the bone to the support and between the extreme rods with which the fragment is fixed. The number of rods (two or three) does not actually affect the movement indicator [16, 21].

EFRs have a number of advantages over other fixators due to minimal tissue trauma and speed of the operation. They can serve as not only the primary method of fixation, but also the final method of treatment, provided that the bone fragments are repositioned and stable.

In case of multifragmentary fracture of the diaphyseal part of the femur, there is often a problem in repositioning the fragments and aligning the axis of the segment. For this purpose, the use of an intramedullary spacer makes it possible to restore the position of the main bone fragments around the internal frame. In addition, the results of the studies indicate a positive effect of the local antibacterial effect of intramedullary spacers, which were used to treat osteomyelitis of long bones, which made it possible to shorten its duration and avoid the development of contracture of adjacent joints [22].

The use of combined fixation "spacer + EFR" makes it possible not only to ensure stable fixation of the fragments, but also to create a channel for the future implementation of blocked intramedullary osteosynthesis during conversion.

The study found that classical fixation of bone fragments in a gunshot fracture of the middle third of the femur using EFRs causes significant stress in the area of injury (62.4 MPa) and equivalent deformation (215.9). This can lead to instability of the fragments and disruption of the axis of the limb segment. Deformation of the bone at the exit points of the rods (121.1) causes their loosening, which causes inflammatory processes in the surrounding soft tissues and general instability of the fixation system.

Based on the analysis, it follows that the installation of an internal fixator in combination with EFRs provides a more uniform distribution of stresses in the model, reduces the load on the bone and increases the safety margin.

Table 2

Comparison of physical and mechanical characteristics of femoral fixation using two options

Characteristics	Femur, fixed with an EFR		Femur, fixed with the "EFR + spacer" system		
	bone	EFR	bone	EFR	spacer
Displacement, mm	11.7	14.4	1.4	0.3	1.4
Stress, MPa	62.4	15.4	13.1	13.1	26.5
Strain, units	215.9	121.1	38.6	12.4	124.1
Safety margin, units	0.14	32.80	1.20	40.10	19.10

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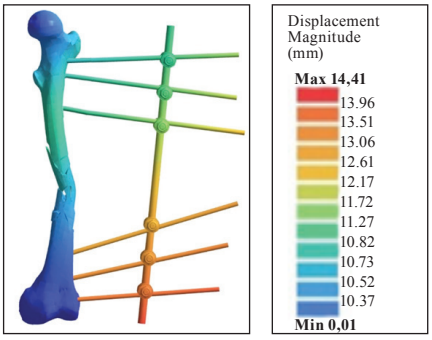

Fig. 3. Movement of femoral fragments under the action of a force of 400 N

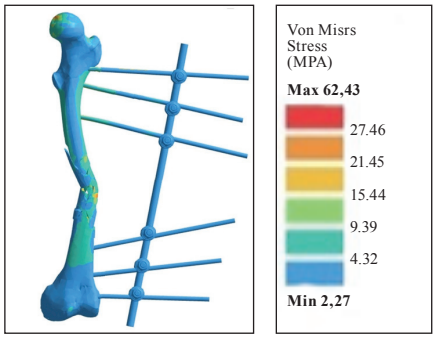

Fig. 4. Stress in the femur and elements of the EFR in force application

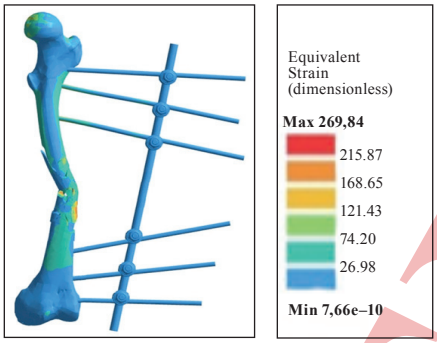

Fig. 5. Deformation occurring in the femur in force application

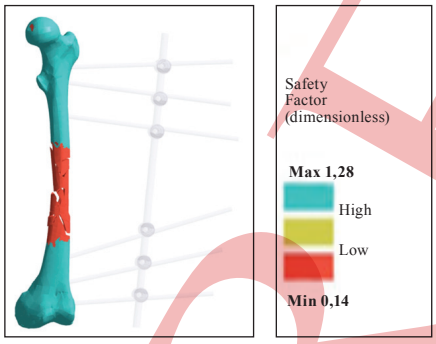

Fig. 6. Safety margin of the femur fixed with an EFR

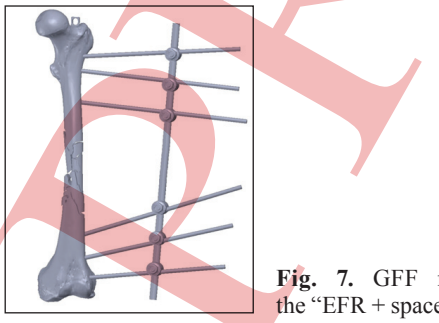

Fig. 7. GFF model fixed with the "EFR + spacer" system

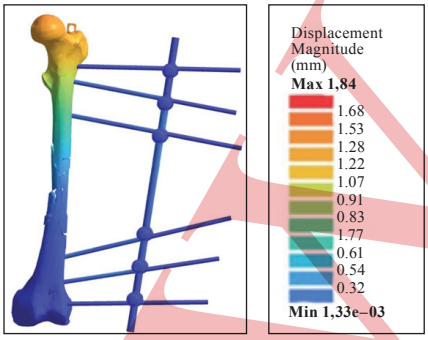

Fig. 8. Movement of bone fragments of the femur fixed with the "EFR + spacer" system

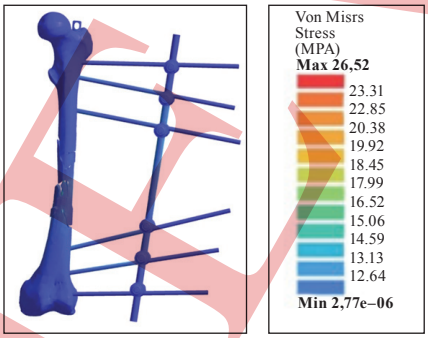

Fig. 9. Stress occurring in the femur fixed with the "EFR + intramedullary spacer" system

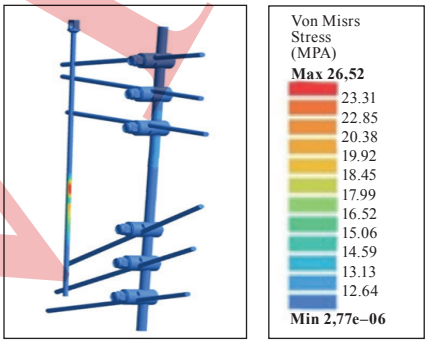

Fig. 10. Stress occurring in the spacer with a force of 400 N applied to the femur with a gunshot fracture

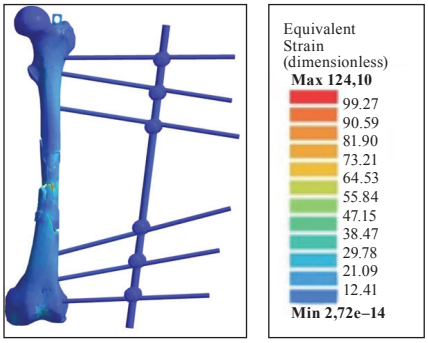

Fig. 11. Deformation of the femur fixed with the "EFR + spacer" system under applied force.

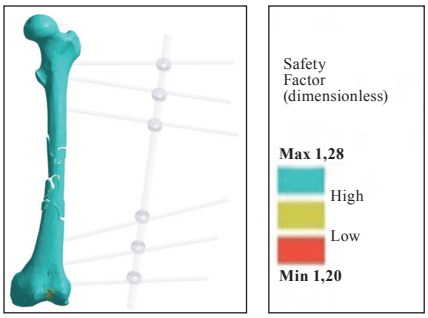

Fig. 12. Safety margin of bone tissue fixed with the "EFR + spacer" system

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Conclusions

Comparative analysis of two methods of fixation of bone fragments of the femur has shown that in the case of using EFRs, the main mechanical load falls directly on the femur, while the EFR only partially stabilizes the fragments from displacement and provides uneven distribution of stress. In the combined fixation option "EFR + intramedullary spacer", the latter performs the function of a frame, significantly increasing the rigidity of the structure and preventing deformation of the femur, loss of stability under the influence of external forces.

The study of the stress-strain state of the femur after its gunshot fracture has revealed that the system "bone + EFR + intramedullary spacer" has an advantage over the system "bone + EFR" in terms of the studied indicators: displacement, stress, deformation and safety margin.

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Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. Future studies should focus on comparing different geometries of the rod device for external fixation in combination with an intramedullary spacer, to better understand the mechanical principles behind the optimal design of such a structure. This will help improve fixation techniques, enhance biomechanical stability, and reduce the risk of complications. Additionally, experimental and numerical modeling, particularly using the finite element method, offers promising potential for optimizing device configurations in various clinical scenarios.

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Authors' contribution. Lurin I. A. — analysis of the findings, critical review of the article, its final approval; Buryanov O. A. — analysis of the findings, final approval of the article; Yarmolyuk Y. O. — review and analysis of related studies, static analysis, critical review of the article; Matviychuk B. V. — review and analysis of related studies, design and modeling, drafting the article.

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ANALYSIS OF THE STRESS-DEFORMED STATE OF THE FEMUR WITH GUNSHOT FRACTURE WITH VARIOUS METHODS OF ITS FIXATION

I. A. Lurin [1, 2], O. A. Burianov [3], Y. O. Yarmoliuk [3, 4], B. V. Matviichuk [3, 5]

[1] National Academy of Medical Sciences of Ukraine, Kyiv
[2] SSI «Center for Innovative health Technologies» of the State Administration of Affairs, Kyiv, Ukraine
[3] Bogomolets National Medical University, Kyiv. Ukraine
[4] National Military Medical Clinical Center «Main Military Clinical hospital», Kyiv. Ukraine
[5] Military Medical Clinical Medical treatment and Rehabilitation Center, Irpin`, Ukraine

✉ Igor Lurin, MD, Prof.: lurinnamn@ukr.net; https://orcid.org/0000-0003-3770-3984
✉ Olexandr Burianov, MD, Prof.: kaftraum@ukr.net; https://orcid.org/0000-0002-2174-1882
✉ Yurii Yarmolyuk, MD, Prof.: Yuo1707@gmail.com; https://orcid.org/0000-0002-9583-1231
✉ Bohdan Matviichuk, MD: godtaken.bm@gmail.com; https://orcid.org/0000-0003-3770-3984

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Bone mineral density and vitamin D status in war veterans after lower limb amputation

N. V. Grygorieva [1], A. B. Vilenskyi [2], O. Z. Stefiuk [3], I. I. Kaut [2], D. Yu. Kurylo [1], A. V. Iniushyna [1]

[1] State Institution «D. F. Chebotarev Institute of Gerontology of the NAMS Ukraine», Kyiv
[2] Charitable Organization «Charitable Fond «Superhumans», Lviv. Ukraine
[3] Danylo Halytsky Lviv National Medical University, Lviv. Ukraine

The study aimed to assess bone mineral density (BMD) and vitamin D status in war veterans after unilateral lower limb amputation (ULLA). Methods. In the case-control study, 64 men aged 20–54 years were examined and divided into two groups: healthy subjects without any diseases or conditions affecting bone metabolism (control group) and men who received ULLA (study group). The analysis was performed depending on the presence and level of amputation. BMD was measured by two energy X-ray absorptiometry, and vitamin D status was assessed by serum dihydroxyvitamin D (25(OH)D) levels. Results. Significantly lower BMD values were found in the femoral neck and the hip of the amputated (p = 0.00002 and p = 0.0002, respectively), byt not in the contralateral side or lumbar spine in amputees compared with controls. Significantly worse BMD indices were found in the femoral neck and the hip in men with transfemoral amputation compared with those with transtibial amputation at the level of the amputation, but not the contralateral side. BMD of the femoral neck of the amputated side significantly correlated with the duration of the post-amputation period (r = –0.47; p = 0.01). Significantly lower serum level of 25(OH)D was found in amputees compared to controls (25.9 ± 4.8) and (32.0 ± 9.8) ng/ml; p = 0.002). 50 % of the control group and 81.25 % of the study group had low side of 25(OH)D. Conclusions. The results demonstrated BMD changes in subjects after ULLA, a significant relationship between BMD and the duration of the post-amputation period, and a high proportion of vitamin D deficiency and insufficiency, which should be taken into account when planning rehabilitation measures in this category of patients.

Мета. Оцінити мінеральну щільність кісткової тканини (МЩКТ) та статус вітаміну D у військовослужбовців після односторонньої ампутації нижньої кінцівки (НК). Методи. Обстежено 64 чоловіків віком 20–54 років, поділених на 2 групи: здорові особи без будь-яких захворювань і станів із визначеним впливом на метаболізм кісткової тканини (контрольна група) та потерпілі після ампутації однієї НК (досліджувана група). Аналіз проводили залежно від наявності й рівня ампутації. Вимірювання МЩКТ здійснювали за допомогою двофотонної рентгенівської абсорбціометрії, статус вітаміну D оцінювали за сироватковим рівнем дигідроксивітаміну D (25(OH)D). Результати. Виявлено достовірно нижчі показники МЩКТ шийки стегнової кістки (ШСК) та проксимального відділу стегнової кістки (ПВСК) ампутованої кінцівки (p = 0,00002 та p = 0,0002, відповідно), проте не контрлатеральної НК чи хребта в ампутованих осіб порівняно з показниками контролю. Зафіксовано достовірно гірші показники МЩКТ ШСК та ПВСК у чоловіків із трансфеморальною ампутацією порівняно з особами з транстібіальною на рівні ампутованої, проте не контрлатеральної НК. МЩКТ ШСК ампутованої НК достовірно корелювала з тривалістю постампутаційного періоду (r = –0,47; p = 0,01). Виявлено достовірно нижчі показники сироваткового рівня 25(OH)D в осіб із ампутацією порівняно з контролем ((25,9 ± 4,8) та (32,0 ± 9,8) нг/мл; p = 0,002). Низькі рівні 25(OH)D мали 50 % осіб контрольної та 81,25 % досліджуваної групи. Висновки. Результати дослідження продемонстрували погіршення стану кісткової тканини на тлі односторонньої ампутції НК, достовірний зв'язок між МЩКТ і тривалістю постампутаційного періоду та високу частку дефіциту й недостатності вітаміну D, що слід ураховувати під час планування реабілітаційних заходів у цієї категорії хворих. Ключові слова. Ампутація нижньої кінцівки; мінеральна щільність кісткової тканини; 25(OH)D; ДРА; остеопороз.

Keywords. Lower-limb amputation; bone mineral density; 25(OH)D; DXA; osteoporosis

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Introduction

The full-scale Russian invasion of Ukraine over the past three years has led to an unprecedented increase in the number of combat gunshot and mine-explosive injuries among both military personnel and civilians. Among these injuries, limb amputations (LAs) occupy a special place, which not only disrupt the integrity of the musculoskeletal system, but are also characterized by profound physiological, psychoemotional, and social consequences for the injured individuals and society as a whole. Important complications of amputations are post-traumatic stress disorder, phantom pain, infectious lesions, and post-immobilization osteoporosis, which impedes adequate rehabilitation of patients and causes the development of low-traumatic fractures in the long term [1–2].

Unfortunately, there is limited recent literature on the development of post-immobilization osteoporosis and its complications in amputees [3–6], and the available information on the impact of amputation on the rate of disease progression is fragmentary and does not fully reflect its real consequences for the health of injured people. Most of the existing studies or systematic reviews on post-immobilization osteoporosis focus on the features of bone loss in astronauts [7, 8] and people with chronic diseases that lead to prolonged immobilization [9, 10], and there are very few high-quality scientific studies on the comprehensive assessment of bone tissue in people after LA. Therefore, further observations of the state of bone tissue in this category of injured people can help to identify the features of its loss, develop personalized approaches to the prevention and treatment of post-immobilization osteoporosis, and also reduce the number of complications due to prolonged rehabilitation and disability. Studying this issue will contribute to the formation of new protocols for physical therapy and drug correction taking into account anatomical and functional changes after amputation. The results will have not only clinical, but also humanitarian and strategic value for the post-war recovery of the country, the reintegration of veterans into society and the formation of an effective military medicine system in the future. Purpose: to assess bone mineral density (BMD) and vitamin D status in servicemen after unilateral amputation of the lower limb.

Material and methods

To achieve this goal, we conducted a study on the basis of the Superhumans Center, Lviv Territorial Medical Association Clinical Hospital for Planned Treatment, Rehabilitation and Palliative Care, and the State Institution "D. F. Chebotaryov Institute of Gerontology of the National Academy of Medical Sciences of Ukraine" (Kyiv) in June–August 2024, a case-control study was conducted with the participation of 64 men aged 20–54 years (mean age 35.0 ± 8.3).

Two groups were selected for analysis: healthy men without any diseases and conditions with a certain impact on bone metabolism (control group, n = 32, mean age (34.9 ± 9.0) years) and individuals who had one lower limb amputation as a result of military operations and were in the "Superhumans" center for the purpose of primary or secondary prosthetics (study group, n = 32, mean age (35.1 ± 7.8) years). In the future, for analysis, men in the second group were divided into two subgroups: A — individuals with transfemoral amputation and B — with transtibial amputation.

The study was conducted in compliance with the requirements and provisions of the Helsinki Declaration on Human Rights (2000), the Council of Europe Convention on Human Rights and Biomedicine (1997), the Fundamentals of Ukrainian Legislation on Health Care (1992), and the current national ethical standards for conducting clinical research. The study was approved by the local ethics committee of the State Institution "D. F. Chebotaryov Institute of Gerontology of the National Academy of Medical Sciences of Ukraine" (Protocol No. 4 dated 20.06.2024). All participants provided written informed consent to participate in it.The study employed general clinical, instrumental and laboratory research methods.

Measurement of the main anthropometric indicators (height and body weight) with calculation of body mass index (BMI) was carried out using a calibrated stationary height meter "Seca202", RP-200 and medical scales "Zdorovya" in the morning, on an empty stomach, in a calm state after urination, in light clothing, without shoes and hats. The results of height measurement were recorded with an accuracy of 1 cm, body weight — up to 0.1 kg.

In the individuals of the study group, the adjusted body weight (weight (corrected)) was also calculated, which reflects the approximate value of the "full" weight in a patient without an amputation using the formula:

$$\text{weight (corrected)} = \text{weight (actual)} - P,$$

where weight (actual) is the patient's body weight (kg) without taking into account the prosthesis; P is the fraction of total body weight lost due to amputation

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(in decimal format, e. g. 0.059 = 5.9 %). For amputation of one limb below the knee joint it is ~ 5.9 % (p = 0.059), above 16%, full foot ~ 1.5% [11].

BMI was calculated using the standard formula (BMI = body weight (kg) / height (m^2)) for the control group and a similar but adapted formula with the adjusted body weight index (adjusted body weight) depending on the level of LA (adjusted BMI = adjusted body weight (kg) / height (m^2)) for the men in the study group.

Bone mineral density was measured using the two-photon X-ray absorptiometry (DXA) method using two DISCOVERY densitometers with automatic calculation of the Z-score using densitometer software. The indicators were measured at the level of the proximal femur (PF) and its neck in the amputated and contralateral limbs, as well as at the level of the lumbar spine (LS) L_I–L_{IV}. The study was performed in the morning by two qualified specialists. Preparation and positioning of the subjects, autocalibration and quality control of densitometers using a QA phantom were performed in accordance with the manufacturer's requirements.

Laboratory studies included measurement of the level of dihydroxyvitamin D (25(OH)D) in blood serum by electrochemiluminescent immunoassay (ECLIA) using an automated analyzer Cobas e411 (Roche Diagnostics) using original Roche reagents. Venous blood sampling of the subjects was performed in the morning on an empty stomach, followed by centrifugation (at 2,000 rpm for 10 min to obtain serum) and analysis.

Statistical analysis was performed using the "Statistika 10.0" Copyright© StatSoft, Inc. 1984–2001 software, Serial number 31415926535897. The nature of the distribution of the results was determined by the Shapiro-Wilk criterion. Under normal distribution conditions, data were presented as mean and standard deviation (M ± SD), under non-normal distribution conditions, as median (Me) and interquartile range [LQ–UQ]. Relationships between indicators were assessed using Pearson or Spearman correlation analysis depending on the nature of their distribution. Differences between quantitative indicators of the studied groups were assessed using Student's t-test for unrelated samples and Mann-Whitney U Test, differences between percentage indicators were assessed using $\chi 2$ and were considered significant at $p < 0.05$.

Results

The analysis of the results showed that the subjects did not differ in age (t = 0.11, p = 0.91), body weight (81.4 ± 13.9) in the control and (77.1 ± 13.8) kg in the study groups, respectively, t = 1.2; p = 0.22), adjusted body weight ((81.4 ± 13.9) and (88.7 ± 16.8) kg, respectively, t = 1.9; p = 0.07) and BMI ((25.2 ± 3.6) and (25.0 ± 4.1) kg/m^2; t = 1.1; p = 0.82), although the individuals of the study group had significantly lower height indicators ((175.6 ± 5.2) and (179.6 ± 6.3) cm, respectively; t = 2.7; p = 0.008) and higher values of adjusted body weight ((28.7 ± 5.0) and (25.2 ± 3.6) kg/m^2, respectively, t = 3.2; p = 0.002).

Traumatic amputation in patients of the study group was confirmed at the level of the lower leg (n = 21) or thigh (n = 11). The duration of the post-amputation period in the examined patients of this group was from 1.5 to 27 months and was, on average, 5.0 (4.0–7.0) months. It did not differ depending on the level of amputation (transtibial (5.0 (3.5–6.0) months or transfemoral (6.0 (4.0–7.0) months; in Z = 1.28; p = 0.20). Also, patients in the study group did not differ among themselves in terms of age (t = 0.62; p = 0.54), height (t = 0.34; p = 0.73), body weight (t = 0.68; p = 0.50) and BMI (t = 0.85; p = 0.40), although men with transfemoral amputation had significantly higher adjusted body weight (t = 2.11; p = 0.04) and BMI (t = 2.20; p = 0.04).

The study of risk factors for low BMD found that among 65.6% of the subjects in the study group and 31.3% of the control group smoked (χ^2 = 7.57; p = 0.006). Previous high-traumatic fractures were reported by 18.8 % of the subjects and 15.6 % of the control group. Concomitant chronic respiratory, cardiovascular, and gastrointestinal diseases were reported by 31.3 % of the subjects and 18.8 % of the control group (χ^2 = 1.22; p = 0.24).

Analysis of DXA indicators (Table 1) in the subjects, depending on the presence of traumatic amputation, revealed significantly lower BMD data in the subjects in the study group compared to control values at the level of the femoral neck (FN) and the PF of the amputated limb (t = 4.7; p = 0.00002 and t = 4.0; p = 0.0002, respectively). In contrast to the above, we did not find any significant differences in BMD at the level of the FN and PF of the limb contralateral to the amputation (t = 0.2; p = 0.84 and t = 1.0; p = 0.33, respectively). BMD at the level of the LS tended to differ but did not reach significant values (t = 1.8; p = 0.07, Table 1).

Low BMD of the FN and PF (Z-index ≤ –2 SD) at the level of the amputated limb was found in 42 and 39 % of cases in the study group and in no patient at the level contralateral to the LA, while in the control

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group, low BMD (Z-index ≤ –2 SD) was not recorded in any man at either the FN or PF levels.

Evaluation of the results of DXA in the study group depending on the level of amputation (Table 2) revealed significantly worse indicators in men with transfemoral amputation compared to those with transtibial amputation at the level of the amputated, but not contralateral to the amputation limb. We did not obtain any significant differences in BMD of the LS depending on the level of amputation.

BMD of the FN (Fig. 1) of the amputated limb significantly correlated with the duration of the post-amputation period (r = –0.47; p = 0.01). Similar relationships at the level of the PF of this limb were less pronounced (r = –0.35; p = 0.06) and absent at the level of the LS (r = –0.09; p = 0.64) and the proximal part of the contralateral. Assessment of the relationship between BMD indices of the FN of the amputated limb and the duration of the post-amputation period in patients in the study group depending on the level of amputation (transfemoral or transtibial) revealed a statistically significant relationship in individuals with amputation at the thigh level (R = –0.78; p = 0.008), but not at the lower leg level (R = –0.20; p = 0.40). Analysis of serum 25(OH)D levels in the subjects depending on the presence of lower limb amputation revealed significantly lower values in the study group compared to the control group ((25.9 ± 4.8) and (32.0 ± 9.8) ng/ml; t = 3.2; p = 0.002). Low serum 25(OH)D levels were found in 50 % of the control group and 81.25 % of the subjects in the study group. Vitamin D deficiency was observed in 6.25 % of men in the study and control groups, 75 and 43.75 % had vitamin D deficiency, and

Table 1

Dual-energy X-ray densitometry measurements in patients based on lower limb amputation status

Indicator / Group	Control group	Study group	t	p
BMD of the LS, g/cm^2	1.06 ± 0.11	1.00 ± 0.11	1.8	0.07
Z-score of the LS, SD	–0.31 ± 1.05	–0.71 ± 1.03	1.5	0.13
BMD of the FN of the contralateral limb, g/cm^2	0.87 ± 0.14	0.87 ± 0.12	0.2	0.84
Z-score of the FN of the contralateral limb, SD	–0.06 ± 0.98	–0.12 ± 0.83	0.3	0.78
BMD of the PF of the contralateral limb, g/cm^2	1.00 ± 0.20	1.04 ± 0.13	1.0	0.33
Z-score of the PF of the contralateral limb, SD	0.07 ± 0.81	0.18 ± 0.83	0.6	0.58
BMD of the FN of the amputated limb, g/cm^2	0.87 ± 0.14	0.66 ± 0.20	4.7	0.000020
Z-score of the FN of the amputated limb, SD	–0.06 ± 0.98	–1.61 ± 1.48	4.8	0.000010
BMD of the PF of the amputated limb, g/cm^2	1.00 ± 0.20	0.78 ± 0.22	4.0	0.000200
Z-score of the PF of the amputated limb, SD	0.07 ± 0.81	–1.51 ± 1.46	5.2	0.000003

Note. SD — sigma deviation.

Table 2

Dual-energy X-ray densitometry indicators in the examined patients depending on the level of lower limb amputation

Indicator / Group	Subgroup A	Subgroup B	t	p
BMD of the LS, g/cm^2	0.97 ± 0.11	1.02 ± 0.12	1.0	0.31
Z-score of the LS, SD	–1.02 ± 0.98	–0.56 ± 1.05	1.2	0.25
BMD of the FN of the contralateral limb, g/cm^2	0.85 ± 0.11	0.87 ± 0.13	0.5	0.65
Z-score of the FN of the contralateral limb, SD	–0.31 ± 0.80	–0.02 ± 0.84	0.9	0.38
BMD of the PF of the contralateral limb, g/cm^2	1.03 ± 0.07	1.04 ± 0.15	0.3	0.75
Z-score of the PF of the contralateral limb, SD	0.08 ± 0.46	0.23 ± 0.96	0.5	0.64
BMD of the FN of the amputated limb, g/cm^2	0.47 ± 0.12	0.76 ± 0.16	5.0	0.000030
Z-score of the FN of the amputated limb, SD	–3.11 ± 0.87	–0.86 ± 1.10	5.6	0.000005
BMD of the PF of the amputated limb, g/cm^2	0.59 ± 0.18	0.88 ± 0.17	4.3	0.000200
Z-score of the PF of the amputated limb, SD	–2.81 ± 1.21	–0.86 ± 1.11	4.4	0.000100

Notes: A — amputation of the lower limb at the thigh level, B — at the shin level.

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18.75 and 50 % had normal serum 25(OH)D levels. However, we did not find any significant differences (t = 0.42; p = 0.68) in the level of 25(OH)D depending on the level of amputation. In the case of transfemoral amputation, it was (25.4 ± 3.84) ng/ml, and in the case of transtibial amputation, it was (26.2 ± 5.21) ng/ml.

Discussion

Due to the Russian invasion of Ukraine, the number of injuries and amputations of limbs has increased dramatically in recent years, both among the civilian population and among military personnel. LA is a complex surgical procedure that has not only important pathophysiological and anatomical consequences, but also significantly affects psychological health and quality of life of patients. One of the critical aspects that often remains underestimated is the impact of amputation on bone health. The loss of a limb leads to dramatic changes in mechanical stress, bone metabolism and overall functioning of the body. However, to date, studies on the impact of amputations on bone health are fragmentary and do not fully reflect the real consequences of war for the health of military personnel. This makes it impossible to plan the necessary medical measures, early diagnosis of post-immobilization osteoporosis and effective rehabilitation of patients.

Loss of sufficient mechanical load is a major factor in the development of post-immobilization osteoporosis following amputation. According to Wolff's Law, formulated by the German anatomist Julius Wolff in the 19th century, bone tissue constantly adapts to the loads acting on it, ensuring an adequate rate of bone remodeling [12]. The presence of increased mechanical load leads to an increase in bone strength, its absence, on the contrary, causes progressive bone loss and the development of post-immobilization osteoporosis. A decrease in mechanical stress on the bone, as occurs after amputation or during prolonged bed rest, leads to an imbalance of remodeling processes with a predominance of bone resorption.

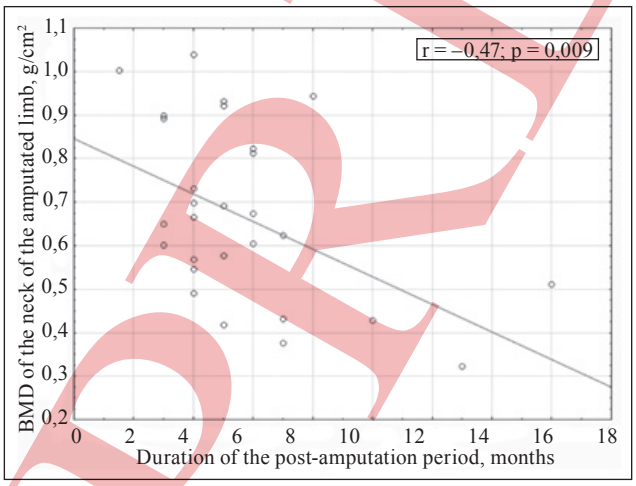

Figure. Relationship between BMD of the femur on the side of amputation and the duration of the post-amputation period in patients in the study group

Post-immobilization osteoporosis, which develops as a result of inactivity (immobilization, prolonged bed rest, paralysis, and amputation), is one of the most powerful factors leading to rapid bone loss [13–15], which exceeds that even in women in the first years after menopause [16]. Post-immobilization osteoporosis involves various pathophysiological components, including changes in bone tissue cells such as reduced osteoblast activity, increased osteoclast activity, and disrupted osteocyte function. These factors result in a higher rate of bone resorption and alterations to bone microarchitecture, such as thinning of trabeculae and fewer connections between them, which contribute to decreased bone strength and a greater risk of fractures. Additionally, local blood circulation and neural regulation may be impaired, further promoting bone demineralization. To date, the effect of amputation on BMD indicators has not been studied sufficiently. Studies and systematic reviews have shown reduced BMD in individuals after amputation [4–6, 17–19]. Most observations are confirmed in the residual limb (stump), and some of them in the preserved limb, which indicates a bilateral effect of amputation. According to scientists, changes in BMD in the contralateral limb are the result of modifications in walking patterns and body weight distribution of the patient. Although the healthy limb is mostly subjected to increased load to compensate for the lost function, it may be insufficient to maintain optimal BMD, or a decrease in overall physical activity leads to systemic effects.

A study by D. A. Bemben et al. [4] demonstrated a rapid and marked loss of bone strength in individuals with traumatic amputations within the first 6 months after surgery, which was not recovered within 12 months after resuming walking. The reduction in regional femoral BMD at the level of the amputated limb was 11–15 %. The study confirmed not only the loss of trabecular but also cortical bone. Similarly, J. H. Flint et al. [5] showed a significant loss of BMD after combat amputation of the lower limb, emphasizing that the traumatic nature of the surgery may additionally influence these processes. In a retrospective case-control study [5] of 156 lower limb amputation patients (121 unilateral, 35 bilateral), 42 % had a lower Z-score (–1.2 ± 1.0 SD) in bilateral amputation patients compared with unilateral ampu-

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tation patients (–0.6 ± 1.1 SD, p = 0.005). In addition, a significant difference in BMD between the intact and amputated limbs was found in unilateral amputation patients (odds ratio (OR) –1.0; 95 % CI –1.1 to –0.8; p < 0.001). Important factors for low BMD were the long period before resumption of walking [OR = 1.39; 95 % CI: 1.003–1.93; p = 0.048] and a higher level of amputation (OR = 7.27; 95% CI: 3.21–16.49; p < 0.001).

The important significance of the level of amputation (transfemoral or transtibial) on BMD obtained in our study was also confirmed by V. D. Sherk et al. [17], which the authors attribute to the features of the changed load redistribution.

The results of our investigation also coincide with the data of another recently published cohort study ADVANCE involving 153 male military personnel from the United Kingdom with lower limb amputees compared with the control group [6]. The authors found a significant decrease in BMD of the femoral neck compared to controls (t-score –0.08 SD vs. –0.42 SD; p = 0.0001). This decrease was significant only at the level of the femoral neck of the amputated limb (p = 0.0001) and was greater for individuals with transfemoral versus transtibial amputations (p < 0.001), with no differences in BMD of the lumbar spine. An important conclusion of the authors of the article is that BMD loss in amputees is mechanical, not systemic, and is caused by altered physical load on the limbs. Therefore, local strategies to stimulate bone turnover, in particular through adequate physical rehabilitation, may be effective in the recovery of individuals with amputees.

However, the idea of local bone loss at the level of the amputated limb is not shared by all researchers. W. Ngo et al. [18] in their review note that amputation can cause systemic adaptations in the entire musculoskeletal system, including changes in muscle strength, balance and walking patterns. This may indirectly affect the BMD of other parts of the skeleton, in particular due to a general decrease in physical activity or a change in load distribution. It is obvious that in order to compensate for the lost function of the amputated limb, the healthy one is often subjected to increased but abnormal load, which can lead to changes in BMD in it or, conversely, to a local increase in density depending on individual movement patterns and the use of the prosthesis.

In view of the above, the results of a retrospective cohort study of 44 British male veterans of World War II with major unilateral lower limb amputations [19] (mean age 73.0 years, and at the time of amputation — 26 years (17–57 years)) are interesting. Transfemoral amputations were in 34% of patients, transtibial — in 66 %. BMD on the amputated side of the femoral neck, trochanter and Ward's triangle was significantly lower than on the contralateral limb (p < 0.0001). The t-score was, respectively, –2.26 SD on the amputated and –1.10 SD on the healthy limb (p < 0.00001). Given the long post-amputation period in the patients of this observation, it becomes obvious that there is no recovery of BMD in the amputated limb even long after amputation. It is obvious that low BMD in the amputated limb can be a significant factor in low-trauma fractures in this category of individuals. Another important factor that affects bone remodeling and the risk of fractures is vitamin D deficiency and insufficiency [20]. According to the results of a recent study in Ukraine, the average level of total vitamin D in serum in men aged 20–40 years is 30.1 ng/ml [21]. Studies of the status of this vitamin in amputees demonstrate a high proportion of its deficiency or insufficiency. Thus, according to É. Smith et al. [22] 68.8 % of men with lower limb amputees had vitamin D deficiency, 10.4 % had its insufficiency. Lower percentages of vitamin deficiency and insufficiency were demonstrated in the study by D. Bemben et al. [4] in subjects in the early post-amputation period in the period before the prosthesis was installed (respectively, 12 % of cases had its deficiency and 25 % had its insufficiency). The results of our observation showed a lower serum level of vitamin D in amputees compared to control values, but there were no significant differences in groups depending on the level of amputation. Low serum 25(OH)D values were found in 81.25 % of men after amputation (vitamin D deficiency was 6.25 %, insufficiency was 75 %), which may have a negative impact on bone tissue remodeling and the rate of its loss. Thus, the results of the study indicate that lower limb amputation is a significant risk factor for the development of post-immobilization osteoporosis. It is obvious that the loss of mechanical load on the stump bones leads to rapid demineralization of bone tissue, while changes in movement patterns and the general level of activity may cause a less pronounced decrease in BMD in the contralateral limbs, increasing the risk of osteoporosis and fractures. Understanding these mechanisms is critical for developing effective prevention and rehabilitation strategies. A comprehensive approach that includes early mobilization, individualized exercise programs [23], adequate nutritional support, and, when necessary, pharmacological treatment is key to minimizing the negative consequences of amputation on bone health and improving functional outcomes for patients.

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Our observation has a number of limitations. These include its design (a single-center case-control study), the small number of subjects and the inclusion of only male patients with unilateral lower limb amputation, and the large range of time from amputation to examination (1.5–27 months).

Conclusions

The results of the study demonstrated a significant decrease in BMD of the femoral neck in men after unilateral amputation at the level of the amputated limb compared with the indicators of healthy men and the absence of significant differences on the contralateral side to the amputation. BMD indicators correlated with the duration of the post-amputation period and were lower in subjects with transfemoral amputation compared with indicators after transtibial.

After unilateral amputation of the lower limb, 81.25 % of cases had low levels of 25(OH)D in the blood serum (vitamin D deficiency — 6.25 %, insufficiency — 75), which may have a negative impact on the development of osteoporosis and low-traumatic fractures in the long term after amputation.

Conflict of interest. The authors declare no conflict of interest.

Prospects for further research. It is obvious that due to the growing consequences of the Russian invasion of Ukraine and the increase in the number of people with injuries and amputations, high-quality multicenter prospective studies using modern instrumental and laboratory methods are needed to study in detail the state of bone tissue and the characteristics of its loss in this category of patients.

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BONE MINERAL DENSITY AND VITAMIN D STATUS IN WAR VETERANS AFTER LOWER LIMB AMPUTATION

N. V. Grygorieva [1], A. B. Vilenskyi [2], O. Z. Stefiuk [3], I. I. Kaut [2], D. Yu. Kurylo [1], A. V. Iniushyna [1]

[1] State Institution «D. F. Chebotarev Institute of Gerontology of the NAMS Ukraine», Kyiv
[2] Charitable Organization «Charitable Fond «Superhumans», Lviv. Ukraine
[3] Danylo Halytsky Lviv National Medical University, Lviv. Ukraine

✉ Nataliia Grygorieva, MD, Prof.: crystal_ng@ukr.net; https://orcid.org/0000-0002-4266-461X
✉ Andrii Vilenskyi , MD, PhD: a.vilensky@superhumans.com; https://orcid.org/0000-0003-7983-3581
✉ Oksana Stefiuk, MD: oksanastefyuk@gmail.com; https://orcid.org/0009-0008-3992-4311
✉ Iryna Kaut, MD: i.kaut@superhumans.com; https://orcid.org/0000-0001-7262-358X
✉ Daryna Kurylo: kurilodarina@ukr.net; https://orcid.org/0009-0005-8075-2644A
✉ Alina Iniushyna: iniushina@ukr.net; https://orcid.org/0009-0005-0435-7343

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Dynamics of biochemical markers of bone metabolism in patients with segmental bone defects treated with the Masquelet technique

S. Magomedov, Yu. V. Polyachenko, A. V. Kalashnikov, Yu. M. Litun, L. V. Polishchuk

SI «National Institute of Traumatology and Orthopedics of the NAMS of Ukraine», Kyiv

Segmental bone defects represent a complex clinical challenge in reconstructive orthopedics, etiologically associated with high-energy trauma, oncological resections, and osteomyelitic processes. The two-stage Masquelet technique with induced membrane formation demonstrates high efficacy in reconstructing critical-size bone defects, however, the molecular-biochemical mechanisms of reparative osteogenesis during its application remain insufficiently investigated. Objective. To evaluate the dynamics of biochemical markers of bone metabolism in patients with segmental defects of long tubular bones during treatment using the induced membrane (Masquelet) technique in order to determine the metabolic characteristics of osteogenesis and to optimize bone regeneration. Methods. The study included 85 patients aged 18 to 65 years. The experimental group consisted of 44 patients with segmental bone defects, while the control group comprised 41 patients with low-energy fractures. Biochemical markers such as alkaline phosphatase, osteocalcin, β-CrossLaps, calcium, phosphorus, and parathyroid hormone were analyzed. Results. Before treatment, significant abnormalities in bone metabolism markers were observed in the experimental group: elevated alkaline phosphatase (175.45 ± 46.2) U/L, osteocalcin (53.70 ± 12.4) ng/mL, β-CrossLaps (0.949 ± 0.271) ng/mL. Following treatment, 75-92 % of patients demonstrated normalization of biochemical parameters, indicating stimulation of reparative osteogenesis. Conclusions. The Masquelet technique effectively stimulates bone regeneration in segmental defects, as confirmed by the normalization of biochemical markers. Comprehensive biochemical monitoring can serve as a valuable tool for assessing treatment efficacy.

Сегментарні дефекти кісток є доволі складною проблемою реконструктивної ортопедії, етіологічно пов'язаної з високоенергетичними травмами, онкологічними й остеомієлітичними процесами. Двохетапна методика Masquelet з формуванням індукційної мембрани демонструє високу ефективність у відновленні критичних кісткових дефектів, проте молекулярно-біохімічні механізми репаративного остеогенезу в разі її застосування залишаються недостатньо дослідженими. Мета. Вивчити динаміку біохімічних маркерів кісткового метаболізму в пацієнтів із сегментарними дефектами довгих трубчастих кісток у процесі лікування з використанням методики індукованої мембрани (Masquelet) для визначення метаболічних особливостей остеогенезу й оптимізації остеорегенерації. Методи. Обстежено 85 пацієнтів віком від 18 до 65 років. Дослідну групу склали 44 особи з сегментарними дефектами кісток, пролікованих за двохетапною методикою Masquelet. Контрольну групу (41 пацієнт) становили хворі з низькоенергетичними переломами. Дослідження включало визначення маркерів кісткового метаболізму (лужна фосфатаза, остеокальцин, β-CrossLaps), показників мінерального обміну (кальцій, фосфор) та регуляторний фактор (паратгормон). Результати. До лікування в пацієнтів із сегментарними дефектами виявлено підвищення рівнів лужної фосфатази (175,45 ± 46,2) мккат/л, остеокальцину (53,70 ± 12,4) нг/мл та β-CrossLaps (0,949 ± 0,271) нг/мл. Після лікування в 75–92 % випадків спостерігалася нормалізація показників біохімічного ремоделювання кісткової тканини, що свідчить про стимуляцію репаративного остеогенезу. Висновки. Методика індукційної мембрани сприяє стимуляції репаративного остеогенезу, що підтверджується нормалізацією біохімічних маркерів. Комплексне оцінювання біохімічних показників є важливим інструментом моніторингу ефективності лікування. Ключові слова. Сегментарний дефект, індукційна мембрана, остеогенез, біохімічні маркери, кістковий метаболізм.

Keywords. Segmental defect, induced membrane, osteogenesis, biochemical markers, bone metabolism

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Introduction

Replacement of segmental bone defects is currently an extremely relevant issue in orthopedics and traumatology. Well-known techniques, such as vascularized fibular autograft or the Ilizarov distraction osteosynthesis method are common. Although they are quite effective, they also have certain drawbacks. In particular, they are technically complex, require highly qualified specialists and modern material and technical support, as well as a large number of complications in the postoperative period [1, 2].

To minimize the number of complications and unsatisfactory results, in 1986 A. Masquelet proposed a two-stage technique, which consists in the implantation at the first stage of polymethyl methacrylate (PMMA) (bone cement) saturated with an antibiotic, which is responsible for the formation of a pseudosynovial membrane. The second stage after the formation of the induced membrane within a period of 6 to 8 weeks implied removal of the spacer and filling the cavity with a spongy autograft. The properties of the membrane are defined by its mechanobiological characteristics: mechanically, it prevents the invasion of fibrous tissue into the recipient site while facilitating the restoration of the damaged segment's anatomy; biologically, it stimulates tissue regeneration, leading to the formation of an induction membrane that revascularizes the bone graft and prevents its resorption [3, 4].

This technique allows to reconstruct significant diaphyseal defects, even if the recipient area has been irradiated or infected, provided that a pre-formed shell is formed to protect and revascularize the bone graft [5].

Stimulation of the osteogenic potential of autografts using growth factors and osteoinductive cells remains an area of active research [6, 7]. Current studies are still in their early stages and require answers to many unresolved questions.

Ultimately, further investigation into the metabolic properties of induction membranes holds great promise for uncovering new mechanisms of bone tissue biology and regeneration. This could significantly improve the quality of care for many patients. The technique of using the induced membrane is unique and has the potential to shift the paradigm for implanting foreign bodies into the human body. Despite being used in practice for over 30 years, scientific and practical studies on its properties are just beginning.

Objective: to assess the time course of biochemical markers of bone metabolism in patients with segmental bone defects during treatment using the induced membrane technique (Masquelet) in order to determine the metabolic features of osteogenesis and optimize osteoregeneration.

Material and methods

The study was conducted on the basis of the Biochemistry Laboratory of the State Institution "Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine". The research was carried out in accordance with the terms of the Declaration of Helsinki with the approval of the Bioethics Committee (Protocol No. 3 dated 26.04.2025). All patients involved in this study signed a voluntary informed consent to participate.

The study involved examination of 85 subjects aged 18 to 65 years (mean age (42.3 ± 8.7) years).

The experimental group included 44 patients with segmental bone defects, mostly lower limbs, in which the two-stage Masquelet method was used. The control group included 41 individuals hospitalized for intra-articular injuries and low-energy closed fractures of the lower limbs. The groups were identical in terms of age and sex.

The clinical observation was based on the quantitative determination of bone tissue remodeling markers by the method of parallel biochromatic and monochromatic adsorption measurement (Automatic electrochemiluminescent analyzer Cobas E 411 and biochemical analyzer Cobas E 311 using Roche Diagnostics test systems).

Laboratory studies included the determination of the following indicators: markers of bone formation (alkaline phosphatase (ALP), osteocalcin), indicators of resorption (β-CrossLaps) and mineral metabolism (total calcium, phosphorus), regulatory factors (parathormone), additional enzymes (creatine phosphokinase (CPK), lactate dehydrogenase (LDH)). Blood sampling was performed in the morning on an empty stomach before the start of treatment and after its completion. The patients' blood serum was analyzed after being separated using an ELMI Centrifuge CM-6MT.

For statistical analysis of values, a descriptive method was used with the calculation of the mean (M), the mean standard error (m). The probability of the difference was assessed depending on the type of data cut by parametric (Student's t-test for unrelated samples) and non-parametric (Pearson's χ^2, Mann–Whitney U-test) methods. The relationship between the parameters studied was revealed by calculating the Spearman correlation coefficient. All data are presented as the mean and standard

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error of the mean. The difference was considered significant at $p < 0.05$. Calculations were performed in the Statistica 12 software.

Results

The analysis of the initial indicators in the study group revealed significant deviations from the reference values. An increased level of alkaline phosphatase (> 129 μkat/l) was observed in 23 % of patients with an average value of (175.45 ± 46.2) μkat/l in the group with an increased level. Deviations from the norm of osteocalcin were detected in 55 % of patients, of which > 22.0 ng/ml in 45 % (up to (53.70 ± 12.4) ng/ml). Increased β-CrossLaps levels were recorded in 42 % of cases (mean value (0.949 ± 0.271) ng/ml), with the highest rates observed in patients with disease duration of more than 2 years. Calcium-phosphorus metabolism disorders were detected in 35 % of cases, including hyperphosphatemia in 18 and hypocalcemia in 12 % (Fig. 1).

After the treatment, positive dynamics were recorded: normalization of alkaline phosphatase levels in 85 % of patients (the average value decreased to (102.3 ± 28.6) μkat/l), restoration of osteocalcin levels to reference values in 75 %. The β-CrossLaps level decreased by an average of 35 % (to (0.621 ± 0.248) ng/ml) with complete normalization of the indicator in 82 % of people. Indicators of mineral metabolism normalized in most patients: calcium levels in 92 %, phosphorus in 88 % of cases.

The indicators of the control group were characterized by stability and were within the reference values: alkaline phosphatase — (103.4 ± 25.6) μkat/l, calcium — (2.52 ± 0.28) mmol/l, phosphorus — (1.28 ± 0.38) mmol/l, β-CrossLaps — (0.621 ± 0.248) ng/ml, osteocalcin — (29.8 ± 11.7) ng/ml, parathormone — (28.9 ± 11.8) pg/ml (Fig. 2).

Discussion

The analysis of the obtained results demonstrates complex changes in biochemical markers in patients with segmental defects of bone tissue. Particular attention is drawn to changes in markers of bone formation and resorption, which showed characteristic changes. Alkaline phosphatase levels were elevated ((102.5 ± 31.2) μkat/l) with significant gender differences ((105.3 ± 29.8) μkat/l in men vs. (97.7 ± 24.6) μkat/l in women, $p < 0.05$). Osteocalcin levels were also elevated ((27.8 ± 10.7) ng/ml), indicating osteoblast activation.

A similar pattern was found in the study by N. S. Rathwa et al., who associated it with compensatory activation of bone formation processes [8, 9]. The β-CrossLaps resorption marker demonstrated an elevated level ((0.64 ± 0.23) ng/ml) with significant individual variability (CV = 35.7 %).

In the publications of F. Perut et al. and S. Wei et al. also noted the high variability of this indicator and its importance for studying the intensity of bone resorption [10, 11]. The data on mineral metabolism were the most stable. The calcium level (2.55 ± 0.23) mmol/l was characterized by the lowest variability (CV = 8.9 %), which indicates the preservation of homeostasis mechanisms.

M. Kumar et al. emphasize the importance of maintaining a stable calcium level for the processes of reparative osteogenesis [12]. Of particular note is the increased level of parathormone (28.2 ± 13.7) pg/ml with high variability (CV = 456 %) and right-sided asymmetry of distribution.

O. W. Omogbai et al. associate this with the activation of compensatory mechanisms of regulation of calcium-phosphorus metabolism [13]. Enzymatic activity also underwent characteristic changes. CPK level was increased (15.3 ± 4.3) U/L with significantly higher values in the female group ($p < 0.05$). LDH

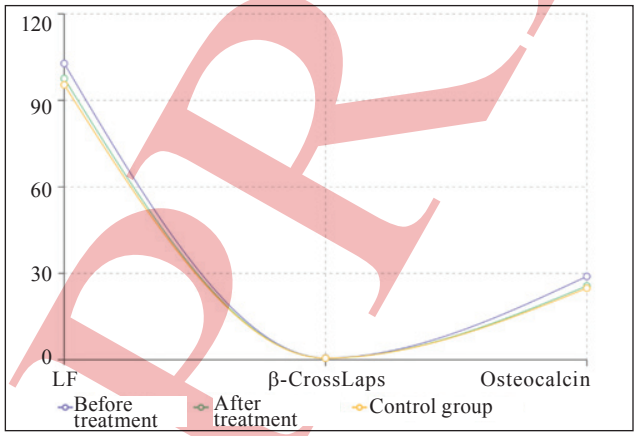

Fig. 1. Changes in the main markers of bone metabolism

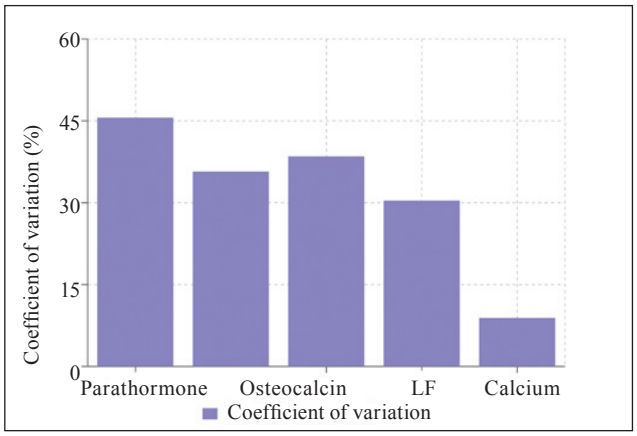

Fig. 2. Coefficients of variation of biochemical parameters

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activity (197.4 ± 47.6) U/L showed a normal distribution of data.

J. A. Nicholson et al. proved similar changes and their significance for assessing the metabolic activity of bone tissue. The identified correlations between markers (LF/osteocalcin r = 0.72, β-CrossLaps/LF r = 0.68) confirm the relationship between the processes of formation and resorption [14].

The results indicate that a comprehensive assessment of biochemical markers can be used to monitor treatment effectiveness. At the same time, it is necessary to take into account the high individual variability of some indicators and their gender characteristics. When analyzing the pathogenic mechanisms of reparative osteogenesis, it is important to note the role of various growth factors and cytokines. An increased level of osteocalcin (27.8 ± 10.7) ng/ml together with high activity of LF (102.5 ± 31.2) μkat/l may reflect the activation of the BMP2-dependent osteogenesis pathway.

S. Martin-Iglesias et al. demonstrated that such changes correlate with BMP2 expression and osteoblast activation [15, 16]. The relationship between markers of bone resorption and formation deserves special attention. An increased level of β-CrossLaps (0.64 ± 0.23) ng/ml with a simultaneous increase in osteocalcin indicates a disruption of the balance of remodeling processes. N. Patel et al. showed that such a combination of changes is characteristic of delayed consolidation [17].

The role of inflammatory factors is also significant. The high variability of parathyroid hormone (CV = 45.6 %) and the right-sided asymmetry of its distribution may reflect the activation of pro-inflammatory mechanisms. H. ElHawary et al. noted similar changes in case of impaired fracture consolidation [18]. The stability of mineral metabolism indicators (calcium CV = 8.9 %) with significant variability of other markers may indicate the preservation of systemic regulatory mechanisms under conditions of local disorders of osteogenesis.

V. Fischer et al. emphasize the importance of maintaining mineral homeostasis for successful consolidation. Gender differences in the levels of LF ((105.3 ± 29.8) μkat/l in men versus (97.7 ± 24.6) in women) and CPK may be associated not only with hormonal characteristics, but also with different intensity of mechanical load [19]. The identified changes also suggest the participation of VEGF-dependent mechanisms in the disruption of reparative osteogenesis. K. Hu et al. noted that the activation of angiogenesis is a critical factor for successful consolidation [20]. Therefore, a comprehensive analysis of biochemical markers opens up new opportunities for understanding the pathogenesis of reparative osteogenesis and optimizing treatment tactics.

Conclusions

The study showed that before treatment, patients had significant bone metabolism disorders, which were manifested by deviations of biochemical markers from reference values.

Patients with segmental bone defects were found to have an increase in the levels of markers of both formation (LF — (102.5 ± 31.2) μkat/l, osteocalcin — (27.8 ± 10.7) ng/ml) and resorption (β-CrossLaps — (0.64 ± 0.23) ng/ml), which indicated a disruption in the balance of remodeling processes.

Most of the studied indicators were within the reference values but were characterized by significant individual variability. Statistically significant gender differences were found for LF indicators ((105.3 ± 29.8) μkat/l in men and (97.7 ± 24.6) in women, $p < 0.05$) and CPK, which should be considered when interpreting the results.

The highest variability was demonstrated by the levels of parathyroid hormone (CV = 45.6 %) and β-CrossLaps (CV = 35.7 %), the lowest by the concentration of total calcium (CV = 8.9 %). The data distribution for most indicators exhibited right-sided skewness, except for calcium and LDH, which displayed a nearly normal distribution.

Correlations were established between markers of bone formation and resorption (r = 0.68–0.72; $p < 0.01$), which confirms the complex nature of metabolic disorders and the need to monitor a wide range of biochemical markers to determine the effectiveness of treatment.

The results demonstrated high efficiency, as evidenced by the normalization of most biochemical indicators.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. The main limitation of this study is the relatively short observation period, which, at this stage, did not influence the outcomes. However, a comprehensive assessment of biochemical markers remains an effective approach for monitoring bone metabolism disorder treatments and offers promising opportunities for further research.

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Authors' contribution. Magomedov S. — analysis of the findings, participation in drafting the article; Polyachenko Yu. V. — determination of research directions; Kalashnikov A. V. — analysis of clinical material, drafting of conclusions; Litun Yu. M. — analysis of clinical material, participation in drafting the article; Polishchuk L. V. — processing and conducting biochemical studies.

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DYNAMICS OF BIOCHEMICAL MARKERS OF BONE METABOLISM IN PATIENTS WITH SEGMENTAL BONE DEFECTS TREATED WITH THE MASQUELET TECHNIQUE

S. Magomedov, Yu. V. Polyachenko, A. V. Kalashnikov, Yu. M. Litun, L. V. Polishchuk

SI «National Institute of Traumatology and Orthopedics of the NAMS of Ukraine», Kyiv

✉ Sadrudin Magomedov, MD, Prof.: alexander@magomedov.kiev.ua; https://orcid.org/0000-1234-5678-9101

✉ Yuriy Polyachenko, MD, Prof. in Orthopedics and Traumatology: poliach.yv@gmail.com; https://orcid.org/00000003-1814-4240

✉ Andrii Kalashnikov, MD, Prof. in Orthopedics and Traumatology: orgitoua@gmail.com; https://orcid.org/0000-0001-8092-3451

✉ Yurii Litun, MD, PhD: litun_yurii@ukr.net; https://orcid.org/0000-0002-7397-5381

✉ Larysa Polishchuk: 2501lora@gmail.com; https://orcid.org/0000-0002-9416-4596

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Biomechanical analysis of short-segment pedicle screw fixation for AO type A fractures at the thoracolumbar junction under extension loading

O. S. Nekhlopochyn [1], V. V. Verbov [1], Ie. V. Cheshuk [1], M. Yu. Karpinsky [2], O. V. Yaresko [2]

[1] Romodanov Neurosurgery Institute of National Academy of Medical Sciences of Ukraine, Kyiv

[2] Sytenko Institute of Spine and Joint Pathology of the National Academy of Medical Sciences of Ukraine, Kharkiv

Thoracolumbar junction fractures account for up to 60 % of all spinal injuries, with more than 20 % classified as burst fractures. These injuries are characterized by instability and an increased risk of kyphotic deformity. Short-segment transpedicular fixation, which has been gradually gaining favor as the treatment of choice for burst fractures in this region, undoubtedly reduces invasiveness but can lead to fixation failure if there is no intermediate support in the body of the injured vertebra. Objective. To evaluate the stress-strain state of the thoracolumbar spine with a burst fracture at Th_{XII} under extension loading, considering screw length and the presence of intermediate fixation. Methods. A finite element model of the spine (Th_{IX}–L_V) with a burst fracture at Th_{XII} was developed. Four variants of short-segment transpedicular fixation were analyzed: short or long (bicortical) screws, with or without additional screws in Th_{XII}. A 350 N load was applied to Th_{IX}, and stresses were determined at control points using the von Mises criterion. Results. The highest stresses in the connecting rods were observed with long screws without intermediate fixation (337.2 MPa). Introducing intermediate screws decreased the stress in Th_{XII} from 16.2 to 9.8 MPa. Short screws with Th_{XII} fixation distributed loads more effectively, reducing peak stresses. Long screws led to overload at the entry points (up to 12.8 MPa in L_I), while their maximum stress reached 95.1 MPa. Conclusions. Intermediate fixation of the injured vertebra reduces stress in both bone structures and the implant, thereby decreasing the risk of correction loss. The most favorable configuration is a combination of short screws with intermediate fixation. Long screws are advisable in cases of osteoporosis, although they increase local stresses — a factor that must be taken into consideration during surgical planning.

Переломи грудопоперекового переходу становлять до 60 % усіх ушкоджень хребта, з них понад 20 % є вибуховими. Такі травми характеризуються нестабільністю та ризиком кіфотичної деформації. Коротка транспедикулярна фіксація, що поступово набуває популярності як метод вибору в разі вибухових переломів цієї ділянки, безумовно зменшує інвазивність, проте за відсутності проміжної опори в тілі ушкодженого хребця може призводити до неспроможності фіксації. Мета. Оцінити напружено-деформований стан грудопоперекового відділу хребта з вибуховим переломом Th_{XII} під час екстензійного навантаження залежно від довжини гвинтів і наявності проміжної фіксації. Методи. Створено скінченно-елементну модель хребта (T_{IX}–L_V) із вибуховим переломом Th_{XII}. Досліджено чотири варіанти короткої транспедикулярної фіксації: короткі та довгі (бікіркові) гвинти, із додатковими гвинтами в Th_{XII} чи без них. Навантаження 350 Н прикладали до T_{IX}, а напруження визначали в контрольних точках за Мізесом. Результати. Найвищі напруження в з'єднувальних балках спостерігалися за довгих гвинтів без проміжної фіксації (337,2 МПа). Використання проміжних гвинтів знижувало напруження в Th_{XII} з 16,2 до 9,8 МПа. Короткі гвинти з фіксацією Th_{XII} більш ефективно розподіляли навантаження, зменшуючи пікові напруження. Довгі гвинти зумовлювали перевантаження в точках входу (до 12,8 МПа в L_I), а їхні максимальні напруження сягали 95,1 МПа. Висновки. Проміжна фіксація ушкодженого хребця знижує напруження в кісткових структурах і металоконструкції, зменшуючи ризик втрати корекції. Оптимальною є комбінація коротких гвинтів із проміжною фіксацією, а довгі доречні за остеопоротичних змін, бо збільшують локальні напруження, що слід ураховувати під час хірургічного планування. Ключові слова. Вибуховий перелом, грудопоперековий перехід, коротка транспедикулярна фіксація, проміжні гвинти, екстензійне навантаження, метод скінченних елементів, біомеханіка хребта.

Keywords. Burst fracture, thoracolumbar junction, short-segment transpedicular fixation, intermediate screws, extension loading, finite element method, spinal biomechanics

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Introduction

Fractures in the thoracolumbar junction, according to various studies, account for approximately 40–60 % of all spinal injuries [1, 2]. More than 20 % of such injuries are classified as burst fractures, which occur mainly as a result of axial loading and are accompanied by damage to the anterior and middle supporting columns of the spine [3]. Such injuries are characterized by pronounced instability of the affected segment, which can lead to the development of kyphotic deformity and prolapse of bone fragments into the spinal canal, increasing the risk of neurological complications [4]. In significant loss of height of the anterior vertebrae, surgical intervention is aimed not only at stabilizing the affected area, but also at preventing progressive kyphosis, which, in turn, can cause secondary compression of the spinal cord [5]. In addition, with the right choice of surgical treatment tactics and timely stabilization, it is possible to achieve indirect decompression of the spinal canal without the need for open access, which helps to reduce intraoperative trauma, reduce blood loss and the risk of infectious complications, as well as accelerate rehabilitation [6, 7]. Despite significant clinical experience, the technique and extent of stabilization for burst fractures remain a subject of debate [8]. In modern practice, short transpedicular fixation has become widely used, which involves the installation of screws in adjacent vertebrae to the damaged one (one above, one below). The main advantages of this approach are less invasiveness and the preservation of a larger number of functionally active spinal motor segments [9]. The technique has demonstrated efficacy in stabilising less burdened thoracic regions; however, its application at the thoracolumbar junction is influenced by both clinical considerations and economic factors. Reducing spinal fusion length in this area can lead to a high risk of early correction loss — up to 50 % according to some studies — and increases the chances of screw loosening or breakage [10]. Long stabilization, covering two levels above and below the fracture, provides better primary stability, but is accompanied by an increase in the volume of surgical intervention and a decrease in mobility due to the immobilization of additional segments. One way to increase the effectiveness of short fixation without increasing its length is to insert additional transpedicular screws into the body of the damaged vertebra, which ensures the formation of a six-screw structure instead of the traditional four-screw [11]. Biomechanical studies show that this approach contributes to an increase in system stiffness, improved retention of kyphotic correction and more uniform load distribution, which reduces peak stresses on each individual screw [12].

One of the key factors in evaluating the biomechanical properties of stabilization methods and predicting their effectiveness is the accurate modeling of loading modes. Most studies focus on flexion, extension, lateral bending, rotation, and axial compression [13, 14]. While flexion is typically considered the most challenging mode for implants, extension loads have their own unique characteristics [15]. Specifically, during extension, similar to flexion, the primary force is applied to the upper screws, while the lower screws experience lower stresses. In the absence of intermediate fixation within the fracture zone, extension may lead to overloading of the connecting beam. Adding two screws to the body of the damaged vertebra creates an additional fulcrum, which provides a more even load distribution, reduces peak stresses in the screws and beams, and improves long-term stability of the correction [16]. In addition, extension affects adjacent motion segments. According to modeling, intervertebral discs above the level of fusion are often subjected to increased loads, which can cause accelerated degeneration and the development of pathological changes [13]. Therefore, the selection of the optimal design for stabilizing burst fractures of the thoracolumbar junction requires a balance between sufficient stiffness to maintain correction and minimizing overload on both implants and adjacent spinal segments, especially during extension movements.

To date, the number of publications on this topic remains limited, highlighting the need for further biomechanical and clinical studies to develop individualized approaches for selecting surgical treatment strategies for patients with burst fractures in the thoracolumbar region.

Objective: To investigate the stress-strain state of a mathematical model of the thoracolumbar spine with a Th_{XII} burst fracture under conditions of various short transpedicular fixation configurations during trunk extension.

Material and methods

The materials of the article were reviewed by the Ethics Committee of the State Institution "Academician A. P. Romodanov Institute of Neurosurgery of the NAMS of Ukraine" (Protocol No. 3 dated 04.05.2018). In the laboratory of biomechanics of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the NAMS of Ukraine", a finite element model of the thoracolumbar

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spine with simulation of a burst fracture of the Th_{XII} vertebral body was created. A detailed description and characteristics of the constructed model are given in previous publications [17, 18].

To simulate a burst fracture (type A4 according to the AOSpine thoracolumbar spine injury classification system), the Th_{XII} vertebral body was divided into separate fragments by several planes, and the gaps between them were filled with a material that, according to its biomechanical characteristics, corresponds to interfragmentary regenerate [19]. Four options for transpedicular fixation of two adjacent vertebrae (superior and inferior) were considered using short and long screws that passed through the anterior surface of the vertebral body; the option with and without two additional short screws in the Th_{XII} body was also evaluated.

When cconstructing the model, the materials were assumed to be homogeneous and isotropic. The poroviscoelastic properties of the spinal tissues were not taken into account, since all loads were considered under quasi-static loading conditions. Given the significant individual variability of the mechanical and anatomical parameters of the spine, adapting the model characteristics to a specific patient was considered impractical. The main task of this study was to identify the stress distribution under different loading schemes with the possibility of further extrapolation of the results to the general population. Therefore, the selected method for simplifying the model is appropriate.

As the basic type of finite element (FE), a ten-node tetrahedron with a quadratic approximation was chosen, which ensures high accuracy of the modeling results. The choice of the FE type is based on the results of a number of studies that have shown the superiority of ten-node quadratic tetrahedra over four-node linear elements both in terms of calculation accuracy and calculation time [20]. In addition, it has been proven that the number of FEs over 1,700 per vertebral body guarantees an error of less than 0.5 % [21]. Our model consisted of 35,161 ten-node tetrahedral isoparametric FEs and 92,958 nodes, which exceeds 3,000 elements per vertebral body.

The FE mesh was generated using modern software packages that automatically determine the size, type, and number of elements thanks to adaptive algorithms that take into account the curvature of surfaces, the optimal geometry of the model, and prevent the formation of elements of unsatisfactory shape.

The mechanical characteristics of biological tissues (cortical and cancellous bones, intervertebral discs, and articular cartilage) were determined based on literature sources [22–24]. Metal structures were modeled from titanium alloy VT-16, and the characteristics of artificial materials were selected from technical reference books [25]. The mechanical properties used for modeling (Young's modulus (E) and Poisson's ratio (ν)) are given in Table 1.

The above models were investigated under the action of a load simulating the extension of the trunk backwards (from front to back), which was applied to the body of the T_{IX} vertebra and the articular surfaces of its processes. The load value was chosen at the level of 350 N, which corresponded to the mass of the upper half of the trunk [26]. The caudal plane of the L_V disc was rigidly fixed, as illustrated in Fig. 1.

For the convenience of analyzing the influence of different options for transpedicular fixation on the stress-strain state, the values of stresses at fixed control points were determined in each model (Fig. 1).

In particular, among them were the vertebral bodies (Th_{IX}–L_V), endplates (lower Th_{XI} and upper L_I), screw entry and passage points (Th_{XI}, Th_{XII}, L_I), and support beams.

The analysis was performed by the finite element method, using the Mises stress as a criterion for assessing the stress state [27]. The modeling was performed in the SolidWorks computer-aided design system, and the stress-strain calculations were performed in the CosmosM environment [28].

Table 1

Mechanical characteristics of materials used in modeling

Material	Young's modulus, MPa	Poisson's ratio
Cortical bone	10000.0	0.30
Cancellous bone	450.0	0.20
Articular cartilage	10.5	0.49
Intervertebral disc	4.2	0.45
Interfragmentary regenerate	1.0	0.45
Titanium BT-16	110000.0	0.30

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Results

The modeling of four variants of transpedicular fixation for a Th_{XII} burst fracture showed significant differences in the stress distribution and behavior of the structure.

Short screws without intermediate fixation — model 1 (Fig. 2)

This variant has a standard short-segment stabilization, when the screws are installed in the vertebra adjacent to the fracture, but without fixation of the fractured Th_{XII} vertebra itself. In this configuration, the load is transmitted through the beams that connect the adjacent vertebrae (Th_{XI} and L_I), forming a rather long "span" above the fracture. As a result, the maximum stresses in the metal structure are observed precisely in the supporting beams, reaching 361.3 MPa.

Regarding bone structures, the highest stresses were recorded in the body L_{IV} (20.6 MPa), L_{III} (17.5 MPa) and L_I (17.4 MPa). In the fractured vertebra Th_{XII}, they were somewhat lower (16.2 MPa), which may be a consequence of insufficient retention of fragments. The lowest stresses among the analyzed vertebral bodies were observed in the thoracic region, specifically in Th_{XI}, where the stress measured 10.4 MPa.

Regarding the screws, the maximum stresses were observed in the screws of Th_{XI}, reaching 79.5 MPa, with somewhat lower stresses recorded in L_I at 75.9 MPa. The highest stresses, particularly at the screw entry zones, were found in the arches of Th_{XI} at 15.4 MPa, while in L_I, this value was slightly lower at 12.4 MPa.

Long screws without intermediate fixation — model 2 (Fig. 3)

The use of long screws in adjacent vertebrae (without fracture fixation) creates a stiffer anchorage in the bone, which leads to stress redistribution. The maximum values in the metal structure are reduced at the support beams to 337.2 MPa, indicating a decrease in the overall load on the system.

In the bone structures, the stress level also decreases: 15.7 MPa in the body of Th_{XII}, 16.2 MPa in L_{III}, and 17.2 MPa in L_I. However, in the arches of L_I, where the long screws penetrate deeper into the vertebra, the stress increases to 12.8 MPa. The most significant increase in stress is observed in the screws of L_I, reaching 95.1 MPa, which is the highest value among all the models. This suggests a potential risk of implant overload in this region.

Short screws with intermediate fixation — model 3 (Fig. 4)

Adding intermediate screws to the body of the affected Th_{XII} vertebra significantly changes the nature of the load distribution. The compressed vertebra begins to be not only a passive structural element, but also actively maintain the stability of the segment. It is characteristic that in this configuration the stress in the body of Th_{XII} decreases to 9.8 MPa, almost half as much as in models without intermediate fixation.

In the metal structures, an increase in stress on the supporting beams is observed, reaching 442.3 MPa, indicating a more active involvement of the fractured vertebra in load transfer. Meanwhile, the stresses in the screws themselves are significantly reduced: in the Th_{XI} screws, the stress drops to 66.0 MPa (compared to 79.5 MPa in the model without intermediate screws), and in the L_I screws, it decreases to 64.4 MPa (down from 75.9 MPa). A reduction in stress is also noted in the Th_{XI} arches, with the value falling to 8.8 MPa (from 15.4 MPa in the previous model).

Therefore, the inclusion of the affected level in the fixation allows to reduce peak loads at key points of the system, which has a positive effect on the durability of the structure.

Long screws with intermediate fixation — model 4 (Fig. 5)

This configuration is the most rigid, as it combines long screws with intermediate fixation. It exhibits the lowest stress levels in the bone structures among all the options. For instance, the stress in the body of Th_{XII} is 9.8 MPa, in L_I it is 14.1 MPa, and in L_{III} it is 13.9 MPa.

At the same time, unlike the model with monocortical screws, in metal structures there is a decrease in the maximum stress on the support beams (436.0 compared to 442.3 MPa), which indicates some reduction in stress in the structure.

However, the stress on the L_I screws remains relatively high at 75.7 MPa, while the stress on the screws in Th_{XII} is 13.5 MPa, which is only slightly higher than in the previously considered model. This suggests a more uniform distribution of the load, although the overall stiffness of the structure remains high.

The values of stresses at all control points of the models for different options for transpedicular fixation are summarized in Table 2.

When comparing the results of the analysis across the considered models, it's important to focus on several key points that hold the greatest clinical significance.

A detailed analysis of the stress-strain state of the elements of the biomechanical system, especially in the areas of connection of the screws with the bone tissue of the vertebrae, is key to determining

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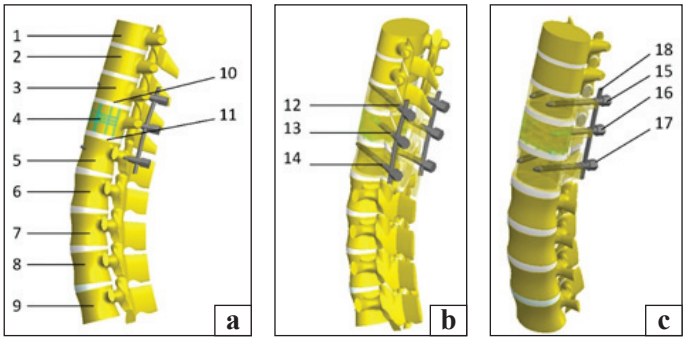

Fig. 1. Schematic location of control points: 1 — vertebral body Th_{IX}; 2 — vertebral body Th_{X}; 3 — vertebral body Th_{XI}; 4 — vertebral body Th_{XII}; 5 — vertebral body L_{I}; 6 — vertebral body L_{II}; 7 — vertebral body L_{III}; 8 — vertebral body L_{IV}; 9 — vertebral body L_{V}; 10 — lower endplate of the vertebral body Th_{XI}; 11 — upper endplate of the vertebral body L_{I}; 12 — entry of screws into the vertebral arch Th_{XI}; 13 — entry of screws into the vertebral arch Th_{XII}; 14 — entry of screws into the vertebral arch L_{I}; 15 — screws in the vertebral body Th_{XI}; 16 — screws in the vertebral body Th_{XII}; 17 — screws in the vertebral body L_{I}; 18 — support beams

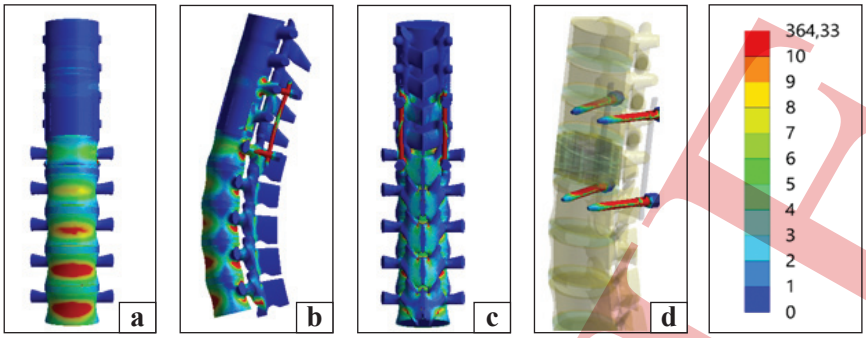

Fig. 2. Stress distribution in the model of the thoracolumbar spine with a burst fracture of the Th_{XII} vertebral body during backward bending of the trunk. Transpedicular fixation with short screws without fixation of the Th_{XII} vertebra view: a — front; b — side; c — back; d — screws

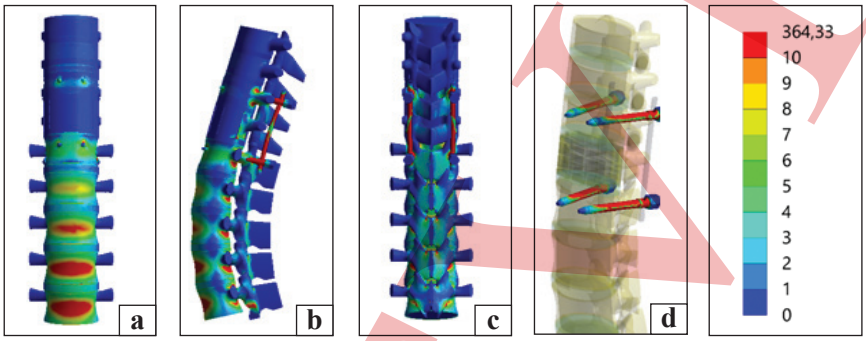

Fig. 3. Stress distribution in the model of the thoracolumbar spine with a burst fracture of the Th_{XII} vertebral body during backward bending of the trunk. Transpedicular fixation with long screws without fixation of the Th_{XII} vertebra view: a — front; b — side; c — back; d — screws

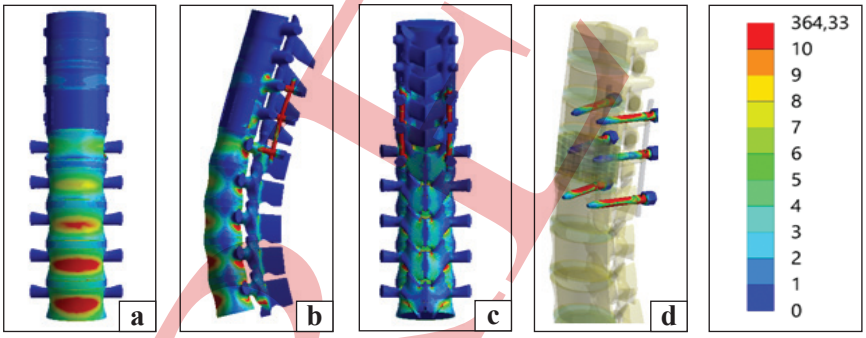

Fig. 4. Stress distribution in the model of the thoracolumbar spine with a burst fracture of the Th_{XII} vertebral body during backward bending of the trunk. Transpedicular fixation with short screws with additional fixation of the Th_{XII} vertebra view: a — front; b — side; c — back; d — screws

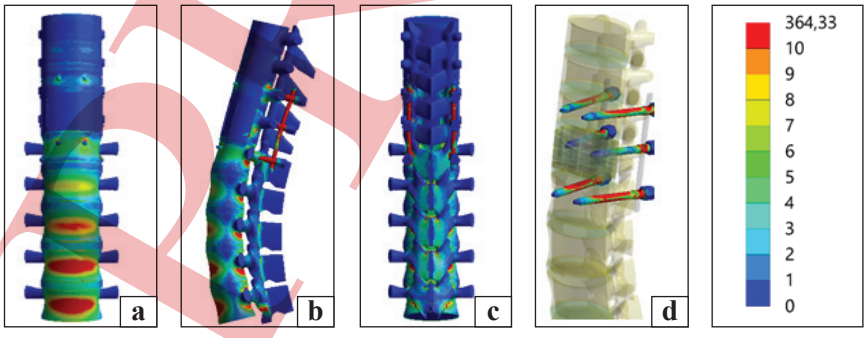

Fig. 5. Stress distribution in a model of the thoracolumbar spine with an explosive fracture of the Th_{XII} vertebral body during backward bending of the trunk. Transpedicular fixation with long screws with additional fixation of the Th_{XII} vertebra view: a — front; b — side; c — back; d — screw

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the effectiveness of various options for transpedicular fixation in the case of an explosive fracture of the body of the Th_{XII} vertebra. Our study revealed that the highest stress values are concentrated in the places where the screws enter the vertebral arches. In particular, in the model without intermediate screws, the maximum stresses at the places where the screws enter the arch of the Th_{XI} vertebra are 15.4 MPa (short) and 14.5 (long). When intermediate screws are added, these values are significantly reduced to 8.8 and 7.7 MPa, respectively. In the Th_{XII} vertebra, where additional intermediate screws are installed, the stresses at the connection points are 2.5 MPa for both types of screws. In the area of screw entry into the L_I vertebral arch, a decrease in stresses was also noted from 12.4–12.8 MPa (model without intermediate screws) to 9.3–10.0 MPa (model with intermediate screws). A detailed analysis of the L_I–L_V vertebral bodies revealed an uneven distribution of stresses with significant differences between individual zones of the vertebral bodies. The highest stresses were recorded in the L_{IV} vertebral bodies (20.6–20.7 without intermediate screws, 18.5–19.1 MPa with intermediate screws) and L_{III} (17.5 without intermediate screws and 13.9–15.1 MPa with intermediate screws). In the L_{II} vertebral body, stresses decrease from 14.7–14.2 MPa in the model without intermediate screws to 12.0–12.5 MPa with intermediate screws. In the L_V vertebra, the stresses are the lowest and almost do not change (15.3 without intermediate, 14.8–14.9 MPa with intermediate screws). At the same time, it should be noted that assessing the nature of stress distribution in the most heavily loaded vertebral bodies, particularly the lumbar region (L_I–L_V), requires a more detailed and comprehensive analysis. Given the high clinical significance of this information, a more detailed analysis of the stress-strain state of these structures could serve as the basis for a separate, more specialized study. Such an investigation would provide a deeper understanding of the mechanisms behind potential complications and help optimize treatment strategies.

The overall analysis of the obtained data demonstrates that the highest peak stresses in the beams were observed in the configuration of long screws without intermediate fixation (337.2 MPa), which potentially makes this model the most loaded for metal elements. Adding intermediate fixation significantly reduced the stresses in the beams, it was especially effective for the structure with short screws,

Table 2

Tension during backward trunk bending in thoracolumbar spine models with explosive fracture of the Th_{XII} vertebral body in different transpedicular fixation options

Control point			Stress, MPa			
			model without intermediate screws		model with intermediate screws	
№	зона		short	long	short	long
1	Bone tissue	Th_{IX} vertebral body	1.6	1.5	1.5	1.4
2		Th_X vertebral body	1.5	1.4	1.4	1.3
3		Th_{XI} vertebral body	10.4	9.8	8.3	8.2
4		Th_{XII} vertebral body	16.2	15.7	9.8	9.8
5		L_I vertebral body	17.4	17.2	15.9	14.1
6		L_{II} vertebral body	14.7	14.2	12.5	12.0
7		L_{III} vertebral body	17.5	16.2	15.1	13.9
8		L_{IV} vertebral body	20.6	20.7	19.1	18.5
9		L_V vertebral body	15.3	15.3	14.9	14.8
10		Lower endplate of Th_{XI} vertebra	3.0	3.1	2.4	2.4
11		Upper endplate of L_I vertebra	8.0	7.7	8.3	8.1
12		Screw entry into vertebral arch Th_{XI}	15.4	14.5	8.8	7.7
13		Screw entry into vertebral arch Th_{XII}	—	—	2.5	2.5
14		Screw entry into vertebral arch L_I	12.4	12.8	10.0	9.3
15	Metal construction	Screw in the vertebral body Th_{XI}	79.5	79.7	66.0	54.0
16		Screw in the vertebral body Th_{XII}	—	—	13.2	13.5
17		Screw in the vertebral body L_I	75.9	95.1	64.4	75.7
18		Support beam	361.3	337.2	442.3	436.0

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where the stresses were 442.3 MPa, but the stability of the structure was significantly improved due to the load distribution by additional attachment points (model 3). Thus, it can be argued that from the standpoint of minimizing stresses in the system, the most favorable configuration is the one with short screws and intermediate fixation, while the most stressed is the model with long screws without intermediate fixation.

Discussion

The effect of screw length on the stress level

The length of the pedicle screws significantly affects the nature of the stress distribution in the structure and bone. Models with long (bicortical) screws demonstrated higher fixation stiffness, which was manifested in an increase in stresses in critical areas of the structure. In particular, the transition from short to long screws (models 1 → 2 and 3 → 4) was accompanied by an increase in the maximum stress in the beams. This is explained by the fact that longer screws are more firmly fixed in the vertebral body and deform less at the point of contact with the bone, due to which more external load is transmitted directly to the metal connecting elements of the system. For example, in modeling without intermediate fixation, additional fixation of the screws in the opposite cortical wall led to an increase in stress in the beams by approximately 30–40 % compared to short screws under the same applied load. Similarly, in the presence of intermediate fixation, long screws also produced higher stresses in the beams, although the relative increase was somewhat smaller (since the presence of an intermediate support partially unloads the connecting elements). Critical zones in the bone—mainly around the screw insertion points (arch roots and adjacent vertebral body) — are also affected by screw length. Models with long screws showed increased local stresses in the pedicle area compared to short ones. This is especially noticeable at the lower supporting vertebra of the construct (in our case, L_I), where the load is maximal. In percentage terms, bicortical fixation increased the stresses in the bone at the base of the screw by approximately 15–20 %. Physically, this means that a more tightly fixed long screw fixes the bone tissue more strongly during loading, concentrating the stresses at the screw entry. In contrast, short (monocortical) screws are somewhat more elastic at the fixation point: they do not reach the opposite wall of the vertebra, so the load is partially damped by a small elastic deformation of the bone around the tip of the screw. As a result, the maximum stresses in the design with short screws are slightly lower, and the force distribution is softer, the stresses are more dispersed along the length of the screw and less concentrated near the pedicle. It is worth noting that the difference in the length of the screws affects the distribution of loads in more than one direction. Long screws, providing better grip, improve the resistance of the screw to extraction and can reduce the risk of its micromovement in the bone under load. In the simulation, this is reflected in slightly lower stresses in the distal (anterior) part of the vertebral body, where the tip of the long screw is fixed, the load is perceived there by an additional support point. Thus, the long screw distributes the forces over a larger volume of bone. However, the main "impact" of the load is taken by the screw entry zone into the pedicle, where the bone material experiences more stress. Therefore, in terms of the likelihood of local overload of the bone (which can lead to its resorption or microfractures around the screw), short screws are more gentle.

Thus, increasing the length of the screws increases the stiffness of the entire structure and reduces micromotions in the screw-bone connection, but is accompanied by an increase in maximum stresses in both the metal elements and the bone near the screws. In the context of modeling, this means that long screws fix more effectively, but can create critical overstress zones that should be taken into account when studying the durability of implants and the safety of bone support.

Effectiveness of intermediate screws

The introduction of screws into the body of the fractured Th_{XII} vertebra (intermediate fixation) has shown high efficiency in improving load distribution and increasing the stability of the structure. A comparison of pairs of models without and with intermediate fixation (1 → 3 and 2 → 4) demonstrates a common trend: the presence of additional supports in the affected vertebra significantly reduces extreme stresses in the structure and changes the path of load transmission.

First, the intermediate screws take on part of the load that would otherwise fall on the beams and adjacent intact vertebrae. In a model experiment, this was manifested in a decrease in the maximum stresses in the beams under the condition of adding intermediate fixation. For the configuration with short screws, adding screws at Th_{XII} reduced the peak stresses in the connecting elements of the structure by a fairly significant amount (about 5–10 % in our calculations). Although this figure may seem modest, the qualitative effect is very important: the shape of the rod bending changed — instead of one

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large span between Th_{XI} and L_I, two smaller spans (Th_{XI}–Th_{XII} and Th_{XII}–L_I) were formed, each with its own support point. This means that the rod works with less deflection and carries the load more evenly, reducing the risk of stress concentration in the middle of the span.

Secondly, intermediate screws change the distribution of forces in the vertebrae themselves. A fractured vertebra equipped with screws begins not only to be an object of support, but also actively perceives the load. Our results showed that the stresses in the Th_{XII} body changed in the presence of screws: instead of the load being concentrated on the anterior and middle columns of the fractured vertebra (as is observed in the case of insufficient support), part of the forces were transmitted through the pedicle screws to the beams. This led to a decrease in the peak stresses in the Th_{XII} body in the model with intermediate fixation. In other words, the additional screws strengthened the fragments from the inside, reducing their mutual displacement and the load on the interfragmentary structures. Such a redistribution is positive in terms of preventing further traumatization of the cancellous bone and promoting conditions for fracture consolidation, since the fragments are held more stably. It is also worth noting that intermediate fixation unloads the adjacent intact vertebrae. In the absence of screws in Th_{XII}, the vertebrae above and below (Th_{XI} and L_I) actually bear the entire moment of force associated with fracture stabilization through the beams. This is manifested by high stresses in their bodies and especially in the places of screw attachment. Adding support in Th_{XII} redistributes part of the moment directly to it. As a result, in models with intermediate fixation, the stresses in the bodies of Th_{XI} and L_I are somewhat lower, and the maximum stresses near their pedicles are also reduced (as can be seen from the comparison of stresses in the screw insertion zones: in model 3 they are lower than in 1; in model 4 they are lower than in 2). This means that additional fixation protects the neighboring vertebrae from overload, taking part of the efforts on itself.

Thus, the effect of additional fixation of the affected vertebra during extension load simulation is generally positive and multifaceted: intermediate screws reduce stresses in the metal structure, reduce their concentration in bone structures, increase stiffness and stability of the damaged segment, and also contribute to a more uniform distribution of loads throughout the "implant-spine" system.

Clinical recommendations

The modeling results have a clear practical reflection, helping to choose the optimal tactics of surgical fixation of a Th_{XII} burst fracture. First of all, the importance of additional fixation of a traumatically affected vertebra has been confirmed. The installation of transpedicular screws in a fractured Th_{XII} significantly increases the initial stability and unloads the implants. Clinically, this means better support of the anterior spinal column and a greater likelihood of preserving vertebral height and correcting kyphosis after surgery. Patients with this fixation are likely to have a lower risk of early deformity or pseudarthrosis of the fracture, since the fragments are securely immobilized. Thus, short-segment fixation with the inclusion of the fracture level (models 3 and 4) seems to be a reasonable choice in the case of burst fractures, this technique has already gained support in clinical practice and our modeling confirms its biomechanical feasibility.

Regarding the length of the screws, the data obtained indicate a certain compromise. Bicortical screw insertion (long screws) provides somewhat better fixation in the bone, which may be critical in cases of osteoporosis or poor bone quality, when there is a risk of screw pullout. In such situations, long screws will help to fix more firmly in the bone tissue and hold the construct; that is, clinically reduce the likelihood of screw pullout or migration under load. However, at the same time, the increased stiffness of the fixation leads to an increase in the loads on the construct itself. Practical conclusion: When using long screws, the surgeon should consider the quality and strength of the supporting beams, opting for those with higher endurance if necessary. Additionally, it is important to account for the need to limit excessive loads on the patient's spine during the postoperative period. Short screws, on the other hand, show lower stress concentrations and may be sufficient in cases where the bone is strong. Clinically, under conditions of sufficient bone mineral density, monocortical screws hold the segment quite reliably and at the same time reduce the risk of damage to the opposing cortical plate and adjacent structures (e. g., vessels, ligaments) during their installation [29]. The results obtained did not reveal a critical advantage over long screws in terms of stress reduction or stability, therefore, from the point of view of the stability/load balance on the structure, short screws with intermediate fixation are the optimal solution in most cases. Long screws can be considered as a means of increasing the reliability of fixation in difficult cases, but their necessity should be weighed against potential risks.

It should be noted that in the context of comparing our data with the results of other studies, there are certain difficulties due to a number of factors. In particular, most of the existing works use simpli-

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fied damage models that do not take into account all the details considered in ours [16, 30–32]. In addition, other researchers often analyze a much smaller number of control points, which may not allow for a full assessment of the load distribution [14, 33, 34]. At the same time, a certain dissonance is introduced by the differences in the loading modes of the models, which also complicates the direct comparison of the results. Despite these differences, our data are generally consistent with the general trends observed in other studies and reliably reflect the nature of the load in the most critical structures [16, 30, 33, 35].

Conclusions

The modeling of various options for short transpedicular fixation of the thoracolumbar junction confirms that under extension loading, the best balance between immediate stability and long-term safety of the structure is achieved when the affected vertebra is involved, using the optimal length of screws for a specific patient. This tactic minimizes the risks of failure of the structure and provides conditions for successful fusion, while reducing undesirable consequences for adjacent spinal segments in the future.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. The nearest prospect is the completion of the analysis of all main loading patterns, which will allow for a comprehensive assessment of the biomechanical behavior of various fixation options. Special attention is planned to be paid to identifying the most critical overload zones in bone structures and elements of metal structures. Based on the obtained data, optimal stabilization configurations will be determined to increase the reliability of fixation and reduce the risk of complications in patients with explosive fractures of the thoracolumbar junction. It is planned to conduct clinical validation of the obtained biomechanical results, as well as develop individualized approaches to choosing a fixation configuration taking into account bone density, fracture morphology, and the degree of destruction of the anterior column. Dynamic modeling, with simulation of the fusion process and prolonged loading, is also considered.

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Authors' contribution. Nekhlopochyn O. S. — idea and concept of the study, analysis of findings, drawing conclusions; Verbov V. V. — clinical interpretation of the obtained data, comparison with literary sources; Cheshuk E. V. — literary search, technical editing of the article; Karpinsky M. Yu. — modeling, collection of initial results, primary analysis of the stress-strain state; Yaresko O. V. — construction of a geometric model, setting of control points.

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BIOMECHANICAL ANALYSIS OF SHORT-SEGMENT PEDICLE SCREW FIXATION FOR AO TYPE A FRACTURES AT THE THORACOLUMBAR JUNCTION UNDER EXTENSION LOADING

O. S. Nekhlopochyn [1], V. V. Verbov [1], Ie. V. Cheshuk [1], M. Yu. Karpinsky [2], O. V. Yaresko [2]

[1] Romodanov Neurosurgery Institute of National Academy of Medical Sciences of Ukraine, Kyiv
[2] Sytenko Institute of Spine and Joint Pathology of the National Academy of Medical Sciences of Ukraine, Kharkiv

✉ Oleksii Nekhlopochyn, MD, PhD: AlexeyNS@gmail.com; https://orcid.org/0000-0002-1180-6881
✉ Vadim Verbov, MD, PhD: v.verbov@gmail.com; http://orcid.org/0000-0002-3074-9915
✉ Ievgen Cheshuk, MD: evcheshuk@gmail.com; https://orcid.org/0000-0002-8063-2141
✉ Mykhailo Karpinsky: korab.karpinsky9@gmail.com; https://orcid.org/0000-0002-3004-2610
✉ Olexander Yaresko: avyresko@gmail.com; https://orcid.org/0000-0002-2037-5964

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Histological changes in adjacent intervertebral discs in a rat model of nucleus pulposus injury and spinal nerve compression

O. O. Barkov, V. Ye. Maltseva, O. A. Nikolchenko, Z. M. Danyshchuk, K. M. Samoylova

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

The prevalence of decompression and stabilization in the thoracic and lumbar spine (LS) is constantly increasing due to the high incidence of degenerative spine diseases among the working-age population. Aim: To analyze histological changes in rats in which the condition of LS was experimentally reproduced as in patients with spinal nerve compression before and after performing decompression and stabilization of the spine. Methods. The study was conducted using 19 white rats, in which the nucleus pulposus in the intervertebral disc was destroyed at the L_V–L_{VI} level. In Model 1, at the level of the damaged disc, the right spinal nerve was ligated with two double knots of suture material. In Model 2, the L_V and L_{VI} vertebral bodies were bilaterally fixed with two metal staples, pressing them on the root area. Results. No signs of inflammation were detected in any of the rats. Degenerative changes were recorded in the adjacent cranial and caudal intervertebral discs, but there was no significant difference in the scores between the adjacent intervertebral discs, both in the case of a general assessment and separately for the annulus fibrosus and the nucleus pulposus. The values obtained were ≈ 6.5 and ≈ 5 points, respectively, for the model. The sum of the scores for the annulus fibrosus of the degenerative disc of Model 1 was significantly higher compared to both adjacent discs ($p = 0.016$; $p = 0.026$), compared to the corresponding values for the cranial or caudal disc of Model 2, no difference was detected. In both models, Wallerian degeneration was detected in the more distal areas of the nerves. Conclusions: Degenerative changes occur in adjacent discs in a rat model of spinal nerve compression and intervertebral disc nucleus pulposus injury. This provides an opportunity to use this model to study treatments for disc degeneration in patients with neurological complications after spinal decompression and stabilization.

Поширення декомпресійно-стабілізуючих втручань на грудному та поперековому відділах хребта (ПВХ) постійно зростає через високу частоту дегенеративних захворювань цієї локалізації серед працездатного населення. Мета. Проаналізувати гістологічні зміни в щурів, яким експериментально відтворили стан ПВХ як у пацієнтів із компресією спинномозкових нервів до та внаслідок виконання декомпресійно-стабілізуючих втручань. Методи. Дослідження проведене з використанням 19 білих щурів, яким руйнували драглисте ядро в міжхребцевому диску на рівні L_V–L_{VI}. Модель 1 — на рівні ушкодженого диска перев'язували правобічний спинномозковий нерв двома подвійними вузлами шовного матеріалу. У Моделі 2 тіла хребців L_V та L_{VI} білатерально фіксували двома металевими скобами, притискаючи ними ділянку корінців. Результати. Ознак запалення не виявлено в жодного з щурів. Зафіксовано дегенеративні зміни в суміжних краніальному та каудальному дисках, проте за оцінкою в балах не було значущої різниці між суміжними міжхребцевими дисками, як у разі загальної оцінки, так і окремо для волокнистого кільця та драглистого ядра. Отримані значення дорівнювали ≈ 6,5 та ≈ 5 балам відповідно моделі. Сума балів для волокнистого кільця ушкодженого диска Моделі 1 була значуще більшою порівняно з обома суміжними дисками ($p = 0,016$; $p = 0,026$), порівняно з відповідними значеннями краніального або каудального диска Моделі 2, різниці не виявлено. У обох моделях зафіксовано у дистальніше розташованих ділянках нервів Валлерову дегенерацію. Висновки. У моделі щурів із компресією спинномозкового нерва й ушкодженням драглистого ядра міжхребцевого диска ПВХ виникають дегенеративні зміни в суміжних дисках, що дає змогу використовувати їх для дослідження методів лікування дегенерації дисків у пацієнтів із неврологічними ускладненнями після декомпресійно-стабілізуючих втручань на хребті. Ключові слова. Дегенерація міжхребцевого диска, щур, компресія спинномозкового нерва, дегенеративні захворювання поперекового відділу хребта, захворювання суміжних сегментів.

Keywords. Iintervertebral disc degeneration, rat, spinal nerve compression, degenerative lumbar disease, adjacent segment disease

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Introduction

The issue of preventing and managing complications arising from decompression-stabilization procedures in the thoracic and lumbar spine remains an ongoing challenge. Transpedicular stabilization of the spine is one of the standard methods of surgical treatment of degenerative diseases of the spine. At the same time, incorrect placement of transpedicular screws is associated with the risk of neurological complications [1]. Neuropathic pain is one of them and is accompanied by a deterioration in the quality of life [2]. In patients presenting with neurological complications resulting from lumbar spine (LS) nerve compression, decompression-stabilization interventions (DSI) may not consistently result in complete recovery for all individuals [3]. Pre-existing neuropathic pain increases the risk of prolonged pain after spinal fusion [4]. In addition, it is important to study the condition of the intervertebral discs adjacent to the degenerative segment due to the corresponding complication that occurs after spinal fusion of the LS in 5–30 % of patients [5]. The solution to this problem involves creating new ways to treat and prevent these complications. That is, it is important to create models that will allow studying the development of changes in the spine in patients with nerve compression in the LS both before and after DSI. This will help to plan the further use of various conservative treatment methods, in particular biological therapy for adjacent segments. Animals, especially small ones, such as mice or rats, are one of the common options for modeling degenerative diseases of the spine [6–11]. S. Shehab et al. found in rats with unilateral ligation of the spinal nerve at the level of L_V that the effect of capsaicin or resiniferatoxin on the adjacent nerves L_{III} and LBI reduced pain and structural changes in the nerves [12]. This provides a direction in the creation of animal models for studying the development of structural changes in the spine similar to those in patients with degenerative spinal diseases and neuropathic pain at the affected and adjacent levels.

Objective: To evaluate histological alterations in rats following the experimental replication of lumbar spine conditions analogous to spinal nerve compression in humans, both prior to and subsequent to decompression-stabilization procedures.

Material and methods

The experimental study was reviewed and approved by the Bioethics and Deontology Committee of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the National Academy of Medical Sciences of Ukraine" (protocols No. 215 dated 19.04.2021, No. 239 dated 18.12.2023). The research was carried out in accordance with regulatory and legislative requirements [13, 14].

Animals

The experiment was performed using 19 nonlinear white rats aged 9–10 months (body weight 430–675 g) from the population of the Experimental Biological Clinic of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the National Academy of Medical Sciences of Ukraine"

Surgical interventions

For anesthesia, rats were injected intramuscularly with medetomidine hydrochloride (0.02 mg/kg) and ketamine (50 mg/kg). The animals were fixed in a supine position. After laparotomy, the abdominal organs were taken out, wrapped in a sterile gauze napkin and irrigated with saline. To access the ventral part of the LS, soft tissues and blood vessels (spiral-lumbar and posterior vena cava) were carefully retracted, protected with a sterile gauze napkin and retractors were installed. In the intervertebral disc at the level of segments L_V–L_{VI}, a standard perforated defect was created with the destruction of the nucleus pulposis (depth 1.5 mm) using a dental bur with a diameter of 1.5 mm.

The animals were divided into groups depending on the pattern of spinal nerve compression:

– *Model 1 (n = 9).* Between the right-sided muscles next to the damaged intervertebral disc, the adjacent spinal nerve (ventral branch of the lumbar nerves, which passes into the sciatic nerve) was visualized and separated with control of the manifestation of the motor reflex in the right pelvic limb of the rat. Then, the spinal nerve was ligated with 2 double knots of non-absorbable suture material (Fig. 1, a);

– *Model 2 (n = 10).* For spinal fusion, two stainless steel staples (medical stapler Manipler® AZ-35W, 6.9 mm × 4.2 mm, grade 316L) were used after shortening their arms to 2 mm. In the adjacent vertebral bodies of the L_V and L_{VI}, four standard perforated defects with a depth of 2 mm were created using a dental bur with a diameter of 1.2 mm bilaterally, two in the caudal part of the L_V and two in the cranial L_{VI}. Then, using the press-fit technique, metal staples were implanted into the defects, pressing the adjacent spinal nerves with them (Fig. 1, b).

Upon completion of the surgical intervention, the abdominal wall and skin wound of all rats were sutured in layers with absorbable suture material and treated with a povidone-iodine solution (10 %).

In Model 1, 2 rats died 5 and 9 days after the intervention. In Model 2, 2 individuals died during

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the operation, another 2 a day later, and another 2 animals after 4 days.

Eight weeks after surgery, 11 rats were removed from the experiment by decapitation, which was due to the need to collect blood for biochemical analysis. Fragments of the L_I–S_I LS were removed for further histological examination.

Histological analysis

For histological analysis, the selected fragments of the lumbar spine L_I–S_I were fixed in 10 % neutral formalin for 5 days. After decalcification in 10 % formic acid solution, 3 fragments with intervertebral discs were cut out: cranial (L_{IV}–L_V), level of injury (L_{IV}–L_V), caudal (L_{VI}–S_I), cutting along the vertebral bodies. After that, the samples were dehydrated in ethyl and isopropyl alcohols of increasing concentration, soaked in a mixture of isopropyl alcohol and paraffin, and embedded in paraffin. Using a sledge microtome, histological sections of 6 μm thickness were made in the coronal plane, which were analyzed under a BX63 light microscope. Digital images were obtained using a DP73 camera.

The assessment of degenerative changes in three intervertebral discs for each rat was performed using the scale developed by A. Lai et al. [15]. According to it, the maximum manifestation of degenerative changes is 16 points, and the normal structure is 0 (Table 1). The assessment was not performed at the level of damage to the nucleus pulposus due to its absence.

Statistical analysis

The obtained indicators are presented as mean and standard deviation. Their comparison within one model was performed using the Wilcoxon test for related samples, and for comparison between models, the Mann-Whitney U-test was used. The difference was considered significant in $p < 0.05$. The analysis was performed using the SPSS Statistics 23 software.

Results

Model 1 (n = 7)

Cranial segment. In the intervertebral disc of the spinal segment located cranially from the damaged disc, in the outer section of the annulus fibrosus, collagen fibers were appropriately organized, only one rat (14 %) was found to have a violation. The cellular composition in the outer section consisted of fibrochondrocytes, and in the inner section of chondrocytes. The cell density was from medium to high. However, in the outer section, interfibrous ruptures/cracks in the laminae were detected in half of the rats, while in the others, there were no structural changes (Fig. 2, i).

In the nucleus pulposus, the matrix was heterogeneous in color in all animals except one. In 70 % of cases, notochondral cells were detected in the nucleus pulposus, while in the others, only chondrocytes were detected, and in one rat, degenerative cells together with chondrocytes (Fig. 2, d). In rats in which notochondral cells were detected, chondrocytes were also recorded. Among the signs of nucleus pulposus degeneration, the following were detected: cell loss in 42% of cases, accumulation of collagen fibers in 57 %, and calcification in 1 (14 %) (Fig. 2, d).

The endplates were without structural abnormalities, except for one rat, in which they were calcified, which was combined with vascular growth. At this level of the spinal segment, no signs of inflammation were detected.

Level of damage. At the level of injury to the intervertebral disc by a dental bur in the fibrous ring, all rats had impaired organization of collagen fibers, in 28 % they were disconnected and torn. The outer and inner sections did not have a pronounced difference in structure, and among the cells, only chondrocytes were determined in half of the rats, in the others both fibrochondrocytes and chondrocytes (Fig. 2, b, i). The cell density was from medium to low, in one animal it was high. Among the preserved plates of the outer section of the fibrous ring, interfibrous gaps were determined in 71 % of cases, which were combined in 28 % with fragmentation of the plates, and in 28 % the presence of detritus was detected.

Nucleus pulposis did not have a characteristic structural structure due to boron damage and was

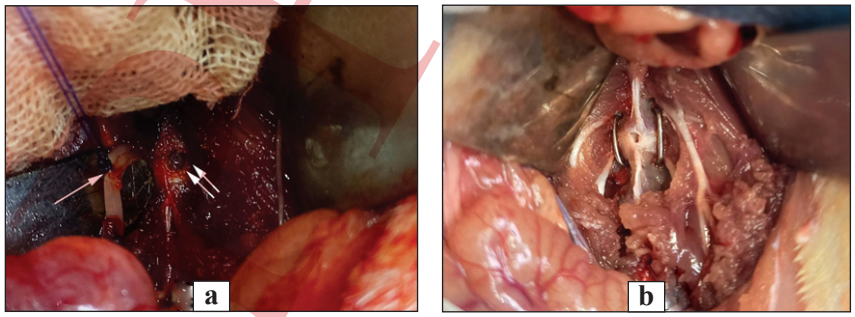

Fig. 1. Surgical site after performing a hole defect in the intervertebral disc at the level of segments L_V and L_{VI} (double arrow) and compression of the adjacent spinal nerve by ligating it with suture material in rats, Model 1 (a) and pressing with implanted metal staples in rats, Model 2 (b)

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actually replaced by other tissues: in 57 % connective, sometimes with capillary-type vessels, with a large number of fibroblasts, single chondrocytes, and in 33 % cartilaginous with chondrocytes and small cells of notochondral cells (Fig. 2, f). In rats with replacement of the nucleus pulposis with cartilage tissue, cracks in the matrix and detritus were found next to them. In one animal out of 7 (14 %) the cartilage tissue in the nucleus pulposis area was combined with newly formed bone tissue cells, capillary-type vessels and detritus. There were no signs of inflammation at this level of the spinal segment.

Caudal segment. In the annulus fibrosus of the intervertebral disc of the spinal segment caudal to the injured level, 57 % of the collagen fibers retained a lamellar structure, while the rest showed signs of disorganization. The cells analyzed were characteristic of the annulus fibrosus — fibrochondrocytes and chondrocytes, which were located near the nucleus pulposus. The cell density was medium to high. Interfibrous gaps in the annulus fibrosus plates were found in half of the rats, while the integrity of the structure was preserved in the others (Fig. 2, o).

In the nucleus pulposus, notochondral cells were identified in only half of the rats, while only chondrocytes were found in the others. Notochondral cells were often combined with chondrocytes. The matrix of the nucleus pulposus was mostly heterogeneously stained. Among the signs of degeneration of the nucleus pulposus, an accumulation of collagen fibers was found in 28 %, while areas of calcification were present in the others (Fig. 2, g).

The endplates were intact with no signs of vascular ingrowth. Inflammation was not detected in any of the studied cases.

At this level, the spinal nerves that formed the lumbar plexus were surrounded by an epineurium of dense connective tissue. (Fig. 3, a, b). In the nerve fibers, degenerative changes in axons were determined in the form of accumulation of amorphous decay products and axon fragmentation (Fig. 3, a). Single Schwann cells were determined (Fig. 3, b).

According to the quantitative assessment of degenerative changes in intervertebral discs in Model 1, no difference was found in the scores between the cranial and caudal adjacent discs (Table 1), and the average score was ≈ 6.5 points. The sum of the scores for the fibrous ring of the damaged disc was significantly higher compared to both adjacent discs ($p = 0.016$; $p = 0.026$).

Model 2 (n = 4).

Cranial segment. The intervertebral disc located cranially from the damaged segment consisted of a fibrous ring and a nucleus pulposis (Fig. 2, a). In the fibrous ring of the intervertebral disc, collagen fibers retained the appropriate structural organization in 80% of rats. Fibrochondrocytes were located in the outer and chondrocytes in the inner part of the fibrous ring. The cell density was average. In the outer part of the fibrous ring, interfibrous gaps and fiber breaks in the laminae were found in 40 % of cases (Fig. 2, p, w).

In the nucleus pulposis, the matrix had a heterogeneous color in 60 % of rats, the cellular composition in all animals was notochordal, and chondrocytes were also found in 40 % of them (Fig. 2, n). Among the degenerative signs, the accumulation of collagen fibers in areas was determined in 60 % of cases. The endplates were calcified in 80 % of the rats, but without vascular growth. No signs of inflammation were found in any animal.

Level of injury. At the level of injury, signs of disorganization of collagen fibers in the annulus fibrosus of the intervertebral disc were determined in 80 % of the individuals (Fig. 2, q, x). Chondrocytes and fibroblasts predominated among the cells. Their density was high in 60 %, and medium or low in the others. Interfibrous gaps in the laminae of the annulus fibrosus and loss of the lamellar structure were also found in 80 %.

The nucleus pulposus did not have a characteristic structure and was replaced in 80 % by cartilage tissue (Fig. 2, r, u, Fig. 4, a), one of these rats was found to have connective and bone tissue simultaneously (Fig. 4, b).

In one animal (20 %), only connective tissue was identified in the area of the nucleus pulposus. In a rat with bone tissue, capillary-type vessels were found in the connective tissue. The cells were appropriate for the type of tissue, fibroblasts in the connective tissue, chondrocytes in the cartilage tissue, osteoblasts and osteocytes in the bone tissue. The endplates were calcified in 60 % of the animals, and in the others they were completely absent. No signs of inflammation were detected.

In the vertebral bodies adjacent to the intervertebral disc, holes were identified that remained from the staples installed during the surgical intervention to stabilize this spinal segment. Bone tissue of a lamellar structure was formed around the holes. Cartilage tissue was also identified along the perimeter of the staples, and connective tissue in small areas (Fig. 5, a). The structure of the vertebral bodies was without signs of disorders. The only peculiarity was that newly formed connective tissue with capillary-type vessels was found on the outside of the vertebral

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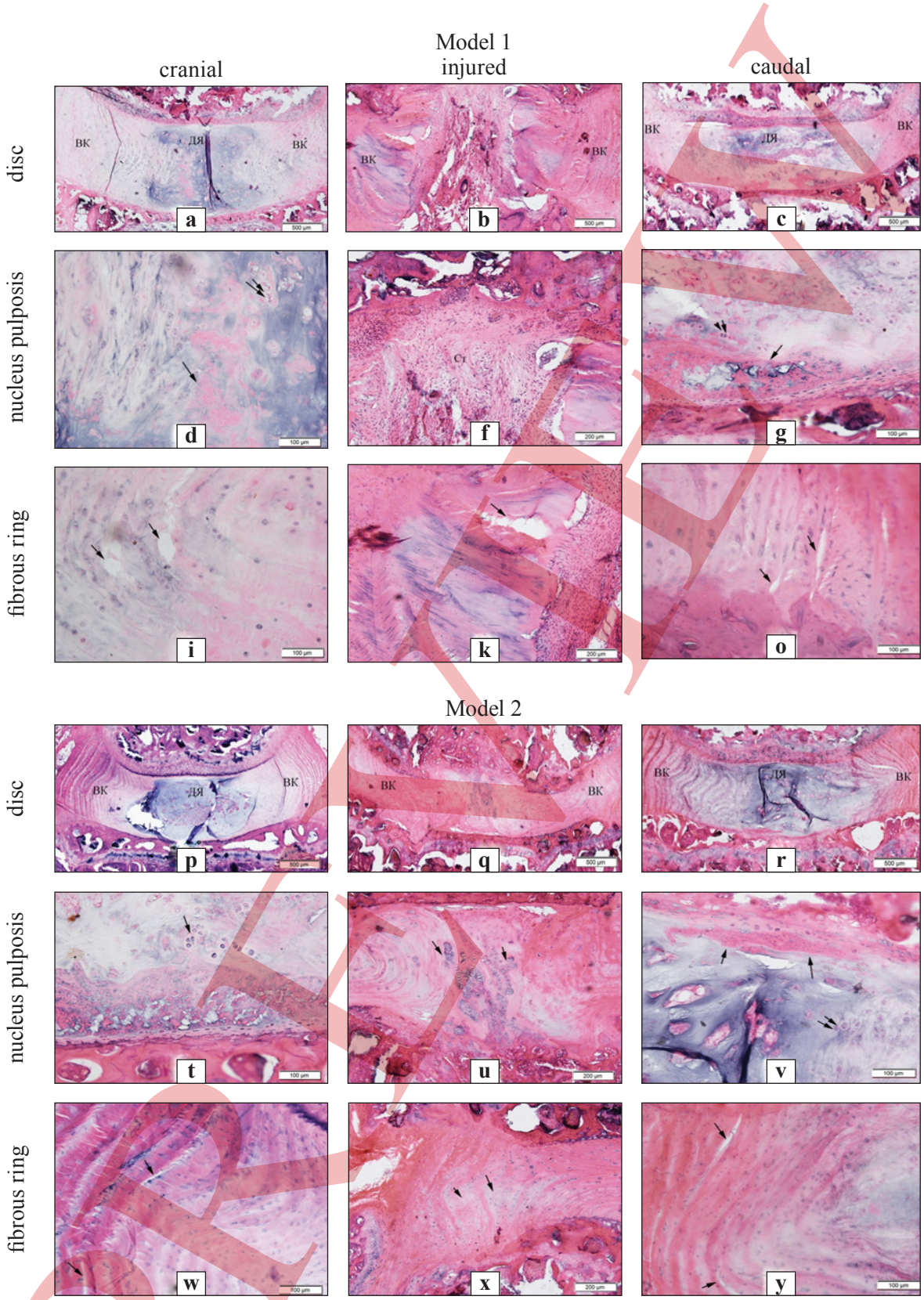

Fig. 2. Structural features of intervertebral discs in Models 1 and 2 at the level of injury and adjacent (cranially and caudally) to this spinal segment. General view of the structure of the intervertebral disc (a–c, p–r). Replacement of the nucleus pulposis with connective tissue (Ct) in Model 1 (b, f) or with cartilage tissue in Model 2 (q) with partial preservation of the structure of the fibrous ring (k, x), violation of the integrity of the locking plate (b, f, q, u). Hypertrophied chondrocytes (arrow) u). Crack between the plates in the outer part of the fibrous ring (arrow) (i, o, w, y). Accumulation of collagen fibers in the nucleus pulposis (arrow) next to clusters of chondrocytes (arrows) (d, g, t, v). Designation: fibrous ring (FR), nucleus pulposis (NP). Hematoxylin and eosin.

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Table

Quantitative assessment of degenerative changes in intervertebral discs (in points) (according to A. Lai et al. [15])

Category	Model 1			Model 2		
	cranial	damaged	caudal	cranial	damaged	caudal
Nucleus pulposus						
Form	1.0 ± 0.6	—	1.4 ± 0.5	1.0 ± 0.0	—	0.7 ± 0.6
Area	0.7 ± 0.5	—	1.6 ± 0.5	0.3 ± 0.6	—	0.7 ± 0.6
Number of cells	1.0 ± 0.8	—	1.2 ± 0.8	1.0 ± 1.0	—	1.0 ± 1.0
Cell morphology	1.1 ± 0.7	—	1.2 ± 0.8	1.0 ± 1.0	—	1.0 ± 1.0
NP sum	3.9 ± 2.2	—	5.4 ± 2.1 p1 = 1.000	3.3 ± 2.5 p3 = 0.833	—	3.3 ± 2.5 p1 = 1.000 p3 = 0.250
NP – AF margin	1.6 ± 0.5	—	1.6 ± 0.9	0.7 ± 0.6	—	1.0 ± 1.0
Fibrous ring						
Lamellar structure	0.3 ± 0.5	2.0 ± 0.0	0.5 ± 0.5	0.0 ± 0.0	1.5 ± 1.0	0.0 ± 0.0
Cracks/ruptures	0.7 ± 0.5	1.7 ± 0.5	0.5 ± 0.5	0.3 ± 0.6	1.8 ± 0.5	0.3 ± 0.6
FR sum	1.0 ± 0.8	3.7 ± 0.5 p1 = 0.016 p2 = 0.026	1.0 ± 1.1 p1 = 0.564	0.3 ± 0.6 p3 = 0.267	3.3 ± 1.5 p1 = 0.157 p2 = 0.157 p3 = 1.000	0.3 ± 0.6 p1 = 1.000 p3 = 0.548
Endplate	0.3 ± 0.5	2.0 ± 0.0	0.5 ± 0.5	1.0 ± 0.0	2.0 ± 0.0	0.3 ± 0.6
Sum	6.7 ± 1.6	5.7 ± 0.5	7.3 ± 2.9 p1 = 1.000	5.3 ± 3.5 p3 = 0.517	5.3 ± 1.5 p3 = 1.000	5.0 ± 3.0 p1 = 0.655 p3 = 0.381

Notes: p1 — comparison with the corresponding indicator of the L_{IV}–L_V disc; p2 — comparison with the corresponding indicator of the L_{VI}–S_I disc; p3 — comparison with the corresponding indicators of Model 1. NP — nucleus pulposus, FR — fibrous ring.

bodies, as well as foci of newly formed spongy bone tissue (Fig. 5, b). The spinal nerves at this level were surrounded by an epineurium consisting of dense connective tissue with fibroblasts between the fibers (Fig. 3, c). In the nerves, similar degenerative changes in axons were detected, as in the case of ligation with a thread: amorphous decay products were found between the fibers, fragmentation of fibers, Schwann cells were rare (Fig. 3, c, d).

Caudal segment. In the fibrous ring, collagen fibers in 80 % of cases retained normal structural organization, only in one rat (20 %) signs of disorganization were detected. The cellular composition also corresponded to the norm and consisted of fibrochondrocytes and chondrocytes. The cell density was mainly average. In 40% of animals, interfibrous gaps were recorded between the plates of the fibrous ring, and in the others, the plates were intact (Fig. 2, y).

In the nucleus pulposis, the matrix was heterogeneously stained in 40 % of the individuals, with notochordal cells and chondrocytes in them, and with chondrocytes in the remaining rats with heterogeneously stained matrix. Signs of degeneration in the form of accumulation of collagen fibers were found in 40 % of cases (Fig. 2, v).

The endplates were intact in 80 % of the animals, with calcified only in one (20 %). In all rats, vascular sprouting was not recorded.

Signs of inflammation were also not detected in any case.

According to the assessment of degenerative changes in rats of Model 2, no significant difference was recorded between the cranial and caudal intervertebral discs, both in general assessment and separately for the annulus fibrosus and the nucleus pulposus (Table). The obtained values were equal to ≈ 5 points. When comparing the values of the annulus fibrosus of the damaged disc with the corresponding values for the cranial and caudal discs, no difference was also found. No difference was found between the models for all discs in the case of a quantitative assessment in the points.

Discussion

As a result of the study, we developed two models of degenerative diseases of the spine with compression of the spinal nerves and destruction of the nucleus pulposus: 1) without fixation of this spinal segment and with ligation of the spinal nerve in the LS with a thread; 2) with fixation of this spinal

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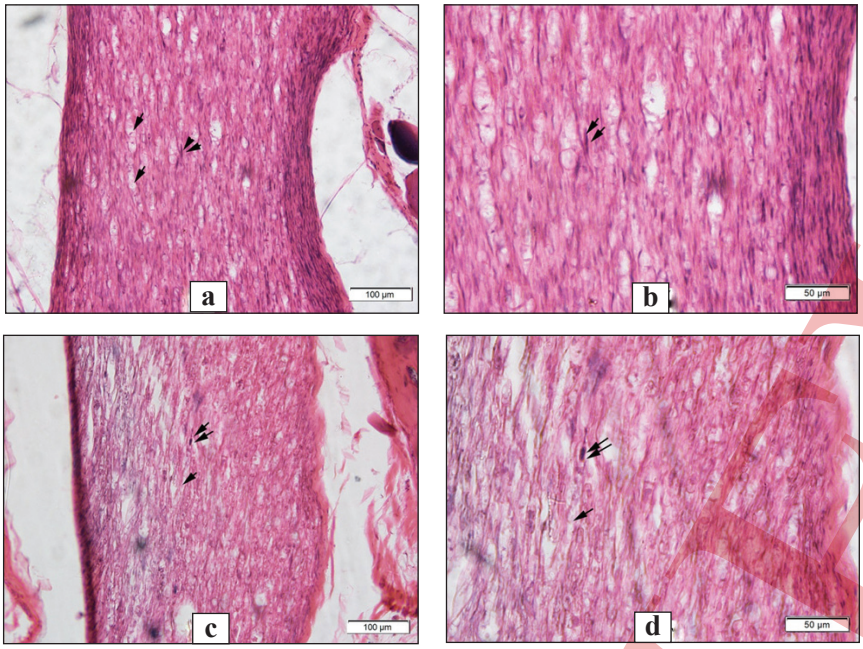

Fig. 3. Spinal nerve distal to nerve root clamp or nerve trunk ligation in rats in Models 1 (a, b) and 2 (c, d). Degenerative changes in axons (arrow) and single Schwann cells (arrows). Hematoxylin and eosin

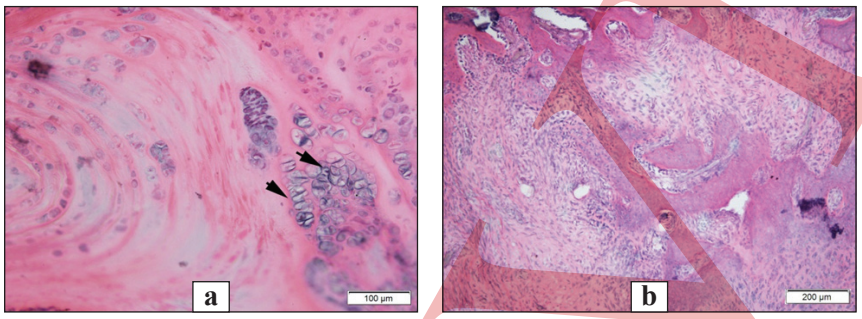

Fig. 4. Structural features of tissue formation in the area of destroyed nucleus pulposus in rats in Model 2. Replacement of the nucleus pulposus with cartilage tissue with hypertrophied chondrocytes (a) or connective tissue with bone formation (b). Hematoxylin and eosin

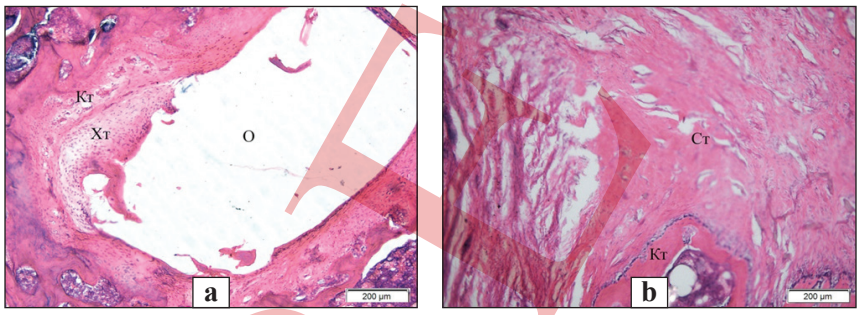

Fig. 5. Fragment of the vertebral body of a rat spinal segment with a destroyed nucleus pulposus in Model 2. Hole (H) from the end of the fixing bracket around which connective tissue (Ct), cartilage tissue (Cart) and bone tissue (Bt) have formed (a). Connective tissue is formed from the outside of the vertebral body and newly formed spongy bone tissue (b). Hematoxylin and eosin

segment with two clamps that pressed on the roots of the corresponding spinal nerves. Reconstruction of intervertebral disc degeneration in animals is often performed by destroying the nucleus pulposis, in particular by puncturing it [8, 16]. In Model 1, we reproduced intervertebral disc degeneration and neuropathy in patients with degenerative spinal diseases before performing decompression-stabilization interventions to analyze how this affects the adjacent segments. Their condition is known to be one of the factors that affect the success of subsequent decompression-stabilization interventions and spinal fusion [17, 18]. In Model 2, we attempted to reproduce the complications caused by spinal nerve root compression due to misplacement of transpedicular screws during decompression-stabilization procedures at the L_{IV}–L_V level or more distally, resulting in neuropathic pain in patients [1, 2, 19]. During nerve compression/ligation, we monitored the animals' limb responses to confirm the accuracy of the procedure. In the models of intervertebral disc degeneration with nerve compression that we developed and reproduced in rats, we found the development of degenerative changes in the discs of adjacent segments in

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both quantitative and qualitative assessments. However, we did not find any differences in the degeneration score [15] between the models for all the intervertebral discs studied. However, structural changes differed between the models in the nucleus pulposus of the intervertebral disc of the spinal segment caudal to the level of injury. Thus, Model 1 showed more pronounced replacement of notochordal cells by chondrocytes, cell death, accumulation of collagen fibers in the matrix, and formation of cracks than Model 2. In a similar study in mice, instability was caused by resection of the posterior elements of the spinal segment of the LS, resulting in degeneration of the nucleus pulposus at the level of the injury, but the adjacent segments were not evaluated [20]. J. Sun et al. in rabbits that underwent spinal fusion recorded degenerative changes in the nucleus pulposus in the adjacent segments [21]. The changes we found may also be due to the fact that disc puncture in rats causes an increase in interleukins in the adjacent discs in the first 14 days after injury, which indicates inflammation [11].

Degenerative changes in adjacent intervertebral discs may also be due to impaired muscle innervation resulting from ligation of the nerve plexus or compression of the spinal nerve roots. Another factor may be dysfunction in the spinal nerve roots, which occurs due to increased interleukin levels in the surrounding tissues due to inflammation in the damaged disc [22]. This negatively affects peripheral nerve function in the LS of the rats. Thus, neuropathy may cause skeletal muscle myopathy in animals [23]. We have previously shown that the development of degenerative changes in the intervertebral discs of rats is associated with atrophic changes in the muscles in the LS paravertebral muscle ischemia model [10]. Thus, a difference was found between the models at the level of the damaged intervertebral disc. In animals from Model 1, where the spinal segment with a damaged intervertebral disc was not stabilized with staples, degenerative changes in the annulus fibrosus of the injured disc, as assessed by the score [15], were greater than in both adjacent discs, which was not found in Model 2. This may indicate the effect of instability on the damaged disc. A. J Michalek et al. [7] showed a 20 % decrease in disc stiffness under different loading conditions (compression and torsion) in a rat model of a punctured intervertebral disc, which may indicate a decrease in its ability to withstand loads. Loss of strength after puncture of the nucleus pulposus has also been found in a cadaveric intervertebral disc during axial loading [24]. Also, in rats of Model 1, in which the replacement of the nucleus pulposus with cartilage tissue was detected, large cracks were detected, which was not the case in Model 2. In our opinion, this may also be due to the presence of instability in Model 1 compared to Model 2. S. Liu et al. [25] also recorded the formation of cracks in the nucleus pulposus in a model of instability of the lumbar spinal segment in mice.

Peripheral nerve injury by compression with a ligature or ligation with a thread is quite common when studying nerve degeneration/regeneration in animal models [26]. A feature of spinal nerve roots is a thinner epinervium and a lower content of collagen fibers compared to peripheral nerves, so the above actions cause more damage [27]. It is known that peripheral nerve compression leads to edema, which causes axonal damage due to increased endoneurial fluid pressure [26, 27]. When peripheral nerves are ligated in rats, the distal parts of the nerve undergo Wallerian degeneration [27], which we observed in both models. We did not detect signs of inflammation or increased macrophage numbers after 8 weeks of modeling, which is likely due to a significant decrease in these manifestations 2 weeks after mechanical nerve injury in rodents [28].

Conclusions

Spinal nerve compression and damage to the nucleus pulposus of the lumbar intervertebral disc in rats leads to degenerative changes in the adjacent discs — cranial and caudal.

The developed rat models can be used to study methods for treating disc degeneration in patients with neurological complications after decompression-stabilizing spinal surgery.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. Search for new methods for treating neurological complications after decompression-stabilizing spinal surgery using the developed models.

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Authors' contribution. Barkov O. O. — concept and design, data analysis, writing a draft of the article, approval of the final version of the article; Nikolchenko O. O. — experimental modeling in rats, approval of the final version of the article; Samoilova K. M. — experimental modeling in rats, approval of the final version of the article; Maltseva V. E. — histological analysis, data analysis, writing a draft of the article, approval of the final version of the article; Danyshchuk Z. M. — histological analysis, approval of the final version of the article.

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HISTOLOGICAL CHANGES IN ADJACENT INTERVERTEBRAL DISCS IN A RAT MODEL OF NUCLEUS PULPOSUS INJURY AND SPINAL NERVE COMPRESSION

O. O. Barkov, V. Ye. Maltseva, O. A. Nikolchenko, Z. M. Danyshchuk, K. M. Samoylova

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

✉ Oleksandr Barkov, MD, PhD in Traumatology and Orthopaedics: a.barkov.79@gmail.com; https://orcid.org/0000-0003-2161-416X
✉ Valentyna Maltseva, Phd in Biol. Sci.: maltseva.val.evg@gmail.com; https://orcid.org/0000-0002-9184-0536
✉ Olga Nikolchenko, PhD in Biol. Sci.: o_nicolchenko@ukr.net; https://orcid.org/0000-0001-9808-9485
✉ Zinayda Danyshchuk, MD: zinada1962@gmail.com; https://orcid.org/0000-0003-2968-3821
✉ Kateryna Samoylova: samoylova_e@ukr.net; https://orcid.org/0000-0003-1806-3467

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The effect of body position on hemodynamic parameters and bispectral index

K. I. Lyzohub

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

Surgical interventions routinely have a significant impact on haemodynamic parameters due to a combination of factors: stress, anaesthetics, specific surgical procedures and perioperative position. Monitoring the bispectral index (BIS) helps to adjust anaesthesia to maintain stable haemodynamic status, minimise consciousness and potentially reduce recovery time. Objective. To assess the effect of body position on haemodynamic parameters and bispectral index during upper limb surgery under general anaesthesia with propofol solution. Methods. A prospective randomised study involved 70 patients divided into two groups: I (n = 35) — operated on in a semi-sitting position (SSP); II (n = 35) — anaesthetised in a standard supine position. The average age of patients in group I was (43.06 ± 11.92), in group II — (40.25 ± 10.14) years. General anaesthesia was maintained with a 1% propofol solution depending on BIS monitoring indicators. To control the depth of sedation and adjust the propofol infusion, BIS monitoring COVIDEN was used. Results. Patients were comparable in terms of age, duration of surgery, and blood loss. When comparing haemodynamic values, the following changes were observed: a statistical difference in SBP (p < 0.001), DBP (p < 0.001), SAT (p < 0.001), slight tachycardia was observed compared to group II, but within the reference values (79.22 ± 9.76) beats per minute and (71.34 ± 7.77) beats per minute, respectively (p < 0.001). Reliable statistical values were obtained when calculating the dosage of 1% propofol solution; in group I, the average value was (4.87 ± 0.24) mg/kg/hour, while in group II it was (6.16 ± 0.49) mg/kg/hour (p < 0.001). Episodes of nausea and vomiting were observed in 12 patients in group I and in 5 patients in group II. The average time to spontaneous breathing recovery was longer in group I (p < 0.001), but no significant difference was found in the average time to extubation (p = 0.55). Conclusions. Anaesthesia monitoring using BIS allows to reduce the recovery time after awakening by reducing the total doses of anaesthetics administered. The infusion of anaesthetics depends not only on haemodynamic parameters but also on the perioperative body position.

Оперативні втручання зазвичай викликають значний вплив на гемодинамічні показники через поєднання таких чинників: стрес, анестетичні засоби, специфічні хірургічні процедури та періопераційне положення. Моніторинг біспектрактрального індексу (BIS) допомагає скоригувати анестезію для підтримки стабільного гемодинамічного статусу, мінімізації свідомості та потенційного скорочення часу відновлення. Мета. Оцінити вплив положення тіла на показники гемодинаміки та біспектрального індексу під час операції на верхніх кінцівках під загальною анестезією зі застосуванням розчину пропофолу. Методи. До проспективного рандомізованного дослідження залучено 70 хворих, розподілених на 2 групи: I (n = 35) — оперовані в напівсидячому положенні (НСП); II (n = 35) — анестезовані в стандартному положенні на спині. Середній вік хворих у I групі складав (43,06 ± 11,92), в II — (40,25 ± 10,14) років. Загальна анестезія підтримувалась розчином пропофолу 1 % залежно від показників BIS-моніторингу. Для контролю глибини седації та корекції інфузії пропофолу використовували BIS-мониторінг COVIDEN. Результати. Пацієнти були співставні за віком, тривалістю операції та крововтратою. Під час порівняння значень гемодинаміки виявлені такі зміни: статистична різниця в показниках СіАТ (p < 0,001), ДіАТ (p < 0,001), САТ (p < 0,001), спостерігається незначна тахікардія, порівняно з групою II, але в межах референтних значень (79,22 ± 9,76) уд. за хв та (71,34 ± 7,77) уд. за хв відповідно (p < 0,001). Достовірні статистичні значення отримано під час розрахунку дозування розчину пропофолу 1 %, в I групі середній показник складав (4,87 ± 0,24) мг/кг/год, тоді як в II — (6,16 ± 0,49) мг/кг/год (p < 0,001). Епізоди нудоти та блювання спостерігались у 12 хворих в I групі пацієнтів, та у 5 II групи. Середній час відновлення спонтанного дихання в I групі довший (p < 0,001), не було виявлено достовірної різниці в середньому часі екстубації (p = 0,55). Висновки. Моніторинг анестезії за допомогою BIS дозволяє скоротити час відновлення після пробудження, за рахунок зменшення введення загальних доз анестетиків. Їх інфузія залежить не лише від показників гемодинаміки, але і від періопераційного положення тіла. Ключові слова. Загальна анестезія, напівсидяче положення, гемодинаміка, BIS-моніторинг.

Keywords. General anaesthesia, BCP, haemodynamics, BIS monitoring

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Introduction

Upper extremity surgery is performed in two main perioperative positions: semi-recumbent (SRP) and standard supine. Upper extremity surgery under general anesthesia requires controlled hypotension (to minimize blood loss and optimize the operating field). However, prolonged hypotension can lead to the development of neurological complications such as stroke, cerebral ischemia, and transient visual loss [1], as blood pressure is a target factor that affects organ perfusion. Hypoperfusion and organ dysfunction are correlated with each other depending on their severity, through the development of hypotension. Intraoperative hypotension is known to be associated with an increased risk of postoperative mortality [2], myocardial ischemia after noncardiac procedures [3], and acute renal failure [4]. SRP of the unanesthetized patient activates the sympathetic nervous system and thereby increases peripheral vascular resistance, which leads to a further increase in blood pressure. However, anesthetics inhibit the baroreceptor response, which is necessary to correct the effect of gravity on cerebral perfusion pressure, therefore, the main changes in hemodynamics occur precisely during the change in the position of the anesthetized patient [1]. One of the most widely used general anesthetics is propofol solution, which has a proven safety record of over 30 years [5]. Most inhalation anesthetics can cause peripheral vasodilation, but its mechanisms are different. Propofol acts by suppressing sympathetic tone, and not directly on the smooth muscles of peripheral vessels [6], therefore, the use of its solution contributes to better visualization of the surgical wound. The occurrence of a vasoplegic effect depends on the dosage, therefore, control of the depth of anesthesia is a critically important aspect of ensuring patient safety during surgical interventions. Traditional monitoring of depth of anesthesia is primarily determined by the patient's clinical signs and symptoms, such as changes in heart rate, blood pressure, and limb movements [7]. The bispectral index (BIS) represents a significant breakthrough in objectively assessing depth of anesthesia, providing valuable real-time feedback [8]. One important application of BIS monitoring is its role in preventing perioperative awakening, a psychologically traumatic event that is exacerbated by the patient's return to consciousness during surgery. In a systematic review, S. R. Lewis et al. found evidence that BIS-controlled anesthesia may reduce the risk of intraoperative awareness compared with standard practice without such monitoring [9]. The monitor processes real-time electroencephalogram data and calculates a numerical score (from 0 to 100) that reflects the degree of brain function suppression. Today, BIS monitoring is used to study the state of the central nervous system, the pharmacodynamic effect of anesthetics [10] and is the standard for monitoring intraoperative sleep levels.

Control of arterial hypotension is crucial during surgery. Hypotension is exacerbated by the use of anesthetics, perioperative body position, and blood loss.

Purpose: to analyze the influence of body position on hemodynamics and bispectral index indicators during surgical intervention on the upper extremities under general anesthesia with the use of propofol solution.

Material and methods

The study was performed at the State Institution "Professor M.I. Sytenko Institute of Spine and Joint Pathology of the NAMS of Ukraine". The study was approved by the local bioethics committee (Protocol No. 231 dated 05.20.2023) of the relevant institution in accordance with the ICH GCP amendment, the Helsinki Declaration of Human Rights and Biomedicine, as well as the current legislation of Ukraine. All involved patients were familiarized with the plan and conditions of the experiment and signed an informed consent.

The prospective randomized study included 70 patients, who were evenly distributed into 2 groups: I (n = 35) — surgical intervention was performed in the SRP; II (n = 35) — anesthetized patients in the standard supine position. The average age of patients in group I was (43.06 ± 11.92), in group II (40.25 ± 10.14) years. Patients with cardiac arrhythmias, angina pectoris, respiratory or hepatic failure, and a history of drug addiction were excluded from the analysis. Considering that BIS is a single number calculated on the basis of subparameters obtained from the electroencephalogram, several factors can change its value without affecting the depth of anesthesia (hypoglycemia, hypovolemia, cerebral ischemia) [11]; therefore, individuals with a history of traumatic brain injury and diabetes mellitus were also excluded. The physical status of the patient in the preoperative period was assessed according to the ASA (American Society of Anesthesiologists) scale, all of whom were classified as class I–II. The initial positioning of the patients in the two groups was in the standard position — lying on their backs. The day before, both groups were prescribed pregabalin 75 mg. Before induction, they received pantoprazole 40 mg, sibazone solution 10 mg. Induction

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included: propofol solution 1 % — 2 mg/kg, fentanyl solution 0.005 % — 0.2 mg, myoplegia during tracheal intubation was provided with suxamethonium solution 0.1 mg/kg, and subsequently myorelaxation was maintained with atracurium besylate solution at a dosage of 0.3 mg/kg. After airway prosthesis and transfer of the patient to artificial lung ventilation with the Drager Atlan A300 device, general anesthesia was maintained with propofol solution 1 % depending on BIS-monitoring indicators. 10 min after induction, patients in group I were transferred to the NSP, patients in group II remained in the supine position. Peripheral blood saturation (SpO_2), non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) were determined by the Mediana YM 6000 monitor. The first measurement was performed immediately after venous access was established and then every 5 min. COVIDEN BIS monitoring was used to control the depth of sedation and correct the propofol infusion; the patient's depth of sedation should be from 40 to 60, an index below 40 corresponds to deep anesthesia, and BIS has a processing delay of 5–10 s [12]. The difference between the predicted and actual BIS was on average (30.09 ± 18.73) s. Given that CO_2 is a vasodilator and low levels are thought to cause cerebral vasoconstriction [13], affect neuroethology, structural histology, neuronal apoptosis, and cerebral edema [14], end-tidal carbon dioxide levels were measured continuously in both groups and were 35–45 mm Hg. The Aldrete system was used to assess the safety of transferring patients from the intensive care unit to the ward.

In the postoperative period, the presence of nausea and vomiting, the time of extubation and the restoration of spontaneous breathing were analyzed, the quality of which was assessed using the Quality of recovery 15 (QoR 15) scale 24 hours after the intervention.

Statistical analysis. The obtained data were analyzed using the IBM SPSS 9.0 software. The normal distribution of the samples was checked using the Kolmogorov-Smirnov test. The mean and standard deviation were calculated. Differences between groups of indicators were assessed using the Student's t-test.

Results

Analysis of primary indicators before perioperative change in body position. Patients in the two groups were comparable in age, duration of surgery and blood loss. The initial data are shown in Table. 1.

When studying the changes in hemodynamic parameters such as: SBP, DBP, pulse and BIS-monitoring values before induction, no significant difference was found, the initial data are shown in Table 2.

When analyzing the two groups after induction, no difference was found between them, a uniform decrease in SBP, DBP and BIS parameters was observed. Hemodynamic and BIS-monitoring data are presented in Table 3.

Analysis of hemodynamic and BIS-monitoring parameters after positioning. When comparing hemodynamic data after positioning patients

Table 1

Comparison of patient age, duration of surgery, and blood loss

Group	Age (years)	Blood loss (ml)	Duration (min)
I	43.06 ± 11.92	232.85 ± 51.71	112.97 ± 21.47
II	40.25 ± 10.14	226.34 ± 84.04	118.86 ± 20.53

Table 2

Comparison of initial hemodynamic parameters

Group	SBP (mm Hg)	DBP (mm Hg)	Pulse (beats per minute)	BIS
I	148.68 ± 24.30	88.8 ± 11.80	77.94 ± 11.80	97.08 ± 1.42
II	148.11 ± 15.71	93.6 ± 7.49	75.57 ± 11.00	95.78 ± 1.56

Table 3

Comparison of hemodynamic and BIS parameters after induction

Group	SBP (mm Hg)	DBP (mm Hg)	Pulse (beats per minute)	BIS
I	114.28 ± 11.00	73.6 ± 11.00	72.62 ± 11.06	47.05 ± 3.94
II	116.74 ± 11.15	76.08 ± 10.26	71.22 ± 10.30	45.2 ± 4.98

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in the SRP and in the supine position, the following changes were found: the average SBP values were (98.28 ± 5.95) mm Hg, while in group II (105.74 ± 7.97) ($p < 0.001$), a significant decrease in DBP in group I — (63.37 ± 4.49) mm Hg ($p < 0.001$), SBP in group I was (75 ± 4.97) mm Hg, while in group II — (81 ± 5.67) mm Hg. There was a significant difference in pulse rates and slight tachycardia, compared with group II, but within the reference values (79.22 ± 9.76) beats per min and 71.34 ± 7.77, respectively ($p < 0.001$). No significant statistical changes were recorded in BIS values, namely in group I the average value was 46.37 ± 4.44, while in group II it was 45.54 ± 4.09 ($p = 0.42$). Significant statistical indicators were obtained when calculating the dosage of propofol solution, in group I the average values were (4.87 ± 0.24) mg/kg/h, while in group II (6.16 ± 0.49) mg/kg/h ($p < 0.001$). Changes in the obtained data are presented in Table 4.

Detection of complications after anesthesia. Episodes of nausea and vomiting were observed in 12 patients in group I and 5 in group II. The average time to restore spontaneous breathing in group I was (11.64 ± 3.82) min, while in group II it was 7.60 ± 2.36 ($p < 0.001$), the average time to extubation in group I was (16.61 ± 5.29) min, and in group II (16.05 ± 3.91) min, no significant difference was found between the groups ($p = 0.55$) (Table 5).

Diagnosis of the safety of transferring a patient from the intensive care unit to the department was performed using the Aldrete assessment system. The quality of recovery after surgery and anesthesia was assessed using the QoR 15 scale. The average value according to Aldrete and QoR 15 in group I was 9.25 ± 0.60 and 140.08 ± 6.17, respectively, in group II the average value according to Aldrete was 9.57 ± 0.60, while QoR 15 was (141.22 ± 8.35) points, no significant difference between the groups was found ($p > 0.001$) (Table 6).

Discussion

The study assessed the change in the dosage of propofol solution depending on the perioperative body position under the control of BIS monitoring during surgical interventions on the upper extremities. The results showed that in the SRP the dosage of propofol solution is significantly less than in the standard position, with the same hemodynamic effects and BIS indicators in the two groups.

Considering that controlled hypotension is the most effective method of stopping bleeding and achieving clear visibility of the surgical field [15],

Table 4

Comparison of changes in SBP, DBP, SAT, pulse, BIS and propofol solution dosage between groups after positioning

Group	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	Pulse (beats per minute)	BIS	Dose of 1% propofol solution (mg/kg/h)
I	98.28 ± 5.95 *	63.37 ± 4.49 **	75 ± 4.97***	79.22 ± 9.76 °	46.37 ± 4.44 °°	4.87 ± 0.24 •
II	105.74 ± 7.97	69.2 ± 5.57	81 ± 5.67	71.34 ± 7.77	45.54 ± 4.09	6.16 ± 0.49

Notes: difference between groups I and II: * $p < 0.001$ — SBP; ** $p < 0.001$ — DBP; *** $p < 0.001$ — MBP; ° $p < 0.001$ — pulse; °° $p = 0.42$ — BIS indicators; • $p < 0.001$ — difference in the dosage of propofol solution between the groups.

Table 5

Complications in the postoperative period

Group	Nausea and vomiting (number of patients)	Time to return to spontaneous breathing (min)	Extubation time
I	12	11.64 ± 3.82 *	16.61 ± 5.29 **
II	5	7.60 ± 2.36	16.05 ± 3.91

Notes: * $p < 0.001$ — difference in time to restore spontaneous breathing; ** $p = 0.55$ — difference in time to extubation.

Table 6

Average score for assessing the safety of transferring a patient from the intensive care unit and the quality of recovery after surgery

Group	Aldrete Scale	QoR 15
I	9.25 ± 0.60 *	140.08 ± 6.17 **
II	9.57 ± 0.60	141.22 ± 8.35

Notes: * $p > 0.001$ — difference in Aldrete scale scores; ** $p > 0.001$ — difference in QoR 15 scores.

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the pressure was maintained in both groups without statistical difference. The study performed by W. Yin et al. with the participation of 130 patients showed that in the case of using standard doses of propofol solution during shoulder arthroscopy, the time to restore spontaneous breathing was prolonged, but no difference was found in episodes of vomiting and nausea [16]. Another study took into account such disadvantages of propofol solution as the development of postoperative nausea and vomiting, although perioperative sedation with this solution does not affect this duration [17]. The time to recovery of spontaneous breathing was longer in the SRP group compared to patients in the standard position, and episodes of nausea and vomiting were observed in 4.2 % of cases.

One of the problems of anesthesia in the case of shoulder arthroscopy is the need for controlled hypotension to reduce intra-articular hemorrhage and thus provide adequate visualization for the surgeon.

T. Tantry et al. compared the efficacy and convenience of target-controlled infusion (TCI) of propofol and the inhaled agent sevoflurane in patients undergoing shoulder arthroscopy. Of the 34 patients, 17 received TCI propofol (target plasma concentration 3 μg/mL) and the same amount of sevoflurane (1.2–1.5 of the minimum alveolar concentration). Propofol TCI helped to achieve lower systolic and mean blood pressure, and the number of interventions required was also lower compared with the sevoflurane group [18].

T. M. Chokshi showed that the propofol group had better visualization of the surgical field. The target plasma concentration used was 3 μg/mL, which corresponds to a dosage of 8 mg/kg/h [19].

In a study by T. Sugiura on elbow surgery, balanced anesthesia was used, consisting of general anesthesia combined with brachial plexus block in the perioperative period under the control of electrocardiography, noninvasive blood pressure, SpO_2, end-tidal CO_2 tension and bispectral index. Propofol infusion was used with a target control infusion of 2 μg × ml^{-1} plasma concentration, corresponding to 6 mg/kg/h [20], and no hemodynamic instability was observed.

In the observation of N. Padhi et al., 9 episodes of hypotension were observed with propofol and no development of bradycardia, because hypotension can lead to increased use of vasoactive drugs and fluids that might otherwise be unnecessary [21].

S. A. Yildirim et al. noted that the development of arterial hypotension occurs due to dilation of veins or arteries, a decrease in cardiac output and systemic vascular resistance, and the manifestation of bradycardia, which is regulated by the antisympathetic effect of propofol [22].

However, M. Matsushima et al. showed that the decrease in heart rate caused by propofol cannot be completely explained by the effect of the central vagus nerve, i. e. this agent may also have a direct inhibitory effect on the sinoatrial node [23].

Conclusions

Monitoring anesthesia with BIS enables a reduction in recovery time following awakening, primarily due to the lower volume of general anesthetics administered and a potential decrease in side effects.

Infusion of anesthetics depends not only on hemodynamic parameters, but also on the perioperative body position. Positioning in a semi-sitting position under general anesthesia significantly prolongs the time of spontaneous breathing recovery, but at a dosage of 4.5 mg/kg/h does not affect the extubation time. SRP does not affect the duration of stay in the recovery room.

Conflict of interest. The author declares the absence of a conflict of interest.

Prospects for further research. This research facilitates enhanced perioperative monitoring and enables more efficient optimisation of patient recovery room stay durations.

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Authors' contribution. Lyzogub K. I. — development of the study concept, analysis of the findings, drafting and editing the article for publication.

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THE EFFECT OF BODY POSITION ON HEMODYNAMIC PARAMETERS AND BISPECTRAL INDEX

K. I. Lyzohub

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

✉ Kseniia Lyzohub, MD, PhD: kslizogub@gmail.com; https://orcid.org/0000-0001-9149-7208

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Evaluation of the efficacy of kinematic and mechanical alignment in primary total knee arthroplasty during the early postoperative period

M. D. Moroz [1], R. A. Kozak [1], O. A. Kostogryz [1], V. I. Bondar [2]

[1] SI «Institute of Traumatology and Orthopedics of the NAMS of Ukraine», Kyiv
[2] Diagnostic Center «M24», Kyiv. Ukraine

Mechanical alignment is widely accepted as a standard technique for total knee arthroplasty (TKA). However, approximately 20 % of patients remain dissatisfied with the outcomes. Recent studies suggest that an alternative method, known as kinematic alignment, could potentially improve functional outcomes and provide more rapid pain relief during the early postoperative period. Objective. To compare early postoperative clinical and functional outcomes of primary total knee arthroplasty performed using either kinematic or mechanical alignment. Methods. We prospectively analyzed the outcomes of 100 patients undergoing primary TKA, with 50 patients receiving mechanical alignment and 50 receiving kinematic alignment. Clinical assessments included pain measurement using the VAS, functional evaluation using the WOMAC, and knee range of motion (ROM). Assessments were conducted preoperatively, at 14 days, and 1.5 months postoperatively. Results. Analysis of key surgical parameters — including operation duration, intraoperative blood loss, and length of hospital stay — revealed no significant differences between the two groups. However, the requirement for additional ligament releases was significantly higher in the mechanical alignment group. According to WOMAC scores, the kinematic alignment group showed consistently better outcomes at all follow-up stages. At postoperative day 14, the kinematic alignment group had significantly better VAS pain scores and greater knee ROM compared to the mechanical alignment group ($p < 0.05$). However, by 1.5 months after surgery, the differences between the two groups were no longer statistically significant ($p > 0.05$). Conclusions. Kinematic alignment leads to superior early pain relief and faster functional recovery in the initial postoperative period compared to mechanical alignment. Nevertheless, differences in pain and function between both groups diminish by 1.5 months after surgery. These findings suggest the need for further studies with a longer follow-up (at least one year) to evaluate long-term outcomes and potential complications.

Ендопротезування колінного суглоба з використанням механічного вирівнювання є загальноприйнятим стандартом, проте близько 20 % пацієнтів залишаються незадоволеними отриманими результатами. Мета. Порівняти ранні післяопераційні клінічні та функціональні результати первинного ендопротезування колінного суглоба, виконаного кінематичним і механічним способами вирівнювання. Методи. Проспективно проаналізовано результати лікування 100 пацієнтів, яким здійснене ендопротезування за механічним (n = 50) та кінематичним (n = 50) вирівнюванням. Аналізували біль (VAS), суб'єктивне оцінювання функції (WOMAC) і амплітуду рухів (ROM) у колінному суглобі перед операцією, на 14-й день та через 1,5 місяці після оперативного втручання. Результати. Аналіз основних хірургічних параметрів, таких як час операції, обсяг інтраопераційної крововтрати й тривалість госпіталізації, не показав суттєвої різниці між групами. Водночас потреба у виконанні додаткових релізів зв'язкового апарата була істотно вищою в групі механічного вирівнювання. За опитувальником WOMAC, кінематичне вирівнювання мало перевагу на всіх етапах спостереження. На 14-ту добу після втручання група кінематичного вирівнювання продемонструвала кращі показники за VAS, інтенсивності амплітуди рухів у колінному суглобі, ніж група механічного ($p < 0,05$). Проте через 1,5 місяці після операції відмінності між групами за цими параметрами вже не були статистично значущими ($p > 0,05$). Висновки. Кінематичне вирівнювання сприяє більш вираженому зниженню болю та швидшому відновленню функції колінного суглоба в ранньому післяопераційному періоді. Проте через 1,5 місяці після операції показники функціонального стану та інтенсивності болю в обох групах вирівнюються. Це вказує на доцільність проведення додаткових досліджень із тривалішим спостереженням для визначення довгострокових результатів і потенційних ускладнень. Ключові слова. Кінематичне вирівнювання, механічне вирівнювання, ендопротезування колінного суглоба, колінний суглоб.

Keywords. Kinematic alignment, mechanical alignment, total knee arthroplasty, knee joint

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Introduction

Osteoarthritis is one of the most common conditions of the knee joint, resulting in degeneration of articular cartilage and significantly reducing the quality of life. According to WHO estimates, this disorder is among the ten most disabling diseases in developed countries, affecting approximately 528 million people worldwide. More than a million knee replacement surgeries are performed annually, making it one of the most effective surgical procedures, significantly reducing pain and improving joint functionality in patients with severe forms of arthritis. In Europe, the leaders in the frequency of such interventions are Switzerland, Germany and Finland (287, 284 and 255 surgeries per 100,000 population, respectively) [1].

Although knee arthroplasty using mechanical alignment is effective and widely used as a standard approach for the treatment of patients with osteoarthritis, about 20 % of patients remain dissatisfied with the results of the intervention. In the postoperative period, patients most often present with persistent pain, limited range of motion of the operated joint, and inconsistency of the actual results with previous expectations [2, 3]. According to the literature, the main reason for dissatisfaction is the significant individual variability of the anatomical structure, which complicates the accurate positioning of the endoprosthesis components. Failure to take into account these anatomical parameters leads to uneven load distribution and disruption of the natural biomechanics of movement in the knee joint, which ultimately causes the above-mentioned symptoms [4, 5]. Mechanical alignment remains the generally accepted method in total knee arthroplasty. At the same time, the results of recent studies indicate a number of advantages of the kinematic approach [8]. According to modern meta-analyses, kinematic alignment provides a more physiological distribution of the load on the medial and lateral parts of the joint, which is accompanied by less pain intensity and better restoration of the amplitude of movements in the early postoperative period [6, 7, 9].

Despite the presence of numerous studies with convincing results in favor of kinematic alignment, the final decision on the optimal technique for positioning the endoprosthesis components remains a subject of debate.

Objective: to conduct a comparative analysis of the results of primary knee arthroplasty in patients with osteoarthritis of the III–IV degrees using kinematic and mechanical alignment methods, with a special emphasis on reducing the intensity of the pain syndrome, improving joint function and recovery rates in the early postoperative period.

Material and methods

The study was conducted at the Department of Traumatology and Orthopedics of the State Institution “Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine” from January 2022 to October 2024.

The study included 100 patients aged 40 to 65 years who underwent knee arthroplasty for deforming arthrosis of stages III–IV according to the Kellgren & Lawrence classification. All patients underwent a comprehensive preoperative examination and postoperative control within 2 months from the moment of surgery.

The study did not include patients with post-traumatic arthrosis, septic arthritis, and knee instability resulting from damage to the capsular ligament apparatus. Patients with arthrosis accompanied by significant defects in the bone tissue of the femoral condyles and/or tibial plateau were excluded, as well as individuals with varus or valgus deformities of the knee joint greater than 15° or those with pronounced contractures of the operated joint exceeding 30°.

The criteria for intergroup distribution were the methods of alignment of the knee joint endoprosthesis components used during primary endoprosthetic repair. The first group (n = 50) underwent surgery using the mechanical alignment technique, while patients in the second group (n = 50) used non-restrictive kinematic alignment. The mean age of the patients in the first group was (51.52 ± 4.92) years (range: 42–63), in the second group — (51.78 ± 4.99) years (range: 41–62). In both groups, a uniform distribution by gender was ensured (25 women and 25 men).

The preoperative planning protocol included performing axial images of the lower extremities with subsequent determination of key reference lines and angles, mechanical lateral distal femoral (mLDFA) and mechanical medial proximal tibial (mMPTA), as well as the Hip–Knee–Ankle (HKA) angle [15, 16]. In the mechanical alignment group, the mean mLDFA value was 88.78° ± 1.49°, in the kinematic group — 88.47° ± 1.53°. The corresponding mMPTA values were 88.03° ± 1.86° and 87.70° ± 1.89°. The mean HKA values were 180.75° ± 2.51° for mechanical and 180.77° ± 2.55° for kinematic alignment. No statistically significant differences were found between the groups ($p > 0.5$).

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Determination of the maximum amplitude of movements in the knee joint was assessed using a goniometer, a comprehensive assessment of the subjective sensations of patients using a visual analogue scale of pain (VAS) and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) questionnaire. The maximum amplitude of movements in patients of the first and second groups was 71.02° ± 7.02° and 69.14° ± 13.87°, respectively. The mean VAS score was 7.5 ± 0.71 in the first group and 7.6 ± 0.7 in the second group. The mean WOMAC score was 54.9 ± 3 and 56.6 ± 3.75 in the first and second groups, respectively. The intergroup differences were statistically significant for WOMAC and maximum range of motion ($p < 0.05$), while demographic parameters and VAS were similar in both groups ($p > 0.05$) (Table 1).

The reason for the surgical intervention was chronic knee pain syndrome, resistant to therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 6 months, with confirmation of the severity of pain using the VAS scale of more than 6 points. Additionally, high WOMAC scores > 40.

The surgical intervention was performed by a single surgical team with all technical aspects of mechanical [10, 11] and non-restrictive kinematic alignment [12, 13]. For surgical access to the knee joint, a medial subvastus approach was performed with mobilization of the *vastus medialis muscle* without its dissection. For all patients, the same model of implant with cement fixation was used, the design and surgical instruments of which allowed implantation of endoprosthesis components using both mechanical and kinematic alignment methods. In addition, in all cases, a medially stabilized tibial insert was used, developed according to the medial pivot concept in accordance with the principles of multimodal analgesia. Analgesia included pre- and intraoperative perifocal blocks, the use of opioids and NSAIDs during surgery, and postoperative analgesia using paracetamol and nonsteroidal drugs [14].

Physical rehabilitation after surgery was carried out under the supervision of a rehabilitation physician in accordance with a unified rehabilitation program. Passive mobilization of the knee joint began on the first postoperative day. Starting from the second day and until discharge, patients underwent daily physiotherapy sessions lasting about one hour, which included a combination of active and passive exercises aimed at gradually restoring the range of motion in the joint, strengthening the muscular system and improving coordination skills.

To study the correct positioning of the endoprosthesis components in patients of both groups on the 14th day after surgery, axial radiography of the lower extremities was performed with subsequent measurement of the main reference lines and angles (Fig. 1).

The clinical results of knee joint prosthetics were assessed by measuring the maximum amplitude of movements using a goniometer before surgery, 2 weeks and 1.5 months after surgery. The time course of improvement in the functional state of patients was analyzed by comparing the indicators obtained on the 14th day and 1.5 months after surgery. The effectiveness of endoprosthetic repair was determined by comparing preoperative values with the results recorded 1.5 months after the intervention.

Table 1

Demographic and clinical data in groups before surgery

Characteristic	Group 1 (n = 50)	Group 2 (n = 50)	p*
Number of patients	50	50	p > 0.05
Male	25	25	p > 0.05
Female	25	25	p > 0.05
Age (M + SD), years	51.52 ± 4.92	51.78 ± 4.99	p > 0.05
Age range, years	42–63	41–62	p > 0.05
mLDFA, degrees	88.78 ± 1.49	88.47 ± 1.53	p > 0.05
mMPTA, degrees	88.03 ± 1.86	87.70 ± 1.89	p > 0.05
HKA, degrees	180.75 ± 2.51	180.77 ± 2.55	p > 0.05
VAS (M + SD), points	7.50 ± 0.71	7.60 ± 0.70	p > 0.05
WOMAC (M + SD), points	54.90 ± 3.00	56.60 ± 3.75	p > 0.05
Maximum range of motion (M + SD), degrees	71.02 ± 7.02	69.14 ± 13.87	p < 0.05

Note. * — The reliability of the differences in results between groups is, accordingly, statistically significant at the $p < 0.05$ level.

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To assess the subjective sensations of patients, the intensity of pain was measured using the VAS scale. Determination of the subjective state of the knee joint using the WOMAC questionnaire was carried out before surgery, on the 14th day and 1.5 months after surgery. The time course of improvement in the subjective state was analyzed by comparing the indicators obtained on the 14th day and 1.5 months after surgery, and the effectiveness of endoprosthetic repair was determined by comparing preoperative data with the results recorded 1.5 months after the intervention.

The study was conducted in strict accordance with the principles of bioethics, legislative requirements, and established standards for conducting biomedical research, as set forth in the Declaration of Helsinki of the World Medical Association (2000), the Constitution of Ukraine (1996), the Civil Code of Ukraine (2006), the Fundamentals of Ukrainian Legislation on Health Care (1992), and the Law of Ukraine "On Information" (1992) with amendments and supplements as of 01 December 2021. Before the start of the study, written voluntary consent was obtained from all participants, and data from medical records were analyzed in accordance with the requirements of the Bioethics Committee of the State Institution "ITO of the NAMS of Ukraine" (Protocol No. 3 of the meeting of the Bioethics Commission dated 29 April 2025).

Statistical data processing was performed using Microsoft Excel and Statistica 8.0 (StatSoft Inc.). The Mann–Whitney test was used to compare independent samples, and the Wilcoxon test was used to analyze repeated measures. The results were analyzed using standard methods of mathematical statistics, including the calculation of the number of samples (n), the arithmetic mean (M), and the standard deviation (SD). The statistical relationship between the studied variables was assessed using the Fisher test. The confidence level was set at 95 %, and the statistical significance was 0.05 ($p = 0.05$).

Results

In the mechanical alignment group, the mean mLDFA value was 89.45° ± 1.10°, in the kinematic group — 88.37° ± 1.47°. The corresponding mMPTA values were 89.46° ± 1.55° and 87.64° ± 1.92°. The mean HKA angles were 179.98° ± 1.55° in the mechanical and 180.73° ± 2.56° in the kinematic alignment groups. No statistically significant differences were found between the groups ($p > 0.5$). Analysis of key radiographic angles before and after surgery confirmed the fulfillment of the preoperative technical tasks: the mean deviation of HKA from the planned was –0.77° ± 0.52° in the mechanical and -0.04° ± 0.31° in the kinematic alignment groups ($p > 0.05$) (Table 2).

In the preoperative period, the intensity of knee pain, measured by the VAS scale, ranged from 7 to 9 points, with a mean value of 7.50 ± 0.71 in group 1 and 7.60 ± 0.70 in group 2. On the 14th day after surgery, the pain score in group 1 decreased from 7.50 ± 0.71 to 4.40 ± 0.70, and during 1.5 months of observation to (3.00 ± 0.45) points. Similarly, in group 2, on the 14th day after surgery, the VAS value decreased from 7.60 ± 0.70 to 4.18 ± 0.52, and after 1.5 months to (2.90 ± 0.95) points.

Subjective assessment of the knee joint using the WOMAC questionnaire, conducted before the intervention and in the postoperative period, showed a significant improvement in the functional state of patients in both groups. At the preoperative examination stage, the WOMAC score was (54.90 ± 3.00) and (56.60 ± 3.75) points in groups 1 and 2, respectively. As early as 14 days after the operation, a decrease in the average score was observed in group 1 to (32.50 ± 4.77), and after 1.5 months to (20.80 ± 4.32). Similarly, in group 2, the WOMAC scores decreased to (24.86 ± 4.50) points on the 14th day and to (19.10 ± 3.12) 1.5 months after the operation.

In the postoperative period, a statistically significant improvement in the subjective assessment of the condition of the operated joint was recorded in both groups ($p < 0.05$). On the 14th day, the intensity of pain on the VAS scale significantly decreased ($p < 0.05$). However, 1.5 months after the start of observation, the difference between the groups no longer reached the level of statistical significance ($p > 0.05$).

Table 2

Main radiological angles before and after surgery in the study groups

Indicator / Group	Mechanical alignment (before → after surgery)	Kinematic alignment (before → after surgery)	p
mLDFA	(88.78° ± 1.49°) → (89.45° ± 1.10°)	(88.47° ± 1.53°) → (88.37° ± 1.47°)	p > 0.05
mMPTA	(88.03° ± 1.86°) → (89.46° ± 1.55°)	(87.70° ± 1.89°) → (87.64° ± 1.92°)	p > 0.05
HKA	(180.75° ± 2.51°) → (179.98° ± 1.55°)	(180.77° ± 2.55°) → (180.73° ± 2.56°)	p > 0.05

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The changes of indicators on the VAS and WOMAC scales before and after the performed surgical intervention in patients of the two groups is presented in Fig. 2, 3.

Analysis of the clinical data showed the following changes in improvement in the amplitude of movements in the knee joint. In group 1, the average ROM increased from 71.02° ± 7.02° (preoperative measurement) to 82.30° ± 5.18° on the 14th day after surgery, and 1.5 months after the intervention it reached 95.34° ± 5.44°. Similarly, in group 2, the average ROM before surgery was 69.14° ± 13.87°, with further improvement to 91.14° ± 5.46° on the 14th day and to 99.20° ± 13.19° 1.5 months after surgery.

On the 14th day after surgery, both groups showed a significant increase in the maximum amplitude of movements in the operated joint ($p < 0.05$). At the same time, after 1.5 months, the difference between the ROM indicators was statistically insignificant ($p > 0.05$).

The time course of the increase in the amplitude of movements in the knee joint before and after the surgery in patients of the two groups is shown in Fig. 4.

The analysis of the main surgical parameters, such as the duration of the operation and hospitalization, the volume of intraoperative blood loss, did not reveal a significant difference between the groups. At the same time, the need for additional releases of the ligamentous apparatus to align the flexion-extension gap was significantly higher in the mechanical alignment group. The mean duration of surgery was (55.7 ± 12.5) minutes in the kinematic alignment group and (57.4 ± 11.8) in the mechanical group ($p > 0.05$). The amount of blood loss was similar: (119.6 ± 18.9) ml for mechanical and

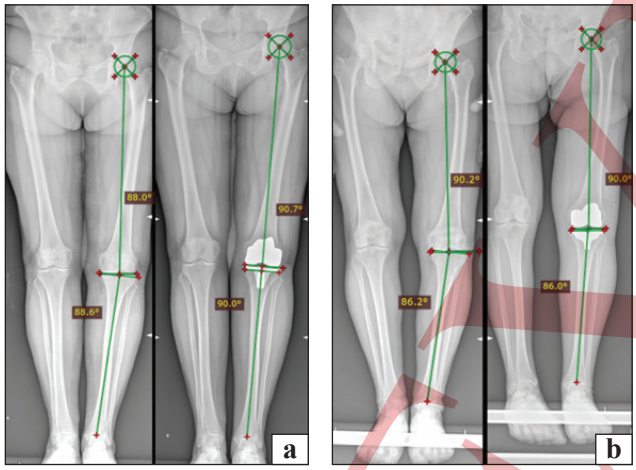

Fig. 1. Radiography findings before and after the installation of the endoprosthesis components according to the preoperative planning (a — mechanical alignment, b — kinematic)

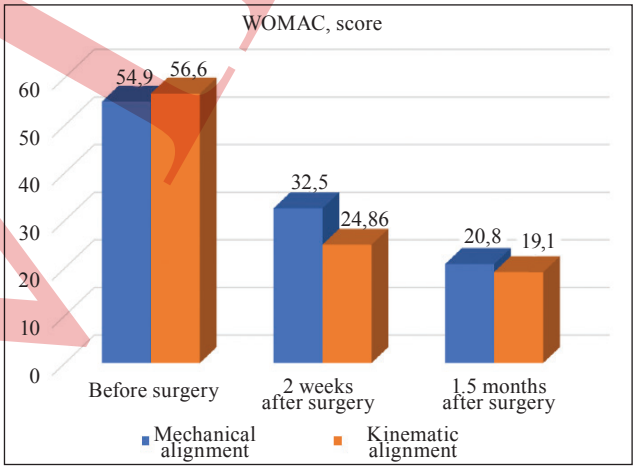

Fig. 3. Indicators of the patient's subjective assessment of the condition of the knee joint on the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) scale in both groups before and after surgical treatment

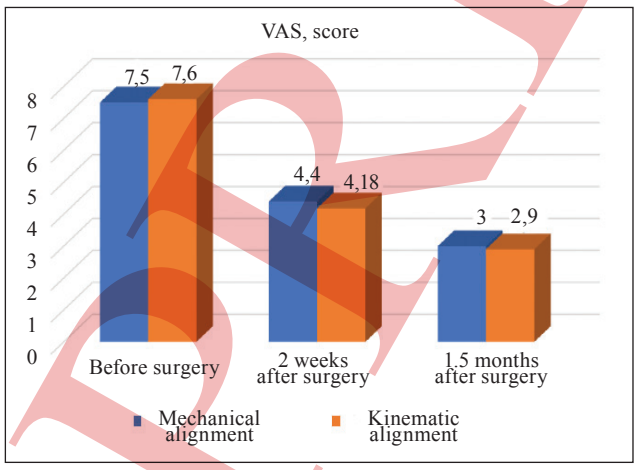

Fig. 2. Indicators of the level of pain syndrome on the VAS scale in both groups before and after surgical treatment

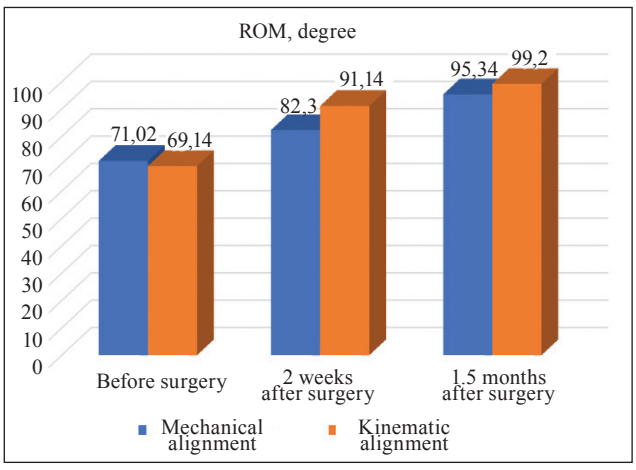

Fig. 4. Amplitude of movements in the knee joint in both groups before and after surgical treatment

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Table 3

Differences in the average values of surgical indicators of mechanical and kinematic alignment methods

Parameter	Mechanical alignment	Kinematic alignment	p
Duration of surgery, min	57.4 ± 11.8	55.7 ± 12.5	p > 0.05
Intraoperative blood loss, ml	119.6 ± 18.9	122.2 ± 15.9	p > 0.05
Hospital stay, days	7.0 ± 1.9	6.0 ± 1.7	p > 0.05
Frequency of soft tissue releases, %	44	8	p < 0.05

(122.2 ± 15.9) for kinematic alignment (p > 0.05). The mean hospital stay was slightly shorter in the kinematic alignment group (6.0 ± 1.7) days compared to the mechanical group (7.0 ± 1.9) (p > 0.05), which is probably due to better functional recovery and reduced pain. Additional soft tissue releases were performed in 8 % of surgical interventions in the kinematic alignment group and in 44 % of cases in the mechanical group (p < 0.05) (Table 3).

Discussion

Throughout the study, both techniques for positioning the endoprosthesis components, kinematic and mechanical, demonstrated comparable accuracy in component placement and similar effectiveness in terms of key surgical outcomes. In particular, the average operation time, intraoperative blood loss, and length of hospitalization did not have statistically significant differences between the groups: (57.4 ± 11.8) min vs. (55.7 ± 12.5); (119.6 ± 18.9) ml vs. (122.2 ± 15.9); (7.0 ± 1.9) vs. (6.0 ± 1.7) days, respectively (p > 0.05) (Table 2). The results obtained are consistent with the data of international studies, which also show no significant differences between these techniques in terms of the specified parameters [7, 17, 18].

At the same time, we found that kinematic alignment required significantly fewer additional soft tissue releases, 8 % compared to 44 % in the mechanical alignment group (p < 0.05). This result is consistent with the theoretical premises of the kinematic alignment concept, according to which the restoration of the individual anatomical axis of the joint minimizes the need for intervention in the ligamentous apparatus. The obtained data also align with the results of individual randomized studies and meta-analyses that report a decrease in the frequency of releases when using the kinematic technique [19–21]. Early functional dynamics demonstrated the superiority of the kinematic method: on the 14th day after surgery, the increase in the flexion amplitude in this group was 43 %, which exceeded the similar indicator in the mechanical alignment group (34 %; p < 0.05). However, 1.5 months after the intervention, a statistically significant difference between the groups was no longer detected. A similar trend was observed for pain syndrome on the VAS scale: on the 14th day, the intensity of pain in the kinematic alignment group was significantly lower (p < 0.05), but at the end of the observation period, the indicators in both groups were equalized (p > 0.05).

The assessment according to the WOMAC questionnaire showed the superiority of kinematic alignment at all stages of observation. The overall improvement was 37.5 points in the kinematic alignment group compared to 34.1 in the mechanical alignment group, while the "pain/discomfort" component showed an improvement of 4.7 versus 4.5 points, respectively (p < 0.05).

Conclusions

The use of kinematic alignment technologically reduces the need for additional soft tissue releases, helping to preserve the individual kinematics of the joint, which contributes to the reduction of pain syndrome and faster functional recovery in the first two weeks after surgery. At the same time, 1.5 months after the intervention, the differences between the groups become statistically insignificant, emphasizing the feasibility of further studies with a longer observation period to determine long-term results and potential complications.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. Study of the effectiveness of kinematic and mechanical alignment with the analysis of clinical results and possible complications within a year after primary knee arthroplasty.

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EVALUATION OF THE EFFICACY OF KINEMATIC AND MECHANICAL ALIGNMENT IN PRIMARY TOTAL KNEE ARTHROPLASTY DURING THE EARLY POSTOPERATIVE PERIOD

M. D. Moroz [1], R. A. Kozak [1], O. A. Kostogryz [1], V. I. Bondar [2]

[1] SI «Institute of Traumatology and Orthopedics of the NAMS of Ukraine», Kyiv
[2] Diagnostic Center «M24», Kyiv. Ukraine

✉ Mykola Moroz: morozn d@ukr.net; https://orcid.org/0000-0003-4134-1322
✉ Roman Kozak: ra.kozak@gmail.com; https://orcid.org/0000-0002-5132-027X
✉ Oleh Kostogryz, MD, DMSci: arztkostogryz@ukr.net; https://orcid.org/0000-0002-9533-9247
✉ Volodymyr Bondar: bondar_cooper@ukr.net; https://orcid.org/0009-0001-1695-0778

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Analysis of risk factors and assessment of prevention of venous thromboembolic complications in patients with hip joint replacement

S. Ye. Bondarenko, O. V. Vysotskyi

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

The issue of thromboembolic complications prevention is one of great importance, since patients have a high risk of developing postoperative venous thromboembolism. Objective. To analyze risk factors contributing to the development of venous thromboembolic complications in patients with hip pathology undergoing arthroplasty, and to substantiate its prophylactic measures. Methods. Depending on age, all patients were divided into groups: 20–40 years — 13 individuals, 41–60 years — 13 individuals, 61–80 years — 42 cases. To assess the effectiveness of thromboprophylaxis, two groups of patients diagnosed with stage III–IV idiopathic coxarthrosis aged 41 to 80 years were compared. 100 patients with various pathologies of the hip who underwent surgical treatment with endoprosthetics were involved. Results. Among the identified nosological forms of pathology, idiopathic coxarthrosis was most frequently diagnosed in patients aged 41 to 80 years. Our study demonstrated dynamic changes in the hemostatic system in patients after total hip arthroplasty when using various drugs for the prevention of thromboembolic complications, taking into account the level of antithrombin-III. In patients of the group I who received nadroparin calcium, the fibrinogen content in the blood before the operation was 4.90 (4.50–5.10) g/l, after 7 days — 4.40 (4.30–4.65), after 14 — 3.54 (2.30–3.75) g/l. In group II, thromboprophylaxis was achieved by taking dabigatran etexilate, before the operation, the fibrinogen content in the blood was 4.87 (4.45–5.15) g/l, after 7 days — 4.30 (4.20–4.50), after 14 — 3.62 (2.35–3.80) g/l. Conclusions. In patients with hip pathology, the main risk factors for venous thromboembolic complications before the endoprosthetic surgery and in the early postoperative period are age 41-80 years, obesity, arterial hypertension, as well as chronic venous insufficiency of the lower extremities. Thromboprophylaxis in total hip arthroplasty should be implemented with an individualized approach, considering not only surgical factors but also the early postoperative period.

Питання профілактики тромбоемболічних ускладнень важливе, оскільки пацієнти мають високий ризик розвитку післяопераційної венозної тромбоемболії. Мета. Проаналізувати чинники ризику розвитку венозних тромбоемболічних ускладнень у хворих із патологією кульшового суглоба після операції ендопротезування й обґрунтувати засоби їхньої профілактики. Методи. Залежно від віку всі пацієнти були поділені на групи: 20–40 років — 13 осіб, 41–60 — 45, 61–80 років — 42 випадки. Для вивчення ефективності тромбопрофілактики сформовано 2 групи хворих із діагнозом коксартроз III–IV стадії віком від 41 до 80 років. Було залучено 100 пацієнтів з різними патологіями кульшового суглоба, яким проводилось оперативне лікування з ендопротезування. Результати. За визначенням нозологічних форм патологій виявлено, що в хворих віком від 41 до 80 років найчастіше діагностовано ідіопатичний коксартроз. Нами досліджено динаміку показників системи гемостазу в осіб після ендопротезування кульшових суглобів із застосуванням різних препаратів для профілактики тромботичних ускладнень з урахуванням рівня антитромбіну-III. У хворих I групи, які одержували надропарин кальцію, до операції вміст фібриногену в крові становив 4,90 (4,50–5,10) г/л, через 7 діб — 4,40 (4,30–4,65), через 14 — 3,54 (2,30–3,75) г/л. У II групі тромбопрофілактику досягали шляхом прийому дабігатрану етексилату, до операції вміст фібриногену в крові становив 4,87 (4,45–5,15) г/л, через 7 діб — 4,30 (4,20–4,50), через 14 — 3,62 (2,35–3,80) г/л. Висновки. У хворих з патологією кульшового суглоба основними факторами ризику венозних тромбоемболічних ускладнень до операції ендопротезування та в ранньому післяопераційному періоді є вік від 41 до 80 років, ожиріння й артеріальна гіпертензія, а також хронічна венозна недостатність нижніх кінцівок. Тромбопрофілактика в разі виконання операцій тотального ендопротезування кульшового суглоба потребує індивідуального підходу до пацієнтів із урахуванням факторів ризику як у доопераційному, так і післяопераційному періодах. Ключові слова. Ендопротезування, ідіопатичний коксартроз, фактори ризику, тромбоемболічні ускладнення, антитромбін-III, тромбопрофілактика.

Keywords. Arthroplasty, idiopathic coxarthrosis, risk factors, thromboembolic complications, antithrombin III, thrombotic prevention

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Introduction

Recently, joint replacement surgeries have been the most common treatment for patients with severe forms of hip joint (HJ) impairments, accounting for 75–80% of all surgical orthopedic interventions. These interventions result in the elimination of pain syndrome in approximately 85–90 % of cases, restoration of joint function, and enable patients to regain a full quality of life [1, 2].

However, with the increasing number of such surgeries, the incidence of complications also rises. Among the early and most common are venous thromboembolic and hemorrhagic complications, particularly blood loss [3]. The prevention of these issues is of great significance, as patients who undergo hip replacement surgery are at high risk for developing postoperative venous thromboembolism [4], which may recur in 25 % of cases within 7–10 years and also contribute to the development of concurrent diseases. The primary complication of deep vein thrombosis (DVT) in the lower extremities is post-thrombotic deep vein syndrome [5].

In addition, many cases of DVT of the lower extremities are asymptomatic. All this significantly worsens the quality of life of patients and requires an individual approach to the diagnosis, treatment and prevention of these thrombotic conditions, the development of appropriate measures and tactics for their implementation with the use of pharmacological agents [6].

Purpose: to analyze the risk factors for the development of venous thromboembolic complications in patients with hip joint disorders after endoprosthetic repair and to substantiate the means of their prevention.

Material and methods

The material for the study was the results of observation of 100 patients with various disorders of the hip joint, who underwent surgical treatment with endoprosthetic repair at the Department of Joint Pathology of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the NAMS of Ukraine" for the period 2018–2024. The analysis examined the influence of age and gender on the progression of the disease, as well as on the outcomes of surgical interventions for hip joint replacement.

The study was reviewed and approved at a meeting of the Bioethics and Deontology Committee of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the NAMS of Ukraine" (Protocol No. 253 dated 03.06.2025).

All patients provided written consent for examination and treatment. The study was performed in compliance with the requirements and provisions of the Helsinki Declaration of Human Rights (2000), including the revision of EC-GCP, the Constitution and the Fundamentals of Ukrainian Legislation on Health Care, and all ethical norms for conducting clinical trials.

Patients were categorised by age as follows: 13 cases in the 20–40 year group, 45 cases in the 41–60 year group, and 42 cases in the 61–80 year group. To study the individual thromboembolic risks of total hip replacement surgery, a validated scale was taken into account according to the Caprini scoring system [7], which provides a consistent, thorough and effective method of stratifying the risk of venous thromboembolism in patients with hip replacements and the recommendations of the American Academy of Orthopaedic Surgery (AAOS). The following criteria were used to determine the risk factors for venous thromboembolism: age, body mass index (BMI), the presence of concomitant conditions, as well as the severity and timing of the intervention.

All endoprosthetic surgeries were performed under spinal anesthesia with bupivacaine solution (5 mm/1 ml), an anterolateral approach up to 10–12 cm long was used. Cementless, cemented and hybrid versions of hip joint endoprostheses were used to fix the implants.

Blood sampling for the study was carried out from the forearm vein in the morning on an empty stomach into a special test tube with sodium citrate, for subsequent plasma collection. To assess the hemostasis system in the blood plasma of patients, the following were determined: fibrinogen content by the Claus method, soluble fibrin-monomer complexes (SFMC), fibrinolytic activity. Determination of antithrombin-III activity in blood plasma was performed by residual thrombin activity after its interaction with antithrombin-III in defibrinated plasma using ready-made reagent sets.

In our clinical study, we used protocols for the prevention of thromboembolic complications approved by the Ministry of Health of Ukraine No. 329 dated 15.06.2007 and recommendations of the American College of Thoracic Surgeons (ACTS), recommendations of the Institute of Health and Clinical Care of England and Wales (NICE).

To study the effectiveness of thromboprophylaxis, 2 groups of patients diagnosed with stage III–IV coxarthrosis aged 41 to 80 years were formed:

– I (n = 16, 8 men and 8 women) — the level of antithrombin-III ranged from 98.0 to 113.0 %. These

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patients were treated with nadroparin calcium with a molecular weight of (2850 IU in 1 ml) in a prophylactic dose of 0.3 ml as a means of preventing thromboembolic complications.

– II (n = 16, 8 men and 8 women) — the level of antithrombin-III ranged from 76.0 to 92.0 %. The means of preventing thromboembolic complications was dabigatran etexilate. This agent was used prophylactically per os — 75 mg per day.

Statistical processing of data was performed using the software packages Microsoft Excel XP and Statsoft Statistica 6.0. Comparison of groups was carried out using the nonparametric Wilcoxon test with calculation of the median (Me) and percentiles (25 — 75) [8].

Results

Analysis of the composition of patients by gender showed that the ratio of men and women was 42 to 58 %, respectively. Thus, endoprosthetic repair was performed more frequently in women than in men. According to the obtained data, the development of hip joint disorders requiring endoprosthetic repair was most commonly diagnosed in patients over the age of 40; in individuals aged 41 to 80 years, it accounted for 87 %.

According to the definition of nosological forms of conditions, idiopathic coxarthrosis was most frequently diagnosed in patients aged 41 to 80 years. In elderly individuals requiring endoprosthetic repair, femoral neck fractures and traumatic instability of the implant were also observed; however, these clinical cases accounted for only 9 %, compared to 24 % in patients diagnosed with idiopathic coxarthrosis. Therefore, idiopathic coxarthrosis is the most common hip joint condition in older patients requiring total hip arthroplasty. (Table 1). In young patients, indications for hip arthroplasty are dysplastic coxarthrosis, aseptic necrosis of the femoral head, and rheumatoid arthritis.

The majority of procedures utilized total cementless arthroplasty (72 cases), while cemented techniques were performed in 18 cases and hybrid methods in 10 cases. Cemented arthroplasty was performed in patients with impaired bone mineral density (BMD), and revision arthroplasty was performed in cases of instability of the arthroplasty and in cases of femoral neck fractures.

Hip replacement surgery is known to be a surgical procedure with a high risk of developing thrombotic conditions. Several constant factors contribute to its increase, including advanced age (over 60 years) and the presence of concomitant conditions such as severe cardiopulmonary diseases, ischemic heart disease, and pulmonary hypertension. [9]. Additionally, risk factors include various comorbid conditions, in particular, high BMI and neuromuscular diseases [10, 11].

Ek. Carlino et al. found an increased rate of complications in patients with higher BMI, although the exact threshold value at which the risk of complications becomes unacceptable remains uncertain. However, there are contradictions in the literature regarding the influence of high BMI on the development of venous thromboembolism [12].

Among the patients included in our study, the BMI distribution was as follows: 37 % had a normal weight, 27 % were overweight, and the remaining 36 % had varying degrees of obesity. Overall, overweight women were more prevalent, comprising 37 out of 63 patients, with the remaining 26 patients being men (Table 2).

The most common risk factors included the development of arterial hypertension: Stage I–II in 20 % of patients, and Stage III–IV in 13 %, respectively. However, it should be noted that the arterial hypertension detected in patients was controlled, that is, patients received antihypertensive therapy.

Considerable attention should also be given to assessing the history of chronic gastric ulcers in patients, as this necessitates an individualized approach

Table 1

Distribution of patients by nosological forms of hip joint conditions

Patient age, years	20–40		41–60		60–80		Total	
Nosology	abs.	%	abs.	%	abs.	%	abs.	%
Idiopathic coxarthrosis	—	—	36	36.0	24	24.0	60	60.0
Dysplastic coxarthrosis	5	5.0	11	11.0	4	4.0	20	20.0
Aseptic necrosis of the femoral head	3	3.0	2	2.0	—	—	5	5.0
Rheumatoid arthritis	1	1.0	3	3.0	2	2.0	6	6.0
Fracture of the femoral neck	—	—	—	—	7	7.0	7	7.0
Traumatic instability of the endoprosthesis	—	—	—	—	2	2.0	2	2.0
Total	9	9.0	52	52.0	39	39.0	100	100.0

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to both the prescription of anticoagulants and the surgical procedure. It is clear that endoprosthetic surgery for such individuals should only be performed when the gastric ulcer is in remission, as the condition may worsen during the postoperative period (Table 3). The percentage of concomitant conditions in patients requiring endoprosthetic surgery was 61.5 % for those aged 20–40 years, 86.7 % for those aged 41–60 years, and 95.2 % for those aged 61–80 years.

We investigated the time course of hemostasis system indicators in patients after hip replacement surgery using various agents for the prevention of thrombotic complications, taking into account the level of antithrombin-III. In patients of Group I who received nadroparin calcium, the fibrinogen content in the blood was 4.90 (4.50–5.10) g/l before surgery, 4.40 (4.30–4.65) after 7 days, and 3.54 (2.30–3.75) g/l after 14 days. In Group II, thromboprophylaxis was achieved by taking dabigatran etexilate; before surgery, the fibrinogen content in the blood was 4.87 (4.45–5.15) g/l, 4.30 (4.20–4.50) after 7 days, and 3.62 (2.35–3.80) g/l after 14 days.

Therefore, one of the important criteria for choosing agents for thromboprophylaxis in patients with joint disorders requiring endoprosthetic repair can be considered antithrombin-III — a heparin cofactor that inactivates thrombin, which prevents the development of thrombosis.

Therefore, antithrombin-III, a heparin cofactor that inactivates thrombin and helps prevent the development of thrombosis, can be considered one of the key criteria for selecting thromboprophylaxis agents in patients with joint disorders requiring endoprosthetic repair. In the case of a decrease in antithrombin-III in the blood due to various factors (in the postoperative period), heparin loses its anticoagulant effect. Low-molecular-weight heparin drugs — Clexane, Fraxiparine — also act in the same way, since their mechanism is binding to antithrombin-III. If its low concentration is detected in the blood of patients before surgery, it becomes inappropriate to prescribe low-molecular-weight heparin drugs that act through antithrombin-III. An alternative option is dabigatran, an anticoagulant agent that operates through a different mechanism by directly inhibiting

Table 2

Distribution of patient groups by BMI before surgery

BMI, kg/m²	Number of patients (n)	Percentage (%)
Normal body mass		
18.50–24.99	37	37.0
Excess body weight (pre-obesity)		
25.00–29.99	27	27.0
First-degree obesity		
30.00–34.99	11	11.0
Second-degree obesity		
35.00–39.99	19	19.0
Third-degree obesity		
40.00–44.99	4	4.0
Fourth-degree obesity		
> 45.00	2	2.0
Total	100	100.0

Table 3

Comorbidity detected in patients before hip replacement surgery

Патологія	Вік (роки) і кількість хворих		
	20–40 (n = 13)	41–60 (n = 45)	61–80 (n = 42)
Arterial hypertension of stages I–II	—	10	10
Arterial hypertension of stages III–IV	—	5	8
Rheumatoid arthritis	1	—	—
Pulmonary disorders	—	1	2
Kidney disorders	—	3	2
A history of gastric ulcer	1	2	3
Hepatitis C	1	1	—
A history of hormone therapy	1	4	5
A history of antibiotic therapy	1	5	—
Granulating vasculitis	1	—	—
Chronic venous insufficiency	—	6	7
A history of lower limb erysipelas	—	2	—
Type II diabetes mellitus	2	1	3
Number of patients with concomitant conditions	8	39	40

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thrombin and preventing thrombus formation. Thus, the preventive effect of thrombus formation is achieved without the participation of its own anticoagulant factor, antithrombin-III [13]. In our opinion, the choice of this approach is fully pathogenetically justified, as there is no consensus among specialists on the optimal method of antithrombotic prophylaxis to balance the risks of thrombosis and minimize bleeding in patients undergoing endoprosthetic surgery.

Discussion

Venous thromboembolism cannot be considered an absolute, but is a relative contraindication to performing hip arthroplasty, as stated by H. Choe et al. However, DVT, especially in the iliac-femoral vein, is an absolute modified contraindication for elective endoprosthetic repair. Surgical intervention can displace existing thrombi, which will potentially cause life-threatening complications [14].

Therefore, it is important to identify patients with a history of venous thromboembolic conditions, which is a dangerous risk factor for complications during hip replacement and requires an individual approach to prevention [15]. In particular, in our study, chronic venous insufficiency of the lower extremities was diagnosed in 15 % of cases.

Also, the development of obesity (BMI > 30 kg/m^2) is a significant risk factor for venous thromboembolism in patients who require hip replacement, because they lead a sedentary lifestyle. Therefore, performing hip replacement is more difficult due to an increase in the average time of the operation (80–120 min) and an increase in the likelihood of hemorrhagic and thrombotic complications. In addition, motor activity decreases in the postoperative period. All these factors cause disruption of the hemostasis system and the development of venous thrombosis and even create risks of pulmonary embolism; therefore they require mandatory thromboprophylaxis [16, 17].

To assess the degree of risk for venous thromboembolism and develop a prevention plan, four main periods were distinguished: the first, preoperative (2–5 days before the intervention); the second, intraoperative; the third, early postoperative (10–14 days after the intervention); and the fourth, late postoperative (2–3 months after the intervention).

In the preoperative period, the main task was to determine the etiological causes of vascular thrombosis in patients. This was achieved through a thorough study of disease histories, in particular, history taking and clinical examination with special attention to the examination of the venous system of the lower extremities and pelvis visually and according to the results of ultrasound examination. The functional state of the cardiovascular system, liver, kidneys, as well as the presence of peptic ulcer of the gastrointestinal tract were analyzed.

Attention was given to the physical condition of patients, including measurements of height, weight, and blood pressure. BMI was calculated, motor activity assessed, and necessary laboratory tests, including biochemical blood tests and coagulation assessments, were performed.

Also of great importance in the preoperative period is the identification of conditions and impairments that may cause violations of the hemostasis system in the intraoperative period. Therefore, it is important to individually plan not only the operation itself, but also to determine risk factors for the justified appointment of preventive measures for the development of venous thromboembolic complications.

In the intraoperative period, minimal trauma is the most important and fundamental aspect. An important point during the operation is the surgeon's rational access to the hip joint, as well as an individual approach to choosing the type of anesthesia. It is mandatory to use a blood content aspiration system during the surgeon's treatment of bone tissue in the acetabular fossa and femoral canal of the femur, especially in places where a blood clot forms. The second important point during the operation is the correct use of the vascular coagulation technique to stop bleeding, because excessive cauterization of the vessels causes a coagulation flow that can cause the development of thrombosis. In addition, it is caused by trauma (compression) of blood vessels with instruments during the operation. Therefore, training assistants during the operation to correctly perform actions using surgical instruments, as well as carefully perform the procedure for dislocation of the femoral head or reduction of the endoprosthesis head, is a necessary prerequisite. These procedures can injure both periarticular nerve and vascular formations, which is also a thrombohazardous moment.

We also evaluated such indicators as the total time of the operation (on average it was (90 ± 20) min) and blood loss, which was on average (300 ± 100) ml, and in cases of cement endoprosthesis, the thermal effect of bone cement on the state of blood pressure and somatic status of the patient. During the intraoperative period, it is rational to administer anesthesia not only for the surgical procedure itself but also to ensure appropriate dilution, use dextrans to improve blood rheology, prevent aggregation of blood cells, and reduce the risk of thrombosis.

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After the operation, it is necessary to use compression elastic bandaging of the lower extremities or use compression knitted stockings as a preventive measure for the development of venous thromboembolism for 10–14 days after the operation, with the exception of patients with chronic venous insufficiency.

The early postoperative period requires special attention, since postoperative complications, such as venous thromboembolism and other diseases, are the main risk factors for mortality in this period. Dynamic control of postoperative wound healing, appropriate infusion therapy, which prevents hemostasis and improves the rheological properties of blood, is of fundamental importance. Patients with various hip joint conditions have been found to have changes in hemostasis system markers following endoprosthetic surgery.

Patients who underwent thromboprophylaxis with low molecular weight heparins have been shown to have a certain percentage of lower limb vein thrombosis in the early postoperative period, which justifies the search for rational schemes. They should be formed taking into account the concentration of antithrombin-III, since its decrease in the blood can serve as a criterion for choosing a thromboprophylactic agent to prevent the development of venous thrombosis [18].

Thus, after hip replacement surgery, activation of blood coagulation is observed in the form of impaired fibrinolysis, and the use of laboratory markers, in particular, the content of fibrinogen and antithrombin-III, allows detecting an imbalance in the fibrinolytic link of hemostasis and forming the principles of thromboprophylaxis.

It is worth noting that impaired hemostasis leads to thrombosis of deep veins of the extremities, therefore, control of biochemical blood parameters should occur before and after surgery.

Conclusions

The main factors contributing to the risk of venous thromboembolic complications in patients with hip joint disorders, both before hip arthroplasty and during the early postoperative period, include age (41 to 80 years), obesity, arterial hypertension, and chronic venous insufficiency of the lower extremities.

Laboratory markers that assess the dynamics of hemostasis changes and predict thromboembolic complications in postoperative patients include blood fibrinogen levels, fibrinolytic activity, and antithrombin-III levels. Its indicator can reasonably be considered one of the most important criteria when choosing drugs for the prevention of thromboembolic complications in patients after arthroplasty.

Thromboprophylaxis in the case of total hip arthroplasty requires an individual approach to patients, taking into account risk factors both in the preoperative and postoperative periods.

Conflict of interest. The authors declare no conflict of interest.

Prospects for further research. Assessing laboratory markers to minimize thromboembolic risks and complications during endoprosthetic repair.

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Contribution of the authors. Vysotsky O. V. — drafting the article and collecting data; Bondarenko S. Ye. — research management, analysis of findings.

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ANALYSIS OF RISK FACTORS AND ASSESSMENT OF PREVENTION OF VENOUS THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH HIP JOINT REPLACEMENT

S. Ye. Bondarenko, O. V. Vysotskyi

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

✉ Stanislav Bondarenko, MD, DSci in Orthopaedics and Traumatology: bondarenke@gmail.com; https://orcid.org/0000-0003-2463-5919

✉ Oleksandr Vysotskyi, MD: vavkherson@gmail.com; https://orcid.org/0000-0002-4845-1615

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Results of reconstruction of the structures of the posterolateral corner in combination with anterior cruciate ligament surgery

M. L. Golovakha [1], A. A. Bezverkhyi [1], W. Orljanski [2]

[1] Zaporizhzhia State Medical and Pharmaceutical University. Ukraine
[2] Vienna Private Clinic. Austria

The results of treatment of patients with damage to the structures of the posterolateral corner in combination with anterior cruciate ligament (ACL) surgery are presented. The purpose of the work was to evaluate the results of reconstruction of combined injuries of the anterior cruciate ligament and structures of the posterolateral corner under arthroscopic control based on a comparative analysis of the results and complications. The study group consisted of 26 patients, the comparison group consisted of 27. As part of the examination, the VAS, IKDS, Tegner, Lysholm and KOOS scales were determined in both groups of patients, and the dynamics of osteoarthritis progression according to the Kellgren and Lawrence classification were also assessed. The results of arthroscopically guided reconstruction of the posterolateral corner, combined with ACL reconstruction, were quite promising: the overall IKDS score was: A19, B5, C2, D0. The majority of patients (87.50 %) were very or moderately satisfied with the treatment results. A comparative analysis of functional and radiological results showed that the stability of the knee joint based on the IKDS score was better in the group of patients with arthroscopically guided reconstruction of the posterolateral corner in combination with ACL reconstruction, and this group also had a lower rate of progression of osteoarthritis. Arthroscopic intervention using the original technology using a tendon graft is combined with the minimally invasive arthroscopic technique "all-inside" for ACL reconstruction. The results of this work argue for the good stability of anatomical reconstruction by arthroscopic intervention technique, which can be recommended as a valuable alternative method of plastic surgery of the structures of the posterolateral corner of the knee joint. Conclusion. Arthroscopic surgery of the structures of the posterolateral corner of the knee joint in case of combined injury with rupture of the ACL can be recommended as an alternative method compared to open surgery.

Наведено результати лікування пацієнтів із ушкодженням структур задньолатерального кута в поєднанні з пластикою передньої схрещеної зв'язки (ПСЗ). Мета. На основі порівняльного аналізу результатів та ускладнень вивчити наслідки реконструкції комбінованих ушкоджень передньої схрещеної зв'язки та структур задньолатерального кута під артроскопічним контролем. Методи. Групу дослідження склали 26 пацієнтів, порівняння — 27 осіб. У межах обстеження в обох групах визначали показники шкал VAS, IKDS, Tegner, Lysholm та KOOS, а також аналізували динаміку прогресування остеоартрозу за класифікацією Kellgren та Lawrence. Результати. Відновлення структур задньолатерального кута під артроскопічним контролем, які поєднувалися з реконструкцією ПСЗ, виявилося досить багатообіцяючим: загальний показник шкали IKDS склав: A19, B5, C2, D0. Більшість пацієнтів (87,50 %) результатом лікування дуже чи просто задоволені. Порівняльний аналіз функціональних і радіологічних даних показав, що стабільність колінного суглоба на підставі шкали IKDS була кращою в групі пацієнтів із відновленням структур задньолатерального кута під артроскопічним контролем у комбінації з пластикою ПСЗ, у цій групі відзначено також меншу питому вагу прогресування остеоартрозу. Артроскопічне втручання за оригінальною технологією з використанням сухожилкового трансплантата комбінується з мінімально інвазивною артроскопічною технікою «all-inside» для реконструкції ПСЗ. Результати цієї роботи аргументують хорошу стабільність анатомічної реконструкції шляхом артроскопічної техніки втручання. Висновок. Артроскопічна пластика структур задньолатерального кута колінного суглоба за комбінованого ушкодження з розривом ПСЗ може бути рекомендована як альтернативний метод порівняно з відкритою пластикою. Ключові слова. Колінний суглоб, травма, нестабільність, передня схрещена зв'язка, реабілітація.

Key words. Knee joint, injury, instability, anterior cruciate ligament, rehabilitation

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Introduction

The diagnosis and management of combined anterior cruciate ligament (ACL) injuries present significant challenges, due to ongoing questions regarding anatomical considerations, biomechanical factors, reconstruction techniques, and evaluation of patient clinical outcomes. ACL injuries are common, and the combination with lesions of the posterolateral corner structures occurs in 9 % of all ACL injuries [1, 3, 4, 10]. Concomitant injury to the posterolateral knee joint components is mostly diagnosed with lesions of the posterior cruciate ligament, the incidence reaches 80 % [2, 7, 11].

Damage to the structures of the posterolateral corner in combination with ACL tears is one of the most difficult cases to detect. Diagnostic criteria are described as very variable [8, 9, 16]. Such injuries occur much more often than they are suspected. Damage to the structures of the posterolateral corner may often go undiagnosed in clinical practice, which can result in repeated ACL ruptures or patients presenting years later with pain in the lateral aspect of the knee joint.

The debate surrounding the surgical approach to the posterolateral corner structures stems from the lack of consensus on the optimal technique and the limited number of published results that demonstrate complete restoration of knee joint stability. A solid understanding of the anatomy and biomechanics of the posterolateral corner is essential for grasping the injury mechanism and determining the appropriate treatment strategy for patients with combined rotational external knee instability.

It is quite difficult to track a large body of data on the results of restoration of the ACL and structures of the posterolateral corner. This is partly because signs of injuries in this area are most effectively detected during a clinical examination of the knee, while MRI can typically visualize them only within the first 2–4 weeks. The indications for reconstructing the posterolateral corner structures remain unclear, and surgical approaches vary depending on the hospital's practices. As a result, there is still much room for improvement, which drives the ongoing search for alternative treatment methods for this condition. The most commonly used approach involves auto- or allotendinous grafts, as described by LaPrade [12, 13], performed via an external approach, involving the preparation of the lateral structures of the knee. Recently, arthroscopic techniques have emerged, utilizing existing instruments and approaches to the knee joint in various ways. By employing a novel arthroscopic method for reconstructing the posterolateral corner structures, we have achieved promising results in restoring function in cases of combined injuries to the posterior cruciate ligament [6, 9, 15]. This method has also been applied in cases of ACL ruptures combined with injuries to the posterolateral corner structures.

Objective: to study the consequences of arthroscopic reconstruction of combined injuries of the anterior cruciate ligament and posterolateral corner structures based on a comparative analysis of outcomes and complications.

In line with the objective, we divided the patients into two groups. The first group consisted of patients who underwent the more commonly used method of arthroscopic ACL reconstruction combined with open surgery to reconstruct the posterolateral corner structures of the knee. The second group included patients who received arthroscopic ACL reconstruction alongside the original arthroscopic technique for restoring the posterolateral corner structures. We then analyzed and compared the outcomes of both groups to evaluate the effectiveness of the treatments.

Material and methods

The analysis of clinical material was carried out in accordance with the protocol of the Bioethics Commission of Zaporizhzhia State Medical and Pharmaceutical University (Protocol No. 8 dated 26.12.2022). The study was carried out in compliance with the requirements and provisions of the Helsinki Declaration of Human Rights (2000), including the revision of EC-GCP, the Constitution and the fundamentals of Ukrainian legislation on healthcare. All patients provided written consent for examination and treatment.

The results of treatment of two different groups of patients were analyzed. The first group comprised 26 patients who underwent arthroscopic reconstruction of the posterolateral angle using an autograft from the semitendinosus tendon and ACL reconstruction using an autograft from the quadriceps tendon. The second group involved 27 patients, ACL reconstruction was also performed using an autograft from the quadriceps tendon, and reconstruction of the posterolateral angle was performed using an open external approach using an autograft from the semitendinosus tendon.

The first group, arthroscopic reconstruction of the posterolateral angle

In the period from 2019 to 2023, 26 patients (22 men and 4 women) were operated on for acute or chronic posterior instability. Combined reconstructive and revision interventions were included in this

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study. In all cases, there was a combined injury to the ACL and the structures of the posterolateral angle. In 11 (42.31 %) patients, the ligament rupture occurred due to sports injuries, in 12 (46.15 %) due to traffic accidents, in 3 (11.54 %) due to other reasons. The diagnosis was made on the basis of clinical examination, radiography and magnetic resonance imaging (MRI). The operations were performed arthroscopically: the ACL was restored with a graft from the quadriceps tendon (QT, one tendon bundle) using the all-inside method. Reconstruction of the posterolateral corner structures was performed using the original technique under arthroscopic control with an autograft from the semitendinosus tendon, the results of which were published previously [9, 15]. Additionally, medication, physical rehabilitation, and splint immobilization were administered according to the standard protocol followed after anterior cruciate ligament reconstruction.

Group 2, open reconstruction of posterolateral angle structures

27 patients (25 men and 2 women) were operated on between 2004 and 2015 for acute or chronic anterior instability. Combined reconstructive and revision interventions were included in this study. In all cases, there was a combined injury to the anterior cruciate ligament and the structures of the posterolateral angle. In 9 (33.33 %) individuals, the ligament rupture occurred due to sports injuries, in 16 (59.26 %) due to traffic accidents, and in 2 (7.41 %) due to other causes. The diagnosis was made on the basis of clinical examination, radiography and MRI. The operations were performed arthroscopically with an autograft from the quadriceps tendon using the all-inside method (QT, one tendon bundle). Reconstruction of the posterolateral angle structures was performed through external access using the LaPrade technique with an autograft from the tendon of the semitendinosus muscle [4, 5, 9, 12–14]. Additionally, medication, physical rehabilitation, and splint immobilization were administered according to the standard protocol followed after anterior cruciate ligament reconstruction.

During the examination, the VAS, IKDS, Tegner, Lysholm, and KOOS scales were determined in both groups, and the time course of osteoarthritis progression was assessed using the Kellgren and Lawrence classification.

Previous surgeries

Two patients in the first group (7.69 %) had previously undergone surgery on the damaged joint: 1 had undergone ACL reconstruction due to a tear; the second had previously undergone ACL refixation.

In the second group, only 1 patient (3.7 %) had previously undergone ACL reconstruction.

Concomitant interventions

Patients of the first group (16 (61.54 %)) underwent additional operations along with reconstruction of the ACL and the structures of the posterolateral angle: 5 (19.23 %) individuals underwent a suture of the lateral meniscus, in 3 (11.54 %) cases a suture of the medial meniscus, in 1 (3.85 %) meniscus, in 7 (26.92 %) patients partial removal of the damaged meniscus was performed.

Patients of the second group (17 (62.96 %)) underwent additional operations along with reconstruction of the posterior cruciate ligament: 4 (14.81 %) — suture of the lateral meniscus, 3 (11.11 %) — suture of the medial meniscus, 4 (14.81 %) — partial removal of the damaged meniscus, 5 (18.52 %) — partial removal of both damaged meniscuses, 1 (3.71 %) — removal of the metal structure.

Statistical processing of the obtained results was carried out using computer variational, nonparametric analysis of variance (Excel and Statistica 7.0 software).

Results

First group

The age of patients at the time of surgery was 13–57 years, average age 32.89 years. In 10 (38.46 %) cases, there was acute and in 16 (61.54 %) cases, there was chronic instability of the knee joint. The time interval between the injury and the provision of first aid was on average (1.38 ± 3.91) (0–20.18) years, and between the date of injury and reconstructive intervention was (1.95 ± 4.24) (0.03–20.27) years. The assessment of the condition of 12 out of 26 patients (46.15 %) was possible using a questionnaire, personal clinical examination and MRI. The status of 14 out of 26 (53.85 %) could only be determined by subjective questionnaires and MRI. All operations were performed by a single traumatologist. On average, the VAS index was (2.46 ± 1.65) (0–7), Tegner 5 (1–9), Lysholm (88.67 ± 18.98) (34–100), IKDC index (87.34 ± 18.53) (35.63–100), KOOS for pain 91–100), KOOS for function (87.3 ± 16.32) (53.57–100), KOOS for activities of daily living (90.16 ± 13.09) (51.47–100), KOOS for sports and leisure (87.74 ± 29.94) (0–10). The total score of the IKDS scale was: A19, B5, C2, D0. Most patients (87.50%) were very or moderately satisfied with the treatment results. They would agree to undergo the same amount of surgery again, knowing the results (Table 1–3).

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A subjective satisfaction assessment was obtained from all 26 (100 %) patients. It indicates that 17 (65.38 %) subjects were very satisfied, 5 (19.23 %) were satisfied, 3 (11.54 %) were moderately satisfied, and 1 (3.85 %) was not satisfied.

Complications after the QT-graft removal on the knee joint were minor. Only one patient presented with pain at the site of the graft removal, as well as a painful sensation due to impaired wound healing. One patient was bothered by a crunching sound in the area of graft fixation for reconstruction of the posterolateral angle structures in the area of the external condyle of the femur.

The second group

The age of the patients was between 23 and 46 years, the average age was 28.92. The time interval between the injury and the provision of first aid was on average (2.18 ± 2.01) (0–14.21) years, and between the date of the injury and the reconstructive intervention was (1.47 ± 4.24) (0.03).

The assessment of the condition of 17 out of 27 patients (62.96 %) was possible using a questionnaire, personal clinical examination and magnetic resonance imaging.

On average, the VAS index was (2.75 ± 1.27) (0–7), Tegner 5 (1–9), Lysholm (76.75 ± 17.18) (38–100), IKDC index (75.42 ± 19.35) (34.36–100), KOOS for pain (80.92 ± 19.75) (25.83–100), KOOS for function (79.34 ± 15.26) (52.71–100), KOOS for activities of daily living (81.62 ± 15.56) (52.45–100), KOOS for sports and leisure (75.68 ± 28). IKDS was A18, B5, C4, D0. Most patients 22 (81.48 %) were very or just satisfied with the treatment results.

Subjective satisfaction was obtained from all 27 (100 %) patients.

Complications after the QT-graft harvest in the knee joint were insignificant.

Radiological evaluation of the results was carried out by comparing the Kellgren and Lawrence osteoarthritis scale before and after the operation.

All patients in the first group (26 people) underwent MRI control. Before the intervention, 19 patients (73.08 %) had doubtful osteoarthritis of stage 0, and 7 (26.92 %) had osteoarthritis of stage I. None were diagnosed with stages II or III (Table 4).

After the operation, magnetic resonance imaging was performed. The following stages of osteoarthritis were detected in the patients: 12 (46.15 %) — 0; 10 (38.47 %) — I; 4 (15.38 %) — II with slightly pronounced osteoarthritis. None of the patients were diagnosed with stage III with severe osteoarthritis (Table 4).

Table 1

Comparative subjective assessment by VAS, IKDC, activity level by Tenger

Scale	First group	Second group	P
VAS	2.46 ± 1.65 (0–7)	2.75 ± 1.27 (0–7)	> 0.05
IKDC	87.34 ± 18.58 (35.63–100)	75.42 ± 19.35 (34.36–100)	< 0.01
Lysholm	88.67 ± 18.98 (34–100)	76.75 ± 17.18 (38–100)	> 0.05
Tegner	5 (1–9)	5 (1–9)	< 0.01

Таблиця 2

Оцінка результатів за шкалою KOOS

Показник	First group	Second group	P
Pain	91.22 ± 18.15 (27.78–100)	80.92 ± 19.75 (25.83–100)	> 0.05
Symptom	87.30 ± 16.32 (53.57–100)	79.34 ± 15.26 (52.71–100)	< 0.01
Activity in daily life	90.16 ± 13.09 (51.47–100)	81.62 ± 15.56 (52.45–100)	> 0.05
Sports and leisure	87.31 ± 29.94 (0–100)	75.68 ± 28.56 (0–100)	< 0.01

Таблиця 3

Оцінка за шкалою IKDC

Показник	First group	Second group
Mobility	A-20, B-6, C-0, D-0; 76.9 %, 23.1 %	A-20, B-5, C-2, D-0; 74.1 %, 18.5 %, 7.4 %
Stability	A-20, B-4, C-2, D-0; 67.9 %, 15.4 %, 7.7 %	A-20, B-4, C-3, D-0; 74.1 %, 14.8 %, 11.1 %
Function	A-16, B-8, C-2, D-0; 61.5 %, 38.8 %, 7.7 %,	A-16, B-7, C-4, D-0; 59.3 %, 25.9 %, 14.8 %
Overall outcome	A-19, B-5, C-2, D-0; 73.1 %, 19.2 %, 7.7 %,	A-18, B-5, C-4, D-2; 66.7 %, 18.5 %, 14.8 %

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All 27 patients (100 %) of the second group underwent MRI. Before the intervention, 11 (40.74 %) of them had no signs of osteoarthritis, 14 (51.85 %) had stage I osteoarthritis, and 2 (7.41 %) had mild stage II osteoarthritis. No patient was diagnosed with stage III (Table 4).

After surgery, MRI revealed that 8 (29.63 %) had no signs of osteoarthritis, 13 (48.15 %) had stage I, 4 (14.81 %) had stage II, and 2 (7.41 %) had stage III. None of the patients were diagnosed with stage IV with severe osteoarthritis (Table 4).

Complications

In the first group, complications were recorded in 1 (3.85 %) case. The patient had a hematoma in the area of graft harvesting in the area of the quadriceps tendon, which did not require drainage, so local hypothermia was performed with a continuation of the antibiotic course.

In the second group, complications were observed in 2 patients (7.41 %). Both had superficial wound healing disorders in the area of the outer knee, which were treated conservatively with dressings and a continuation of the course of antibacterial therapy.

A possible complication of this operation is damage to the peroneal nerve, which is located in the area of the instrument (needle, drill) around the posterior edge of the lateral condyle of the tibia, so its protection is a priority during such an operation.

Recurrent injury

In the first group, one patient (3.85 %) out of 26 experienced a recurrent injury. Upon examination, it was found that the patient had damage to the internal meniscus, which was subsequently repaired with suturing.

In the second group, 3 (11.11 %) out of 27 patients were injured again. Two had damage to the internal meniscus after the suture, one had an injury to the internal meniscus (which was intact during the operation).

Comparative analysis of both groups

A comparative analysis of the treatment results of patients in both groups was performed by constructing comparative tables and determining the reliability of differences in numerical indicators between the groups (Tables 1–4).

In general, statistical processing showed that the results in both groups were similar. However, there was a tendency towards better indicators in the first group of patients after arthroscopic reconstruction of the posterolateral angle structures. Some values differed more significantly in favor of this group. For example, the IKDC index, KOOS symptoms, and the progression of osteoarthritis according to Kellgren and Lawrence (Table 3–4).

Subjective comparative assessment using the VAS, IKDC, KOOS, Lysholm, and Tegner scales also showed slightly better results in the first group (Table 1–2). Moreover, a significant difference was obtained only for the VAS and IKDC. That is, the KOOS and Lysholm scales, which are recommended for use in osteoarthritis, did not reveal a significant difference.

Tegner activity was practically the same. The main differences were determined by the IKDC scales, which characterizes knee stability, and the VAS, which subjectively assesses pain syndrome.

Some heterogeneity of the IKDC scale indicators is due to the fact that in the second group there were slightly more meniscal injuries. In addition, it should be noted that arthroscopic precise positioning of the graft fixation point during the reconstruction of the hamstring muscle [15], undoubtedly, provided better stability of the structures of the posterolateral corner, which was reflected in the assessment of the results according to this scale (Table 3). It is clearly seen that the stability indicators of the knee joint are better in the first group of patients.

The progression of osteoarthritis was greater in the second group. Also, the stability indicators of the knee joint according to the results of the assessment according to the IKDC scale were slightly worse.

It is important to note that, while the KOOS and Lysholm scale results showed only minor differences,

Таблиця 4

Результати оцінки динаміки остеоартрозу за Kellgren та Lawrence

Стадія	First group		Second group		
	before surgery	after surgery	before surgery	after surgery	P
0	19 (73.08 %)	12 (46.15 %)	11 (40.74 %)	8 (29.63 %)	> 0.05
I	7 (26.92 %)	10 (38.47 %)	14 (51.85 %)	13 (48.15 %)	> 0.05
II	—	4 (15.38 %)	2 (7.41 %)	4 (14.81 %)	< 0.01
III	—	—	—	2 (7.41 %)	< 0.05
IV	—	—	—	—	—

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the IKDC scale assessments were significantly more favorable in the first group of patients, who underwent the arthroscopic technique for reconstructing the structures of the posterolateral corner.

Discussion

Reconstructions of the posterolateral angle of the knee joint result in only partial restoration of the intact relationships [2, 3, 12, 14, 16]. A significant factor influencing the functional outcome is the correct position (positioning) of the graft in the area of the posterior edge of the lateral condyle of the tibial bone. In addition, we reconstruct the hamstring muscle by augmenting it with a much stiffer tendon graft. The ideal drill channel in the area of the lateral condyle of the tibial bone is formed in an anterior-posterior direction through the tibia to the projection of the place where the hamstring tendon passes. Biomechanical studies have indicated that this results in early loss of graft tension, thinning, and possible failure [4, 15, 16].

The results of arthroscopically guided reconstruction of the posterolateral angle, combined with ACL reconstruction, were quite promising: the overall IKDS score was: A19, B5, C2, D0. The majority of patients (87.50 %) were very or fairly satisfied with the treatment results. A comparative analysis of functional and radiological results showed that the stability of the knee joint based on the IKDS score was better in the group with arthroscopically guided reconstruction of the posterolateral angle in combination with ACL reconstruction, and this group also had a lower rate of osteoarthritis progression. The wide variety of surgical techniques, with a wide selection of grafts, the small number of observations and the short periods of post-operative examination limit the reliability of the results. The ideal scope of care for injuries to the posterolateral angle of the knee has diametrically different approaches in terms of surgical technique and graft selection. Arthroscopic intervention using the original technology using a tendon graft is combined with the minimally invasive all-inside arthroscopic technique for reconstruction of the ACL. The goal of ACL reconstruction is to restore the function of the knee joint. At the same time, there are numerous treatment methods (conservative and surgical), experimental concepts and recommendations (ESSKA) for the optimal elimination of posterolateral rotational instability. The results of this study argue for the good stability of anatomical reconstruction by arthroscopic intervention technique, which can be recommended as a valuable alternative method of plastic surgery of the structures of the posterolateral angle of the knee joint. The average subjective and objective results over time are promising, as evidenced by patient satisfaction, restored stability, return to sports, and a low incidence of osteoarthritic degeneration. The rate of complications is also within an acceptable range. However, this study is based on a small and heterogeneous sample of patients, meaning that the results should be interpreted with caution.

Conclusion

Arthroscopic reconstruction of the posterolateral angle of the knee joint in case of combined injury with rupture of the anterior cruciate ligament can be recommended as an alternative method compared to open reconstruction. The number of complications is low; however, it is important to note the progression of osteoarthritis and the potential risk of iatrogenic injury to the common peroneal nerve, which must be carefully protected during surgery.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. It is planned to determine the impact of restoration of the posterolateral angle of the knee joint structures on the development of secondary osteoarthritis of the knee joint and to evaluate the differential indications for partial restoration of the posterolateral angle structures at different degrees of their damage.

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RESULTS OF RECONSTRUCTION OF THE STRUCTURES OF THE POSTEROLATERAL CORNER IN COMBINATION WITH ANTERIOR CRUCIATE LIGAMENT SURGERY

M. L. Golovakha [1], A. A. Bezverkhyi [1], W. Orljanski [2]

[1] Zaporizhzhia State Medical and Pharmaceutical University. Ukraine
[2] Vienna Private Clinic. Austria

✉ Maxim Golovakha, MD, Prof. in Traumatology and Orthopaedics: golovahaml@gmail.com; https://orcid.org/0000-0003-2835-9333
✉ Andrii Bezverkhyi, MD: andreybezverxiyl9@gmail.com; https://orcid.org/0009-0000-4858-7865
✉ Weniamin Orljanski, MD, Prof. in Traumatology and Orthopaedics: orljanski@hotmail.com

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Patellar tendinopathy after arthroscopic meniscus resection, with «anterior knee pain» syndrome

A. S. Gerasymenko, O. E. Yurik, S. I. Gerasymenko, A. M. Babko, D. M. Poluliah, V. V. Hromadskyi

National Institute of Traumatology and Orthopedics of the NAMS of Ukraine, Kyiv

Patellar tendinopathy is a common problem in patients after arthroscopic interventions, accompanied by chronic pain and limitations in knee joint function. The purpose of the study was to analyze the dynamics of clinical and functional parameters in patients with patellar tendinopathy within 3 months after surgery and standard rehabilitation. Methods. The study involved 196 patients with diagnosed patellar tendinopathy (29.1 %) who underwent arthroscopic meniscus resection. All patients received a standard course of rehabilitation measures. Control was performed after 2 weeks, 6 weeks and 3 months, assessing the level of pain on the VAS scale, functional capacity on the KSS and AKPS scales, as well as quality of life on the SF-36 scale. Results. It was found that in patients who underwent comprehensive rehabilitation, the level of pain decreased from 6.9 ± 1.0 to (2.2 ± 0.6) points (68.12 % decrease). According to the AKPS scale, functional capabilities increased from 62 ± 4.4 to (64 ± 1.6) points (an increase of 3.2 %). The restoration of motor and psychological functions contributed to a significant improvement in the quality of life: the SF-36 score increased to (78.2 ± 4.6) points, which is 15% more than the initial score and confirms the effectiveness of integrated approaches. Conclusions. Analysis of the results shows that in patients who developed patellar tendinopathy after arthroscopic meniscus resection, even 3 months after surgery, the level of functional ability and quality of life remained lower than before surgery. Overall, physical functioning decreased by 6.7 % (from 75 to 70 points). Role limitations related to physical health decreased from 65 to 22. Psychological indicators also improved: emotional well-being rose from 50 to 75, although it remained below the preoperative level. Social functioning decreased from 88 to 78, a decrease of 11.36 %. Pain levels decreased by 27.3 % (from 55 to 70), but pain sensations remain pronounced. Thus, most indicators failed to reach preoperative levels, although significant progress in recovery and functionality has been observed.

Тендинопатія наколінка — поширена проблема в пацієнтів після артроскопічних втручань, що супроводжується хронічним болем і обмеженнями у функціональності колінного суглоба. Мета. Проаналізувати динаміку клінічних і функціональних показників у пацієнтів із тендинопатією наколінка протягом 3 міс. після хірургічного втручання та стандартної реабілітації. Методи. У дослідженні взяли участь 196 осіб із діагностованою тендинопатією наколінка (29,1 %) після артроскопічної резекції меніска. Усі пацієнти отримували стандартний курс реабілітаційних заходів. Контроль проводили через 2 і 6 тижнів, 3 міс., оцінюючи рівень болю за шкалою ВАШ, функціональні можливості — за шкалами KSS і AKPS, а також якість життя за SF-36. Результати. Виявлено, що в хворих після комплексної реабілітації рівень болю знизився з (6,9 ± 1,0) до (2,2 ± 0,6) бала (зменшення на 68,12 %). За шкалою AKPS функціональні можливості підвищилися з (62 ± 4,4) до (64 ± 1,6) бала (зростання на 3,2 %). Відновлення рухових і психологічних функцій сприяло значному підвищенню якості життя: SF-36 зросло до (78,2 ± 4,6) бала, що на 15 % більше початкового і підтверджує ефективність комплексних підходів. Висновки. Аналіз результатів довів, що у пацієнтів, у яких розвинулася тендинопатія наколінка після артроскопічної резекції меніска, навіть через 3 міс. після операції рівень функціональної здатності й якості життя залишився нижчим ніж до втручання. Фізичне функціонування знизилося на 6,7 % (з 75 до 70 бала). Обмеження фізичного здоров'я зменшилося з 65 до 22. Психологічні показники також покращилися, а емоційне благополуччя піднялося з 50 до 75. Щодо соціального функціонування, воно зменшилося з 88 до 78, що становить зниження на 11,36 %. Стосовно болю, рівень зменшився на 27,3 % (з 55 до 70), але больові відчуття все ще залишаються вираженими. Отже, більшості показників не вдалося досягти доопераційного рівня, хоча спостерігається значний прогрес у відновленні та функціональності. Ключові слова. Тендинопатія наколінка, артроскопія колінного суглоба; реабілітація; синдром «переднього болю» колінного суглоба.

Keywords. Patellar tendinopathy, knee arthroscopy; rehabilitation; anterior knee pain syndrome

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Introduction

Patellar tendinopathy is a common complication in patients with various types of knee injuries, presenting with pain, decreased function, and may lead to chronic movement disorders [1, 2]. Of particular concern is the development of tendinopathy in those who have undergone arthroscopic meniscal resection, one of the most popular surgical procedures for meniscal injuries in young and active individuals [3, 4]. Although this procedure is generally considered to be minimally invasive, several studies have reported postoperative complications, including tendinopathy and anterior pain syndrome [5].

According to J. Amestoy et al., after arthroscopic interventions, some patients report pain symptoms localized to the anterior part of the knee joint, have greater atrophy of the quadriceps femoris muscle, as well as a significant loss of electrical contractility and muscle strength 6 weeks after surgery compared with the control group, and worse postoperative functional outcomes. Postoperative anterior pain is observed in individuals who have undergone different types of knee joint interventions: anterior cruciate ligament reconstruction or total knee arthroplasty. However, the authors note that there are no studies that have analyzed postoperative anterior pain after arthroscopic partial meniscectomy [3]. Other investigators emphasize in a clinical case report that patellar tendinopathy is not common after arthroscopic knee procedures. These degenerative changes are a complex clinical problem that requires long-term treatment. Pain relief is achieved after a period of more than 8 months, and signs of knee ligament regeneration are observed after a year [5].

As of 2025, no study has been conducted to analyze the incidence of patellar tendinopathy in non-athletes who have undergone arthroscopic meniscal resection. Therefore, it is very important to determine the prevalence of anterior knee pain in patellar tendinopathy in patients after meniscal resection and to identify the impact on knee function and quality of life in this group of patients.

Purpose: To analyze the incidence of patellar tendinopathy, knee function, and the impact on quality of life in patients with anterior knee pain with existing patellar tendinopathy that developed after arthroscopic meniscal resection.

Material and methods

Study design and population

We conducted a prospective study that included the following stages: examination of patients before surgery, 14 days, 6 weeks and 3 months after surgery.

The study was performed at the clinical base of the Department of Joint Diseases in Adults of the State Institution "Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine" and was approved by the Bioethics Commission of this institution (rotocol No. 5 dated 09.02.2023).

The study involved 196 subjects with a meniscus resection performed using arthroscopic techniques (88 women aged (29.4 ± 6) years and 108 men (34.8 ± 6) years).

Inclusion criteria: patient age from 18 to 50 years, BMI < 30, confirmed meniscus injury (Stoller 3A-3B) on MRI, without injury to other intra-articular structures, arthroscopic intervention on the knee joint (resection of part of the meniscus), development of pain in the anterior part of the knee joint in the area of the patellar ligament, its tendinopathy according to clinical data within 14 days of surgical intervention.

Exclusion criteria: patients who had concomitant injuries of the knee joint structures (chondromalacia, damage to the anterior/posterior cruciate or collateral ligaments, loose bodies in the joint cavity) or dysplasia in the knee joint, high kneecap (patella alta), degenerative changes in the kneecap identified during MRI examination.

All patients provided written informed consent to participate in the study in accordance with the requirements of the Declaration of Helsinki (version 2013) and current legislation of Ukraine.

Research methods

Methods of subjective pain assessment used in the study included the visual analogue scale (VAS) [7], allowing the patients to independently assess the level of pain from 0 (absence) to 10 (maximum pain), the Knee Society Score (KSS), Kujala/Anterior knee pain score (AKPS) and Short Form Health Survey (SF-36).

The KSS classification consists of an assessment of knee pain and function and allocates a maximum of 100 points for the indicators of range of motion (1 point per 5°, maximum 125°), stability (medial/lateral (15 points) and anterior/posterior (10 points)) and pain (50 points) with deduction of extension lag, presence of flexion contracture and curvature (if the axis of the lower limb is < 5° or > 10° on radiographic examination). The maximum score of 100 points means a well-aligned knee joint with an amplitude of motion of 125°, almost complete absence of either anteroposterior or mediolateral instability, and pain. The functional analysis considers walking distance (50 points) and stair climbing (50 points) with the use of assistive devices. A patient who can walk with-

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out limitation and has no difficulty climbing stairs receives the maximum score on the Function Score subscale, 100 points.

The Anterior Knee Pain Scale (AKPS, Kujala) is a 13-item self-report questionnaire that measures subjective responses to certain activities and symptoms known to be associated with anterior knee pain syndrome. The AKPS is scored from 0 to 100, with 100 being the highest possible score. Lower scores reflect greater pain and disability.

Anterior knee pain often leads to impairments that cause difficulty performing activities that place stress on the knee joint (running, squatting, and climbing stairs), and the AKPS assesses these activities. This index has high test-retest reliability and is a valuable tool for studying the patient's condition over time [8, 9]. The four formats of the AKPS scale were found to have acceptable standard errors of measurement (0.82 to 3.00), high internal consistency (αcoef = 0.83–0.91), equivalence between the short and long forms (r = 0.98), and moderate to high criterion validity as determined by physician diagnosis: 0.92 (13-item form), 0.90 (long form), and 0.90 (short 6-item form). The AKPS questionnaire is an effective epidemiological screening tool with a valid and reliable assessment of anterior knee pain [10].

Another subjective method of the study was the use of the SF-36 scale [11], which assessed the quality of life of the subjects according to five main criteria: mobility, self-care, usual activities, pain/discomfort and psycho-emotional state. Patients filled out a questionnaire before treatment and during follow-up, which allowed to identify the impact of therapy on general well-being. The tool includes scales for physical and social functioning, role limitations due to physical or emotional problems, mental health, energy, pain and general perception of health. A high score corresponds to a better health status. The SF-36 questionnaire has been validated in patients with musculoskeletal conditions and is widely used in clinical practice.

A dynamic analysis was used to assess changes in pain, joint function, and quality of life over the entire follow-up period (preoperative, 14 days, 6 weeks, and 3 months postoperatively).

Clinical analysis

Clinical assessment is the most appropriate tool and standard criterion for diagnosing patellar tendinopathy.

The first clinical task is to determine whether the tendon is the source of the patient's symptoms. The most common finding on manual examination is focal tenderness [12, 13]. Although pain can occur along the entire length of the patellar tendon, it most commonly occurs at the lower part and distal attachment to the tibial tuberosity.

Pain has been reported to be exacerbated by weight-bearing on the knee extensors.

Functional tests for patients with patellar tendinopathy include jumping and landing afterwards [14].

The main differential diagnosis of this disease is patellofemoral pain syndrome, which is defined as a form of nonspecific, nonstructural pain in the knee, around or behind the kneecap. This syndrome is characterized by crepitus or "creaking" under the kneecap during knee flexion and tenderness along the patellar facets [34].

Statistical analysis was performed using standard approaches. The average values of patient indicators were used for it. Quantitative indicators (mean (M) and its standard deviation (SD)) in the study groups were compared with each other and in the time course of observation.

The relative reduction in the severity of symptoms (% reduction in pain intensity and functional improvement) was calculated. The incidence of complications was analyzed, which was presented as a percentage of the total number of patients.

Results

The main demographic and diagnostic characteristics of the participants: the mean age was (29.4 ± 6) years in women (18 %) and (34.8 ± 6) years in men (82 %). The mean body mass index (BMI) of the examined was (28.6 ± 6.0) kg/m^2. The most common type of surgical intervention performed on patients was arthroscopic resection of the damaged part of the meniscus (74 %) and debridement of fibrous growths that create impingement with articular structures (26 %).

Using clinical and instrumental examination (ultrasound) on the 14th day after surgery, patients were divided into 2 groups. Group 1 comprised patients exhibiting both clinical signs of tendinopathy and sonographic alterations in the patellar ligament, whereas group 2 consisted of patients without these manifestations.

Significant differences were found in the two groups of patients according to the above signs ($p < 0.001$). Table 1 presents the clinical symptoms of patellar tendinopathy and their manifestation on the 14th day after surgery.

Table 2 presents the sonographic signs of patellar tendinopathy and their manifestation by patient groups on the 14th day after surgery.

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Instrumental examination showed that patients with clinical symptoms of tendinopathy (group 1) had significant sonographic differences in the knee ligament, which were not observed in group 2 ($p < 0.001$). Patients in group 1 had changes in the smoothness of the ligament contour, a decrease in its echogenicity and increased vascularization, while group 2 patients were found to have the opposite sonographic presentation. In both groups, thickening of the patellar ligament was observed, which cannot be considered a characteristic change for tendinopathy and manifestations of pain syndrome ($p > 0.1$). Table 3 presents data on the time course of changes in the level of pain according to the pain scales and the function of patients during observation.

An examination of the results indicates that patients with patellar tendinopathy who undergo surgical intervention experience a slower-than-anticipated and incomplete recovery of knee joint function during rehabilitation.

According to the VAS scale, the pain level decreased by 68.12 %, from 6.9 to 2.2 points, but even after 3 months the pain remained relatively moderate and did not decrease significantly. This indicates that it persists and is still a concern, which is confirmed by the high proportion of patients with unsatisfactory or moderate function.

With respect to functional indicators, the KSS scale exhibited a decline of approximately 48.65 % after two weeks. While a notable improvement was recorded at three months, with an increase of 52.70 %, overall functioning remained suboptimal, reaching only 58 out of 100 points.

The level of AKPS indicators in patients with patellar tendinopathy demonstrates significant dynamics of the condition. Before surgery, it was 68 points. During the first 2 weeks after the intervention, this indicator deteriorated significantly and decreased to 28 points, manifesting a decrease of approximately 58.82 % from the initial level. This reflects a significant decrease in functional capacity in the postoperative period.

However, 6 weeks after surgery, an improvement was observed, the AKPS level increased to 54 points,

Table 1

Clinical symptoms of patellar tendinopathy and their manifestation in patients on the 14th day after surgery

Clinical symptom	Patient (n = 96)		Yates corrected Chi-square
	before surgery	14th day after surgery	
Focal pain in the lower (distal) part of the patellar tendon (infrapatellar point)	7 (3.6 %)	52 (26.5 %)	38.35
Pain along the tendon (diffuse)	4 (2.0 %)	48 (24.5 %)	41.00
Pain during resisted knee extension	17 (8.7 %)	55 (28 %)	23.29
Pain when squatting on the operated limb (single leg squat)	21 (10.7 %)	57 (29 %)	19.61
Pain associated with exercise (strengthening after jumping)	14 (7.1 %)	54 (27.5 %)	27.06
Pain during maximum vertical jump (decreased jump height)	9 (4.6 %)	55 (28 %)	37.81

Note. Pearson's criterion in all cases was $p < 0.001$.

Table 2

Sonographic signs of patellar tendinopathy and their manifestation by patient groups on the 14th day after surgery

Сонографічний параметр		Group 1 (n = 57)	Group 2 (n = 139)
Contours (evenness, clarity)	not changed	3 (5.3 %)	124 (89.2 %)
	changed	54 (94.7 %)	15 (10.8 %)
Ligament structure, thickness (compared to the opposite side)	enlarged	55 (96.4 %)	128 (92 %)
	not enlarged	2 (3.6 %)	11 (8 %)
Echogenicity	not changed	5 (8.8 %)	121 (87 %)
	changed (decreased)	52 (91.2 %)	18 (13 %)
Vascularization	not changed	5 (8.8 %)	133 (95.6 %)
	changed	52 (91.2 %)	6 (4.4 %)

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Table 3

Time course of changes in the studied parameters before and after surgical intervention in patients of groups 1 and 2 (M ± SD)

Parameter	VAS	Assessment by KSS		AKPS	p
		pain	function		
Group 1 (n = 57)					
Before surgery	6.9 ± 1.0	74 ± 5.2	62 ± 4.4	68 ± 4.3	p < 0.001
After surgery: 2 weeks	5.2 ± 1.2	38 ± 8.6	32 ± 7.2	28 ± 8.8	p < 0.001
6 weeks	3.8 ± 0.3	48 ± 6.5	52 ± 4.8	54 ± 5.8	p < 0.001
3 months	2.2 ± 0.6	58 ± 4.7	60 ± 3.8	64 ± 1.6	p < 0.050
Group 2 (n = 139)					
Before surgery	6.8 ± 1.1	76 ± 4.2	61 ± 4.7	89 ± 2.2	p < 0.001
After surgery: 2 weeks	3.9 ± 1.4	49 ± 7.4	46 ± 3.8	58 ± 8.5	p < 0.001
6 weeks	2.8 ± 0.2	62 ± 4.3	68 ± 6.9	77 ± 3.2	p < 0.001
3 months	1.2 ± 0.3	79 ± 4.5	82 ± 4.8	86 ± 3.6	p < 0.050

which is approximately 92.86 % more than the lowest level (28 points) and 20.59 % less than the initial 68. Despite some improvement in the dynamics of AKPS indicators, the level of residual symptoms and functional limitations were acutely felt even after 3 months, which indicates moderately satisfactory or unsatisfactory results.

This emphasizes the need to develop more effective rehabilitation and therapy methods for patients with patellar tendinopathy, since not all patients achieve full restoration of functions and reduction of pain. Fig. 1. shows the results of assessing the quality of life on the SF-36 scale in patients with clinical signs of this disease.

Analysis of the indicators shows that, despite significant recovery, in most patients who developed patellar tendinopathy, the level of quality of life after surgery remained lower compared to the preoperative state.

Physical functioning before the intervention was estimated at 75 points. In 3 months the indicator increased to 70 points, which is 13.3 % less than the initial one. Despite significant recovery, the level of physical functioning did not return to the preoperative level.

Role limitations due to physical health decreased from 65 to 22 — (67.16 %) — however, at the final stage, in the 3-month period, the level increased to 68 points. This means that patients were already able to perform role functions, but the level remained slightly lower than the initial one — only 3 %.

Role limitations due to emotional state decreased from 67 to 22 — a decrease of 67.18 %. After 3 months, this indicator increased to 65, by 38.6 % compared to the postoperative level, which indicates a partial improvement in the psychological state, but it remained worse than before the operation.

As for the energy/fatigue level, it decreased from 50 to 32, by 36.0 %. In 3 months, this indicator increased to 80, which is 60 % higher than the initial level, but much higher than the postoperative level. This indicates the restoration of vitality and energy potential, increased motivation.

Emotional well-being decreased from 65 to 50 (by 23.08 %). In 3 months, it increased to 75, which is 50 % higher than the minimum level after the operation and 15.38 % higher than the initial level.

The level of social functioning before surgery was 88 points. In 3 months, this indicator decreased to 78 (11.36 % less than before surgery). This indicated that although there was significant progress in restoring the social functioning of patients, there was no return to the preoperative level. As for pain, it changed from 55 to 70 (27.3 %), which indicates a rapid decline in pain, but it still remained quite pronounced. Analysis of the results shows that for most indicators, patients after surgery did not reach the level of quality of life that they had before surgery. Data after 3 months remain lower than before surgery (by 3–7 %), or at the level of 12–15 %, which indicates incomplete recovery and the need for additional rehabilitation measures to achieve full balance. There was a noticeable increase in energy and well-being; however, differences in social and physical functioning compared to preoperative indicators continued to be present.

Limitations

The study has a number of limitations that should be taken into account when interpreting the results:

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the age of the patients is over 50 years, the presence of obesity (BMI > 30). In particular, the analysis did not include patients with damage to the articular cartilage (chondromalacia 1–4 grades according to Outerbridge), the capsular-ligamentous apparatus of the knee joint (damage to the anterior/posterior cruciate or collateral ligaments, patellar tendons, quadriceps tendon injuries), osteoarthritis II–IV grades according to Kellgren-Lawrence, and dysplasia of the knee joints, which limits the possibility of extending the results to severe forms of the disease. Another limitation is the relatively short observation period, which did not exceed 3 months. This does not allow for an objective assessment of the long-term efficacy and safety of the studied methods of treatment and the risks of developing AKPS in the long term. Large-scale prospective studies with standardized treatment approaches, clear assessment criteria, and long-term follow-up are needed to draw definitive conclusions.

Discussion

The study was conducted using clinical scales (VAS, KSS, AKPS). The importance of early and comprehensive rehabilitation in patients with patellar tendinopathy after arthroscopic meniscus resection was confirmed. A notable reduction in pain and improvement of functional indicators is commonly observed in the short term in clinical settings; however, the presence of residual symptoms after 3 months reflects aspects of pathogenesis and regenerative processes within this cohort.

The results of our study coincide with the data of a number of authors who noted that the restoration of knee joint functionality is a slow process. Thus, A. Schwartz et al. have shown that in patients with tendinopathies of the knee joint, when using modern rehabilitation complexes (injection methods, eccentric exercises and surgical intervention), treatment with symptoms characteristic of such a nosology can last 24 months [18].

The psychological factor plays a significant role in recovery. According to B. Nwachukwu et al., psychological motivation and positive mood of patients are associated with high rates of functional recovery, and low levels of psychological support can cause prolonged recovery or chronicity of symptoms [19–21] in different groups of patients. Our results confirm this, since the increase in psychological indicators, such as emotional well-being and motivation, immediately correlated with the improvement of physical functions, which is relevant for the further application of complex approaches taking into account psychological support.

Another critical aspect is the nature of regenerative processes in tendons and muscle tissues after microtrauma. Numerous studies have demonstrated that regenerative processes in damaged knee ligaments occur slowly and are difficult to treat [22, 24–26]. In our observation, standard rehabilitation protocols were used, but residual symptoms indicate the need to integrate new technologies.

Taking into account modern experience, the use of robotic systems to restore lower limb functions has

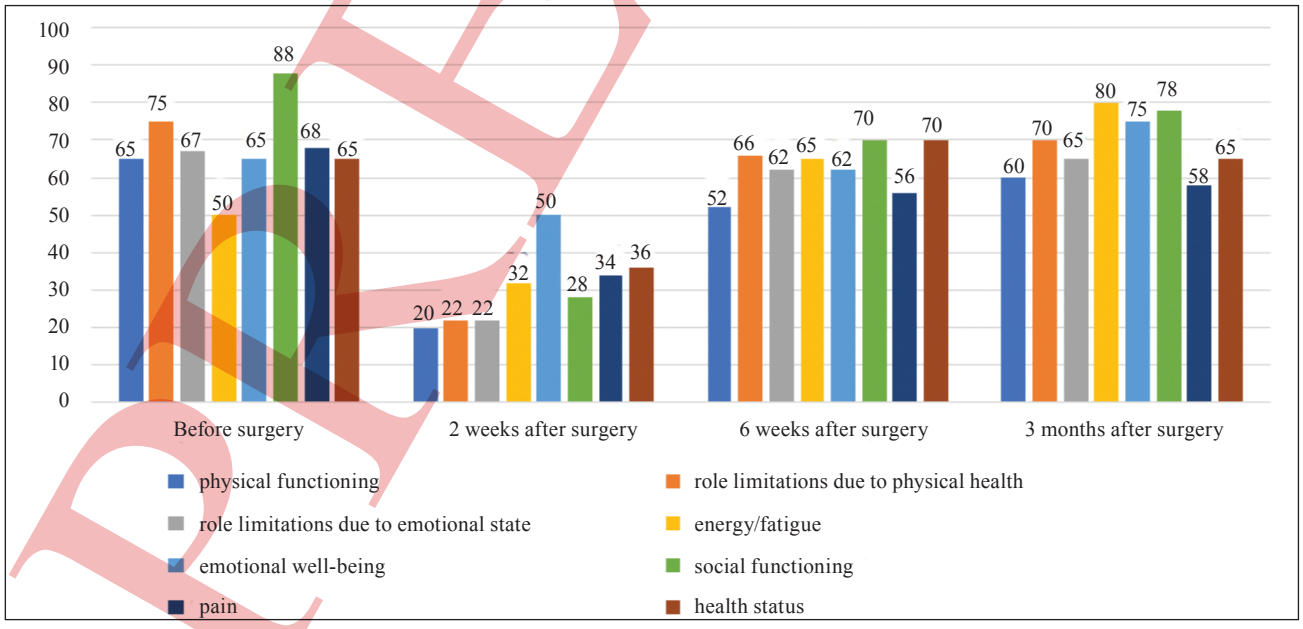

Figure. Results of the SF-36 quality of life assessment

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been shown in numerous studies. Thus, R. Riener et al. have shown the effectiveness of such systems in accelerating rehabilitation processes and reducing pain syndrome, especially in the case of chronic lesions [27–30].

In addition, an important aspect is an individual approach and the use of combined therapy methods that combine physiotherapy, psychological support and modern technologies. Therefore, we emphasize the importance of a multidisciplinary approach to restoring functions and reducing symptoms in case of damage to the musculoskeletal system.

The study showed that patients with patellar tendinopathy after arthroscopy have significant difficulties in restoring knee joint functionality, as evidenced by insufficient pain relief and residual limitations even 3 months after surgery. This is consistent with the literature, which indicates that such chronic tendinopathies have a complex pathogenesis and require a long-term and comprehensive approach to treatment [32–34]. They develop due to microdamage in the patellar ligament due to overload, degenerative changes or impaired blood supply, which complicates rapid recovery.

Overall, our findings emphasize the importance of a comprehensive approach to the treatment and rehabilitation of patients with patellar tendinopathy after arthroscopic treatment. There is a pressing requirement for more extensive research employing advanced technologies and tailored interventions.

Conclusions

Analysis of the results indicates that patients who experienced patellar tendinopathy following arthroscopic meniscus resection exhibited reduced levels of function and quality of life for at least three months postoperatively. In particular, the level of physical functioning decreased by 6.7 % (from 75 to 70 points), which indicates the inability to fully restore physical capabilities. Role limitations due to physical health decreased from 65 to 22, by 67.16 % but by the 3-month period the level increased to 68 and remained slightly lower than the initial level (by 3 %).

Psychological indicators also improved: the level of role limitations due to emotional state decreased from 67 to 22, but after 3 months it increased to 65 (by 38.6 %) from the postoperative level and remained 2.99 % lower than the initial level. The level of energy/fatigue increased from 50 to 80 points — 60 % higher than the initial level, which indicates the restoration of vitality and motivation. Emotional well-being increased from 50 to 75, by 50 % but its level remained 15.38 % lower than the initial level. Similarly, social functioning decreased by 11.36 % (from 88 to 78), recovering only partially.

From the point of view of pain syndrome, the level decreased by 27.3 % (from 55 to 70), which indicates a rapid improvement, but pain sensations still remained pronounced.

Thus, by most measures, patients did not achieve the level of quality of life that was before the operation, regardless of significant progress in the restoration of certain functional areas. This emphasizes the need for the implementation of additional rehabilitation measures to achieve full balance and restore functionality.

Conflict of interest. The authors declare that there is no conflict of interest.

Prospects for further research. According to the authors, future studies should pay attention to the role of rehabilitation programs and their impact on the recovery process of patients. Studies can also study the relationship between individual anatomical features of the knee joint and the risk of developing tendinopathy. In addition, it is necessary to study the long-term results of various therapeutic approaches to better understand their effectiveness in preventing and treating this condition, and to study the role of psychological factors and pain level in shaping long-term consequences and the treatment process. An important direction of research development is the creation of individualized rehabilitation protocols for patients with different degrees of damage and risk profiles, using modern instrumental methods, such as robotic orthoses. Advancing diagnostic precision through high-resolution ultrasound or MRI techniques enables a more accurate characterization of tendinopathy, while facilitating the examination of autonomic regulation in the lower limb.

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Authors' contribution. Gerasimenko S. I., Poluliakh D. M., Gerasimenko A. S. — concept and design of the study, analysis of the obtained data, editing of the article; Babko A. M. — statistical processing and analysis of the obtained data; Hromadsky V. V. — selection of patients, diagnosis, literature review, editing of the article; Yurik O. E. — development of the rehabilitation program.

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PATELLAR TENDINOPATHY AFTER ARTHROSCOPIC MENISCUS RESECTION, WITH «ANTERIOR KNEE PAIN» SYNDROME

A. S. Gerasymenko, O. E. Yurik, S. I. Gerasymenko, A. M. Babko, D. M. Poluliah, V. V. Hromadskyi

National Institute of Traumatology and Orthopedics of the NAMS of Ukraine, Kyiv

✉ Andrii Gerasymenko, MD, PhD, DSc: corado734@ukr.net; https://orcid.org/0000-0002-6378-1196
✉ Olha Yurik, MD: olhayuryk01@gmail.com; https://orcid.org/0000-0003-2245-9333
✉ Sergii Gerasymenko, MD, PhD, DSc, Prof.: kievorto3@gmail.com; https://orcid.org/0000-0002-6378-1196
✉ Andrii Babko, MD, PhD, DSc, Prof.: orthokiev@i.ua; https://orcid.org/0000-0001-5919-5429
✉ Dmytro Poluliah, PhD: dmpoluliakh@gmail.com; https://orcid.org/0000-0002-8895-6917
✉ Vadym Hromadskyi, MD: gromadsky94@gmail.com; https://orcid.org/0000-0002-4399-4741

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The effect of carboxytherapy and its combination with diclofenac sodium and chondroitin sulfate on TNF-A and TGF-B1 expression in monoiodoacetate-induced osteoarthritis in rats

V. V. Shtroblia [1], R. V. Lutsenko [2]

[1] Uzhhorod National University. Ukraine
[2] Poltava State Medical University. Ukraine

Osteoarthritis remains one of the leading causes of disability worldwide, associated with chronic inflammation and progressive destruction of articular cartilage. Current therapeutic approaches show limited efficacy in restoring damaged tissues, which drives interest in novel adjuvant methods, particularly physiotherapeutic techniques such as carboxytherapy. Objective. To investigate the effects of carbon dioxide monotherapy and its combinations with diclofenac sodium or chondroitin sulfate on the expression of the pro-inflammatory cytokine TNF-α and the regenerative factor TGF-β1 in rats with experimentally induced osteoarthritis. Methods. An osteoarthritis model was induced by intra-articular injection of monoiodoacetic acid. Treatment included CO_2 monotherapy or its combination with chondroitin sulfate or diclofenac sodium. On days 14 and 28, serum levels of TNF-α and TGF-β1 were measured using the ELISA method. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test; 95 % confidence intervals and effect sizes (Cohen's d) were calculated. Results. All interventions involving CO_2 led to a statistically significant reduction in TNF-α levels on days 14 and 28 (ANOVA: $F = 2551$ and $F = 4057$, respectively; $p < 0.001$), with the most pronounced effect observed in the «CO_2 + diclofenac» group (a decrease of –54.7 %). Concurrently, an increase in TGF-β1 levels was noted across all treatment groups (ANOVA: $F = 1492$ and $F = 3492$; $p < 0.001$), particularly in the «CO_2 + chondroitin» group (+99.4 % compared to the pathology group). Large effect sizes were recorded for key comparisons (Cohen's $d > 0.8$), indicating the clinical relevance of the observed changes. Conclusions. The combined application of carboxytherapy with diclofenac sodium or chondroitin sulfate promotes a reduction in inflammatory response and activation of regenerative mechanisms in an osteoarthritis model, supporting the rationale for further preclinical and clinical investigations.

Остеоартрит залишається однією з провідних причин інвалідизації у світі через хронічні запалення і поступову деструкцію суглобового хряща. Сучасні терапевтичні підходи мають обмежену ефективність у відновленні уражених тканин, що зумовлює інтерес до нових ад'ювантних методів, зокрема фізіотерапевтичних, таких як карбокситерапія. Мета. Дослідити вплив монотерапії вуглекислим газом і його комбінацій з диклофенаком натрію або хондроїтином сульфатом на експресію прозапального цитокіну TNF-α і регенераторного фактора TGF-β1 у щурів із експериментальним остеоартритом. Методи. Модель остеоартриту відтворювали шляхом внутрішньосуглобового введення монойодоцтової кислоти. Лікування включало монотерапію CO_2 або його поєднання з хондроїтином сульфатом чи диклофенаком натрію. На 14-й і 28-й день визначали рівні TNF-α і TGF-β1 у сироватці крові методом ELISA. Для статистичного аналізу застосовували однофакторний дисперсійний аналіз (ANOVA) з пост-хок тестом Тьюкі; обчислювали 95 % довірчі інтервали й ефекти розміру (Cohen's d). Результати. Усі втручання, що включали CO_2, спричиняли статистично значуще зниження рівня TNF-α на 14-й і 28-й день (ANOVA: $F = 2551$ та $F = 4057$ відповідно; $p < 0,001$), із найбільш вираженим ефектом у групі «CO_2 + диклофенак» (зниження до –54,7 %). Паралельно в усіх терапевтичних групах відзначено підвищення рівня TGF-β1 (ANOVA: $F = 1492$ і $F = 3492$; $p < 0,001$), особливо в групі «CO_2 + хондроїтин» (+99,4 % до патології). Для основних порівнянь зафіксовано великі розміри ефекту (Cohen's $d > 0,8$), що вказує на клінічну релевантність змін. Висновки. Комбіноване застосування карбокситерапії з диклофенаком натрію або хондроїтином сульфатом спричинює зниження запального компонента й активацію регенераторних механізмів у моделі остеоартриту, що обґрунтовує доцільність подальших доклінічних і клінічних досліджень. Ключові слова. Остеоартрит; карбокситерапія; CO_2; диклофенак натрію; хондроїтину сульфат; TNF-α; TGF-β1; експериментальна модель; монойодоцтова кислота; комбіноване лікування.

Keywords. Osteoarthritis; carboxytherapy; CO_2; diclofenac sodium; chondroitin sulfate; TNF-α; TGF-β1; experimental model; monoiodoacetic acid; combined treatment

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Introduction

Osteoarthritis (OA) is one of the most common musculoskeletal conditions, affecting more than 300 million people worldwide, experiencing a significant increase due to the aging of the population [1]. Characterized as a chronic degenerative-inflammatory disease of the joints, OA leads to significant limitation of mobility, chronic pain and a decrease in the quality of life of patients [2]. Its pathogenesis is extremely complex and involves the interaction of local (mechanical) and systemic (metabolic and immunological) factors that cause progressive degeneration of articular cartilage, remodeling of subchondral bone, synovitis and neoangiogenesis [3, 4].

One of the key components of the pathophysiology of OA is inflammation mediated by pro-inflammatory cytokines, among which tumor necrosis factor-alpha (TNF-α) and interleukin-1β (IL-1β) play a leading role [5]. They activate the NF-κB and p38MAPK signaling pathways, which induce the expression of matrix metalloproteinases (MMPs), cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and lead to chondrocyte apoptosis and extracellular matrix degradation [4, 6]. In addition, TNF-α is able to disrupt TGF-β-dependent signal transduction in chondrocytes by inhibiting Smad signaling, which in turn prevents cartilage regeneration and extracellular matrix synthesis [7, 8]. Despite significant progress in understanding the pathogenesis of OA, effective disease-modifying agents are still lacking [9]. The mainstay of treatment remains nonsteroidal anti-inflammatory drugs (NSAIDs), particularly diclofenac sodium, which, although effective in relieving pain, has serious side effects (gastrointestinal, renal, cardiovascular) with prolonged use [10, 11]. This has prompted the scientific community to search for safer alternative or adjuvant therapies [12]. One promising approach is carboxytherapy, the therapeutic use of carbon dioxide (CO_2), which has historically been used in vascular diseases and is now considered a potential anti-inflammatory agent. CO_2 therapy is increasingly gaining attention as a tool for modulating the tissue microenvironment by improving oxygenation, blood flow, stimulating angiogenesis, and inhibiting pro-inflammatory cytokines such as TNF-α and IL-6 [15]. The mechanisms of action of CO2 therapy include activation of VEGF and TGF-β, induction of nitric oxide synthase, and reduction of HIF-1α levels, suggesting its potential efficacy in the treatment of hypoxia-induced and chronic inflammatory damage.

Of particular scientific interest is the potential for combining carboxytherapy (CO_2) with traditional treatments for osteoarthritis. One promising avenue is the combination of CO_2 with nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac sodium. This combination may enhance the anti-inflammatory effects of NSAIDs, allowing for a reduction in the required dosage and, consequently, minimizing the risk of side effects — an essential consideration given the chronic use of NSAIDs in osteoarthritis management.

Additionally, the use of CO_2 in combination with chondroitin sulfate, a well-known chondroprotector with regenerative and partially anti-inflammatory properties, could potentially promote chondrogenesis and help stabilize the tissue microenvironment. Some research suggests that CO_2 might simultaneously reduce inflammation and stimulate tissue repair mechanisms, potentially through the regulation of cytokines. This dual action, both anti-inflammatory and regenerative, opens up new possibilities for improving the clinical management of osteoarthritis, particularly in cases where conventional treatments fall short.

At the same time, the effect of combining CO_2 with diclofenac sodium or chondroitin sulfate on the expression of key pro-inflammatory and anti-inflammatory markers in an animal model of osteoarthritis (OA) remains insufficiently studied and requires further investigation and verification. The model of osteoarthritis induced by intra-articular injection of monoiodoacetic acid (MIOA) is widely used to study the effectiveness of new therapeutic approaches. This model reliably reproduces the key pathomorphological signs of OA, including synovitis, cartilage erosion, synovial hyperplasia, and increased expression of TNF-α [13, 14]. Utilizing this model enables an objective assessment of inflammatory biomarkers and allows for the monitoring of morphological changes in joints under the influence of experimental interventions.

In previous experimental studies, we demonstrated the effectiveness of carboxytherapy (CO_2) both in monotherapy and in combination with traditional anti-inflammatory agents (diclofenac sodium, chondroitin sulfate) in formalin and carrageenan models of inflammation in rats. In particular, analgesic [16], anti-inflammatory [17], and antioxidant properties of CO_2 were revealed [18, 19]. The combined use of CO_2 with NSAIDs or chondroprotectors demonstrated a synergistic effect, which was manifested in a decrease in the intensity of pain, edema, temperature, a decrease in pro-inflammatory markers (integrated indices of inflammation and immune response in rats with a carrageenan model of inflammation) and an

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increase in antioxidant protection [20, 21]. The results obtained became the basis for further study of the effect of CO_2 in the OA model in rats.

Objective: to experimentally study the effect of carbon dioxide monotherapy, as well as its combined use with diclofenac sodium or chondroitin sulfate on the expression level of tumor necrosis factor-α (TNF-α) and transforming growth factor-β1 (TGF-β1) in a model of osteoarthritis induced by monoiodoacetic acid in rats.

Material and methods

The study used 80 sexually mature white outbred male rats (body weight 180–220 g), which were kept in standard vivarium conditions: air temperature — 21–23 °C, relative humidity — 50–60 %, light regime — 12 h light / 12 h dark. The animals had free access to water and standard laboratory food. Before the start of the experiment, all rats underwent 7-day acclimatization. All animal manipulations were carried out in accordance with the International Directive on the ethical use of laboratory animals (Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes).

The osteoarthritis model was reproduced according to the modified protocols of M. Udo et al. [22] and R. Riewruja et al. [23]. Under ether anesthesia, rats were injected once with 0.05 ml of 3 % solution of MIOA into the cavity of the right knee joint of the hind limb. The solution was prepared ex tempore in 0.9 % NaCl. The control (intact) group was injected with an equivalent volume of saline.

Twenty-four hours after the induction of osteoarthritis, the animals were randomized into eight groups (five animals per subgroup) to assess the effects of therapy on the 14th and 28th days:

– intact animals (I) — without interventions;

– intact + NaCl (II) — intraperitoneal administration of 0.9 % NaCl;

– MIOA (III) — pathology group (osteoarthrosis without treatment);

– MIOA + diclofenac 8 mg/kg (IV) — intraperitoneally;

– MIOA + chondroitin sulfate 3 mg/kg (V) — intraperitoneally;

– MIOA + CO_2 0.5 ml (VI) — subcutaneously, periarticularly;

– MIOA + diclofenac sodium 4 mg/kg + CO_2 0.5 ml (VII) — combination therapy;

– MIOA + chondroitin sulfate 3 mg/kg + CO_2 0.5 ml (VIII) — combination therapy.

Diclofenac sodium (4 or 8 mg/kg) and chondroitin sulfate (3 mg/kg) were administered intraperitoneally every 3 days according to the protocol, based on the effectiveness of such doses in animal models of osteoarthritis [11, 32]. Carbon dioxide was applied locally — subcutaneously above the affected knee (0.5 ml every 3 days) for 14 or 28 days.

On the 14th or 28th day of the experiment, the animals were euthanized in accordance with the recommendations of the AVMA Guidelines for the Euthanasia of Animals (2020). Thiopental sodium was used to induce anesthesia at a dose of 50 mg/kg intraperitoneally. The state of deep anesthesia was determined by the absence of reflexes (corneal and painful) and a decrease in respiratory rate. After confirmation of deep anesthesia, cardiopuncture was performed with subsequent blood sampling until cardiac arrest.

Serum was obtained by centrifugation at 3000 rpm for 10 min at +4 °C and stored at −20 °C until analysis.

The concentrations of cytokines TNF-α and TGF-β1 in serum were determined by sandwich ELISA in triplicate using commercial kits FineTest® (China):

– TNF-α — Rat TNF-α ELISA Kit, cat. no. ER1 393; measurement range: (3.906–250) pg/ml; sensitivity: 2.344 pg/ml.

– TGF-β1 — Rat TGF-β1 ELISA Kit, cat. no. ER1 378; measurement range: (31.25–2000) pg/ml; sensitivity: 18.75 pg/ml.

Before the analysis, all reagents were incubated at room temperature for 20 min. The washing buffer was prepared by diluting with distilled water in a ratio of 1 : 25 according to the manufacturer's instructions.

Optical density was measured at a wavelength of 450 nm using a LabLine-026 microplate photometer.

Cytokine concentrations were calculated based on calibration curves using CurveExpert 1.4 software, which provides automatic selection of a mathematical model for constructing a standard curve.

The changes in the levels of the pro-inflammatory cytokine TNF-α and the anti-inflammatory mediator TGF-β1 in the serum of rats with experimental osteoarthritis was studied on the 14th and 28th day of treatment with different therapeutic regimens using carboxytherapy both in the case of monotherapy and combined use with traditional drugs (diclofenac sodium, chondroitin sulfate).

Statistical data processing was performed using Jamovi software, version 2.3.21. The results are presented as mean ± standard deviation (M ± SD). Normality of distribution was checked using the Shapiro–Wilk test.

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For intergroup comparisons with normal distribution, Welch's t-test or ANOVA with Tukey's post hoc test was used. In case of deviation from normality, the Kruskal–Wallis test with Bonferroni correction was used. Results were considered statistically significant at $p < 0.05$. For the main comparisons, 95 % confidence intervals (CI) and effect sizes (Cohen's d) were calculated, which allows assessing both the statistical and clinical significance of the results.

Results and their discussion

The study showed that under the conditions of a single injection of 0.05 ml of 3 % MIOA solution into the knee joint cavity of experimental animals, a long-term significant increase in both TNF-α and TGF-β1 levels was observed, which indicates the presence of an inflammatory process (Table 1).

Thus, on day 14, a significant increase in TNF-α levels was observed in group III — (29.97 ± 0.50) pg/ml, which was 4.36 times higher than the value of the intact group ((6.87 ± 0.44) pg/ml, $p < 0.001$). All interventions that included the use of CO_2 — both as monotherapy and in combination with diclofenac or chondroitin — significantly reduced TNF-α levels compared to group III (ANOVA: $F = 2,551$, $df = 7$; 13.5; $p < 0.001$). The greatest decrease in TNF-α levels was found in group VII — (18.81 ± 0.28) pg/ml (37.3 % reduction relative to pathology; Mean difference = –11.16, 95 % CI [–11.66; –10.66], Cohen's $d = –27.5$; $p < 0.001$). The combination of chondroitin with CO_2 was also effective: (22.15 ± 0.35) pg/ml (–26.1 %, $p < 0.001$, Cohen's $d = –18.1$).

The difference in TNF-α levels between group III and all treated experimental groups (IV; V; VI; VII; VIII) was statistically significant (ANOVA: $F = 2,551$, $df = 7$; 13.5; $p < 0.001$).

On day 28, TNF-α levels remained elevated in group III ((29.59 ± 0.10) pg/ml). The lowest values were observed in group VII — (13.41 ± 0.52) pg/ml (–54.7 %, $p < 0.001$; Cohen's $d = –43.2$), while in group VIII the TNF-α level was (20.17 ± 0.45) pg/ml (–31.8 %; $p < 0.001$; Cohen's $d = –24.3$).

The difference in TNF-α levels between group III and all experimental groups remained statistically significant on the 28th day of observation (ANOVA: $F = 4,057$; $df = 7$; 12.8; $p < 0.001$).

Thus, the use of MIOA led to a significant increase in TGF-β1 levels — from (567.12 ± 19.4) pg/ml (intact) to (840.56 ± 7.87) pg/ml in group III (+48.2 %; $p < 0.001$).

On day 14, the highest level of TGF-β1 was recorded in group VIII — (1570.12 ± 18.50) pg/ml (an increase of 86.9 % compared to MIOA, $p < 0.001$; Mean difference = +730, 95 % CI [704.1; 755.9], Cohen's $d = 22.0$). The combination of CO_2 with diclofenac also showed efficacy: (1202.30 ± 11.56) pg/ml (+43.1 %; $p < 0.001$; Cohen's $d = 11.6$).

The difference in TGF-β1 levels between group III and all experimental groups receiving treatment (IV; V; VI; VII; VIII) was statistically significant (ANOVA: $F = 1,492$; $df = 7$; 13.5; $p < 0.001$).

On day 28, the highest value of TGF-β1 levels was again found in group VIII — (1658.91 ± 14.66) pg/ml, which is 99.4 % higher than pathology ((831.89 ± 6.19) pg/ml; $p < 0.001$, Mean difference = +827, CI [805.7; 848.3], Cohen's $d = 26.7$). The combined regimen with diclofenac + CO_2 maintained high values ((1226.35 ± 5.91) pg/ml, +394.5 pg/ml, Cohen's $d = 12.7$, $p < 0.001$).

The difference in the level of TGF-β1 between group III and all experimental groups remained statistically significant on the 28th day of observation (ANOVA: $F = 3,492$; $df = 7$; 12.6; $p < 0.001$).

In the groups that received treatment (IV; V; VI; VII; VIII), the level of TNF-α significantly decreased between the 14th and 28th days ($p < 0.001$). The largest decrease was recorded in group IV — by 9.28 % (from 25.43 to 23.07 pg/ml).

In parallel, a statistically significant increase in TGF-β1 levels was observed in all the indicated therapeutic groups, most significantly in group V by 206.2 pg/ml (+19.5 %, $p < 0.001$).

In this case, the results obtained indicate the prospects for the use of carboxytherapy (CO_2) as a monotherapeutic approach, as well as in combination with NSAIDs (diclofenac sodium) and chondroprotectors (chondroitin sulfate) in the conditions of an experimental model of OA induced by monoiodoacetic acid. In the groups receiving CO_2, a significant decrease in TNF-α levels was observed on the 14th and 28th day of the experiment, which indicates the anti-inflammatory potential of carboxytherapy. The most pronounced decrease (–54.7 %) relative to the pathology group was recorded in animals that were administered CO_2 in combination with diclofenac, which suggests the presence of a synergistic effect between these compounds.

One possible mechanism for this synergy is the effect of CO_2 on MAPK-dependent regulation of proinflammatory cytokines, including TNF-α and IL-6 [24]. In addition, CO_2 is known to promote local vasodilation, improve microcirculation and activate endothelial NO synthase, which leads to improved tissue oxygenation and create conditions for the repair

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Table

Effect of CO_2 in monotherapy and combinations on the levels of pro-inflammatory cytokine TNF-α and anti-inflammatory factor TGF-β1 in the serum of rats with experimental osteoarthritis (14^{th} and 28^{th} day of observation)

Animal group	Day 14 TNF-α, pg/ml	Day 28 TNF-α, pg/ml	Day 14 TGF-β1, pg/ml	Day 28 TGF-β1, pg/ml
I	6.87 ± 0.44	6.87 ± 0.44	567.12 ± 19.40	567.12 ± 19.40
II	6.85 ± 0.33	6.85 ± 0.32	572.15 ± 21.25	572.15 ± 21.25
III	29.97 ± 0.50	29.59 ± 0.10	840.56 ± 7.87	831.89 ± 6.19
IV	25.43 ± 0.71***	23.07 ± 0.56***	917.93 ± 7.73***	907.25 ± 1.81***
V	27.90 ± 0.20***	26.55 ± 0.57***	1055.69 ± 26.13***	1261.88 ± 20.63***
VI	28.09 ± 0.66***	26.42 ± 0.35***	1133.62 ± 13.59***	1192.39 ± 20.42***
VII	18.81 ± 0.28***	13.41 ± 0.52***	1202.30 ± 11.56***	1226.35 ± 5.91***
VIII	22.15 ± 0.35***	20.17 ± 0.45***	1570.12 ± 18.50***	1658.91 ± 14.66***
Statistical significance of between-group difference	F (7; 13.5) = 2 551, p < 0.001	F (7; 12.8) = 4 057, p < 0.001	F (7; 13.5) = 1 492, p < 0.001	F (7; 12.6) = 3 492, p < 0.001
Shapiro-Wilk test	W = 0.985; P = 0.877	W = 0.986; P = 0.892	W = 0.985; P = 0.849	W = 0.969; P = 0.331

Notes: Data are presented as mean ± standard deviation (n = 5 in each group). No statistically significant deviations from normal distribution were found for all variables (Shapiro–Wilk test, p > 0.05), which allowed the use of one-way analysis of variance (ANOVA) with Tukey's post hoc test. *** p < 0.001 — significant difference compared to the pathology group.

of damaged structures [25, 26]. Although most of these effects have been studied in the skin, similar microvascular responses may also be relevant for joint tissues, especially the subchondral plate. In our study, an increase in the level of TGF-β1, a cytokine that plays an important role in chondrogenesis and cartilage matrix repair, was also recorded. The highest levels of TGF-β1 (1658.91 ± 14.66) pg/ml were found in the group receiving chondroitin sulfate in combination with CO_2. It is known that TGF-β1 stimulates the production of aggrecan, proteoglycans and type II collagen in chondrocytes, which ensures the renewal of the extracellular matrix [27].

The obtained data emphasize the potential of carboxytherapy as an adjuvant approach in the treatment of OA. High expression of TGF-β1 in group VIII correlates with the activation of reparative processes in articular cartilage, which is consistent with the literature data on the role of TGF-β1 as a key mediator of chondrogenesis, maintenance of tissue homeostasis and cartilage remodeling [28]. At the same time, it should be noted that with prolonged stimulation, TGF-β1 may also play a fibrogenic role, which necessitates further observation and morphological analysis of its long-term effects.

Indirect confirmation of the reparative potential of CO_2 is provided by the data of R. Amano-Iga et al. [29], where it was proven in a skin injury model that percutaneous CO_2 administration stimulates the expression of VEGF and TGF-β, and also suppresses HIF-1α, IL-6 and IL-1β, which is accompanied by accelerated tissue healing. Despite the different type of model, the general mechanisms — anti-inflammatory effect, activation of growth factors — may be relevant for cartilage tissue. Similarly, in the study of K. Takeshita et al. [30] it was shown that hypercapnic state inhibits cytokine-induced activation of NF-κB, and the work of C. Brandi et al. [31] demonstrated the ability of CO_2 to improve microcirculation and stimulate tissue regeneration. These effects create a favorable microenvironment for repair, in particular through stimulation of TGF-β1.

In addition to statistical significance, the effects obtained are potentially clinically relevant: the effect size values (Cohen's d > 0.8) for the reduction in TNF-α and the increase in TGF-β1 indicate pronounced biological changes. This may provide the basis for the development of combined therapeutic strategies with the possibility of reducing the dosage of NSAIDs, which in turn will reduce the risk of side effects and potentially enhance the chondroprotective effect of the treatment.

At the same time, the interpretation of the obtained results should take into account certain limitations. First, the study was conducted on an animal model, which only partially reflects the pathophysiology of human osteoarthritis. Second, the number of animals in each group was limited (n = 5), which reduces statistical power. Third, the study did not include morphological analysis of tissues (histology, immunohistochemistry), which narrows the completeness of the morphofunctional interpretation. In addition,

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only two cytokines (TNF-α, TGF-β1) were studied, while other important mediators of inflammation and matrix degradation, such as IL-1β, IL-6, IL-17, MMP-13, remained outside the scope of the analysis.

Given this, further studies should be aimed at expanding the molecular profile, morphological confirmation of changes in tissues, increasing the sample, and studying the effectiveness of combined CO_2 therapy in clinical models.

Conclusions

Carboxytherapy (CO_2) demonstrated a pronounced anti-inflammatory effect, as evidenced by a significant decrease in the level of the pro-inflammatory cytokine TNF-α in rats with experimental osteoarthritis on both the 14th and 28th day of observation.

The use of CO_2 in combination with diclofenac sodium or chondroitin sulfate enhanced the anti-inflammatory effect, providing greater efficacy compared to monotherapy. The most pronounced decrease in TNF-α was recorded in group VII.

Simultaneously with the anti-inflammatory effect, combined treatment with CO_2 promoted the stimulation of reparative processes, which was confirmed by a significant increase in the level of TGF-β1, especially in group VIII, where the highest values of this indicator were recorded.

The effect sizes (Cohen's $d > 0.8$) in key comparisons confirm not only the statistical but also the potential clinical significance of the use of CO_2 as an adjuvant therapeutic factor in osteoarthritis.

The obtained data confirm the feasibility of further preclinical studies aimed at elucidating the molecular mechanisms of action of CO_2, with the prospect of transitioning to clinical trials for the development of combined strategies for the treatment of OA using carboxytherapy.

Conflict of interest. The authors declare the absence of a conflict of interest.

Prospects for further research. In the future, further studies are needed, in particular, morphological verification of the effects of CO_2 both in monotherapy and in combination with diclofenac sodium or chondroitin sulfate, assessment of long-term effects on cartilage tissue, as well as expansion of the panel of studied mediators, including cytokines (IL-1β, IL-6, VEGF) and cartilage matrix degradation enzymes, in particular MMP-1, MMP-3, MMP-13, as well as aggrecanases ADAMTS-4 and ADAMTS-5. Of particular importance is the clinical validation of the results obtained, by conducting studies on the effectiveness of carboxytherapy in combination with diclofenac or chondroitin in real clinical practice of treating osteoarthritis.

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Contribution of the authors. Shtroblya V. V. — study concept, experimental work, statistical analysis, interpretation of results, drafting the main text of the article; Lutsenko R. V. — scientific supervision, correction of the study design, critical editing, generalization of conclusions.

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THE EFFECT OF CARBOXYTHERAPY AND ITS COMBINATION WITH DICLOFENAC SODIUM AND CHONDROITIN SULFATE ON TNF-A AND TGF-B1 EXPRESSION IN MONOIODOACETATE-INDUCED OSTEOARTHRITIS IN RATS

V. V. Shtroblia [1], R. V. Lutsenko [2]

[1] Uzhhorod National University. Ukraine
[2] Poltava State Medical University. Ukraine

✉ Viktor Shtroblia, MD: viktor.shtroblia@uzhnu.edu.ua; https://orcid.org/0009-0003-3299-4329
✉ Ruslan Lutsenko, MD, DMSci, Prof.: farmaluru@gmail.com; https://orcid.org/0000-0003-0277-0458

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Risk factors for recurrent vertebral compression fractures after percutaneous vertebroplasty in osteoporotic patients: a systematic review and meta-analysis

A. I. Popov [1], M. V. Moloduk [1], V. O. Kutsenko [1], M. M. Nessonova [2]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] Private higher educational institution «Kharkiv International Medical University». Ukraine

Recurrent vertebral compression fractures (rVCFs) after percutaneous vertebroplasty (PVP) impair quality of life in osteoporotic patients, yet their risk factors remain debated, necessitating a systematic evaluation. Objective. To synthesize clinical data and quantitatively assess the impact of demographic, morphometric, and technical factors on rVCF incidence post-PVP. Methods. A search was conducted in PubMed, Scopus, Medline, and Google Scholar (2010–2024) using MeSH terms: «vertebroplasty», «compression fractures», «osteoporosis», «risk factors», «recurrence». Twenty cohort studies (7,923 patients) were included. Continuous variables were pooled using the Sidik–Jonkman random-effects model (Cohen's d), and categorical variables using the Paule–Mandel model (odds ratio, OR). Heterogeneity was assessed with I^2 and prediction intervals; sensitivity analyses were performed. Evidence certainty was evaluated using GRADE. Results. Significant risk factors for rVCFs included absence of anti-osteoporotic therapy (AOT) (OR = 1.97, I^2 = 40 %), cement leakage (OR = 1.92, I^2 = 68 %), and low bone mineral density (BMD) (d = –0.55, I^2 = 72 %), with moderate GRADE certainty. Female sex (OR = 1.30, I^2 = 39 %) and older age (d = 0.24, I^2 = 62 %) showed weaker associations with low certainty. Cement volume, body mass index, kyphotic angle, its correction, vertebral height restoration, and thoracolumbar junction involvement were not associated with rVCFs. Conclusions. The most significant rVCF risk factors are absence of AOT, cement leakage, and low BMD, nearly doubling the risk. Female sex increases risk by approximately one-third, and older age has a minor effect. These findings highlight the importance of AOT and technical precision in PVP to prevent rVCFs.

Нові компресійні переломи хребців (НКПХ) після пункційної вертебропластики (ПВП) погіршують якість життя пацієнтів з остеопорозом. Чинники ризику залишаються дискусійними, що зумовило необхідність систематичного аналізу. Мета. Узагальнити клінічні дані та кількісно оцінити вплив демографічних, морфометричних і технічних факторів на частоту НКПХ після ПВП. Методи. Проведено пошук у PubMed, Scopus, Medline, Google Scholar (2010–2024 р.) за MeSH-термінами: «vertebroplasty», «compression fractures», «osteoporosis», «risk factors», «recurrence». Включено 20 когортних досліджень (7 923 пацієнти). Кількісні змінні аналізували моделлю Sidik-Jonkman (d Коена), якісні — Paule-Mandel (OR). Гетерогенність оцінювали за I^2 і прогнозними інтервалами, виконано чутливі аналізи. Упевненість доказів оцінено за GRADE. Результати. Виявлено значущі фактори ризику НКПХ: відсутність антиостеопоротичної терапії (АОТ) (OR = 1,97; I^2 = 40 %), витік кісткового цементу (OR = 1,92; I^2 = 68 %), низька мінеральна щільність кісткової тканини (МЩКТ) (d = –0,55; I^2 = 72 %) — помірний рівень упевненості за GRADE. Жіноча стать (OR = 1,30; I^2 = 39 %) і старший вік (d = 0,24; I^2 = 62 %) мають слабший вплив із низькою впевненістю. Обсяг цементу, індекс маси тіла, кіфотичний кут, його корекція, відновлення висоти хребця та ураження Т-L з'єднання не асоціювалися з НКПХ. Висновки. Найвагоміші чинники ризику НКПХ — відсутність АОТ, витік цементу та низька МЩКТ, які підвищують ризик удвічі. Жіноча стать збільшує ризик на третину, похилий вік — незначно. Ці дані підкреслюють важливість АОТ і технічної точності ПВП для профілактики НКПХ. Ключові слова. Вертебропластика, остеопороз, нові компресійні переломи, метааналіз, чинники ризику.

Keywords. Vertebroplasty, osteoporosis, recurrent compression fractures, meta-analysis, risk factors

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Introduction

Vertebral compression fractures (VCFs) are the most common injury resulting from osteoporosis. Studies suggest that their incidence ranges from 30 % to 50 % in individuals over 50 years of age, regardless of gender [1–4]. Population-based research indicates an annual incidence of 10.7 % in women and 5.7 % in men [5]. For those aged 80 and older, the incidence rises to approximately 30 %, while in younger age groups (up to 80), it typically varies between 5 % and 10 % [6].

Vertebral compression fractures (VCFs) can lead to severe pain, spinal deformities, limited mobility, and a significant reduction in quality of life. One of the primary surgical treatments for VCFs is percutaneous vertebroplasty (PVP). First described by H. Deramond and P. Galibert, this technique was originally used to treat vertebral body hemangiomas [7]. Over time, it gained widespread use for treating VCFs caused by osteoporosis, myeloma, or traumatic injuries. PVP has proven to be both safe and effective, especially when compared to conservative treatment options. It provides rapid relief from pain, restores mobility, and facilitates quicker rehabilitation [8, 9].

However, despite the rapid relief of pain and improvement in functional status, some patients may develop complications: new fractures, spinal cord compression, infectious processes, nerve root damage and embolism. The most common and most thoroughly studied complication is new vertebral compression fractures (NVCF) in both adjacent and distant segments. Previous studies have identified a number of factors that influence the risk of NVCF: age, female gender, bone mineral density (BMD), location of the primary fracture, bone cement (BC) distribution, volume of injection and migration, endplate status, primary kyphotic angle (KA), percentage of KA and vertebral height recovery, absence of anti-osteoporosis therapy (AOT), body mass index (BMI), T-L junction [11]. However, the results of observations are often inconclusive or contradictory. This led us to undertake a systematic review aimed at summarising the available evidence regarding risk factors for new vertebral compression fractures following PVP.

Objective: To summarize and analyze the results of clinical trials on risk factors for new vertebral compression fractures after puncture vertebroplasty and to quantify their impact in order to identify factors that significantly increase the likelihood of new vertebral compression fractures in adjacent and distant segments.

Material and Methods

Eligibility Criteria. This systematic review and meta-analysis was registered in PROSPERO (CRD420251068792) and was performed according to the PRISMA guidelines. The PICOS inclusive design was used, in which the population (P) was patients who underwent PVP. The intervention group (I) was individuals with VCFs. Comparisons were made with a group (C) in which NVCFs were detected. The primary outcomes (O) of interest were differences in the presence of NVCF risk factors in these groups. Only comparative studies (S) were considered for inclusion — original articles (prospective, retrospective studies). Publications where vertebroplasty was considered for non-osteoporotic lesions; experimental or preclinical studies (*in vitro, in vivo* on animals) that do not contain clinical data on humans; duplicates of the same article in different databases; non-original sources that do not disclose any quantitative or qualitative data on the risk of NCP — were excluded.

A literature search was conducted in PubMed, Scopus, Medline, and Google Scholar from 2010 to 2024. There were no language restrictions.

A combination of MeSH (Medical Subject Headings) and free text terms was used for the search, using the logical operators AND, OR, and NOT. Key terms were Vertebroplasty, Percutaneous Vertebroplasty, Transpedicular Vertebroplasty, Spinal Fractures, Compression Fractures, Osteoporosis, Risk Factors, Recurrent Compression Fractures, Prediction of Compression Spine Fractures.

The risk of bias in included studies was assessed using the Newcastle–Ottawa (NOS) scale for non-randomized cohorts and cross-sectional studies. Two independent reviewers completed the NOS checklist (domain Selection, Comparability, Outcome; range 0–9); disagreements were resolved by a third expert. The total scores were interpreted as follows: 7–9 — low, 4–6 — moderate, ≤ 3 — high risk of bias. Among the 20 included studies, 10 had low, 9 — moderate, and 1 — high risk of bias.

Findings. Effect size for quantitative measures was estimated based on the standardized mean difference using Cohen's d. In some studies (e. g., [27, 28]), descriptive statistics for quantitative measures were provided as medians and interquartile ranges; in these cases, the mean and standard deviation values needed to calculate Cohen's d were approximated based on the approaches provided in [10]. For qualitative measures, the odds ratio (OR) was used as a measure of effect size.

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The pooled effect size (OR) for each potential risk factor was estimated using a random effects model, in which the variance estimate (τ^2) due to different studies was calculated during the analysis of quantitative indicators using the Sidak–Jonkman method due to the high variability of the data and using the Paule–Mandel method using the analysis of qualitative indicators [12]

In addition, point and interval estimates of other indicators of heterogeneity between studies are provided, namely, the I^2 statistic (Higgins & Thompson's I^2 statistic) and the H statistic (Higgins & Thompson's H statistic).

All calculations were performed at a confidence interval of 95 %. For all indicators, the limits of the prediction interval were calculated, which shows the range within which the effect observed in a new study randomly selected from the general population can fall with a probability of 95% [13, 14].

The analysis was mainly performed using the functions of the Meta, Metafor, and Dmetar packages of the R programming language; for some auxiliary calculations, the MS Excel 2021 spreadsheet was used.

The confidence in the combined evidence for each potential factor (age, low BMD, absence of AOT, cement leakage, female gender) was determined using the GRADE approach using the online GRADEpro GDT platform (version 2025.3).

Results

Study Selection

A search of electronic databases yielded 454 articles. Initially, duplicates, case reports, letters, reviews, and non-comparative study designs (n = 243) were removed, leaving 211 titles and abstracts for screening. Two independent reviewers then assessed eligibility, excluding 183 publications that did not provide numerical data on group differences in patients with VCFs and NVCFs. This resulted in 28 articles being considered for inclusion. After in-depth review, 11 studies were excluded because they did not meet the eligibility criteria for comparing groups of patients with VCFs and NVCFs. The screening process identified 17 publications for inclusion. Reference lists were also manually reviewed, which resulted in 3 additional studies that met the criteria. Any disagreements between reviewers at any stage were resolved by discussion. In total, 20 comparative studies were included in the meta-analysis, as shown in the PRISMA flowchart (Fig. 1).

Characteristics of included studies

The systematic review included 20 publications published between 2011 and 2024 (Table 1), which were conducted: 12 in China, 5 in South Korea, 1 each in Japan, Ukraine, and Germany. Most of them were retrospective cohort studies (n = 19), and one study was cross-sectional. The total number of patients was 7,923, of whom 1,487 (18.6%) had new vertebral compression fractures (NVCFs). The follow-up period ranged from 5 to 36 months, most often 12. The mean age of the participants ranged from (64.3 ± 11.9) to (74.8 ± 7.8) years, with a predominance of older individuals in all samples, the size of which varied from 60 to 2202 subjects. The proportion of patients with NVCFs ranged from 18.3 to 51.9 % within individual studies. The following possible risk factors for NVCF were considered in the reviewed publications: age; gender (female); BMI; absence of AOT; bone cement leakage; bone cement volume; BMD; CC; T–L junction damage in the case of primary fracture; percentage of KA recovery and vertebral height.

Overall, the included studies differed in design, country of origin, follow-up period, and proportion of new fractures, which allowed for multivariate risk analysis (Tables 2–4).

Risk factor assessment

Age

The effect of patient age on the occurrence of NVCF was investigated in 19 studies included in the meta-analysis. In some studies, older age was associated with an increased risk of NVCF, demonstrating a moderate to large effect, but a significant proportion of them did not show an effect of age (Fig. 2, a).

The estimated pooled effect (0.2891; 95 % CI: 0.1289–0.4494) indicates a statistically significant but small association of age with the risk of NVCF. High heterogeneity (I^2 = 87.3 %; τ^2 = 0.0950) resulted in a wide prediction interval that encompassed zero. After excluding 5 publications — statistical outliers, heterogeneity decreased (I^2 = 24.9 %; τ^2 = 0.0281), and the pooled effect remained stable (0.2278; 95 % CI: 0.0971–0.3584), indicating a stable but weak relationship (Fig. 2, b).

Body mass index

Eleven studies assessed the relationship between BMI and NVCF. Only S. Cai et al. revealed a significant positive effect, while most of the results had intervals that included zero and indicated the absence of a statistically significant effect. The pooled effect was –0.0670 (95 % CI: –0.2859; 0.1519), which also does not confirm the presence of an association. Heterogeneity was high (I^2 = 78.8%; τ^2 = 0.1032; H = 2.173).

After excluding the study by S. Cai et al., heterogeneity decreased to I^2 = 47.6% (τ^2 = 0.0428; H = 1.382),

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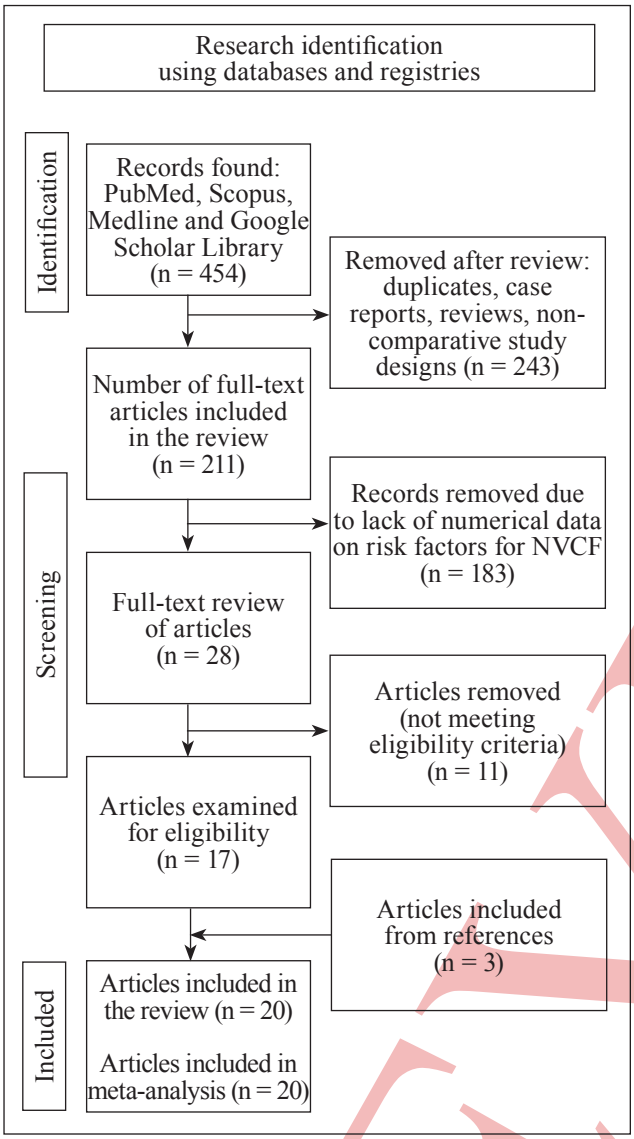

Fig. 1. Flowchart of study selection

but the adjusted effect of –0.1502 (95 % CI: –0.3209; 0.0206) remained statistically insignificant (Fig. 3).

Bone cement volume

Nine studies analyzed the effect of bone cement volume on the risk of NVCF. All standardized mean differences (Cohen's d) indicated no significant effect (Fig. 4). The pooled effect was 0.0321 (95 % CI: –0.0736; 0.1379), and the prediction interval (–0.162; 0.226) confirmed the absence of an association. The results of the studies were consistent, there was no heterogeneity: τ^2 = 0.0042 (95 % CI: 0.000–0.0173), I^2 = 0.0 %, H < 1.

BMD

A significant association between reduced BMD and the risk of NVCF was found in 13 studies: the pooled effect was –0.6076 (95 % CI: –0.8881; –0.3271), which corresponds to a moderate or strong

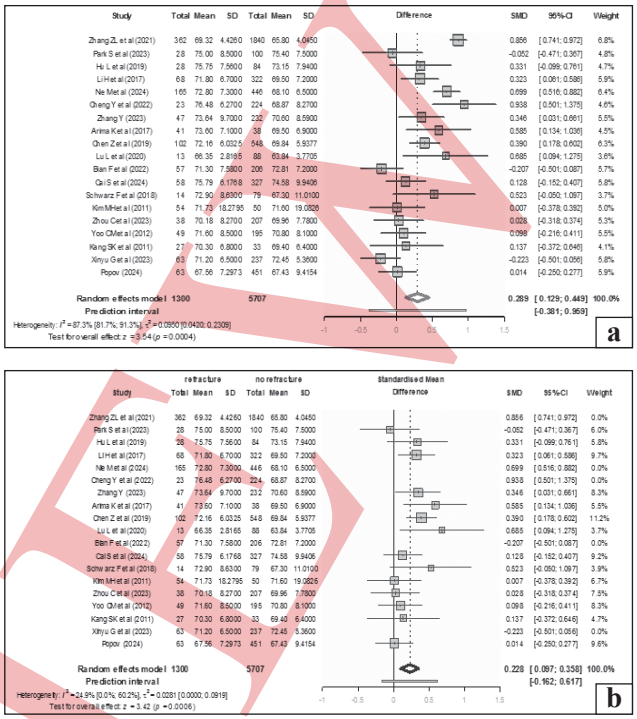

Fig. 2. Forest plot of the association of age of patients with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after exclusion of statistical outliers

effect (Fig. 5, a). At the same time, high heterogeneity (I^2 = 88.8 %; τ^2 = 0.2289; H = 2.982) is due to the variability of the results between studies.

After excluding statistical outliers, heterogeneity decreased (I^2 = 72.1 %; τ^2 = 0.0537; H = 1.892), and the adjusted effect size was –0.5515 (95 % CI: –0.7248; –0.3783 (Fig. 5, b)) confirming the consistent effect of low BMD on the risk of NVCF. The prediction interval (–1.104; 0.001) indicates that similar results should be expected in future studies.

Kyphotic angle

Data regarding the value of KA prior to surgical intervention were identified in only four published studies.

Based on the compilation of their data, we estimated the pooled effect size for this indicator at 0.0805 with 95 % CI: –0.172; 0.333 and a prediction interval of –0.6217 to 0.7827 (Fig. 6). The findings suggest that KA does not have a significant effect on the incidence of NVCF.

Statistical data according to Higgins-Thompson H = 1.3508 with 95 % CI: (1.00; 2.34) and I^2 = 45.195 % with 95 % CI: (0.0; 81.7) % indicated moderate heterogeneity, which was also confirmed by the data of the total variance τ^2 = 0.0321 with 95 % CI: (0.0000; 0.7587), but at the same time no statistical outliers were detected.

Percentage of recovery of the kyphotic angle

Only 2 studies assessed the effect of relative recovery of the KA after surgery on the risk of NVCF.

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Table 1

Baseline data of included studies

Author / Year	Country / Design	Total number of patients	Group with NVCF	Group without NVCF	Follow-up months	Age, years	NOS
Zhang Z. L. 2021 [15]	China / RC	2202	362	1840	14.7	69.32 ± 4.43	8
Park S. 2023 [16]	Korea / RC	128	28	100	12.0	73.00 ± 7.00	7
Bian F. 2022 [17]	China / RC	371	81	290	24.0	71.60 ± 8.00	8
Chen Z. 2019 [18]	China / RC	650	102	548	24.0	73.50 ± 7.90	7
Li H. 2017 [19]	China / RC	390	68	322	18.0	70.00 ± 7.00	7
Hu L. 2019 [20]	China / RC	198	28	170	12.0	74.50 ± 7.80	6
Zhou C. 2023 [21]	China / RC	245	38	207	12.0	70.70 ± 7.00	7
Nie M. 2024 [22]	China / RC	611	165	446	36.0	71.80 ± 9.00	8
Cheng Y. 2022 [23]	China / RC	247	23	224	24.0	69.60 ± 8.40	7
Seo D. H. 2014 [24]	Korea / RC	206	29	177	14.0	72.50 ± 6.90	6
Arima K. 2017 [25]	China / RC	556	96	460	12.0	64.30 ± 11.90	6
Lu L. 2020 [26]	China / RC	101	21	80	24.0	68.20 ± 8.40	6
Zhang Y. 2023 [27]	China / RC	279	47	232	18.0	71.10 ± 8.80	8
Cai S. 2024 [28]	China / RC	385	58	327	12.0	70.20 ± 8.10	8
Kim M. H. 2011 [29]	Korea / RC	104	54	50	12.0	71.40 ± 7.50	6
Yoo C. M. 2012 [30]	Korea / RC	244	49	195	12.0	71.40 ± 7.50	6
Kang S. K. 2011 [31]	Korea / RC	60	27	33	12.0	71.00 ± 7.20	6
Guo X. 2023 [32]	China / RC	300	100	200	22.4	71.60 ± 8.60	6
Schwarz F. 2018 [33]	Germany / RC	93	19	74	12.0	68.10 ± 9.40	6
Popov A. 2024 [34]	Ukraine / RC	553	92	461	12.0	69.00 ± 8.00	3

Note. RC is a retrospective cohort.

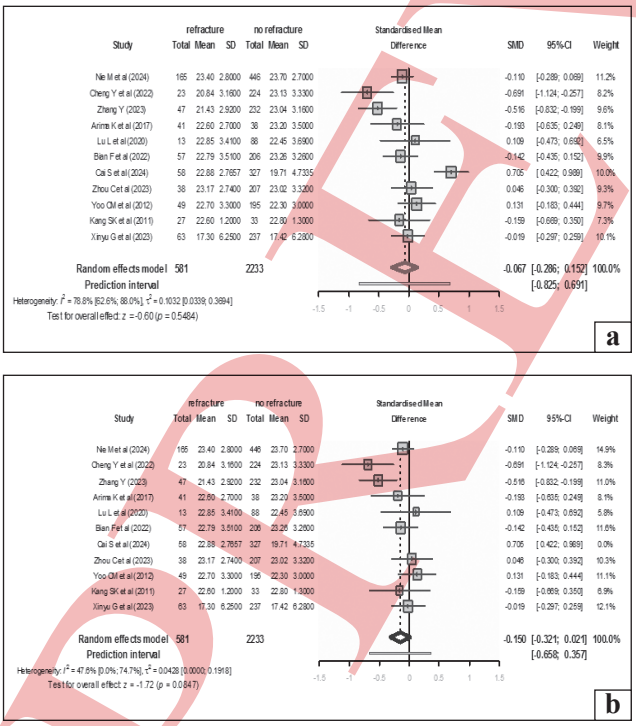

Fig. 3. Forest plot of the association of BMI of patients with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after exclusion of statistical outliers

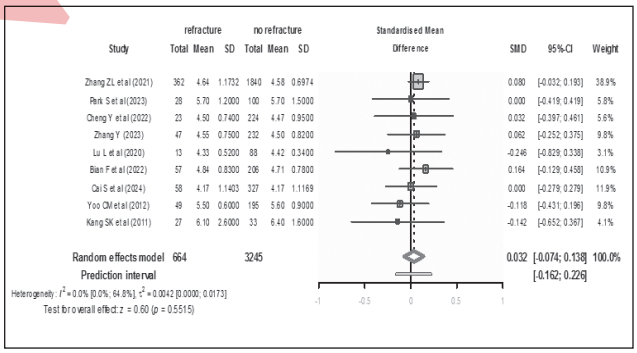

Fig. 4. Forest plot of the association of bone cement volume with new spinal fractures (results of meta-analysis)

One result indicated a moderate effect, the other indicated no effect (Fig. 6). The pooled effect was 0.247 (95 % CI: –0.144; 0.638), which does not allow us to conclude that there is a statistically significant association. The prediction interval (–3.448; 3.942) is almost symmetric, indicating uncertainty in future studies. The data obtained may be limited by the small number of included studies. Heterogeneity was assessed as moderate: $I^2 = 57.0$ %, $\tau^2 = 0.0449$, $H = 1.526$.

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Table 2

Investigated risk factors for NVCF

№	Author / Year	Risk factor
1	Zhang Z. L. 2021 [15]	Age, cement volume, cement leakage, BMI, BMD, KA
2	Park S. 2023 [16]	Age, gender, cement volume, cement leakage, AOT, BMI, KA, % KA recovery, T-L junction, % recovery of vertebral height
3	Bian F. 2022 [17]	Age, gender, AOT, BMI, BMD, T-L junction
4	Chen Z. 2019 [18]	Age, gender, cement volume, cement leakage, BMI, T-L junction
5	Li H. 2017 [19]	Age, gender, cement volume, cement leakage, BMI, T-L junction
6	Hu L. 2019 [20]	Age, gender, cement volume, cement leakage, AOT, BMI
7	Zhou C. 2023 [21]	Age, gender, cement volume, cement leakage, BMD, T-L junction, KA, % KA recovery
8	Nie M. 2024 [22]	Age, gender, cement leakage, BMD, % KA recovery
9	Cheng Y. 2022 [23]	Age, gender, cement leakage, BMI, BMD, T-L junction
10	Seo D. H. 2014 [24]	Age, gender, cement volume, cement leakage, BMI, BMD, T-L junction, % KA recovery
11	Arima K. 2017 [25]	Age, cement volume, cement leakage, BMI, BMD, KA
12	Lu L. 2020 [26]	Age, gender, BMI, BMD, KA, % recovery of vertebral height
13	Zhang Y. 2023 [27]	Age, gender, cement leakage, BMD
14	Cai S. 2024 [28]	Age, gender, cement volume, cement leakage
15	Kim M. H. 2011 [29]	Age, cement volume, cement leakage, BMI, BMD, KA
16	Yoo C. M. 2012 [30]	Age, gender, cement volume, cement leakage, AOT, BMI, KA, % KA recovery, T-L junction, % recovery of vertebral height
17	Kang S. K. 2011 [31]	Age, gender, AOT, BMI, BMD, T-L junction
18	Guo X. 2023 [32]	Age, gender, cement volume, cement leakage, BMI, T-L junction
19	Schwarz F. 2018 [33]	Age, gender, cement volume, cement leakage, BMI, T-L junction
20	Popov A. 2024 [34]	Age, gender, cement volume, cement leakage, AOT, BMI

Notes: BMI — body mass index, BMD — bone mineral density, KA — kyphotic angle, AOT — anti-osteoporotic therapy, BC — bone cement.

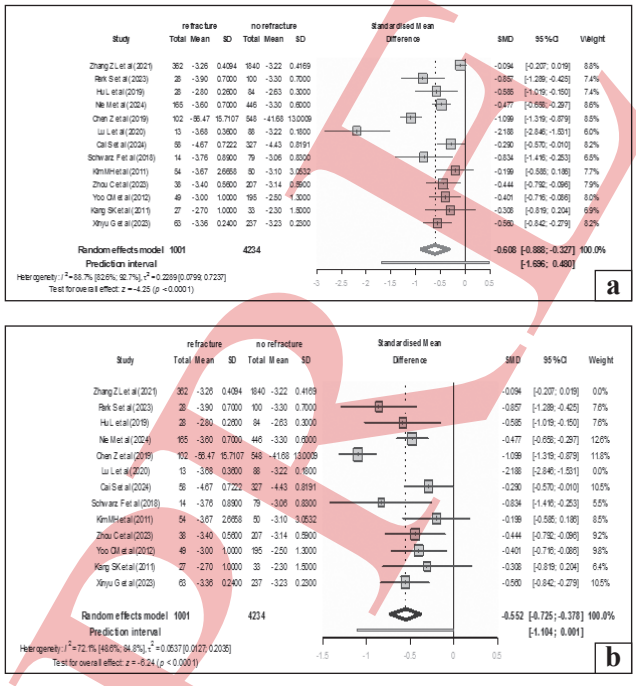

Fig. 5. Forest plot of the association of BMD with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after removal of outliers

Percentage of vertebral height recovery after vertebroplasty

Three studies evaluated vertebral height and its percentage recovery following surgical intervention. The results of these studies showed moderate heterogeneity (Higgins-Thompson H = 1.1727 with 95 % CI: 1.00; 3.64; I^2 = 27.282 % with 95 % CI = (0.0; 92.4) %; τ^2 = 0.0315 with 95 % CI: 0.0000; 2.6329), and the pooled effect was 0.2397 with 95 % CI: –0.0755; 0.5549. The data show that spinal height restoration after surgery does not have a measurable impact on NVCF incidence. However, it is important to note that further publications on this topic are needed to draw definitive conclusions. (Fig. 7).

Female gender

4 of 17 publications found a potential association between female gender and the risk of new vertebral compression fractures, one study (G. Xinyu et al.) showed the opposite effect.

In the remaining studies, the odds ratios were not statistically significant (95 % CI included 1), and the pooled effect was 1.20 (95 % CI: 0.91–1.58),

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which does not support an association. Heterogeneity was significant: $I^2 = 59.1$ %, $\tau^2 = 0.1785$, $H = 1.56$.

After excluding the outlier (G. Xinyu et al.), the heterogeneity decreased to moderate ($I^2 = 39.3$ %; $\tau^2 = 0.0873$; $H = 1.28$), and the adjusted effect increased to 1.30 (95 % CI: 1.03–1.66), indicating a significant increase in the risk of new vertebral compression fractures in women (≈ 30 %). The prediction interval (0.66–2.58) indicates possible variability of the effect in future studies (Fig. 8, 9).

Absence of anti-osteoporosis treatment

Studies on the effect of absence of AOT on the incidence of NVCF showed moderate heterogeneity ($\tau^2 = 0.0395$ with 95 % CI: (0.0000; 0.4898), $H = 1.2862$ with 95 % CI: 1.00; 1.98, $I^2 = 39.553$ % with 95 % CI: (0.0; 74.6) %). The pooled effect estimate for this risk factor was 1.9695 with 95 % CI: 1.5498; 2.5030 and a prediction interval of 1.1129 to 3.4856 (Fig. 10), which allows us to conclude that the chances of NVCF in the absence of AOT are doubled.

Bone cement leakage

The effect of BC leakage on the risk of NVCF was statistically significant: the pooled effect was 2.13 (95 % CI: 1.33–3.42), indicating an almost two-fold

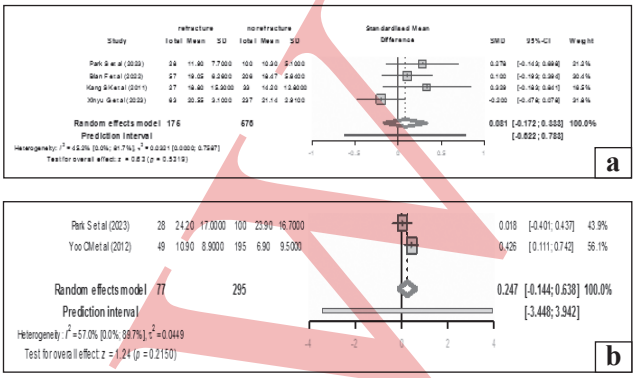

Fig. 6. Forest plot of the association of: a) kyphotic angle with new spinal fractures; b) percentage of kyphotic angle recovery due to surgery for new spinal fractures. Results of meta-analysis

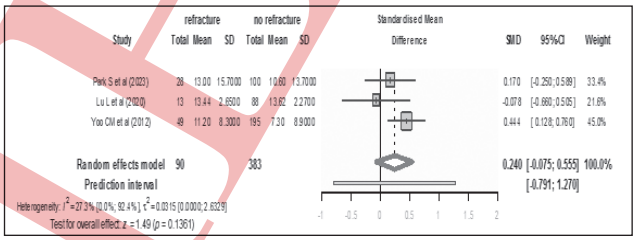

Fig. 7. Forest plot of the percentage of vertebral height recovery after surgery for new spinal fractures (results of meta-analysis)

Table 3

Results of a meta-analysis on the impact of possible risk factors (quantitative indicators) on the incidence of new spinal fractures

Factor	Pooled effect size	Effect	Number of studies	Heterogeneity index		
	Cohen's d (95 % CI)			Higgins & Thompson's H,	*τ^2 (95 % CI)	I^2 (%) (95 % CI)
**Patient's age	0.289 (0.129; 0.449)	weak	19	2.810	0.095 (0.042; 0.231)	87.3 (81.7; 91.3)
Patient's age	0.228 (0.097; 0.358)	weak	14	1.154	0.028 (0.000; 0.092)	24.9 (0.0; 60.2)
**BMI	–0.067 (–0.286; 0.152)	absent	11	2.173	0.103 (0.034; 0.369)	78.8 (62.6; 88.0)
BMi	–0.150 (–0.321; 0.021)	absent	10	1.382	0.043 (0.000; 0.192)	47.6 (0.0; 74.7)
BC volume	0.032 (–0.074; 0.138)	absent	9	0.678	0.004 (0.000; 0.017)	0.0 (0.0; 64.8)
**BMD	–0.608 (–0.888; –0.327)	moderate	13	2.982	0.229 (0.0799; 0.724)	88.8 (82.6; 92.7)
BMD	–0.552 (–0.725; –0.378)	moderate	11	1.892	0.054 (0.013; 0.204)	72.1 (48.6; 84.8)
Kyphotic angle	0.081 (–0.172; 0.333)	absent	4	1.351	0.032 (0.000; 0.759)	45.2 (0.0; 81.7)
% kyphotic angle recovery	0.247 (–0.144; 0.638)	absent	2	1.526	0.045 (N/A)	57.0 (0.0; 89.7)
% vertebral height recovery	0.240 (–0.076; 0.555)	absent	3	1.173	0.032 (0.000; 2.633)	27.3 (0.0; 92.4)

Notes: * — total variance between studies (τ^2) estimated by the Sidak-Jonkman method; ** — data before exclusion of statistical outliers.

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increase in odds (Fig. 11). However, heterogeneity was significant (I^2 = 72.3 %; τ^2 = 0.5846; H = 1.90).

After excluding statistical outliers (L. Lu et al.), the effect remained significant — 1.92 (95 % CI: 1.30–2.82), the prediction interval narrowed (0.53–6.97), and the heterogeneity decreased to I^2 = 67.8 % (τ^2 = 0.3129; H = 1.76), but remained moderately high.

T–L junction

The pooled effect estimate for T–L junction injury did not reveal a significant association with NVCF (effect 0.9017; 95 % CI: 0.5132–1.5843; Fig. 12).

The initial heterogeneity was very high (I^2 = 92.7 %; τ^2 = 1.8336; H = 3.69), with statistical outliers in the studies of H. Li and D. H. Seo et al.

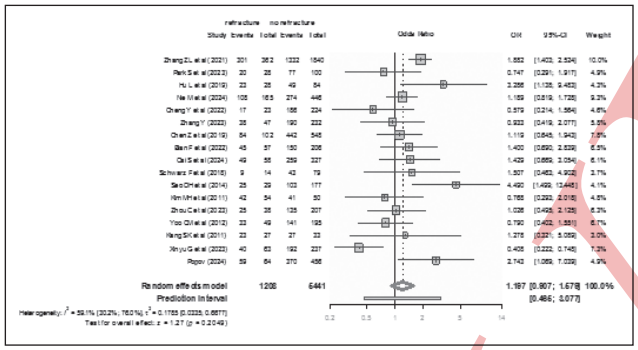


Fig. 8. Forest plot of the association of female gender with new spinal fractures (results of meta-analysis)

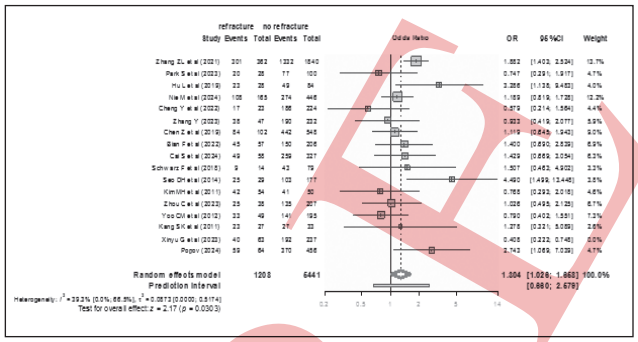


Fig. 9. Forest plot of the association of patient gender with new spinal fractures (results of meta-analysis after excluding statistical outliers)

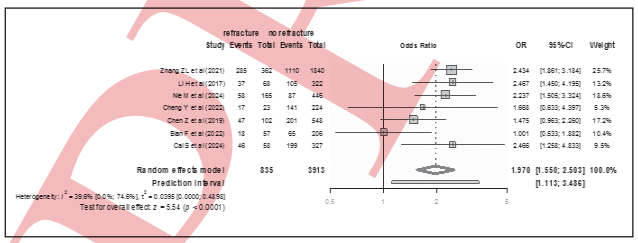


Fig. 10. Forest plot of the association of lack of anti-osteoporotic therapy with new spinal fractures (results of meta-analysis)

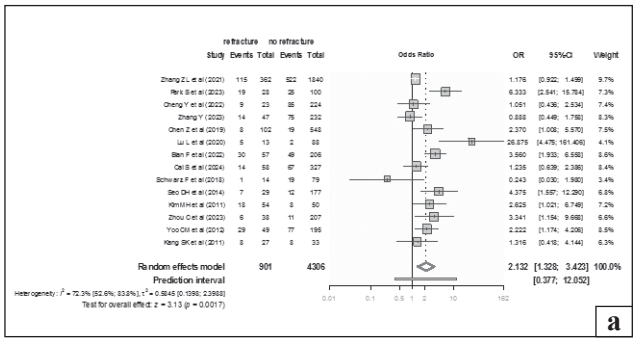
After their exclusion, the heterogeneity decreased but remained high (I^2 = 74.5 %; τ^2 = 0.4795; H = 1.98), and the adjusted effect remained statistically insignificant.

For the indicators whose pooled effect was significant, we additionally assessed the evidence profile using the GRADE approach (Table 5).

Discussion

Comparison of our meta-analysis with previous systematic reviews demonstrates both a consistent convergence of results and fundamental differences that are clinically relevant. First of all, all studies confirm the key role of low BMD in shaping the risk of NVCF after vertebroplasty. In our study, the effect was moderate (d ≈ –0.55) and remained stable in sensitive analyses, which is consistent with the data of G. Zhai et al. (SMD ≈ –0.41) and partly with the results of S. Dai et al. (WMD ≈ –0.38). Therefore, timely diagnosis and aggressive correction of osteoporosis remain an indispensable link in the prevention of new fractures [35, 36].

Bone cement leakage was also a notable factor. In our analysis, it almost doubled the risk of fracture (OR ≈ 1.92), which is practically identical to the meta-analysis by Dai et al. [36] (OR ≈ 2.05) and supports the conclusions of a previous review by Mao et al. [37]. A recent study by Wu et al. detailed the anatomical prerequisites for cement leakage, namely



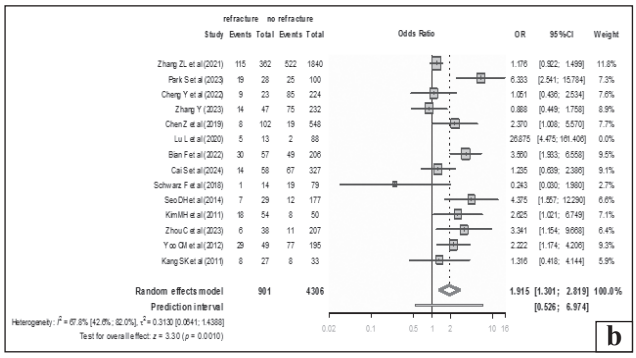


Fig. 11. Forest plot of the association of bone cement leakage with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after removing statistical outliers

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Table 4

Results of a meta-analysis on the impact of possible risk factors (qualitative indicators) on the incidence of new spinal fractures

Factor	Pooled effect size	Number of studies	Heterogeneity index		
	OR (95 % CI)		Higgins & Thompson's H,	*τ^2 (95 %–CI)	I^2 (%) (95 %–CI)
**Female gender	1.966 (0.9066; 1.5792)	17	1.5640	0.1785 (0.0335; 0.6677)	59.12 (30.2; 76.0)
Female gender	1.3041 (1.0256; 1.6583)	16	1.2840	0.0873 (0.000; 0.5174)	39.1 (0.0; 66.5)
Lack of osteoporotic treatment	1.9695 (1.5498; 2.5030)	7	1.2860	0.0395 (0.000; 0.4898)	39.55 (0.0; 74.6)
**Bone cement leakage	2.1318 (1.3276; 3.4233)	14	1.8990	0.5846 (0.1398; 2.3988)	72.275 (52.6; 83.8)
Bone cement leakage	1.9152 (1.3013; 2.8186)	13	1.7630	0.3129 (0.0641; 1.4388)	67.82 (42.6; 82.0)
**Damage to the T–L junction	0.9069 (0.3765; 2.1847)	10	3.6898	1.8336 (0.7846; 6.4829)	92.66 (88.6; 95.3)
Damage to the T–L junction	0.9017 (0.5132; 1.5843)	8	1.9807	0.4796 (0.1153; 1.5843)	74.51 (48.5; 87.4)

Notes: * — total variance between studies (τ^2) estimated by the Paule–Mandel method; ** — data before exclusion of statistical outliers.

Table 5

GRADE profile of risk factors for new vertebral compression fractures after puncture vertebroplasty

Factor	Number of studies/patients	Pooled effect (95 % CI)	I^2, %	Confidence level
Absence of AOT	7 / 4 748	OR = 1.97 (1.55;2.50)	40	⊕⊕⊕ Moderate
Bone cement leakage	13 / 5 106	OR = 1.92 (1.30;2.82)	68	⊕⊕⊕ Moderate
Low BMD	11 / 2 932	Cohen's d = 0.55 (0.38;0.73)	72	⊕⊕⊕ Moderate
Advanced age	14 / 3 384	Cohen's d = 0.29 (0.13;0.45)	25	⊕⊕ Low
Female gender	16 / 6 349	OR = 1.30 (1.03;1.66)	39	⊕⊕ Low

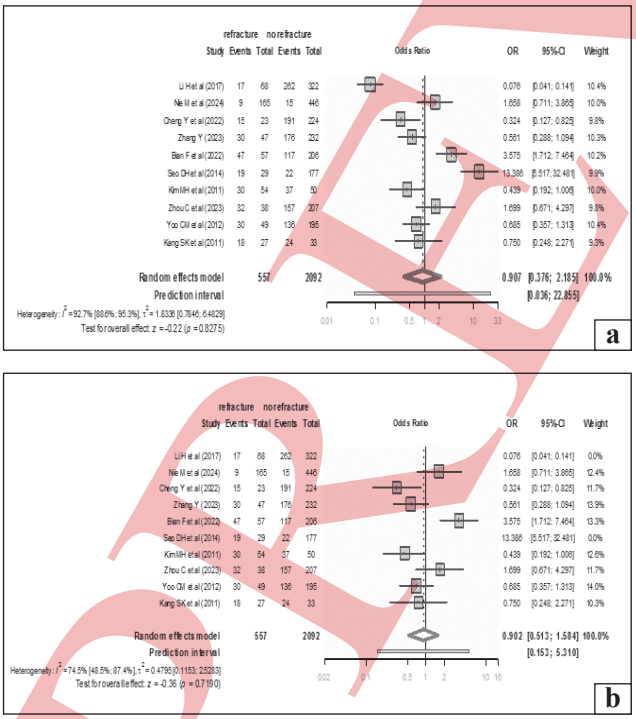

Fig. 12. Forest plot of the association of T–L junction damage in a primary fracture with new vertebral fractures: a) meta-analysis results; b) meta-analysis results after removing statistical outliers

cortical disruption and vacuum gap, emphasizing the importance of neutralizing these factors during intervention [38].

A notable contribution of our work is the quantitative analysis of the consequences of not receiving anti-osteoporotic therapy. Our findings reveal that the absence of drug therapy nearly doubles the risk of new fractures, whereas most prior reviews have merely described this association without statistical validation [36, 37]. This underscores the importance of AOT as a central component of secondary prevention strategies.

Regarding demographic variables, female gender was associated with an almost 30 % increased risk, which was consistent with the estimates of S. Dai, although statistical significance was not reached in the review by G. Zhai. Age showed a small but reproducible effect: in our pooled effects, the weighted average difference was about 2–3 years, which is practically the same as the results of S. Dai, while the review by G. Zhai, limited to the sample up to 2017, did not find a signal effect.

Interestingly, neither cement volume nor body mass index showed a significant association with

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the incidence of new fractures in our study or in previous reviews. This finding suggests that efforts to adjust these parameters in an attempt to reduce risk are not supported by evidence.

Methodologically, our study is distinguished by a wider involvement of almost 7000 patients from different regions and the use of modern statistical approaches (Sidik–Jonkman, Paule–Mandel, predictive intervals, GRADE), while most of the predecessors used the classic DerSimonian–Laird model without grading the certainty of evidence. This provides higher external validity and practical applicability of our findings.

Limitations

First, the vast majority of the studies we included had a retrospective cohort design (19 out of 20), which limits the evidence of the conclusions due to the potential risk of systematic errors. Second, there was significant heterogeneity between studies for factors such as age, BMD, and cement leakage ($I^2 > 70$ %), suggesting variability in methodologies, population characteristics, and interpretation of results across studies. Although sensitive analyses were performed to exclude outliers, residual heterogeneity remained. Third, some potentially important risk factors had insufficient numbers of included studies (% vertebral height recovery, % KA recovery, KA), limiting the validity of conclusions about them.

It should be noted that the majority of studies used for the analysis (91 % of cases (18 of 20 cases)) considered the Asian population. This is significant given that race is necessarily taken into account when assessing BMD, as representatives of this population have a lower risk of osteoporosis compared with Caucasians.

Conclusions

A systematic review and meta-analysis of 20 studies identified the most significant predictors of new vertebral compression fractures following percutaneous vertebroplasty: the absence of anti-osteoporotic therapy, bone cement leakage, and low bone mineral density. The first two factors were found to approximately double the risk of new fractures, with the quality of evidence assessed by GRADE as moderate. Female gender increases the likelihood by approximately one-third, and older age has a statistically significant but small effect; for these, the level of confidence remains low. In contrast, cement volume, amount and correction of kyphosis, restoration of vertebral height, body mass index, body weight and T–L junction involvement did not show a significant association with new fractures.

Conflict of interest. The authors declare that there is no conflict of interest.

Prospects for further research. The prospect of future research will be the creation of a unified system of treatment, prevention and prognosis of NVCF after PVP, as well as its implementation in the treatment protocols of such patients in hospitals in Ukraine.

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Contribution of the authors. Popov A. I. — development of the research concept, participation in data collection, analysis of the results; Molodyuk M. V. — data collection, analysis of the results, drafting the article; Kutsenko V. O. — development of the research concept, participation in data collection; Nessonova M. M. — statistical processing of digital data and description of indicators. All authors participated in drafting the article and approved the final manuscript.

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RISK FACTORS FOR RECURRENT VERTEBRAL COMPRESSION FRACTURES AFTER PERCUTANEOUS VERTEBROPLASTY IN OSTEOPOROTIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. I. Popov [1], M. V. Moloduk [1], V. O. Kutsenko [1], M. M. Nessonova [2]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] Private higher educational institution «Kharkiv International Medical University». Ukraine

✉ Andrii Popov, MD, DSci in Orthopaedics and Traumatology: aipopovdoc@gmail.com; https://orcid.org/0000-0002-9006-7721
✉ Mykyta Moloduk, MD: NikitaMoloduk@gmail.com; https://orcid.org/0009-0005-0058-424X
✉ Volodymyr Kutsenko, MD, DSci in Orthopaedics and Traumatology: kutsvlad1956@gmail.com; https://orcid.org/0000-0001-7924-6553
✉ Maryna Nessonova, PhD in Technology: m.nessonova@khimu.edu.ua; https://orcid.org/0000-0001-7729-317X

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Nonsteroidal anti-inflammatory drugs in the management of degenerative spinal disorders: efficacy, safety, and future perspectives

I. F. Fedotova, I. V. Korzh, K. O. Fedik

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

Objective. To analyze the current literature on the pathogenetically justified use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with degenerative spinal diseases, considering the growing use of this drug class in recent years during the perioperative period of spinal surgery as well as in conservative treatment, and to identify potential risks and prospects for optimizing therapy. Methods. A literature review was conducted using electronic databases such as PubMed, covering the past 10 years. Results. Relevant studies were selected that highlight the pathogenesis of degenerative spinal disorders (DSD), the role of inflammatory mediators, the mechanisms of NSAID action, and their impact on pain and inflammation. The key role of inflammatory processes in intervertebral disc degeneration was emphasized, with increased expression of cytokines IL-1β, TNF-α, and IL-6. This cascade promotes extracellular matrix degradation, triggers neurovascular ingrowth, and enhances nociceptive sensitization. Comparative clinical trials demonstrate that NSAIDs with varying degrees of cyclooxygenase isoform selectivity reduce pain scores and improve functional outcomes, though they differ in tolerability profiles. For chronic use, special attention is required regarding gastrointestinal and cardiovascular risk assessment, minimal effective dosing, and the use of protective co-medications. Conclusion. Accumulating experimental evidence suggests that NSAIDs should be regarded not only as symptomatic analgesics but also as potential modulators of the inflammatory microenvironment of the intervertebral disc. This opens perspectives for their combination with biological agents or antioxidants to slow down the degenerative process. Future research should focus on developing personalized treatment protocols integrating pharmacological, physical, and rehabilitative interventions with consideration of inflammatory biomarkers.

Мета. Проаналізувати сучасну літературу щодо висвітлення питання патогенетично обумовленого застосування нестероїдних протизапальних препаратів у хворих із дегенеративними захворюваннями хребта з урахування збільшення використання в останні роки кількості вищенаведеної групи препаратів у періопераційному періоді лікування дегенеративних захворювань хребта та як частки консервативного лікування, а також визначити можливі ризики та перспективи вдосконалення терапії. Методи. Проаналізовано літературу з електронних баз даних, таких як PubMed, за останні 10 років. Результати. Відібрано актуальні дослідження, які висвітлюють патогенез ДЗХ, роль запальних медіаторів, механізм дії НПЗП та їхній вплив на біль і запалення. Підкреслено ключову роль запальних процесів у дегенерації міжхребцевих дисків, що супроводжується підвищеною експресією цитокінів IL-1β, TNF-α та IL-6. Виявлено, що такий каскад підтримує деградацію позаклітинного матриксу, провокує нейроваскулярну інвазію й посилює ноцицептивну сенситизацію. Порівняльні клінічні дослідження демонструють, що препарати з різним ступенем селективності до ізоформ циклооксигенази забезпечують зниження больового індексу та покращення показників функції, проте відрізняються профілем переносимості. За умов хронічного призначення акцент робиться на ретельній оцінці гастроінтестинального й серцево-судинного ризику, мінімально ефективних дозах і необхідності протекторних супутніх засобів. Висновок. Накопичені експериментальні дані дозволяють розглядати НПЗП не лише як симптоматичні анальгетики, а й як потенційні модулятори запального мікросередовища диска, що відкриває перспективи їхньої комбінації з біологічними агентами або антиоксидантами для уповільнення дегенеративного процесу. Подальші дослідження мають бути спрямовані на розроблення персоналізованих схем, де фармакологічні, фізичні та реабілітаційні втручання інтегруватимуться з урахуванням біомаркерів запалення. Ключові слова. Дегенеративні захворювання хребта, запалення, нестероїдні протизапальні препарати.

Key words. Degenerative spinal diseases, inflammation, nonsteroidal anti-inflammatory drugs

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Introduction

Degenerative spinal diseases (DSD), primarily driven by intervertebral disc degeneration, are a major cause of chronic back pain and significantly impair patients' quality of life [1]. The main clinico-morphological manifestations include spinal pain, inflammation of the structures within the motion segment, and structural changes in intervertebral discs and the spinal articular–ligamentous system.

In all patients, involutional processes in spinal tissues follow a similar trajectory: disc dehydration with subsequent loss of height and overload of the facet joints; dehydration of hyaline cartilage of the facet articular surfaces; decreased bone mineral density of vertebral bodies; reduced elasticity of ligaments and facet joint capsules; degeneration of paravertebral muscles with reduced strength and endurance. These processes are frequently accompanied by pain: starting pain during transitions from rest to movement, when bending the trunk forward, or under conditions of prolonged axial load [2].

Nonsteroidal anti-inflammatory drugs (NSAIDs) play a central role in the treatment of DSD, providing both potent analgesic and anti-inflammatory effects [3]. This work reviews current scientific data regarding the efficacy, mechanisms of action, side effects, and perspectives of NSAID use in patients with DSD, both during the perioperative period and as part of conservative treatment regimens.

Objective. To analyze recent literature addressing the pathogenetically justified use of NSAIDs in patients with degenerative spinal diseases, taking into account the increasing utilization of these agents in recent years in both perioperative management and conservative treatment, and to determine potential risks and prospects for therapeutic optimization.

Materials and Methods

A literature search was conducted in the PubMed electronic database using MeSH keywords with the following queries: "Degenerative spine disease / inflammation" AND "Degenerative spine disease / metabolism"; "Intervertebral disc degeneration / metabolism"; "Low Back Pain / etiology" AND "Low Back Pain / therapy." Only articles published in the past 10 years were considered.

Inclusion criteria comprised original experimental and clinical studies published in English. A total of 29 studies were analyzed.

Results and Discussion

The use of NSAIDs in degenerative spinal diseases (DSD) is supported by a number of biochemical alterations that provide a rationale for their application in degenerative processes of the spinal motion segment.

In the studies by Z. Li et al., the inflammatory theory of DSD was demonstrated, highlighting the role of chronic inflammation in the development of degenerative changes in intervertebral discs and spinal joints. Evidence shows that degenerative processes in these structures are associated with increased production of pro-inflammatory cytokines such as interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and other inflammatory mediators, which promote extracellular matrix degradation and death of nucleus pulposus cells [4]. These molecules are among the most critical pro-inflammatory cytokines, given their strong inflammatory activity and ability to stimulate the secretion of multiple mediators. Their expression is markedly elevated in degenerative intervertebral discs, where they contribute to pathological processes such as inflammatory responses, matrix breakdown, cellular senescence, autophagy, apoptosis, and impaired cell proliferation, ultimately leading to pain and functional impairment. This cascade reduces the cushioning capacity of the disc, leads to water loss, and increases the mechanical load on adjacent spinal structures (ligaments, facet joints, paravertebral muscles) [5].According to M. Lund et al., IL-1β significantly enhances the expression of IL-6, IL-8, and IL-17 in human intervertebral disc cells, initiating an inflammatory cascade. This results in a cycle of reciprocal cytokine activation that sustains chronic local inflammation. Additionally, increasing evidence highlights the role of vascular endothelial growth factor (VEGF), a key regulator of angiogenesis, in degenerative processes. VEGF expression is markedly elevated in degenerative discs, partly induced by pro-inflammatory cytokines [6].

Maintaining the balance between catabolic and anabolic processes in the extracellular matrix is critical for preserving the structural and functional integrity of intervertebral discs. The extracellular matrix, composed of proteins (collagen, elastin), glycoproteins, and proteoglycans, forms the structural scaffold of the tissue, providing mechanical support and regulating cellular behavior [7]. When catabolic activity exceeds anabolic activity, disc degeneration ensues. Key enzymes involved in extracellular matrix breakdown include ADAMTS (A Disintegrin and Metalloproteinase with Thrombospondin motifs), as well as matrix metalloproteinases [8].

Recent findings also emphasize the link between inflammatory processes and oxidative stress.

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Y. Wang et al. demonstrated that pro-inflammatory cytokines induce excessive production of reactive oxygen species (ROS) in intervertebral disc cells, leading to oxidative damage [9]. Cellular senescence, defined as irreversible cell cycle arrest, may result from oxidative stress, cytokine exposure, or DNA damage. Although metabolically active, senescent cells exhibit a strongly pro-inflammatory and catabolic phenotype. Y. Zhang et al. reported that pro-inflammatory cytokines accelerate cellular senescence, thereby increasing the production of matrix-degrading enzymes and further worsening the disc microenvironment [10]. Elevated concentrations of inflammatory mediators in blood plasma have been shown to correlate with the degree of disc degeneration and severity of low back pain [11, 12]. Elucidation of these mechanisms may significantly contribute to the integration of molecular insights into clinical practice, paving the way for novel therapeutic strategies.

Overall, the evidence underscores that inflammation plays a central role in the pathogenesis of intervertebral disc degeneration [13]. Consequently, anti-inflammatory therapy represents a pathogenetically justified approach in the management of degenerative spinal conditions.

It should also be noted that the vertebrology clinic of the State Institution Sytenko Institute of Spine and Joint Pathology, National Academy of Medical Sciences of Ukraine, has for decades been addressing the problem of degenerative spinal diseases [14]. Their studies confirm that involutional processes in spinal tissues follow a similar pattern in all patients: disc dehydration with loss of height and overload of facet joints; dehydration of facet joint hyaline cartilage; reduction of vertebral body bone mineral density; decreased elasticity of ligaments and facet joint capsules; and degeneration of paravertebral muscles with reduced strength and endurance.

Both conservative and surgical treatment of patients with degenerative spinal diseases (DSD) should aim to eliminate:

1) trauma to neurovascular structures resulting from compression within the degeneratively altered spinal canal or nerve root canals;

2) hypoxia of the cauda equina roots caused by venous plexus circulatory disorders, impaired microcirculation with the development of peri- and intraneural edema, and axonal dysfunction;

3) disturbances of cerebrospinal fluid circulation and hypertensive changes in the epidural and subarachnoid spaces.

Thus, the management of DSD is based on several principles: elimination of factors driving disease progression; relief of pain syndrome; reduction of local inflammation; modulation of metabolism and biochemical processes; and restoration of impaired functions (motor, sensory, and autonomic). Therefore, the rationale for NSAID use in DSD cannot be overstated [14].

At the same time, the wide variability of DSD symptoms reflects their multifactorial nature. The severity of comorbidities, biochemical profiles of connective tissue markers and lipid peroxidation systems, and the presence of depressive disorders associated with chronic pain syndrome all play decisive roles in determining the complexity of disease progression. These factors may explain unsatisfactory outcomes of both surgical and conservative treatments. Consequently, although NSAID therapy plays a central role, the overall clinical status of each patient must be comprehensively considered for therapeutic success.

According to international scientific guidelines, NSAIDs are first-line agents for managing pain syndromes, as they inhibit all cyclooxygenase (COX) isoforms, thereby reducing prostaglandin production and, in turn, inflammation and pain [15]. Studies by Y. Wang et al. [16] indicate that the pathological processes underlying intervertebral disc degeneration are closely linked to chronic inflammation and disrupted metabolic pathways, making NSAIDs a critical component of treatment.

In their review, F. Atzeni et al. systematized data regarding the dual (peripheral and central) mechanisms of diclofenac in chronic musculoskeletal pain. The authors emphasize that classical COX-2 inhibition, which reduces prostaglandin E production, only partially accounts for its analgesic effect. Diclofenac also modulates the L-arginine/NO/cGMP pathway, opens ATP-sensitive potassium channels, and indirectly influences NMDA receptor-mediated transmission in the spinal cord. Furthermore, diclofenac demonstrates high affinity for the PPAR-γ receptor, inhibiting microglial activation and cytokine synthesis, thereby potentially reducing neuroinflammation. This combination of peripheral and central actions justifies its use not only as a symptomatic analgesic but also as an agent capable of modulating mechanisms of central sensitization in osteoarthritis, rheumatoid arthritis, and vertebrogenic pain.Diclofenac, a nonselective NSAID belonging to the phenylacetic acid class, possesses anti-inflammatory, analgesic, and antipyretic properties. Compared with other traditional NSAIDs, it shows relatively higher selectivity for COX-2 than for COX-1. Recent studies have demonstrated that the degree of COX-2 selectivity of diclofenac is comparable to that of celecoxib.

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The two most commonly used groups of NSAIDs are nonselective (diclofenac, ibuprofen) and selective COX-2 inhibitors (meloxicam, nimesulide, celecoxib, rofecoxib, parecoxib). Globally, the "gold standard" of NSAID therapy is diclofenac (150 mg/day), whose analgesic effect surpasses that of celecoxib (200 mg/day), naproxen (1000 mg/day), and ibuprofen (2400 mg/day) [17].

Modern pharmacological data indicate that, in terms of COX-2 isoenzyme inhibition, diclofenac is not inferior to the selective inhibitor celecoxib. In addition to the classical COX-related mechanism, diclofenac modulates several ion channels and the NO/cGMP signaling pathway, providing a faster onset of analgesia compared to celecoxib and showing a more stable reduction of pain scale scores already on the first day of treatment [18]. The combination of equivalent COX-2 selectivity, multimodal anti-inflammatory action, superior local exposure, and diverse pharmaceutical formulations justifies diclofenac as a first-line drug for degenerative–inflammatory pain syndromes of the spine.

Special attention is given to the safety profile. Compared with other NSAIDs, diclofenac demonstrates moderate gastrointestinal risk at doses ≤ 75 mg/day; however, cardiovascular events may increase at 150 mg/day [17]. The risk of cardiovascular adverse effects (myocardial infarction, thrombosis) at high diclofenac doses (≥ 150 mg/day) is comparable to that of rofecoxib, celecoxib, or high-dose ibuprofen. Since adverse events are dose-dependent, dose reduction is recommended for patients with cardiovascular or gastrointestinal risk factors [19].

The principle of "lowest effective dose/shortest duration" should be strictly followed, with consideration of individual gastro- and cardiological risks; proton pump inhibitors should be co-prescribed when needed. In the future, combination therapy of diclofenac with anti-cytokine agents or antioxidants may enhance the anti-inflammatory effect and reduce adverse outcomes. Taken together, these findings demonstrate that diclofenac remains one of the most studied and pathogenetically justified molecules for chronic pain management in degenerative and inflammatory musculoskeletal disorders.

The combination of high tissue penetration with a wide range of dosage forms (oral, parenteral, rectal, transdermal) allows therapy individualization, minimizing systemic burden and improving patient adherence. Diclofenac sodium, administered as an enteric-coated tablet, is detected in the synovial fluid for ≈ 11 hours, and after a prolonged-release 100 mg form—for up to 24–25 hours. Notably, its concentration in joint tissue and synovial fluid exceeds plasma levels and remains within the therapeutic range [20]. Such prolonged local exposure correlates with a significant reduction in prostaglandin E, as well as pro-inflammatory cytokines (e.g., interleukin-6, substance P), confirming the peripheral anti-inflammatory potential of diclofenac. Experimental intervertebral disc models support these clinical observations: diclofenac not only blocks the COX-2/PGE pathway but also modulates MMP-3 and MMP-13 expression, inhibiting extracellular matrix degradation and cytokine-mediated nociceptor sensitization. Thus, its sustained tissue presence, proven anti-inflammatory activity, and ability to affect the disc microenvironment provide strong rationale for diclofenac as a first-line drug in degenerative–inflammatory processes of both peripheral joints and the spine [21].

Although other NSAIDs (dexketoprofen, ibuprofen, nimesulide) are also available in fast-dissolving formulations or complexes, the cumulative evidence, diversity of forms, and pharmacoeconomic considerations make potassium diclofenac the most justified choice for rapid relief of acute or chronic vertebrogenic pain. In the 1980s, potassium diclofenac tablets with immediate release in the stomach were developed to ensure rapid absorption and prompt pain relief. This pharmacological profile has been confirmed in patients with vertebrogenic pain. In a systematic review on acute and subacute low back pain, a combination of potassium diclofenac (25–50 mg immediate-release) with the muscle relaxant thiocolchicoside provided significantly faster analgesia and greater reduction in visual analog scale (VAS) pain scores within the first 2 hours compared to placebo or monotherapy with either agent [21]. A randomized controlled trial using a fixed intramuscular combination (diclofenac 75 mg + thiocolchicoside 4 mg) demonstrated that clinically meaningful pain relief was achieved within 30 minutes, and pain intensity was halved by 6 hours, compared to NSAID monotherapy [22]. Therefore, the immediate-release potassium diclofenac formulation ensures rapid absorption and, when combined with muscle relaxants, provides additional benefits for early control of vertebrogenic pain syndromes.

In a randomized controlled trial, K. Iliopoulos et al. evaluated the clinical utility of a single intramuscular injection of a fixed combination of diclofenac 75 mg and thiocolchicoside 4 mg in patients with acute low back pain. Within 30 minutes after administration, the mean pain intensity on the VAS decreased by 38 mm, compared to 24 mm in the control group receiving diclofenac monotherapy

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($p < 0.01$). By 24 hours, 74 % of patients in the combination group achieved clinically significant pain relief (≥ 50 %) versus 49 % in the comparison group, accompanied by significant improvement in the "fingertip-to-floor" test. Adverse effects were mild and transient (local injection site discomfort). These findings confirm that a single injection of an NSAID + muscle relaxant provides faster and more pronounced analgesia in acute lumbalgia compared to monotherapy, while remaining safe for outpatient use [23].

A systematic review by C. Costa et al. analyzed strategies for rational NSAID prescription in geriatric patients with chronic vertebrogenic pain. Despite clear clinical guidelines, the use of high doses of diclofenac and ibuprofen in individuals ≥ 65 years remains substantial, while gastroprotective measures are underutilized. The authors emphasized the need for multi-step stratification of gastrointestinal and cardiovascular risks, implementation of "deprescribing" protocols, and active monitoring of adverse reactions, which is particularly important in long-term treatment regimens for vertebrogenic pain [24].

A meta-analysis by H. Huang et al. compared the efficacy and safety of celecoxib and diclofenac sodium in patients with knee osteoarthritis. Both drugs achieved comparable reductions in pain index and improvements in functional outcomes; however, the incidence of gastrointestinal complications was significantly lower in the celecoxib group (relative risk 0.57), while no differences in cardiovascular events were observed. The authors concluded that the choice between nonselective and selective NSAIDs should be based on the individual risk profile, consistent with current recommendations for pharmacotherapy of degenerative spinal diseases [25].

In a double-blind randomized study, U. Shah et al. compared parenteral paracetamol and diclofenac for postoperative pain control. During the first 2 hours after laparoscopic procedures, patients who received diclofenac had significantly lower VAS scores ($p < 0.05$) and required fewer additional analgesics compared to the paracetamol group; by 6 hours, the difference had disappeared, indicating a faster onset of action with diclofenac. Adverse events were rare and predominantly mild. The investigators concluded that for the early phase of acute pain — particularly after microdiscectomy or spinal stabilization surgery — a single diclofenac injection may provide more effective analgesia without clinically significant complications [26].

Y. Garg et al. assessed the efficacy and safety of several NSAIDs in patients with knee osteoarthritis in an open parallel design. Treatments were evaluated by changes in the WOMAC index and adverse event profiles over 6 weeks. All tested agents, including diclofenac, produced comparable reductions in total WOMAC scores and VAS improvements ($p < 0.001$ vs baseline). Diclofenac demonstrated a faster onset of analgesia (mean ± SD: 2.3 ± 0.4 days) and was associated with fewer dyspeptic symptoms compared with reference drugs, which the authors attributed to careful dose titration and concomitant use of gastroprotective agents. These results support the safe and effective use of diclofenac for short-term management of joint and vertebrogenic pain in outpatient practice [27].

In a systematic review and meta-analysis, Z. Cao et al. analyzed 34 randomized controlled trials investigating combinations of paracetamol with other analgesic agents in patients with low back pain and osteoarthritis (a total of 6,082 participants). Compared to paracetamol monotherapy, combinations with NSAIDs or weak opioids provided additional pain reduction of −0.9 cm on the 10-cm VAS (95 % CI −1.3 to −0.5) and moderate improvement in functional scales (SMD −0.27). Combinations with caffeine or muscle relaxants showed smaller, though still statistically significant, effects. The incidence of adverse events was slightly higher in the "paracetamol + NSAID" groups (NNH ≈ 45), primarily due to dyspepsia; no serious hepato- or cardiotoxic events were reported. The authors concluded that combined analgesia may be considered as a second-line option in patients with insufficient response to monotherapy, provided careful monitoring of gastrointestinal risk and short treatment duration. These results complement evidence supporting the rationale of multimodal regimens for vertebrogenic and osteoarthritis-associated pain [28].

In another systematic review and meta-analysis, A. Cashin et al. examined the efficacy of nonsurgical and noninvasive interventions for low back pain based on placebo-controlled randomized trials. The analysis included 52 studies (over 8,700 participants) covering exercise programs, manual therapy, cognitive-behavioral interventions, acupuncture, and thermal procedures. NSAIDs, particularly diclofenac, demonstrated moderate efficacy for short-term low back pain. The pooled effect size was a mean reduction of −0.32 standard mean differences (SMD) versus placebo (95 % CI −0.42 to −0.22), corresponding to approximately 7 mm on the 100-mm VAS — classified as small but statistically significant. The greatest benefit was observed with active exercise programs and cognitive-behavioral approaches (SMD −0.45), while isolated manual therapy and heat applications

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showed minimal differences from placebo. Adverse event rates did not differ significantly from controls. However, the authors emphasized that the analgesic effect of NSAIDs remains limited compared with placebo, underscoring the importance of an integrated treatment approach that combines pharmacological and nonpharmacological modalities. This observation supports the role of NSAIDs as an important component of low back pain therapy but highlights the need for further studies to optimize their use and develop more effective strategies [29].

Conclusion

Current evidence on the pathogenesis of degenerative spinal disease (DSD), the role of inflammation, and the effectiveness of NSAIDs — particularly diclofenac—confirms that inflammatory processes play a central role in intervertebral disc degeneration. Pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6 drive extracellular matrix breakdown and amplify pain syndromes.

At present, diclofenac at a daily dose of 150 mg is among the most effective NSAIDs for pain management in DSD, with analgesic efficacy equivalent to that of selective NSAIDs. Diclofenac has also proven effective for postoperative pain control in patients with moderate intraoperative trauma. Its efficacy is dose-dependent, but even the lowest effective therapeutic doses provide substantial analgesia, thereby reducing the risk of gastrointestinal or cardiovascular complications. Modern pharmaceutical formulations of diclofenac sodium further minimize adverse effects. Moreover, owing to its lipophilic properties, topical diclofenac achieves significant local analgesia while limiting systemic exposure.

Conflict of interest. The authors of the article are consultants of the company "Berlin-Chemie".

Prospects for further research. Prospects for further research include the development of safer and more effective therapeutic approaches, such as combination therapy with anti-cytokine drugs or antioxidants, as well as studying the possibilities of personalized medicine based on biomarkers of inflammation. The combination of pharmacological, physical and rehabilitation methods may be the key to improving the quality of life of patients with DZH.

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NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN THE MANAGEMENT OF DEGENERATIVE SPINAL DISORDERS: EFFICACY, SAFETY, AND FUTURE PERSPECTIVES

I. F. Fedotova, I. V. Korzh, K. O. Fedik

Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

✉ Inga Fedotova, MD, DMSci: ibolokadze@ukr.net; https://orcid.org/0000-0003-2069-7020
✉ Iryna Korzh, MD, PhD: ikorzh@ukr.net; https://orcid.org/0009-0000-1028-6768
✉ Kateryna Fedik: fedikkaterina09@gmail.com

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K. F. Vegner — an outstanding scientist, founder of the national orthopedics and traumatology

V. O. Tankut [1], I. V. Golubeva [1], L. V. Filipenko [2], O. G. Shevchenko [1]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] Kharkiv National Automobile and Road University. Ukraine

The main stages of the research achievements of the outstanding scientist orthopedic and traumatologist Professor Karl Fedorovych Wegner are characterized and presented. His significant contribution to the development of a functional method of treating bone fractures and his use of the skeletal traction method for treating a femoral fracture are outlined. Objective. To show the contribution of K. F. Wegner to the formation and development of domestic orthopedics and traumatology, in particular to the technology of treating bone fractures and bone tuberculosis, the organization of narrow-profile orthopedic and traumatological care for victims with industrial injuries, and the development of the concept of «emergency surgery». Methods. An information search was conducted in electronic databases, archives, and the library of the State Institution «Institute of Spine and Joint Pathology named after Prof. M. I. Sytenko of the National Academy of Medical Sciences of Ukraine». Results. Karl Fedorovych also revealed in detail the concept of what a bone fracture is, analyzed the mechanisms of its occurrence. The works of K. F. Wegner are analyzed, the professor's contribution to the formation of domestic orthopedics and traumatology is highlighted. The phenomenon of elitist thinking of Karl Fedorovych Wegner, which became the foundation of the collective medical experience of the Kharkiv School of Orthopedists and Traumatologists, of which he is the founder, is characterized in a multi-vector manner. Conclusion. It is proven that Professor Wegner is the founder of the modern system of providing medical care to patients with occupational injuries of the musculoskeletal system. Special attention is paid to the methods of treating bone tuberculosis introduced by him.

Схарактеризовано й подано основні етапи дослідницького доробку видатного вченого ортопеда-травматолога професора Карла Федоровича Вегнера. Окреслено його значний внесок у розвиток функціонального способу лікування переломів кісток і використання ним методу скелетного витягнення для лікування перелому стегнової кістки. Мета. Показати внесок К. Ф. Вегнера в становлення і розвиток вітчизняної ортопедії та травматології, зокрема в технології лікування переломів кісток і кісткового туберкульозу, організацію вузькопрофільної ортопедо-травматологічної допомоги постраждалим з виробничими травмами, розробку концепції «хірургії невідкладних станів». Методи. Проведено інформаційний пошук в електронних базах, архівах і бібліотеці ДУ «Інститут патології хребта та суглобів ім. проф. М. І. Ситенка НАМН України». Результати. Проаналізовано роботи К. Ф. Вегнера, висвітлено внесок професора в становлення вітчизняної ортопедії та травматології. Різновекторно схарактеризовано феномен елітарного мислення Карла Федоровича Вегнера, яке стало фундаментом колективного лікувального досвіду Харківської школи ортопедів-травматологів, засновником якої він є. Карл Федорович детально розкрив поняття, що таке перелом кісток, проаналізував механізми його виникнення. Висновок. Доведено, що професор К. Ф. Вагнер є засновником сучасної системи надання медичної допомоги хворим із виробничими травмами опорно-рухової системи. Особливу увагу звернено на запроваджені ним способи лікування кісткового туберкульозу. Ключові слова. Виробнича травма, переломи, лікування, кістковий туберкульоз, організація медичної допомоги.

Keywords. Industrial injury, fractures, hip, treatment, bone tuberculosis, organization of medical care

Introduction

In recent decades, there has been growing interest among researchers in studying the biographies of scientists who have made significant contributions to various fields of science. These individuals have not only identified promising research areas but also provided crucial impetus for the further advancement of science and offered examples of problem-solving for young scientists. Examining their life paths allows for the identification of the features and patterns in the development of science, shaped by the prevailing social conditions of their time.

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The analysis of the scientific achievements of Professor K. F. Wegner contributes to a deeper understanding of the formation and development of orthopedics and traumatology in Ukraine, as well as to the improvement of the planning and organization of scientific research in these fields.

Purpose: to show the contribution of Professor K. F. Wegner to the formation and development of domestic orthopedics and traumatology, in particular in the technology of treating bone fractures and bone tuberculosis, the organization of orthopedic and traumatological care.

Material and methods

An information search was conducted in electronic databases, utilizing data on the life of K. F. Wegner, as well as memoirs from his students. The professor's own works, housed in the library of the State Institution "Professor M. I. Sytenko Institute of Spine and Joint Pathology of the National Academy of Medical Sciences of Ukraine", were also analyzed. The figure of Karl Fedorovych captures the attention of both orthopedic traumatologists and historians of medicine, as well as local historians. His biographical information is presented in the work of O. Kuptsov (History of the City of Yenakiyevo) [1]. Memories of Karl Fedorovych and accounts of his collaboration with others can be found in the publications of his students, including the renowned orthopedic traumatologist Professor V. D. Chaklin [2] and V. Ya. Tarkovskaya [3]. In their work on the history of orthopedic development in Kharkiv, employees of Professor M. I. Sytenko Institute presented a socio-psychological portrait of Karl Fedorovych, highlighting his family ties [4]. K. K. Silvay and T. P. Galitsa, in their article [5], focused more on his professional activities.

Fig. 1. Photo of K. F. Wegner 1886 (a), 1914 (b)

Results

Karl Fedorovich (Teodorovich) Wegner was born on 12 December 1864 in Kamianets-Podilskyi. After graduating from high school in 1885, he studied at the Mathematics Faculty of St. Petersburg University, but in 1887 he transferred to the Medical Faculty of Yuriev (Derpt) University (Estonia). In 1892–1893, while still a student, Karl Fedorovich worked as an assistant in a clinic in Dorpt. In 1893, after graduating, he was accepted as a resident physician at the Yuzivka Factory Hospital (now Donetsk), where Karl Fedorovich thoroughly studied the characteristics of injuries in workers in the mining and mining industry and established himself as a talented doctor who had his own progressive views on the organization of medical care for patients. He developed a plan for the creation of a new institution, according to which in 1896 the Petrovsk Factory Hospital was built, where he later worked as a senior doctor [1].

The rise in industrial injuries and worker disabilities in the mining sector during this period prompted the decision to establish a specialized orthopedic hospital for the treatment of musculoskeletal injuries. In May 1907, the Council of Miners of the South of Russia sent Karl Fedorovich to Germany to study the organization of medical care for accident patients and methods for assessing the loss of working capacity among injured workers. He was entrusted with this responsibility due to his expertise in the field and his reputation as a creative organizer capable of leading this important initiative. Following his trip, Wegner authored an article titled "On Workers' Insurance in Germany", which was published in several issues of the magazine Mining Leaflet [1].

Using the experience he gained, Karl Fedorovich developed a project for a scientific and medical institution specializing in orthopedics and traumatology. Based on this project, the Medical and Mechanical Institute was established and opened in Kharkiv on 08 June 1907, with Wegner appointed as its head. The institute was tasked with treating workers injured in the mining and industrial sectors, addressing functional disorders resulting from musculoskeletal injuries, and evaluating the degree of working capacity loss among the injured [6].

K. F. Wegner, as a traumatologist, was a strong advocate of the functional method for treating bone fractures. From the very beginning of the institute's work, under his leadership, this approach became a priority in patient care. To support this, specialized technical equipment was acquired for the institute.

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In 1909, based on the results of his research, K. F. Wegner published an article titled “On the Recognition of Femoral Neck Fractures” [7], in which he analyzed the diagnostic errors made by doctors when identifying femoral neck fractures in injured workers. He stressed that diagnosing a femoral neck fracture is a challenging task for doctors without the use of an X-ray machine. Even then, Karl Fedorovich advocated for recognizing “accident medicine” as an independent branch of scientific and practical medicine, calling for the specialization of doctors in “accident surgery” and the establishment of hospitals equipped specifically for the diagnosis and treatment of accident-related injuries [7].

In 1910, Karl Fedorovich performed the first operation in the country at the Medical-Mechanical Institute using the “skeletal extension” technique for the treatment of a femoral fracture [6] (Fig. 2).

Thanks to his scientific work, the functional method of treating bone fractures, which was progressive for its time, was introduced across the country. Under the leadership of K. F. Wegner, his team contributed many innovative approaches to the treatment of such fractures. One notable advancement was the combined method of extraction, which involved simultaneous application of nail traction on one segment and adhesive plaster traction on the other [5].

Several of his scientific works from this period highlight K. F. Wegner's active efforts in addressing the challenges of fracture treatment, including "On Indirect Fractures of the Spine" (1910), "On the Question of the Occurrence of False Joints", "Zur Behandlung veralter Oberschenkelbrueche" (1911), and "On the Steinmann Method in the Treatment of Hip Fractures" (1912). In 1914, Wegner presented his experience in fracture treatment at the 13th Congress of Surgeons in a report titled “Modern Principles of Fracture Treatment” [6]. That same year, he successfully defended his doctoral dissertation on “Closed Fractures of the Femur Diaphysis” [8].

Fig. 2. Patient who was first treated with permanent skeletal traction in domestic practice

As senior physician and later director of the Medical-Mechanical Institute, K. F. Wegner prepared annual reports for the Council of the Congress of Miners. In these reports, he provided detailed histories of diseases, treatment methods, and outcomes for patients with orthopedic injuries. His reports offered valuable practical insights into fracture treatment, the management of their consequences, and the restoration of function in damaged support and movement organs [6].

From the outset of his career in traumatology, Karl Fedorovich was deeply engaged with the issues surrounding the organization of medical care for workers injured in industrial accidents. He dedicated several of his works to this problem, in which he emphasized the specific challenges involved in organizing medical care for injured workers. K. F. Wegner frequently delivered reports at meetings of the Society of Mining Doctors, the Pirogov Congresses of Doctors, and various international medical congresses.

Karl Fedorovich was elected a member of the permanent presidium of the International Congress on Combating Accidents [1]. Through his business trips, K. F. Wegner reported to the Council of the Congress of Mining Workers, detailing the results of fracture treatments presented at the congresses. He also addressed the issue of organizing the cooperation between doctors of insurance companies and health insurance funds (hospitals) [9].

During the First World War (1914–1918), in accordance with the Council's decision, K. F. Wegner organized wards for soldiers with severe gunshot fractures at the Institute. He also oversaw the operation of a 225-bed infirmary opened in Kharkiv for the treatment of soldiers with gunshot fractures of the limbs, where he applied the functional treatment methods he had already tested.

In 1916, K. F. Wegner published the scientific work “Principles of Functional Treatment in Case of Injuries and Diseases of the Limbs”. Drawing from his experience at the Medical-Mechanical Institute, he concluded that active movements in injured limbs are a crucial therapeutic tool, particularly in preventing future joint contractures. He demonstrated that systematic use of active movements promotes normal blood circulation in the tissues, aiding in the “resorption and physiological neutralization of painful infiltrates and pathological elements”, while also improving functional state of the limbs. Wegner believed that active movements, combined with stretching and

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positioning the limb in a half-bent state, were particularly effective in treating joint contractures [10].

During the war, the Institute, under Wegner's leadership, was the first in the country to organize training courses for paramedical personnel, where 28 “sisters of mercy” were trained. After graduation, 20 of them took positions in the local hospital, while 8 were sent to military medical units on the front lines [6].

Between 1918 and 1925, the patient demographic expanded to include children with various orthopedic conditions. Karl Fedorovich remained deeply involved in medical work, personally performing closed reduction of congenital hip dislocations in young children using the Lorenz method, and employing skeletal traction with the Steinmann nail [3].

A notable achievement of Professor K. F. Wegner was his work on treating bone and joint tuberculosis, a widespread disease in the 1920s. In 1922, 16 % of the patients at the Medical and Mechanical Institute were diagnosed with this condition. Wegner applied functional treatment methods for managing bone and joint tuberculosis, including creating a solarium on the roof of the Institute for patients. To prevent joint contractures and alleviate pain, joints were unloaded through stretching, and a specialized diet was also introduced for patients [2]. Several of his works are dedicated to this issue, such as “The Current State of the Treatment of Tuberculosis of Bones and Joints” (1922), “On the Treatment of Tuberculosis of Bones and Joints” (1922), and “On the Fight Against Bone and Joint Tuberculosis” (1925) [5].

Karl Fedorovych was deeply committed to studying the experiences of European clinics, regularly delivering lectures on advanced methods for treating orthopedic and traumatological patients based on these studies, which generated significant interest [3].

He was particularly devoted to the training of young orthopedic traumatologists. Under his mentorship, several notable scientists took their first steps at the institute, including M. P. Novachenko, V. D. Chaklin, M. I. Sitenko, V. O. Marx, and A. P. Prykhodko. It was Karl Fedorovych who laid the foundation for the development of the Kharkiv school of orthopedic traumatologists, and his student, V. D. Chaklin, later founded the Sverdlovsk school [6].

V. D. Chaklin, in his memoirs, highlights Karl Fedorovych’s extraordinary diligence, accuracy, and punctuality. He worked tirelessly, often 12-hour days, and was demanding both of himself and his students. Wegner was meticulous in observing patients postoperatively and during the treatment of bone fractures using the functional method, which was grounded in a thorough understanding of muscle physiology and pathophysiology in the context of bone fractures, as well as joint biomechanics. Wegner was a well-rounded physician, fluent in four foreign languages, and actively participated in European orthopedic and traumatology congresses, staying abreast of new advancements in research [2].

In addition to his leadership role at the institute, Karl Fedorovych was a professor at Kharkiv Medical Institute. At his initiative, the Ministry of Health of Ukraine granted permission to establish a department of orthopedics at the university [2]. In 1921, he became the head of the department of orthopedic surgery and a professor of operative surgery with topographic anatomy at the institute [11].

From 1926 onward, Professor K. F. Wegner headed the orthopedic department at the State Institute of Phthisiology and Orthopedics in Moscow. He played an active role in organizing and hosting the First All-Russian Conference on Industrial Traumatology in December 1926.

In the same year, Wegner’s seminal work “Fractures and Their Treatment” was published, and by decision of the Scientific Council of the People’s Commissariat of Health, it was adopted as a textbook for students [12]. This monograph compiled data on 3,892 cases of fractures treated at Kharkiv Medical and Mechanical Institute. Wegner thoroughly explored the concept of bone fractures and analyzed the mechanisms behind their occurrence. He emphasized the importance of fully understanding the presentation before starting treatment, including hemorrhages, ruptures of muscles, fascia, tendons, ligaments, the nature of bone destruction, and damage to vessels and nerves. In the section “Diagnosis of Fractures”, Wegner provided a detailed description of fracture symptoms, which was particularly important in cases where radiography was not possible. He also listed the classification of fractures, explained the displacement of bone fragments, the process of fracture healing, and laid out the foundational principles for their treatment [13].

Wegner served as a consultant in orthopedics at the polyclinic of the People’s Commissariat of Health of the USSR and was actively involved in the publication of the Journal of Modern Surgery [1].

In 1929, Karl Fedorovych moved to Switzerland, settling in Bern, where he worked in the clinic of the renowned Dr. Steinmann. Unfortunately, little is known about his time in Switzerland, and further research is needed to better understand this period

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of his life. Karl Fedorovych Wegner passed away in December 1940 [1].

Conclusions

Professor Karl Fedorovich Wegner was a remarkable scientist in the field of orthopedics and traumatology during the 19th and 20th centuries. He made a profound contribution to the development of both the theory and practice of bone fracture treatment. Wegner is particularly recognized as the founder of the skeletal extension method for treating fractures, a technique that dominated the field at the time.

Additionally, K. F. Wegner pioneered the use of metal structures in the treatment of bone fractures, an innovation that paved the way for the development of key areas in modern orthopedic surgery, such as intramedullary fixation and bone osteosynthesis. His work laid the foundation for significant advancements in fracture treatment techniques, influencing the field for generations to come.

Professor K. F. Wegner made a profound contribution not only to the treatment of bone tuberculosis but also to the organization of medical care for patients with bone fractures, particularly in the context of combat trauma. He developed plans for establishing the Petrovskaya Factory Hospital and the Medical-Mechanical Institute, laying down the foundational principles for organizing specialized orthopedic and traumatological institutions to provide care for injured individuals.

Wegner is credited with founding the first domestic school of orthopedics and traumatology, where he mentored a distinguished group of scientists, including M. I. Sytenko, M. P. Novachenko, V. D. Chaklin, and many others. His influence extended far beyond his own time, and the legacy of his work continues to shape modern orthopedic practice.

The scientific achievements of Professor K. F. Wegner remain a valuable resource not only for the history of medicine but also for contemporary practices. Some of his treatment methodologies for musculoskeletal system pathologies still retain their relevance and importance today.

Conflict of interest. The authors declare no conflict of interest.

Prospects for further research. Future research could continue exploring Wegner's contributions to the organization of traumatology medical institutions, as well as investigating his life and activities during his time in Switzerland.

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K. F. VEGNER — AN OUTSTANDING SCIENTIST, FOUNDER OF THE NATIONAL ORTHOPEDICS AND TRAUMATOLOGY

V. O. Tankut [1], I. V. Golubeva [1], L. V. Filipenko [2], O. G. Shevchenko [1]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] Kharkiv National Automobile and Road University. Ukraine

✉ Volodymyr Tankut, MD, Prof.: ipps-konf@ukr.net; https://orcid.org/0000-0002-9901-4036
✉ Inna Golubeva: ipps-konf@ukr.net
✉ Larysa Filipenko, PhD in Historical Sci: filosof_it@khadi.kharkov.ua; https://orcid.org/0000-0003-4409-1672
✉ Olena Shevchenko: ipps-konf@ukr.net

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Mykola Ivanovych Berezka

First of September marked the 70th anniversary of the famous scientist, Doctor of Medical Sciences, Professor of the Department of Emergency and Urgent Medical Care, Orthopedics, Traumatology and Prosthetics of Kharkiv National Medical University, Mykola Ivanovych Berezka.

The jubilarian was born in Sumy region, where he studied at the medical school. In 1982, he graduated from Kharkiv Medical Institute with honors and continued studying there from 1982 to 1984 in clinical residency, specializing in orthopedics and traumatology.

From 1984 to 1988, Mykola Ivanovych worked as a traumatologist in the second traumatology department of Meshchaninov Emergency Care Hospital, from 1988 to 2000 as the head of the adult traumatology department at Kharkiv Regional Clinical Hospital - Emergency Medical Care and Disaster Medicine Center, then as its chief physician until April 2010.

Long-term work was reflected first in the candidate's thesis (1992), and then in the doctoral thesis "Clinical and organizational principles of treatment of patients with polytrauma in the conditions of an industrial region" (2011).

Mykola Ivanovich has maintained a longstanding association with Kharkiv National Medical University, dedicating nearly three decades of his career to the institution. In 2012, M. I. Berezka was awarded the academic title of professor, and since 2012 he has been teaching advanced training courses in the field of "Traumatology and Orthopedics". In 2012, he was appointed first acting Head of the Department of Anesthesiology, Traumatology and Extreme Medicine, then Head. Currently, he is a professor of the department.

Berezka's scientific achievements include 120 publications, 5 patents and 1 copyright certificate, 3 textbooks on orthopedics and traumatology in different languages in co-authorship. Under his leadership, 4 candidate and 1 doctoral dissertations were planned and defended, 3 more are planned.

He is a member of the following medical associations and societies: All-Ukrainian public organization "Ukrainian Association of Orthopedic Traumatologists"; AAOS; ESTES; SICOT; ISAKOS; All-Ukrainian public organization "Ukrainian Association of Sports Traumatology, Knee Surgery and Arthroscopy"; Association of Preventive and Anti-Aging Medicine.

The professor has been repeatedly awarded for his contribution to the development of medicine: an honorary diploma of the Ministry of Health of Ukraine (2000), gratitude of the mayor (2005, 2006), a diploma of the Verkhovna Rada of Ukraine (2006), gratitude and diplomas of Kharkiv National Medical University (2017, 2020, 2025).

Today, Mykola Ivanovych has not stopped his career. He is a reviewer of numerous monographs, textbooks, methodological guidelines, abstracts for obtaining a scientific degree, an official opponent during the defense of dissertations, a member of the editorial board of the "Journal of Clinical and Experimental Medical Research" of Sumy State University.

Dear Mykola Ivanovych! Please accept our sincere congratulations on the occasion of your anniversary. We extend our sincere wishes for your continued good health, sustained energy, notable scientific and professional accomplishments, appreciative students and colleagues, as well as enduring family comfort and prosperity. May every day bring you joy, inspiration and new victories!

All-Ukrainian public organization "Ukrainian Association of Orthopedics and Traumatologists"
Editorial Board of the Journal "Orthopedics, Traumatology and Prosthetics"
Staff of Kharkiv National Medical University

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Oleksandr Ivanovych Korolkov

On 15 August Oleksandr Ivanovych Korolkov, a famous pediatric orthopedist-traumatologist, scientist, lecturer, teacher, well-known specialist in the field of orthopedics and traumatology, turned 60 years old.

O. I. Korolkov was born on 15 August 1965 in the village of Shiryaev, Odesa region, in 1988 he graduated from M. I. Pirogov Odesa Medical Institute with a degree in "Medical practice". From 1989 to 1992 he worked at Frunzovsky Central Regional Hospital of Odesa region (now the village of Zakharivka) as a traumatologist, then as a clinical resident, and from 1994 to 1997 he was a full-time postgraduate student at the "M. I. Sytenko Ukrainian Research Institute of Orthopedics and Traumatology". In 1997–2000, he worked in the children's clinic at the same institution as a junior, later as a senior researcher, from September 2006 to February 2018 as the head of the scientific and organizational department. During this period, O. I. Korolkov actively participated in the organization and holding of dozens of scientific and practical conferences, seminars, symposiums of various levels, 6 plenums and 3 congresses of the Ukrainian Association of Orthopedists and Traumatologists.

In 1999, O. I. Korolkov defended his candidate's thesis "Post-repositional hyperpressure syndrome in congenital hip dislocation", and in 2011 his doctoral thesis "Recurrences of congenital dislocation and subluxation of the hip (diagnosis, treatment, prevention)".

In July 2002, he was awarded the academic title of senior researcher.

The growth of Oleksandr Ivanovych as a specialist and a person with extraordinary human qualities was facilitated by his professional training and informal communication with such bright personalities as professors I. G. Herzen, V. P. Topor, S. D. Shevchenko, O. V. Rolik, academician O. O. Korzh and many others.

Since March 2018, O. I. Korolkov has been working at the Communal Non-Profit Enterprise "Lviv Regional Children's Clinical Hospital of Lviv Regional Council "OKHMATDYT", has been heading the clinic of neuroorthopedics, traumatology and rehabilitation of children. Professor Korolkov teaches at Danylo Halytskyi Lviv National Medical University and works as a professor of the Department of Traumatology, Orthopedics and Military Field Surgery part-time. His scientific achievements include about 500 publications, as well as 47 patents of Ukraine and an invention.

To date, under the supervision of Oleksandr Ivanovych, 4 candidate and one doctoral theses have been defended, a PhD thesis and a master's thesis are being completed.

O. I. Korolkov is the vice-president of the NGO "Ukrainian Association of Pediatric Orthopedists and Traumatologists", a member of the board of Public Organization "Ukrainian Association of Orthopedists and Traumatologists", and a number of international associations. He is a member of the editorial board of the journals "Social Pediatrics and Rehabilitation" and "Moldavian Journal of Pediatric Surgery".

Professor Korolkov takes an active part in organizing and conducting scientific and practical conferences, seminars, symposiums, congresses of various levels. He regularly delivers reports at scientific and practical conferences. On his initiative, several international conferences and symposiums on topical issues of neuroorthopedics and pediatric orthopedics and traumatology were held with the participation of specialists from many countries of the world.

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O. I. Korolkov was repeatedly encouraged by the Honorary Certificates of the Verkhovna Rada Committee on Health (2007, 2013), the Ministry of Health of Ukraine (2011), the National Academy of Medical Sciences of Ukraine (2010, 2015). In 2023, he received the National Prize "Treasure of the Nation" in the nomination "Best Doctor of the Year". He enjoys well-deserved authority and respect among students, patients and colleagues, and has an active public position.

Oleksandr Ivanovych is an example of high professionalism, dedication to his chosen cause and boundless care for patients. His many years of work combine scientific activity, clinical experience and pedagogical work, which made his name authoritative among colleagues in Ukraine and abroad.

Throughout his career, the jubilant has made a significant contribution to the development of modern approaches to the treatment of hip and foot pathology in children, the introduction of modern methods of rehabilitation of children with cerebral palsy, actively develops the latest technologies and standards, and promotes the integration of Ukrainian science into the world space.

His students are doctors of a new generation who adopt not only knowledge, but also high moral principles, love for the profession and a sincere desire to help people.

Dear Oleksandr Ivanovich! Please accept our heartfelt congratulations on your anniversary, wishes of good health, many years of active creative and professional activity, new scientific achievements and human happiness.

May your path continue to be full of fruitful work, recognition of colleagues, respect of students and gratitude of patients.

Editorial Board of the Journal "Orthopedics, Traumatology and Prosthetics"
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