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Osseointegrative prosthetics: opportunities, challenges, and prospects for its application in the rehabilitation of patients with amputated limbs (literature review)

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Rehabilitation of patients with amputated limbs is a pressing medical and social issue in modern society. A novel method for partial restoration of limb function is osseointegrative prosthetics. Its main advantage lies in the fact that the implant allows mechanical loads and forces to be transmitted directly to the bone, whereas in traditional prostheses, they mainly act on soft tissues. Despite nearly 30 years of experience with osseointegrative implants globally, these technologies have not yet been implemented in either scientific or clinical practice in Ukraine. Objective. To conduct a literature review of the global practical experience with the use of osseointegrative prosthetics in patients with amputations and to identify its main features, advantages, and disadvantages. Methods. The information search was performed in the bibliographic databases PubMed, Scopus, and Google Scholar. Results. The analysis of literature sources allowed us to distinguish the main types of osseointegrative implants, which differ in terms of design, materials, and surgical techniques: either single-stage or two-stage procedures, and fixation by threading or press-fitting. The rehabilitation period ranges from 6 months to 2 years. Within the first two years, certain complications such as bone infections and skin inflammation should be expected. However, most of these pathological conditions can be effectively managed. Conclusions. Successful fixation of osseointegrative implants requires optimizing the patient's bone, the prosthetic surfaces, and the 'skin-implant' interface. The implementation of these technologies requires multidisciplinary teams of specialists, including physicians, engineers, and rehabilitation experts. Osseointegrative implants significantly enhance patients' functional abilities and quality of life, opening up greater opportunities for the use of bionic and robotic prosthetics.

Реабілітація хворих з ампутованими кінцівками є актуальною медико-соціальною проблемою сучасного суспільства. Новітнім методом часткового відновлення функції кінцівок є остеоінтегративне протезування. Основна його перевага полягає в тому, що імплантат дозволяє передавати механічні навантаження та сили безпосередньо на кістку, тоді як у традиційному протезі, вони переважно діють на м'які тканини. Незважаючи на майже 30-річний досвід використання остеоінтегративних імплантатів у світі, в Україні відповідні технології ще не впроваджені ні в наукову, ні в клінічну практику. Мета. Провести літературний огляд щодо практичного світового досвіду застосування методики остеоінтегративного протезування в пацієнтів із ампутаціями та визначити його основні особливості, недоліки і переваги. Методи. Інформаційний пошук виконувався в бібліографічних базах даних PubMed, Scopus та GoogleScholar. Результати. Аналіз літературних джерел дозволив виділити основні види остеоінтегративних імплантатів, які відрізняються, як за конструкцією й матеріалом, так і за хірургічною технікою їхнього встановлення: одним чи двома втручаннями, різьбовою фіксацією чи впресуванням. Час реабілітації хворих складає від 6 міс. до 2 років. За перші 2 роки слід очікувати ті чи інші ускладнення і септичні процеси кістки та запалення шкіри. Проте більшість цих патологічних станів вдається ефективно нейтралізувати. Висновки. Для успішної фіксації остеінтегративних імплантатів необхідно оптимізувати кістку пацієнта, поверхні протеза та інтерфейс «шкіра – імплантат». Упровадження відповідних технологій вимагає наявності багатопрофільних команд фахівців: лікарів, інженерів, реабілітологів та ін. Остеоінтегративні імплантати суттєво збільшують функціональну здатність пацієнтів, якість їхнього життя; з'являються більші можливості до використання біонічних, роботизованих протезів. Ключові слова. Ампутація, кістково-якірний протез, остеоінтегративні імплантати, штучні кінцівки, інфекція, реабілітація, якість життя.

Keywords. Amputation, bone-anchored prosthesis, osteointegrative implants, artificial limbs, infection, rehabilitation, quality of life

Introduction

Rehabilitation of patients with amputated limbs is an urgent medical and social problem of modern society. Life quality is inextricably linked to mobility, therefore the limited ability to walk in case of loss of the lower limbs and the absence of upper limb function reduces household and social activity. The average frequency of amputations in the world ranges from 0.2 to 25 cases per 100,000 population [1]. The most frequent causes are the consequences of diabetes with occlusive phenomena of blood vessels, malignant tumors of the musculoskeletal system, injuries at work, accidents, wounds during combat operations. The number of amputation cases in 2019 due to injuries increased in 204 countries by 16.4 % (552.45 million) compared to 1990 [2]. Prostheses are used to increase mobility, independence, safety and quality of life after the loss of limbs. However, despite the more than 500-year history of the development of this technology, to this day the general idea of their arrangement is constant — the remains of the limb are connected to the stump-receiving sleeve of the prosthesis in one way or another [3]. Only approaches to construction and materials have changed. Due to the incorrect formation of the stump, physiological features of the body, mechanical stress on soft tissues, prosthetic repair can result in chronic pain syndrome or skin irritation, ulcers, which, in turn, induces intolerance to prostheses, reduced mobility and deterioration of the quality of life [4] .

Considering these consequences, approximately 44 % of people with upper limb amputations and 5–20 % with lower limb amputations do not use their prostheses. At the same time, most patients (34–63 %) who use lower limb prostheses due to poor proprioception and imbalance have a high risk of falling (50 %), which in 7 % leads to stump bone fractures [5].

A new stage in the development of prosthetic repair was the discovery of the process of osseointegration in experiments on animals. R. T. Bothe, L. E. Beaton and H. A. Davenport (1940) discovered bone formation on titanium implants; G. Leventhal et al. (1951) described the process of osseointegration of titanium screws into the femur of rats [6]; P. I. Branemark (1952) investigated the blood flow at the place of implantation of titanium rods in the bone of a rabbit and introduced the concept of “osteointegration” [7]. Now this term implies the development of a direct structural-functional connection between the living bone and the surface of the artificial implant due to the formation of new bone tissue by the body, which is connected to the surface of the integrated body.

The discovery of this phenomenon made it possible to develop implants of the same name for humans, first for dental purposes [8], and later for limbs [9]. Thus, in 1990, the work of P. I. Branemark was expanded by his son, R. Branemark, as a result of which the first osteointegrative prosthesis (OP) of the lower limb was installed on 15 May 1990 in Sweden [10]. OP is a biocompatible metal device that is implanted into the residual bone of the stump with the possibility of further osseointegration. Its opposite end protrudes outwards and after some time a limb prosthesis can be attached to it, which eliminates the need to use a sleeve-type device [11]. The mechanical load is transferred from the limb prosthesis to the adapter (abutment), then from the abutment to the fixator, and finally from the latter to the bone. Usually, implantation is performed in two separate operations, but it can also be performed during one intervention in patients with acceptable bone quality [12].

Today, the corresponding prosthetic techniques are already widely used in Europe, the USA, and Australia. However, implant design, surgical manipulation and rehabilitation techniques are still being researched and improved. Therefore, OP is recommended only for those patients in whom the use of traditional implants is impossible.

The relevance of the implementation of the osteointegrative implantation technique in Ukraine relates to the need to rehabilitate a large number of wounded servicemen due to the war with Russia and determines the necessity of our research.

Purpose: to conduct a literature review of clinical world experience in the use of the technique of osteointegrative prosthetic repair in patients with amputations and to determine the main features, disadvantages and advantages.

Material and methods

Information search was performed in PubMed, Scopus and GoogleScholar bibliographic databases. The main search keywords were: Amputees [Mesh], amputation; Artificial Limbs [Mesh], prostheses; implants; rehabilitation; osseointegration; osseointegrated reconstruction and rehabilitation; limb reconstruction; extremity amputations. The search period was 10 years, and it included English-language articles. 269 sources were found from which 57 original articles and 4 systematic reviews remained after excluding duplicates and inconsistencies with the research objective.

Results and their discussion

Modern varieties of OP and their manufacturers

The main advantage of OP is the transfer of mechanical load and force during human movement directly to the bone by the implant, while in the sleeve prosthesis these forces act mainly on soft tissues. This redistribution of loads provides better limb proprioception [11]. The world experience of using OPs is only 34 years, so clinical research on the results of their use is still ongoing. At the same time, the number of OP manufacturers is limited and each of them offers its own types of designs. All OPs consist of several elements, so it is more correct to call them a system of implants.

The main types of OP are listed in Table 1 [11, 13]. All of them are at various stages of development, research and approval for use. The oldest of them is OPRA (1998), then ILP (1999), Compress® Device (2012), then OPL (2013), OFP (2016) [14, 15]. The newest one is the POP prosthesis [16], and the ITAP was not approved for production after negative results of a clinical trial [9].

Most OP manufacturers make it from a titanium alloy, except for ILP, which is a cobalt-chromium-molybdenum alloy. Their coating is usually rough, which is achieved due to plasma or laser sputtering of titanium, or porous (Compress® Device, POP). The surface of the outer part of the abutment, which is in contact with the skin in all OPs, is polished. For OPRA, ILP and POP, the surgical installation technique is two-stage (S1 and S2), while the OPL, Compress® Device provides a one-stage surgical option. The OFP prosthesis can be installed in two or one stage (in cases where the residual bone is not covered by soft tissues) (Table 2) [9, 12].

In the case of a two-stage surgical technique, during the primary intervention (S1), a part of the implant is implanted into the remaining bone tissue of the amputated limb, which directly participates in osseointegrative processes and in the future ensures reliable mechanical stability of the "bone-implant" system.

During the second surgery (S2), usually after 3–6 months, a permanent abutment is installed. Let us briefly discuss the features of this technique using OPRA as an example.

If OPRA is used during the S1 stage, after drilling and cleaning the residual bone channel, an implant element (Biofixture) is integrated into it, which has a self-tapping thread on the outer surface. This design minimizes the probability of mechanical damage to the bone and ensures close contact of the prosthesis with its endosteum due to a significant increase in the effective contact surface of the implant with the bone for the physiological process of osseointegration [54].

Table 1

Main types/models of prostheses for osseointegrative prosthetic repair and their use in the world practice

Bone implant interface	Implant system	Level of amputation	Status	Clinical studies
Threaded	OPRA	Transfemoral, transtibial, transhumeral, transradial, thumb, digital	Approved by EU countries, Australia, USA (FDA Class III)	[12, 13, 25, 26, 27, 28, 17, 18, 19, 20, 21, 22, 23, 24]
Press-Fit	ILP	Transfemoral, transtibial, transhumeral	Approved by EU countries, Australia	[9, 12, 37, 3 8, 39, 40, 29, 30, 31, 32, 33, 34, 35, 36]
	OPL	Transfemoral, transtibial	Approved by EU countries, clinical studies	[12, 29, 45, 30, 32, 33, 35, 41, 42, 43, 44]
	OFP	Femoral implant	Approved by EU countries	[46, 47]
	POP	Transfemoral	Clinical studies	[16, 48, 49, 50]
	ITAP	Transfemoral, transhumeral	Not manufactures	[51]
Compression/Pin Lock	Compress® Device	Transfemoral, transhumeral	Custom, FDA клас II	[52, 53]

Notes: OPRA — Osseointegrated Prostheses for the Rehabilitation of Amputees, (Integrum AB, Melndal, Sweden); ILP or ESKA Endo-Exo — Integral Leg Prosthesis (ESKA Orthopaedic, Lübeck, Germany); OGAP–OPL —Osseointegration Group of Australia–Osseointegration Prosthetic Leg (Permedica, s. p. a, Milan, Italy); POP — Percutaneous Osseointegrated Prosthesis (DJO Global, Austin, USA); ITAP — The Intraosseous Amputation Prosthesis (Stanmore Implants Worldwide, Watford, United Kingdom); OFP or BADAL X™ (sometimes OTN Implants or BADAL X™) — Osseointegrated Femur Prosthesis (OTN Implants BV, Arnhem, Netherlands); Compress® Device — custom prostheses (Zimmer Biomet, Warsaw, Indiana, USA); FDA — Food and Drug Administration (USA).

Table 2

Comparison of the main characteristics of different OP models [9, 12]

OP type	Material	Bone-implant interface	Amount of surgeries	Time to full load after surgery
OPRA	Titanium	Titanium Laser engraving (nanoporosity)	2	3–18 months
ILP*	Cobalt-chromium-molybdenum	"Czech hedgehog" 1.5 mm (macroporosity)	2	2–3 months
OPL	Titanium	Plasma coating of titanium 0.3–0.5 mm (microporosity)	1	2–3 months
OFP	Titanium	Plasma coating of titanium or porous mesh coating	1 або 2	11 weeks
POP	Titanium	Porous coating	2	Not known
Comp-ress	Titanium	Porous coating	1	12 weeks

Note. * This prosthesis does not involve the process of osseointegration due to the cobalt-chromium-molybdenum alloy from which it is made.

The fixator is deepened 20 mm proximal to the surface of the osteotomy, and not flush with it [12]. If necessary, the autograft is removed from the crest of the iliac bone and transplanted to the bone end, supporting it with compression during the consolidation period. The skin is closed with sutures and drained for 24 hours; antibiotic prophylaxis is prescribed. Between S1 and S2, patients can use their socket prosthesis. Stage S2, during which the abutment is placed, is performed through the final scar, while the subcutaneous fat is removed in the place where it is to pass. The remaining muscles are shaped and sutured to the periosteum 5–10 mm proximal to the end of the bone by myodesis. Then a round entrance hole is cut, through which the abutment screw is inserted into the endoprosthetic part of the device and compression is applied with the screw, after which the skin is sutured and drained for 24 hours.

Recommendations, contraindications and precautions

Despite the implementation of OP in the health care system in various countries, the technology is still being improved and many of its elements are of a research nature. This determines a rather conservative selection of patients for this type of rehabilitation.

The main recommendations during the establishment of OP are the impossibility of using the diseased sleeve prosthesis and the presence of chronic and pronounced clinical complications because of its use. Thus, the OPRA implant was approved by the FDA (USA) in 2020 for use in patients with transfemoral or below-the-knee amputations due to trauma or oncology, due to the lack of a positive rehabilitation effect when using a sleeve prosthesis (FDA class III) [55].

Indications for establishing OP [12]: amputations due to tumor diseases or traumatic; lack of effect from the sleeve prosthesis (periodic skin infections and ulcers in the contact area; pain; a short stump that prevents its use; scars on soft tissues); problems with maintaining the prosthesis due to excessive sweating; limited mobility.

The main contraindications for OPRA according to the FDA, which also apply to other implants, are [11]: incomplete growth of the skeleton; its atypical anatomy; less than 2 mm of cortical bone around the prosthesis in the patient, if there is already an implant; osteoporosis; age over 65 or under 22; body weight over 100 kg, including prosthesis; pregnancy; inability of the patient to comply with the requirements of treatment, rehabilitation and follow-up; severe diseases of peripheral vessels; diabetes mellitus with complications; skin diseases of the residual limb; neuropathy or severe phantom pain; active or dormant infection.

The FDA (USA) believes that OPs, which belong to class III devices, require a high degree of control to guarantee the safety and effectiveness of the device. Post-approval requirements include annual manufacturer reports. Therefore, the impossibility of clinical observation of the patient and completion of a full course of rehabilitation is considered a separate contraindication.

Precautions that should be considered during the installation of OP include obesity; increased risk of infection; disorders of the joints, inflammation of joints; concomitant diseases requiring administration of systemic steroids and intensive chemotherapy or radiation therapy.

Clinical complications

In published clinical studies of OP, the authors mostly evaluated the frequency of infection, periprosthetic fractures, and mechanical complications of OP.

Infectious ones are among the most frequent complications of OP [5, 56, 57] and by type they are divided into superficial soft tissue and deep bone. Also, some researchers use the classification proposed by

Al Muderis et al. [34], in which 4 degrees of infection are distinguished: 1) soft tissues of a low degree, 2) soft tissues of a high degree), 3) deep bone, 4) septic instability of the implant. The longest follow-up studies were conducted for OPRA (15 years), for other systems the duration was three times shorter, 5 years for ILP, and not exceeding 2 years for OPL and POP, and one year for OFP (Table 3).

For ILP, more information has been accumulated on the incidence of infectious complications, which ranges from 7.9 to 77 % over a follow-up period of 1 to 5 years. Superficial lesions of soft tissues were mainly recorded, cases of deep infection were reported in 2 investigations [31, 37], the largest of which was 5 % in the results of a study that lasted 5 years [31]. Within a year, soft tissue infections were found in 42 % (21) of patients with ILP or OPL, but only 3 underwent surgery to remove these tissues, and the rest were treated with antibiotics [29]. In 13 months 7.9 % (5 subjects) had infectious complications, of which: 1 — deep bone infection, 1 — abscess due to hematoma after the first operation, all were successfully treated with antibiotics without removing the implant [37]. In 34 months 34 % (29) of ILP patients developed a low-grade or high-grade soft tissue infection, 4 had an abscess removed, and the rest were treated with antibiotics alone [34]. For 5 years, D. Reetz et al. [31] recorded infectious complications in 77 % (30) of cases, of which 5 % (4 people) had a deep infection that occurred in the first 2 years.

For OPRA, the results of long-term studies have been published, according to which the incidence of infectious complications (over 5-15 years) was 88 to 94% in the lower extremities. During 5 years of observation, R. P. Brånemark et al. [17] found this type of complication in 88 % (45) of patients, of whom 34 had a superficial infection and 11 had a deep infection, of whom 4 patients had the implant removed. For more than 10 years, D. J. Matthews et al. [23] recorded infectious complications in 94 % of patients (17 out of 18) with OPRA, 11 of them in the area of penetration of the implant into the stump, and in 5 subjects it was removed.

The incidence of osteomyelitis among patients with OPRA was also assessed. J. Tillander et al. [25] found it in 17 % (16) of cases during 7.9 years of observation with an average time to the onset of osteomyelitis of 2.6 years, of whom 10 had the implant removed, 4 were treated with antibiotics, and 2 had relapse or chronic infection. The risk of its development was estimated as 20 % (95 % CI; 0.12–0.33) within 10 years.

For upper limbs G. Tsikandylakis et al. [26] over 15 years observed infectious complications in 33 % (6 of 18) of patients with transbrachial amputation using OPRA, of whom 1 had a deep infection 3.5 years after S1, which was treated with antibiotics.

There is insufficient information regarding the frequency of these complications in patients with OPL. During one year of observation, they were detected in 51 % (16) of cases, of which 1 was septic instability of the implant (successful explantation was performed), and other superficial infections were treated with antibiotics [43]. According to L. McMenemy et al. [42] over 2 years, 100 % (7) of patients had cases of only superficial infection treated with antibiotics.

For POR and OFP, only soft tissue infections are known, but for a short period of observation (1–2 years) [16, 47]. During the follow-up year, 23 % (21 people) with an OFP prosthesis R. Atallah et al. [47] found soft tissue infections of low and high levels of activity. For almost 2 years, S. Sinclair et al. [16] recorded only 1 (10 %) case of superficial infection among 10 patients with POR.

Bacterial cultures in patients with OP were also assessed. M. Lenneras et al. [28] most often detected *Staphylococcus aureus* (47 % of cases) in the bone canal in 27 out of 30 patients who had an OPRA abutment replaced, and less often *Streptococcus, Enterococcus faecalis*, coagulase-negative staphylococci (CoNS), including *Staphylococcus lugdunensis*. Similar bacteria were recorded by D. J. Matthews et al. [23] in 5 subjects who had their OPRA implant removed due to infection. Namely, methicillin-resistant *Staphylococcus aureus; Staphylococcus epidermidis, Enterococcus*, and group B hemolytic streptococcus. Among patients with osteomyelitis and OPRA, the most common infections isolated because of surgery were *Staphylococcus aureus* and coagulase-negative staphylococci [25]. G. Tsikandylakis et al. [26] found *Escherichia coli* infection in one case of a deep upper extremity OPRA patient, which was treated with antibiotics.

Similar bacteria have been found in patients with ILP prostheses. M. Al Muderis et al. [34] detected *Staphylococcus aureus* or coagulase-negative staphylococci in 91 % (21) of cases with soft tissue infections, and group B Streptococcus in 2. At the same time, *Staphylococcus aureus, Staphylococcus spp.* and *Streptococcus spp.* are characteristic of normal skin microflora, and they are the predominant ones in the stoma of patients with ILP prostheses [37].

Currently, there is insufficient information on risk factors that affect the development of infectious complications. M. Al Muderis et al. [34] analyzed them

Table 3

Characteristics of patients with osteointegrative prostheses in clinical studies of infectious complications and periprosthetic fractures

Author, year	Number of patients	Amputation level	Gender	Age (years)	Observation term	Prosthesis
OPRA						
Branemark R. P. et al., 2019 [17]	51	transfemoral unilateral (45), bilateral (6)	28 male, 23 female	44 (20–65)	3; 6 months; 1; 2; 5 years	OPRA
Hagberg K. et al., 2023[21]	51	transfemoral	28 male, 23 female	32	5; 10 years	OPRA
Lennerås M. et al., 2017 [28]	30	transfemoral unilateral (28), bilateral (2)	24 male, 6 female	51 ± 13 (25–76)	2 years	OPRA
Matthews D. J. et al., 2019 [23]	18	transfemoral unilateral	15 male, 3 female	26,8 (24–30) 37,8 (21–49)	11,4 years — before* 12,3 years — after	OPRA
Tillander J. et al., 2017 [25]	96	transfemoral unilateral (90), bilateral (6)	60 male, 36 female	43,5 (19–65)	7,9 (1,5–19,6) years	OPRA
Tsikandylakis G. та співавт., 2014 [26]	18	transhumeral	16 male, 2 female	42 (19–69)	6 months and in 1; 2; 3; 5; 7; 10; 13 and 15 years	OPRA
ILP						
Al Muderis M. et al., 2016 [34]	86	transfemoral unilateral (81), bilateral (5)	65 male, 21 female	25–81	34 months (24–71)	ILP
Al Muderis M. et al., 2016 [29]	50	transfemoral unilateral	34 male, 16 female	49,4 (24–73)	1 year	ILP; OPL
Orgel M., Aschoff H. H. et al., 2022 [37]	66	transfemoral unilateral (62), bilateral (4)	37 male, 29 female	50,8 ± 12,3 (26–75)	3; 6; 12; 24 months	ILP
Reetz D. et al., 2020 [31]	39	transfemoral unilateral (38), bilateral (1)	30 male, 9 female	48,7 ± 13,9	5 years	ILP
OPL						
McMenemy L. et al., 2020 [42]	7	transfemoral bilateral	7 male	29,8 (24–33)	2 years, average 46 months (36–52)	OPL
Reif T. J. et al., 2021 [43]	31	ттransfemoral (18) transtibial (13)	11 male, 7 female 8 male, 5 female	49,6 ± 12,0 51,3 ± 14,1	1 year	29 — OPL; 2 — Signature Orthopaedics implants
POP						
Sinclair S. et al., 2022 [16]	10	transfemoral unilateral	10 male	48,8 ± 12,1 (32–68)	≈ 2 years (104 weeks)	POP
OFP						
Atallah R. et al., 2020 [47]	91	transfemoral, transtibial	65 male, 26 female	54 ± 14	1 year	OFP

Note. * — groups that were fitted with a prosthesis before and after the established OPRA protocol.

in case of severe infection among 86 patients with ILP and found that women had a 6-fold higher risk (OR = 6.5; 95 % CI = 1.1 to 38.15). The risk of mild infection in case of obesity (BMI > 25) is 3 times, smoking is 7 times. At the same time, J. Tillander et al. [25] found no effect of gender, age, uncomplicated diabetes, overweight, frequency of abutment replacement on the risk of infection in a study of 96 patients with OPRA prostheses.

It is also not known for certain whether the frequency of deep infection increases over time. K. Hagberg et al. [21] did not indicate a significant difference in the number of incidents of its manifestation between the first 5 years and the following 5 years after OPRA implantation, which was 0.3 per person-years (CI: 0.1–0.5).

J. S. Hoellwarth et al. [9] suggested that the risk of infection is reduced if soft tissue treatment is improved. Since it is inevitable if bacteria colonize the implant before its integration into the tissues, good sealing of the interface between the implant and the soft tissues is necessary to prevent infectious complications [56]. It is believed that the risk of infection, including removal of the implant, is somewhat lower than that of one-stage surgical tactics [5, 56]. However, it is too early to draw unequivocal conclusions, since the results of treatment depend on the technique of intervention, which is constantly being improved, on the experience of specialist doctors, the conditions for conducting the main stages of therapy, the duration of observations, comprehensive monitoring at the quantitative level of objective data, which has not been sufficiently developed in practice medicine

Periprosthetic fractures are infrequent complications (from 8 to 10 %) compared to infectious ones, and only in rare cases lead to implant removal.

L. McMenemy et al. [42] found a periprosthetic fracture after trauma in 14 % (1 of 7) of patients with OPL. In cases of ILP, M. Al Muderis et al. [29] reported such fractures in 8 % (4) of people, 3 had osteoporosis. In both studies, fractures were successfully treated with screw fixation without removing the implant [34, 42]. One of the works gives an example of a periprosthetic fracture that occurred in 1 (10 %) patient. As a result of the injury, the POP implant was removed [16]. J. S. Hoellwarth et al. [35] analyzed the data of 458 subjects with OPL or IPL, of whom 17 had upper limb amputation, and the rest had lower limb amputation, and found these fractures in 5 % (22) of cases and only in the femur (15 — OPL, 7 — ILP). Most fractures (19 of 22) occurred up to 2 cm from the proximal end of the implant and all resulted from falls. In addition, this study showed that women have a 3.9-fold increased risk compared to men.

Besides periprosthetic fractures, cases of femoral fractures proximal to the implants were recorded, which were also treated without their removal [34, 43]. M. Al Muderis et al. [34] found an intertrochanteric fracture proximal to the IPL implant in 3 % (3) of patients. In another study, displaced fractures of the proximal femur occurred in 6 % (2) of individuals with OPL [43].

Mechanical complicatiopns associated with OP system components are quite common. Thus, the failure rate of a prosthesis or abutment is from 0 to 40 %. In addition, loosening of the implant occurs, their frequency is from 0 to 29 %; 0–3 % with transfemoral amputation and up to 29 % with transtibial amputation [5, 56].

Functional results of using OP

The following questionnaires/tests are used to analyze functional results in patients after osteointegrative prosthetics: Q-TFA (Questionnaire for Persons with Transfemoral Amputation); SF-36; K-levels (a rating system for determining a person's rehabilitation potential in Medicare); Amputation Mobility Predictor (AMPPRO); 2- or 6-minute walking test, timed up and go tests; time spent in the prosthesis (wearing time (PUS)); PRO measures (use of prosthesis, mobility, quality of life related to physical health); Patient-Reported Outcomes Measurement Information System (PROMIS).

According to the SF-36 questionnaire, the quality of life in patients with OP improved after one year for ILP [29], after 2 [20, 23], 5 and 10 years [21] for OPRA, after 2 years for OPL [42], than to osteointegrative prosthetic repair in case of transfemoral amputation. The different duration of quality-of-life assessment is related to the different duration of rehabilitation protocols for everyone with an osseointegrative prosthesis.

According to the Q-TFA questionnaire, which analyzes mobility, problems and health status in general, in patients with transfemoral/transtibial amputation, the indicators also improved: with ILP [29, 31], with OPRA [18, 20, 21, 23], with OPL [42, 43], with OFP [47], with POP [16]. Compared to patients with a sleeve prosthesis, subjects with OP (ILP) had fewer problems with the implant, and therefore a higher quality of life according to the Q-TFA questionnaire [40].

Already one year after osseointegrative prosthetic repair, patients' walking improved according to the 6-minute walking test, which is shown for ILP [29], OPL [42–44], POP [16]. Longer prosthesis

wear times are reported for OFP [47] and OPRA [19]. At the same time, R. S. Gailey et al. [58] compared the sensation of body balance during walking (10-meter walking test) in individuals with sleeve prostheses (n = 11) and with OP (n = 11) and found no difference between them.

In separate studies, the following questionnaires were used to analyze the functional status of patients with OP: Amputation Mobility Predictor (AMPPRO) [29], PRO measures [17], PROMIS [43] and better data were found than before osteointegrative prosthetic repair.

So, analyzing the functional indicators of people with OP, we note that their quality of life, as well as walking, improves, the number of problems associated with the use of a prosthesis decreases, due to which the time of its use increases.

Rehabilitation and support of patients

Osteointegrative implants are high-tech products, their effective use requires a multidisciplinary approach, both during the planning of surgical intervention and its implementation, and at the next stage of patient rehabilitation. This process is long-term and essentially, taking into account the social aspect of the problem, it takes a lifetime. The coordinated interaction of doctors and people with OP, which consists of long-term and careful observation by doctors of the patient, their keeping clear medical documentation to objectify the time course of physiological processes and the conditions of their course, and the patient's compliance (a selection factor for OP implantation) gives it is possible to improve the quality of life and eliminate complications in a timely manner.

A fairly clear and strict patient rehabilitation protocol was developed for OPRA prostheses [4, 10]. It includes basic measures that must be carried out both after two stages of surgical interventions and during almost two years of active use of prostheses and appropriate training. Features of rehabilitation in the case of bilateral transfemoral limb amputation under the conditions of using OPRA prostheses are described by Hagberg K. et al. and R. A. Leijendekkers et al. [19, 59]. Rehabilitation and physiotherapy protocols have also been developed: for transtibial osseointegration of OPL [60]; post-traumatic transfemoral amputation and ILP [59, 61]. In Australia and the Netherlands, osseointegrative prostheses with press-fit fixation are widely used, therefore rehabilitation protocols called Osseointegration Group of Australia Accelerated Protocol (OGAAP-1 and OGAAP-2) [29, 59, 62] have been introduced.

One of the factors that reduces the speed of introduction of various OPs into broad practical medicine is the insufficiently comprehensive monitoring of the patient's functional and psychological state and his performance of timely procedures. Therefore, in addition to maintaining purely clinical databases, it is necessary to monitor other indicators with the corresponding regular survey of the patient [60].

Prospects for further development

One of the common problems in the use of prostheses is to increase their functionality to perform useful work for the patient and to maximize the recovery of the receptor/sensory properties of the limb. Appropriate strategies for solving these issues are the use of robotic implants that are controlled by biophysical signals [15, 63, 64]. To ensure this connection, during amputation, it is necessary to preserve nerve fibers, in the projection of which electrodes are connected directly to them [65]. The process of teaching the patient to control the prosthesis is long-term (years), but it significantly increases functional capabilities. Such new technologies should also influence the performance of classical amputations, where the use of OP was not planned from the beginning, in order to maximize preserve intact tissues and have the opportunity to improve the quality of life in the future due to the installation of other prostheses, in particular, osseointegrative prostheses. However, the use of skin electrodes leads to the development of a large number of electromechanical interference, and with long-term use causes skin irritation. This greatly complicates the learning process and limits the possibilities of management in general. OP prostheses can directly pass electrical conductors through the channels of the implant and connect them subcutaneously/intravenously to the nerve fibers (or to the nerves directly) [65, 66]. This increases the reliability and speed of signal transmission, increases immunity to interference, and the number of information channels. It should be noted that for the correct and timely management of technical systems, it is necessary to provide "prosthesis-patient" feedback, that is, to guarantee sensory sensitivity. At the same time, OPs are directly embedded in bone tissue and partially automatically perform this function.

In addition, the use of OP can potentially provide automatic diagnosis of the state of the implant, the "implant-bone" contact and other physiological processes, acting as an intermediate chain between measuring devices and the body [67].

Conclusions

Osteointegrative prostheses are the newest and most modern strategy for helping people with amputated limbs. Relevant engineering and clinical technologies have a high speed of development and implementation in practice. Successful OP fixation requires optimization of the patient's bone, the implant surface, and the skin-implant interface. Osseointegration should be approached with caution, guided by indications and contraindications, and adherence to the rehabilitation protocol.

Currently, 6 main types of OP are used all over the world: OPRA, ILP, OPL, OFP, POR, Compress. Of these, OPRA has the most clinical experience (it was launched in 1996 and received FDA approval for transfemoral prosthetics). All of them are made of titanium alloy, except ILP, and consist of an implant that integrates into the bone and abutment. However, their installation (number of surgical stages, technique) and rehabilitation protocols differ. There is insufficient information regarding the clinical experience of using OP in women, as well as in persons with upper limb amputations.

Among the complications that have been recorded for implants are mechanical ones related to OP components; infectious; periprosthetic fractures. The most common soft tissue infectious complications are treated well with antibiotics, but cases of deep bone infection sometimes require removal of the implant. There is insufficient information on the risk factors that provoke this type of complication and the timing of their occurrence after OP implantation. The high frequency of infectious complications necessitates the development of a system of preoperative and postoperative measures for their prevention. Periprosthetic fractures mostly occur after a fall and are mostly treated with screw fixation without removing the implant. To prevent these fractures and mechanical complications, it is necessary to develop measures for the prevention of falls, for example, complexes of exercises for muscle endurance, body balance training, etc. The introduction of reliable methods for assessing the quality of implant and bone osseointegration deserves special attention.

The introduction of technologies related to OP significantly expands the clinical possibilities for the care and treatment of people with amputation; wider possibilities for the use of bionic, robotic prostheses appear.

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OSSEOINTEGRATIVE PROSTHETICS: OPPORTUNITIES, CHALLENGES, AND PROSPECTS FOR ITS APPLICATION IN THE REHABILITATION OF PATIENTS WITH AMPUTATED LIMBS (LITERATURE REVIEW)

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