УДК 616.728.2-007.2-089.28-005.1-08-07-084:615.273.53

DOI: http://dx.doi.org/10.15674/0030-598720251107-113

Hemostatic system disorders in patients with coxarthrosis of III–IV stages after total hip arthroplasty (literature review)

O. V. Vysotskyi

Municipal Non-Profit Enterprise «Kherson Regional Clinical Hospital». Ukraine

Objective. To analyze the current state of diagnosis and prevention of hemostatic disorders in patients with Kellgren-Lawrence grade III-IV coxarthrosis after total hip arthroplasty based on scientific literature. Methods. A search was performed in PubMed, Web of Science, Google Scholar and Scopus. Using MeSH and keywords such as: "inflammatory markers", "coxarthrosis", "thromboembolism", "tranexamic acid", "anticoagulants", "inflammation", "fibrinolysis", "D-dimer", "arthroplasty", "hypercoagulability", "plasminogen". Results. An important issue in the prevention of thromboembolic complications during total hip arthroplasty is to determine the dynamics of fibrinolysis disorders. Thus, it was found that hip arthroplasty is characterized by an increase in inflammatory markers in the blood and hemostatic disorders. Conclusions. In clinical orthopedics, after hip arthroplasty in patients with coxarthrosis of III-IV stages, complications often occur in the form of hemostatic disorders, which are accompanied by the development of deep vein thrombosis of the extremities, in severe cases — pulmonary embolism. These complications are monitored based on the results of determining the markers of the hemostatic system, which are examined before and after surgery. It has been proven that there are many different factors that affect the development of hemostatic disorders in the body. The age factor, as elderly patients have their own metabolic characteristics and altered rheological properties of blood. Increased body weight, in particular, obesity, is also an important factor that cannot be ignored in clinical practice. To date, clear clinical and laboratory criteria for assessing the hemostatic system and a list of biochemical markers of connective tissue to monitor the condition of patients before and after joint replacement in the context of modern anticoagulant regimens remain to be defined.

Мета. На основі досліджень наукової літератури проаналізувати сучасний стан діагностики та профілактики порушень у системі гемостазу у хворих із коксартрозом III–IV ст. за Kellgren-Lawrence після операцій тотального ендопротезування кульшового суглоба. Методи. Здійснено пошук у PubMed, Web of Science, Google Scholar і Scopus. З використанням MeSH і ключових слів, таких як: «маркери запалення», «коксартроз», «тромбоемболія», «транексамова кислота», «антикоагулянти» «запалення», «фібриноліз», «Д-димер», «ендопротезування», «гіперкоагуляція», «плазміноген». Результати. Важливим питанням профілактики тромбоемболічних ускладнень під час тотального ендопротезування кульшових суглобів є визначення динаміки порушень фібринолізу. Встановлено, що ендопротезування кульшового суглоба характеризується збільшенням маркерів запалення в крові та порушенням гемостазу. Висновки. У клінічній ортопедії після операцій ендопротезування кульшових суглобів у хворих із коксартрозом III–IV стадій часто виникають ускладнення у вигляді порушень системи гемостазу, які супроводжуються розвитком тромбозу глибоких вен кінцівок, у важких випадках — тромбоемболією легеневої артерії. Контроль цих ускладнень проводиться за результатами визначення маркерів системи гемостазу, які досліджуються до та після оперативного втручання. Доведено, що існує велика кількість різноманітних чинників, які впливають на розвиток порушень системи гемостазу в організмі. Віковий фактор, адже пацієнти похилого віку мають власні особливості метаболізму, а також змінені реологічні властивості крові. Збільшення маси тіла, зокрема, ожиріння, також є важливим чинником, який не можна не враховувати в клінічній практиці. На сьогодні залишаються не до кінця визначені чіткі клініко-лабораторні критерії оцінювання системи гемостазу та перелік біохімічних маркерів сполучної тканини для контролю стану пацієнтів до та після ендопротезування суглобів на фоні застосування сучасних схем призначення антикоагулянтів. Ключові слова. Гемостаз, ендопротезування, кульшовий суглоб, тромбоемболія, плазміноген.

Keywords. Hemostasis, endoprosthetics, hip joint, thromboembolism, plasminogen

Introduction

Total hip arthroplasty is an effective method of treating patients with grades III–IV coxarthrosis by Kellgren-Lawrence, as it allows 85–95 % to obtain positive results and restore the musculoskeletal function of the lower extremities [1]. However, during such operations, severe thromboembolic complications (deep vein thrombosis, pulmonary embolism) occur in 24–62 %. Therefore, blood loss control is an important aspect of orthopedic surgery [2]. Hemorrhagic shock from trauma has been proven to be a cause of mortality in both the military and the civilian population. It is also known that effective hemostasis during surgery is of great importance for medical practitioners, as it prevents diffuse bleeding from capillaries and venules, which close the surgical field and increase the time of surgery and the risk of infection [3].

The study of hemostasis system disorders in patients after total joint replacement surgery is currently relevant and requires further study [2–6].

Purpose: based on analysis of scientific literature, to assess the current state of diagnosis and prevention of hemostasis system disorders in patients with grades III–IV coxarthrosis by Kellgren-Lawrence after total hip replacement surgery.

Material and methods

A search was conducted in PubMed, Web of Science, Google Scholar and Scopus. Using MeSH and keywords such as: "inflammatory markers", "coxarthrosis", "thromboembolism", "tranexamic acid", "anticoagulants", "inflammation", "fibrinolysis", "D-dimer", "endoprosthetics", "hypercoagulation", "plasminogen". A comprehensive review of publications and meta-analyses was conducted to evaluate the functionality of the hemostasis system in patients undergoing endoprosthetic procedures. The study criteria were original and clinical studies, presented in English, high level of evidence, year of publication (2012–2025).

In total, 1,723 sources were identified by searching the literature in electronic databases, and 73 potentially suitable publications were selected from them during a detailed review. Ultimately, 46 publications were retained following further analysis.

Results and discussion

During joint replacement, localization of bleeding is especially important for obtaining satisfactory surgical results. Considering that it is very difficult to arrest bleeding from both intramedullary canals and bone surfaces mechanically, the use of pharmacological agents (epinephrine, desmopressin, tranexamic acid, aminocaproic acid, etc.) may be a reasonable addition for this purpose [3, 7].

The fibrinolytic system of the blood is involved in hemostasis, removing blood clots after vascular damage is repaired. In recent years, scientists have evaluated the effectiveness and safety of antifibrinolytic agents in reducing perioperative bleeding [8–10].

Some conditions that clearly require the use of antifibrinolytic drugs include trauma, postpartum hemorrhage, cardiac surgery, spinal surgery, and knee or hip replacement [11–23]. There is currently little research on the perioperative features of the fibrinolytic system. The physiology of fibrinolysis, its relationship to thrombus structure, and perioperative preparation have been described [24]. Pathophysiological mechanisms relevant to clinical practice and their possible designs are discussed according to the proposed classification [25]. Today, there is a need to provide physicians with a broader understanding of the normal functioning of fibrinolysis, the mechanisms of possible deviations from the norm in the perioperative period, the pathophysiological rationale supporting the current indications for antifibrinolytic drugs, and some recent results obtained during their use [26–28].

An important issue in the prevention of thromboembolic complications during total hip arthroplasty is determining the dynamics of fibrinolysis disorders. Their diagnosis involves an assessment of the level of fibrinolytic activity, indicators of fibrin degradation products and thromboelastography results, which are decisive for prescribing therapy to prevent thrombosis. Blood was taken from patients who underwent arthroplasty to study the level of D-dimer and fibrin degradation products before, during and after surgery within 6, 12, 24 and 48 hours. Thromboelastography indicators and D-dimer levels correlated with coagulation and fibrinolysis data, all were within normal limits, although higher than before surgery. In addition, the dynamics of D-dimer and fibrin degradation products correlated with blood loss during surgery. As a result, they were found to be quite effective and informative diagnostic indicators for predicting fibrinolytic activity in the postoperative period, in particular, 6 hours after the intervention [29]. In addition, postoperative complications, such as venous thromboembolism, cerebrovascular and cardiac diseases, were the main sources of mortality risk in the early postoperative period [30–33]. Therefore, acute deep vein thrombosis is an absolute contraindication for elective hip or knee arthroplasty. Surgery may displace existing thrombi, which will lead to potentially

life-threatening complications, such as pulmonary embolism.

In the following studies, inflammatory markers were determined after hip arthroplasty. 70 subjects of different sexes were examined, the average age of which was (68.4 ± 10.9) years. Inflammatory markers were determined before, the next day, and 5 days after surgery. Thus, after surgery, their significant increase was found, in particular, C-reactive protein by almost 10 times. Interleukin-6 increased significantly the day after surgery, but decreased on the 5th day. The number of leukocytes and the ratio of neutrophils and lymphocytes, as well as platelets and lymphocytes, was significantly increased compared with the indicators before surgery. Thus, it was established that hip arthroplasty is characterized by an increase in inflammatory markers in the blood and impaired hemostasis. Therefore, determining their number can provide useful information for monitoring patients at risk of cardiovascular thromboembolic complications [34–35].

F. Hartono et al. evaluated the clinical significance of deep vein thrombosis after total hip and knee arthroplasty, which was accompanied by metabolic changes in biochemical markers, namely collagen types I and IV, tissue factor, P-selectin and nitric oxide. Patients were classified into three categories: the first group received total arthroplasty, the second group underwent hemiarthroplasty, and the third group received open reduction internal fixation. In all groups of patients, thromboprophylaxis was not performed.

Blood tests were carried out on the 3rd and 6th day after the intervention. Deep vein thrombosis was detected, which was confirmed by ultrasound Doppler and venography 6 days after the operation. Deep vein thrombosis was diagnosed in 18 patients (10 after total arthroplasty, 5 after hemiarthroplasty, 3 after open reduction internal fixation). Thus, the risk of this complication in patients after total arthroplasty was found to be 3.5 times higher than after open reduction internal fixation. Moreover, biomarkers (type I collagen) and nitric oxide underwent changes as early as 3 days after the operation. This study established that traumatization of the metaepiphyseal spongy bone tissue of the joints affects the frequency of deep vein thrombosis, confirmed by an increase in biochemical markers. Three days after the operation, they became the most informative for predicting the development of thrombosis. Other biochemical parameters used in the study (type IV collagen, tissue factor, and P-selectin) were not diagnostic. The authors also emphasize the need for further research on this topic [36].

O. E. Dahl et al. emphasize that hip joint implantation with bone cement intraoperatively affects the development of cardiovascular and vascular complications. They proved that patients after prosthetics using cement often posthumously detected microemboli and fibrin deposition in the lungs. The reasons for such changes are, apparently, the launch of the hypercoagulation mechanism and the local reaction to methyl methacrylate, based on which bone cement is created. A significant amount of toxic substances is formed at the implantation site, which, together with cell fragments, are released by damaged tissues. These fragments are transported by blood to the lung tissue, where they accumulate with the development of microcirculation disorders and the formation of emboli. Thus, circulatory disorders occur in the lungs with concomitant hypercoagulation, which can cause significant dysfunction of various organs and tissues with an impact on the brain, cardiovascular system, renal blood flow, and also lead to hemodynamic disorders. In a number of patients, these changes lead to fatal outcomes, particularly in the elderly with femoral neck fractures. Thus, the pathophysiological mechanisms underlying the above-mentioned abnormalities in cemented hip arthroplasty may have serious consequences in the form of hypercoagulable complications due to cell destruction and toxic reactions to bone cement, which are also associated with vasoactive substances [37]. A. Abedi et al. indicate that the risk of venous thromboembolism (VTE) increases after total hip and knee arthroplasty. Although most VTE prophylaxis regimens are prescribed postoperatively, activation of the blood coagulation system begins during the intervention. During prosthetic repair, after reaming the femur for prosthesis installation, it is manifested by increased levels of thrombin-antithrombin complex, prothrombin fragment 1+2, fibrinogen peptide A and D-dimer. Intraoperative heparin significantly reduces the level of fibrinopeptide A and prothrombin F1.2, which indicates a decrease in the synthesis of thrombin and fibrin, but does not affect the thrombin-antithrombin complex [38]. F. J. Conway et al. investigated the role of vitamin C in the development of connective tissue impairment and hemostasis after hip arthroplasty. Ascorbic acid is a well-known water-soluble vitamin that has many diverse metabolic functions in the human body. In particular, it has the properties of a universal antioxidant that can protect cells from damage, as well as an effect on hemostasis. In addition, vitamin C is involved in the synthesis of some hormones, collagen, carnitine, as well as the formation of bile salts and affects the normal absorption of iron

by the human body. There are also publications that prove that there is a correlation between the content of ascorbic acid in human blood plasma and the systemic inflammatory process, which is controlled by the concentration of C-reactive protein in the blood. Changes in the content of vitamin C and tocopherol in the blood of patients and their correlation with tissue damage by free radicals as components of systemic inflammation were revealed. During the observation, blood tests were performed 1, 2, 3 and 90 days after hip replacement. It determined such biochemical markers as ascorbic acid, malondialdehyde, cholesterol, C-reactive protein, tocopherol and albumin levels. A significant decrease in the blood content of vitamin C was found by 74, tocopherol by 36, cholesterol by 40, malondialdehyde by 38, albumin by 29 %. At the same time, the content of C-reactive protein increased by as much as 160 times due to the systemic inflammatory process after surgery. Three months after surgery, all indicators that were analyzed at the beginning of the study returned to their previous values.

As a result, it was found that the content of ascorbic acid can be an important and informative biochemical marker in the case of the development of a severe systemic inflammatory response in patients after surgical interventions on hip joint replacement. Therefore, a decrease in the content of vitamin C in the blood is apparently associated with its use by the body as an antioxidant to support the regenerative capacity of tissues and repair damage during the intervention, which caused a severe systemic inflammatory reaction [39]. N. Guler et al. investigated the mechanisms of fibrinolysis disorders in patients after total hip joint replacement, which, in their opinion, remains an incompletely studied issue. As is known, violations of the fibrinolytic link of hemostasis in various inflammatory processes and their activation after surgical interventions are not always sufficiently pathogenically justified. We investigated the fibrinolysis system disorders in patients in the first 24 hours after surgery for total hip arthroplasty. They can lead to both thrombosis and bleeding in clinical practice. We studied the medical histories of 98 patients who underwent arthroplasty. Among the fibrinolysis indicators, D-dimer and plasminogen activator inhibitor, as well as tissue plasminogen activator were determined using the enzyme-linked immunosorbent assay method, and the antiplasmin indicator was also studied. The level of fibrinolysis markers, except antiplasmin, before surgery was found to be significantly higher in patients compared to clinically healthy individuals. However, the percentage of antiplasmin before surgery was lower than in the control group. The levels of plasminogen activator inhibitor and D-dimer in patients were elevated, and the level of antiplasmin was lower, compared to the values before surgery. Changes in tissue plasminogen activator are insignificant. No correlation between the content of plasminogen activator inhibitor and D-dimer was also established.

The results obtained by the authors confirm the violation of the fibrinolysis system in patients after surgery for total joint replacement. They also determined that during surgical intervention, control of the fibrinolysis system is mandatory, since its violation can lead to complications in the form of bleeding, hematomas and the need for blood transfusion [40]. A. Burleson et al. conducted a study on the influence of perioperative factors on the fibrinolysis system in patients who underwent endoprosthetic repair of large joints. It is widely recognized that the majority of patients requiring total joint replacement, particularly hip and knee, are elderly individuals who often present with concomitant diseases, an elevated body mass index, and impaired carbohydrate metabolism. All these factors can affect the fibrinolysis system both before and after surgery. The authors revealed the influence of age, body mass index and the use of tranexamic acid in the treatment of patients on the fibrinolysis system. A total of 99 patients who underwent total hip and knee arthroplasty were examined. Blood tests were performed on patients before surgery and on the first day after surgery, and the levels of D-dimer, plasminogen activator inhibitor, and tissue plasminogen activator were determined using enzyme-linked immunosorbent assay methods, as well as the level of antiplasmin. Data on the age, sex, hemoglobin level, and body mass index of patients were systematized during the study of their medical histories.

Blood levels of D-dimer and tissue plasminogen activator were shown to have a positive correlation with the age of patients, while the antiplasmin index before surgery was negatively correlated with age. Body mass index is associated only with the preoperative level of tissue plasminogen activator. The type of surgical intervention had no effect on the value of fibrinolysis. There was no significant difference in the D-dimer, plasminogen, tissue plasminogen activator, or antiplasmin data between patients who received tranexamic acid and those who did not. The concentration of D-dimer and tissue plasminogen activator showed significantly lower results in individuals who received this acid. The data obtained by the authors confirmed that the advanced age

of patients and an increased body mass index affect the disruption of the fibrinolysis system after endoprosthetic repair, while the use of tranexamic acid reduces its level [41, 42].

Tranexamic acid is a potent antifibrinolytic agent with recognized efficacy. Its use during joint endoprosthetic repair is approved by clinical boards [43]. The use of tranexamic acid covers almost 95 % of patients after endoprosthetics worldwide [44]. The MATTER study (Tranexamic Acid in Surgery) included 896 patients and found a 6.5% reduction in mortality in patients receiving tranexamic acid [45].

Currently, therapeutic attention is focused on the fibrinolytic system, including the mechanisms regulating the formation and activity of plasmin on cell surfaces, fibrin, and extracellular matrix proteins, the effects of plasminogen/plasmin on platelet aggregation induced by various agonists, and its pro-inflammatory function. Charithani B. Keragala et al. reported that plasminogen administration improves thrombolysis and accelerates wound healing. Most of these findings have been based on in vitro or animal studies, but the use of antifibrinolytic agents to reduce bleeding in patients has been shown to have clinically significant benefits, including a reduced risk of infection that is independent of their hemostatic properties [46].

Conclusions

In clinical orthopedics, after hip joint replacement surgery in patients with grades III–IV coxarthrosis, complications are often observed in the form of hemostasis system disorders, accompanied by the development of deep vein thrombosis of the extremities, and in severe cases, pulmonary embolism. These complications are monitored based on the results of determining hemostasis system markers, which are examined before and after surgery.

Today, there is no clear consensus among orthopedic specialists, as well as anesthesiologists, therapists and specialists in hemostasis disorders regarding the rational, safe and effective use of anticoagulants, in particular, their correct combination in order to minimize the risks of postoperative complications from the blood coagulation/anticoagulant system.

Numerous factors have been identified that significantly impact the development of disorders within the hemostasis system. They include age factor, because elderly patients have their own metabolic characteristics, as well as altered blood rheological properties. Weight gain, in particular obesity, is also an important factor that cannot be ignored in clinical practice. In addition, cardiovascular disorders are reflected in the development of arterial hypertension, changes in the structure of vessels, and cause the formation of thrombi and microthrombi. All this must be taken into account when choosing the prevention of hemostasis system disorders in patients who require joint replacement.

Today, clear clinical and laboratory criteria for assessing the hemostasis system and a list of biochemical markers of connective tissue for monitoring the condition of patients before and after joint replacement against the background of the use of modern anticoagulant prescription schemes remain incompletely defined.

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

Prospects for further research. Development of an algorithm for the diagnosis and treatment of patients with grades III–IV coxarthrosis is a further perspective of our research.

Information on financing. Financing by expenditures of the state budget of Ukraine.

Contribution of authors. Vysotsky O. V. — analysis of literary sources, writing of the text of the article, editing of the text.

References

1. Filipenko, V. A., Tankut, V. A., Bondarenko, S. E., Tankut, A. V., & Akondjom M. (2016) Hip replacement with complications after osteosynthesis of the proximal femur. *Trauma: scientific and practical journal, 17*(3), 29–30. (In Ukrainian)
2. Choe, H., Indelli, P. F., Ricciardi, B., Kim, T., Homma, Y., Kigera, J., Veloso Duran, M., & Khan, T. (2025). What are the absolute contraindications for elective total knee or hip arthroplasty? *The journal of arthroplasty, 40*(2), S45-S47. https://doi.org/10.1016/j.arth.2024.10.041
3. Beig Mirza, S., Elawady, K., Kashif Abbas, S., A. Gangoo, S., & S. Panesar, S. (2020). Hemostasis and *Biosurgicals in trauma and orthopedic surgery. Biosurgicals — The next frontier in operative approaches [working title].* https://doi.org/10.5772/intechopen.92805
4. Tanghe, K. K., Chalmers, B. P., Blevins, J. L., Figgie, M. P., Carli, A. V., Agrusa, C. J., Sculco, P. K., & Gausden, E. B. (2022). Hemostatic agents in orthopedic surgery. HSS Journal®: *The musculoskeletal journal of hospital for special surgery, 19*(2), 247–253. https://doi.org/10.1177/15563316221134270
5. Korzh, M., Filipenko, V., Leontyeva, F., Tankut, O., Malyk, R., & Yakovenko, N. (2012). Use of dabigatran etexilate for preventing thromboembolic complications in hip joint arthroplasty. *Orthopaedics, traumatology and prosthetics, 0*(4), 94. https://doi.org/10.15674/0030-59872012494-98
6. Filipenko, V., Leontyeva, F., & Podgayskaya, O. (2012). Prevention of thromboembolic complications in replacement arthroplasty with use of enoxiparin. *Orthopaedics, traumatology and prosthetics, 0*(4), 99. https://doi.org/10.15674/0030-59872012499-103
7. Tang, S., Zhou, Z., Yang, J., Kang, P., Shen, B., Pei, F., & Shi, X. (2022). Effects of tranexamic acid on vascular occlusive events and perioperative resuscitation in patients with atrial fibrillation undergoing total joint arthroplasty. Chinese medical journal, 135(19), 2354–2356. https://doi.org/10.1097/cm9.0000000000002114
8. Klein, A., Agarwal, S., Cholley, B., Fassl, J., Griffin, M., Kaakinen, T., Paulus, P., Rex, S., Siegemund, M., & Van Saet, A. (2022). A review of European guidelines for patient blood management with a particular emphasis on antifibrinolytic drug administration for cardiac surgery. *Journal*

of clinical anesthesia, 78, 110654. https://doi.org/10.1016/j.jclinane.2022.110654
9. Park, J., Han, S., Park, J., Moon, S., & Jang, W. (2023). A decline in Overutilization of transfusion after total knee arthroplasty using pharmacological agents for patient blood management in South Korea: An analysis based on the Korean national health insurance claims database from 2008 to 2019. *Clinics in orthopedic surgery, 15*(6), 942. https://doi.org/10.4055/cios22312.
10. Abedi, A. A., Tuncay, I., Adi, M. M., Tarabichi, S., Memtsoudis, S., Buttaro, M., & Parvizi, J. (2025). Should intravenous heparin be administered during total knee or total hip arthroplasty? *The journal of arthroplasty, 40*(2), S60–S62. https://doi.org/10.1016/j.arth.2024.10.072
11. Kornblith, L. Z., Moore, H. B., & Cohen, M. J. (2019). Trauma-induced coagulopathy: The past, present, and future. *Journal of thrombosis and haemostasis, 17*(6), 852–862. https://doi.org/10.1111/jth.14450.
12. Peck, K. A., Ley, E. J., Brown, C. V., Moore, E. E., Sava, J. A., Ciesla, D. J., Sperry, J. L., Rizzo, A. G., Rosen, N. G., Brasel, K. J., Kozar, R., Inaba, K., & Martin, M. J. (2020). Early anticoagulant reversal after trauma: A western trauma association critical decisions algorithm. *Journal of trauma and acute care surgery, 90*(2), 331–336. https://doi.org/10.1097/ta.0000000000002979
13. Hofer, S., Blaha, J., Collins, P. W., Ducloy-Bouthors, A., Guasch, E., Labate, F., Lança, F., Nyfløt, L. T., Steiner, K., & Van de Velde, M. (2022). Haemostatic support in postpartum haemorrhage. *European journal of anaesthesiology.* https://doi.org/10.1097/eja.0000000000001744.
14. Giouleka, S., Tsakiridis, I., Kalogiannidis, I., Mamopoulos, A., Tentas, I., Athanasiadis, A., & Dagklis, T. (2022). Postpartum hemorrhage: A comprehensive review of guidelines. *Obstetrical & gynecological survey, 77*(11), 665–682. https://doi.org/10.1097/ogx.0000000000001061
15. Klein, A., Agarwal, S., Cholley, B., Fassl, J., Griffin, M., Kaakinen, T., Paulus, P., Rex, S., Siegemund, M., & van Saet, A. (2022). A review of European guidelines for patient blood management with a particular emphasis on antifibrinolytic drug administration for cardiac surgery. *Journal of clinical anesthesia, 78*, 110654. https://doi.org/10.1016/j.jclinane.2022.110654
16. Wang, M., Zheng, X., & Jiang, L. (2015). Efficacy and safety of Antifibrinolytic agents in reducing perioperative blood loss and transfusion requirements in scoliosis surgery: A systematic review and meta-analysis. *Plos one, 10*(9), e0137886. https://doi.org/10.1371/journal.pone.0137886
17. Yuan, L., Zeng, Y., Chen, Z., Zhang, X., Mai, S., Song, P., & Tao, L. (2019). Efficacy and safety of antifibrinolytic agents in spinal surgery. *Chinese medical journal, 132*(5), 577–588. https://doi.org/10.1097/cm9.0000000000000108
18. Huang, F., Wu, Y., Yin, Z., Ma, G., & Chang, J. (2015). A systematic review and meta-analysis of the use of Antifibrinolytic agents in total hip arthroplasty. *HIP International, 25*(6), 502–509. https://doi.org/10.5301/hipint.5000285
19. Ma, Q., Han, G., Li, B., Li, X., & Jiang, T. (2020). Effectiveness and safety of the use of antifibrinolytic agents in total-knee arthroplasty. *Medicine, 99*(20), e20214. https://doi.org/10.1097/md.0000000000020214
20. Tang, K., Wu, Y., Mu, Y., Li, R., Nie, M., & Yin, L. (2020). Intramedullary hemostasis further reduces postoperative anemia in patients over 70 years old undergoing total hip arthroplasty. *Journal of orthopaedic surgery, 28*(3). https://doi.org/10.1177/2309499020965624
21. Zhao, Z., Ma, J., & Ma, X. (2019). Comparative efficacy and safety of different hemostatic methods in total hip arthroplasty: A network meta-analysis. *Journal of orthopaedic surgery and research, 14*(1). https://doi.org/10.1186/s13018-018-1028-2
22. Bai, F., Feng, S., Xu, C., Xu, Z., Chen, J., & Zheng, Y. (2019). Transurethral resection versus holmium laser enucleation of the prostate. *Medicine, 98*(15), e15223. https://doi.org/10.1097/md.0000000000015223
23. Muñoz, M., Peña-Rosas, J. P., Robinson, S., Milman, N., Holzgreve, W., Breymann, C., Goffinet, F., Nizard, J., Christory, F., Samama, C., & Hardy, J. (2017). Patient blood management in obstetrics: Management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfusion Medicine, 28*(1), 22–39. https://doi.org/10.1111/tme.12443
24. Bondarenko, S., Filipenko, V., Morozenko, D., Leontyeva, F., Vysotskyi, O., & Maltseva, V. (2022). Analysis of the relationship between degenerative changes in the joint under conditions of hip osteoarthritis with hemostasis disorders in patients based on the results of a biochemical study. *Orthopaedics, traumatology and prosthetics*, (3–4), 62–67. https://doi.org/10.15674/0030-598720223-462-67
25. Marinho, D. S. (2021). Perioperative hyperfibrinolysis – physiology and pathophysiology. *Brazilian journal of anesthesiology (English Edition), 71*(1), 65–75. https://doi.org/10.1016/j.bjane.2020.12.007
26. Kuijpers, M. J., Heemskerk, J. W., & Jurk, K. (2022). Molecular mechanisms of Hemostasis, thrombosis and thrombo-inflammation. *International Journal of molecular sciences, 23*(10), 5825. https://doi.org/10.3390/ijms23105825
27. Adelborg, K., Larsen, J. B., & Hvas, A. (2021). Disseminated intravascular coagulation: Epidemiology, biomarkers, and management. *British journal of haematology, 192*(5), 803–818. https://doi.org/10.1111/bjh.17172
28. Williams, B., Zou, L., Pittet, J., & Chao, W. (2024). Sepsis-induced Coagulopathy: A comprehensive narrative review of pathophysiology, clinical presentation, diagnosis, and management strategies. *Anesthesia & Analgesia, 138*(4), 696–711. https://doi.org/10.1213/ane.000000000000688
29. Wang, Y., Xie, J., & Pei, F. (2021). Plasma D-dimer and FDP are promising biomarkers to predict perioperative fibrinolysis and bleeding following primary total joint arthroplasty. *Medicine, 100*(20), e26058. https://doi.org/10.1097/md.0000000000026058
30. Tsantes, A., Papadopoulos, D., Lytras, T., Tsantes, A., Mavrogenis, A., Korompilias, A., Gelalis, I., Tsantes, C., & Bonovas, S. (2019). Association of malnutrition with periprosthetic joint and surgical site infections after total joint arthroplasty: A systematic review and meta-analysis. *Journal of hospital infection, 103*(1), 69–77. https://doi.org/10.1016/j.jhin.2019.04.020
31. Onggo, J. R., Ang, J. J., Onggo, J. D., De Steiger, R., & Hau, R. (2021). Greater risk of all-cause revisions and complications for obese patients in 3 106 381 total knee arthroplasties: A meta-analysis and systematic review. *ANZ journal of surgery, 91*(11), 2308–2321. https://doi.org/10.1111/ans.17138
32. Carender, C. N., Fruth, K. M., Lewallen, D. G., Berry, D. J., Abdel, M. P., & Bedard, N. A. (2024). Obesity and primary total hip arthroplasty: The absolute versus relative risk of Periprosthetic joint infection at 15 years. *The journal of arthroplasty, 39*(9), S436–S443.e1. https://doi.org/10.1016/j.arth.2024.03.033
33. Chen, J., Zhang, F., Liu, C., Yuan, Q., Di, X., Long, S., Shang, H., & Jia, Y. (2019). Impact of chronic kidney disease on outcomes after total joint arthroplasty: *A meta-analysis & systematic review.* https://doi.org/10.21203/rs.2.14747/v1
34. Poredos, P., Poredos, P., Jezovnik, M. K., Mavric, A., Leben, L., Mijovski, M. B., Maia, P., Haddad, S., & Fareed, J. (2021). Time course of inflammatory and Procoagulant markers in the early period after total hip replacement. *Clinical and applied thrombosis/hemostasis, 27*. https://doi.org/10.1177/1076029620985941
35. Man, C., An, Y., Wang, G., Mao, E., & Ma, L. (2025). Recent advances in pathogenesis and anticoagulation treatment of sepsis-induced Coagulopathy. *Journal of inflammation research, 18*, 737–750. https://doi.org/10.2147/jir.s495223

36. Hartono, F., Yusuf, I., Suhadi, B., Fachruddin, A., & Augustinus, Y. (2021). Trauma magnitude of the meta-epyphyseal cancellous affects the incidence of deep vein thrombosis. A prospective cohort study on the dynamic of collagen I, collagen IV, tissue factor, P-selectin and nitric oxide in the thrombus formation following hip and knee surgeries. *Annals of medicine & surgery, 63*. https://doi.org/10.1016/j.amsu.2021.102190
37. Dahl, O. E., Pripp, A. H., Jaradeh, M., & Fareed, J. (2023). The bone cement Hypercoagulation syndrome: Pathophysiology, mortality, and prevention. *Clinical and applied thrombosis/hemostasis, 29*. https://doi.org/10.1177/10760296231198036
38. Abedi, A. A., Tuncay, I., Adi, M. M., Tarabichi, S., Memtsoudis, S., Buttaro, M., & Parvizi, J. (2025). Should intravenous heparin be administered during total knee or total hip arthroplasty? *The Journal of arthroplasty, 40*(2), S60–S62. https://doi.org/10.1016/j.arth.2024.10.072
39. Conway, F., Talwar, D., & McMillan, D. (2015). The relationship between acute changes in the systemic inflammatory response and plasma ascorbic acid, Alpha-tocopherol and lipid peroxidation after elective hip arthroplasty. *Clinical Nutrition, 34*(4), 642–646. https://doi.org/10.1016/j.clnu.2014.07.004
40. Guler, N., Burleson, A., Syed, D., Banos, A., Hopkinson, W., Hoppensteadt, D., Rees, H., & Fareed, J. (2015). Fibrinolytic dysregulation in total joint arthroplasty patients. *Clinical and applied thrombosis/hemostasis, 22*(4), 372–376. https://doi.org/10.1177/1076029615597060
41. Burleson, A., Guler, N., Banos, A., Syed, D., Wanderling, C., Hoppensteadt, D., Rees, H., Fareed, J., & Hopkinson, W. (2015). Perioperative factors and their effect on the Fibrinolytic system in arthroplasty patients. *Clinical and applied thrombosis/hemostasis, 22*(3), 274–279. https://doi.org/10.1177/1076029615611251
42. Karunakaran, G., Menon, J., Nema, S., & Basu, D. (2020). Plasma D-dimer levels in non-prosthetic orthopaedic implant infection: Can it aid diagnosis? *Indian journal of orthopaedics, 54*(S1), 76–80. https://doi.org/10.1007/s43465-020-00120-8
43. Fillingham, Y. A., Ramkumar, D. B., Jevsevar, D. S., Yates,A. J., Bini, S. A., Clarke, H. D., Schemitsch, E., Johnson, R. L., Memtsoudis, S. G., Sayeed, S. A., Sah, A. P., & Della Valle, C. J. (2018). Tranexamic acid use in total joint arthroplasty: The clinical practice guidelines endorsed by the American Association of hip and knee surgeons, American society of Regional Anesthesia and Pain Medicine, American Academy of orthopaedic surgeons, hip society, and knee society. *The journal of arthroplasty, 33*(10), 3065–3069. https://doi.org/10.1016/j.arth.2018.08.002
44. Patel, P. A., Wyrobek, J. A., Butwick, A. J., Pivalizza, E. G., Hare, G. M., Mazer, C. D., & Goobie, S. M. (2022). Update on applications and limitations of perioperative Tranexamic acid. *Anesthesia & Analgesia, 135*(3), 460–473. https://doi.org/10.1213/ane.0000000000006039
45. Morrison, J. J. (2012). Military application of Tranexamic acid in trauma emergency resuscitation (MATTERs) study. *Archives of Surgery, 147*(2), 113. https://doi.org/10.1001/archsurg.2011.287
46. Keragala, C. B., & Medcalf, R. L. (2021). Plasminogen: An enigmatic zymogen. *Blood, 137*(21), 2881–2889. https://doi.org/10.1182/blood.2020008951

The article has been sent to the editors	Received after review	Accepted for printing
11.01.2025	23.02.2025	27.02.2025

HEMOSTATIC SYSTEM DISORDERS IN PATIENTS WITH COXARTHROSIS OF III–IV STAGES AFTER TOTAL HIP ARTHROPLASTY (LITERATURE REVIEW)

O. V. Vysotskyi

Municipal Non-Profit Enterprise «Kherson Regional Clinical Hospital». Ukraine

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