

## Improvement of Perioperative Management of Patients Undergoing Surgical Treatment for Hip Periprosthetic Joint Infection

Andrei A. Kochish, Svetlana A. Bozhkova, Vasilii A. Artyukh, Vitaly N. Liventsov, Alexander V. Afanas'ev, Sergei S. Toropov


*Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia*

### Abstract

Two-stage revision arthroplasty in chronic hip periprosthetic infection is the gold standard technique. First stage debridement leads to large intraoperative and drainage blood loss using standard protocols for thromboprophylaxis and drainage of the surgical wound, which is a significant disadvantage of perioperative management of such patients. **The aim of the study** was to determine the effect of modified management protocol with delayed start of thromboprophylaxis and a short period of drainage on the blood loss and the effectiveness of debridement with antibiotic-impregnated spacer placement in patients with hip periprosthetic joint infection. **Materials and Methods.** A single-center prospective study was conducted. 90 patients underwent endoprosthesis components removal and antibiotic-impregnated spacer placement. Patients were divided into 3 groups: start of thromboprophylaxis before surgery and 3–4 days of drainage; start of thromboprophylaxis no earlier than 12 hours after surgery and 3–4 days of drainage; start of thromboprophylaxis no earlier than 12 hours after surgery and 1 day of drainage. **Results.** There was a statistically significant ( $p < 0.05$ ) decrease of drainage and total blood loss, and transfused blood volume in cases with the delayed start of thromboprophylaxis and a short period of drainage. The proposed protocol was safe for prevention of venous thromboembolic complications and did not affect the frequency of periprosthetic hip joint infection recurrence. The effectiveness of the first stage of treatment — 89%, the second stage — 99% in 1 year after rehabilitation according to the second international consensus on musculoskeletal infection criteria. **Conclusion.** The modified protocol of perioperative management is an effective and safe as a blood-saving strategy and can be proposed for widespread use.

**Keywords:** hip periprosthetic infection, perioperative management, thromboprophylaxis, postoperative wound drainage.

**Funding:** state budgetary funding.

 **Cite as:** Kochish A.A., Bozhkova S.A., Artyukh V.A., Liventsov V.N., Afanas'ev A.V., Toropov S.S. [Improvement of Perioperative Management of Patients Undergoing Surgical Treatment for Hip Periprosthetic Joint Infection]. *Travmatologiya i ortopediya Rossii* [Traumatology and Orthopedics of Russia]. 2021;27(1):143-152. (In Russian). <https://doi.org/10.21823/2311-2905-2021-27-1-143-152>.

 **Andrei A. Kochish;** e-mail: [kochishman@gmail.com](mailto:kochishman@gmail.com)

Received: 14.12.2020. Accepted for publication: 15.02.2021.

## Introduction

The two-stage surgical technique is a gold standard in the treatment of patients with chronic hip deep periprosthetic infection (PPI) [1, 2, 3]. At the first stage, radical surgical treatment of the infection focus is performed, the endoprosthesis is removed and an antimicrobial spacer from methyl methacrylate bone cement is implanted. When the remission of the infectious process is achieved, the antimicrobial cement spacer is removed and the revision hip joint arthroplasty is performed [4, 5, 6].

It is known that debridements in patients with hip PPI are accompanied by significant blood loss, which is facilitated by a number of known factors. First, the removal of large joint endoprosthesis with the antimicrobial cement spacer implantation, as well as total hip arthroplasty, significantly increases the risk of venous thromboembolic complications (VTE) [7, 8]. Prevention of VTE requires the appointment of anticoagulants: low molecular weight heparins and/or direct oral anticoagulants, which leads the coagulation system of patients to a state of hypocoagulation and can increase the volume of perioperative blood loss [9, 10]. The traditional approach to thromboprophylaxis involves its initiation before surgery, which leads to the state of hemostasis above mentioned. However, in the clinical recommendations for the prevention of VTE in traumatology and orthopedics, the first administration of drugs is allowed in the interval – 12 hours before the operation and up to 12 hours after it [11].

Secondly, the PPI focus debridement implies a large amount of surgical aggression against the background of a high paraarticular concentration of inflammatory mediators. Radical surgical treatment of the PPI focus inevitably leads to the formation of massive defects in the surgical site due to the removal of all non – viable tissues, infected compo-

nents of the endoprosthesis and bone cement fragments [12, 13]. The duration of such surgery with careful implementation of all stages usually takes at least 3 hours, which leads to significant intraoperative blood loss [14]. Thirdly, drainage of a postoperative wound is a traditional method of mechanical antiseptics for PPI, which prevents the reproduction of the pathogen in the forming massive hematoma, inevitably leads to significant postoperative blood loss through drains [15].

It should be noted that the standard criterion for removing drains from the postoperative wound in patients who have undergone debridement for hip joint PPI is the absence of drainage discharge, which usually persists for 3-4 days after such intervention and determines the duration of drainage [16, 17]. At the same time, about 500 ml of fluid is drained from the wound through drains during this period, which determines a significant amount of drainage blood loss in the postoperative period. In addition, the loss of a large volume of drainage discharge during 3-4 days decreases the local concentration of antibiotics in the postoperative wound, released by an antimicrobial cement spacer, in the most critical period after the infectious focus debridement [18]. It is known that it can reduce the effectiveness of patients with PPI complex treatment and increases the risk of the infectious process relapses [19].

Thus, large volumes of intraoperative and drainage blood loss after debridement in patients with hip joint PPI with a standard approach to thromboprophylaxis and drainage of postoperative wound are significant disadvantages of the traditional approach to the perioperative management of such patients.

The aim of the study was to determine the effect of the modified tactics of patients with hip PPI management, assuming delayed start of thromboprophylaxis and short drainage period, on the volume of blood loss and the effectiveness of debridement with the antimicrobial cement spacer implantation.

## Materials and Methods

*Research design:* a prospective single-center study.

The study included 90 patients with chronic PPI after primary total hip arthroplasty, who were treated in the department of purulent surgery in 2017-2019.

*The inclusion criterion* is the planned debridement with removal of the endoprosthesis and the spacer implantation.

*Criteria for non-inclusion:* the presence of additional hardware in the wound, any debridements in the anamnesis, 3B defects of the acetabulum and 3B and 4 defects of the femur according to W. Paprosky, type IV PPI according to D.T. Tsukayama and the risk of cardiovascular complications of the 4th degree.

The groups were formed sequentially, including 30 patients with different tactics of perioperative management. In group I, a standard scheme of thromboprophylaxis was used with the introduction of sodium dalteparin 12 hours before surgery, then on the day of surgery (no earlier than 6 hours after its completion) and drainage for 3-4 days. In group II, a modified thromboprophylaxis regimen was used with the first administration of sodium dalteparin no earlier than 12 hours after surgery and a drainage duration of 3-4 days. In group III, a modified thromboprophylaxis regimen with low molecular weight heparins was used (the first administration not earlier than 12 hours after surgery) and a short drainage period-for one

day. On day 5, patients of all clinical groups were transferred to the oral anticoagulant-dabigatran etexilate for 30 days.

The results of the patients' treatment were tracked for a year after the debridement. At the same time, the following indicators were taken into account and compared: the gender and age of patients, the duration of surgery, the volume of intraoperative and total blood loss, the amount of drainage discharge, the amount of puncture aspirate, pre- and postoperative hemoglobin and C-reactive protein (CRP) levels, the number of red blood cells. The volumes of transfused erythrocyte mass and fresh-frozen plasma in the intra- and postoperative periods, the frequency of the chronic infectious process relapses after the first and second stages were also studied.

The average age of patients was 60 (interquartile interval (IQI) 51-69) years. The comparison groups were comparable by age and gender of the included patients (Table 1). The prevalence of men over women was established in all groups.

All patients underwent ultrasonography of the lower extremities veins within 10-12 days after the operation to exclude deep vein thrombosis (DVT).

Medium-term results of treatment were obtained during the study of the electronic register of endoprosthetics, created on the basis of the R.R. Vreden Center, the local register of the department of purulent surgery and a telephone survey of patients.

Table 1

Demographic characteristics of patients

Group	Parameters		
	Average age, Me (IQI)	Male, n (%)	Female, n (%)
I	61 (53-70)	16 (53)	14 (47)
II	57 (48-68)	19 (63)	11 (36)
III	62 (55-68)	18 (60)	12 (40)

The control points for evaluating the effectiveness of the treatment were: the absence of PPI signs at admission to the 2nd stage of treatment and the absence of PPI signs a year after the debridement. Remission of the infectious process was understood as a clinical situation with the absence of systemic and local signs of inflammation, hip joint fistulas after completing a course of oral antibiotic therapy.

Revision arthroplasty was performed on average 175 days (IQI 135-208) after the 1st stage. Further, the average follow-up period was 182 days (IQI 120-240) after the revision arthroplasty.

### Statistical analysis

The obtained data was registered in the form of MS Office Excel, 2007 spreadsheets (Microsoft, USA) and processed using the Statistica for Windows (version 10). Due to the non-compliance of the presented sample with the law of normal distribution, the median (Me) was used as a measure of the central trend, and the lower and upper quartiles (25-75% IQI) were used as scattering measures. Statistical analysis to check the equality of the medians of several samples was

performed using the Kraskel-Wallis test, for two samples-using the Mann-Whitney test.

To test hypotheses about the relationships between variables, Spearman's correlation coefficient (CC) was used, for which the required sample size is  $n_1 \geq 5$  and  $n_2 \geq 5$ , and the correspondence of the distribution to the normal form is optional. The CC was interpreted based on the level of the bond strength. The CC values can vary in the range from -1 (negative correlation) to +1 (positive correlation). The differences in the indicators were taken as statistically significant at  $p < 0.05$ .

### Results

All groups were comparable in terms of the preoperative level of laboratory parameters (Table 2). At the same time, there were medium-strength reliable inverse correlations of the hemoglobin level with the patient's age (CC -0.370;  $p < 0.05$ ) and with the level of CRP (CC -0.300,  $p < 0.05$ ).

A comparative analysis of intraoperative data showed that the average duration of performed debridements in all groups was about 200 minutes, and small differences in this indicator were not statistically significant ( $p > 0.05$ ).

Table 2

**Blood parameters in the groups before and after surgery**

Parameter	Group I, Me (IQI)	Group II, Me (IQI)	Group III, Me (IQI)	<i>p</i>
<i>Before surgery</i>				
CRP, mg/l	16,4 (11,1–51,8)	20,1 (11,5–53,6)	23,0 (12,0–38,9)	0,902
Hemoglobin, g/l	118 (108–131)	125 (105–133)	125 (112–134)	0,419
Erythrocytes, $10^{12}/l$	4,5 (4,1–4,9)	4,5 (3,9–4,9)	4,5 (4,3–4,6)	0,959
<i>After surgery</i>				
CRP, mg/l	20,7 (11,3–27,03)	13,4 (8,6–27,4)	20,0 (13,3–27,1)	0,583
Hemoglobin, g/l	100 (89–106)	100 (96–111)	97 (92–105)	0,284
Erythrocytes, $10^{12}/l$	3,5 (3,4–4,05)	3,6 (3,4–4,1)	3,7 (3,3–3,8)	0,832

Comparison of intraoperative blood loss medians according to the Kraskell-Wallis criterion did not reveal a statistically significant difference ( $p = 0.221$ ) between the studied parameters (Table 3). Since only a modification of thromboprophylaxis can theoretically affect the amount of blood lost during surgery, a narrowly focused analysis was performed according to the Mann-Whitney criterion between the medians of groups I and III having the maximum difference. This analysis established statistical differences between the groups in terms of blood loss ( $p = 0.028$ ).

The combination of delayed start of thromboprophylaxis with a short drainage period was accompanied by a statistically significant decrease in the volume of drainage ( $p < 0.0001$ ) and total blood loss ( $p = 0.001$ ). At the same time, the volume of puncture aspirate in the groups also significantly differed ( $p = 0.0049$ ), this indicator was the highest in group III (Fig. 1). Apparently, the smaller volume of punctate in groups I and II compared to group III is associated with the outflow of wound discharge through drains.

Table 3

The surgery duration and the volume of blood loss in the groups

Parameter	Group I, Me (IQI)	Group II, Me (IQI)	Group III, Me (IQI)	$p^*$
The surgery duration, min.	208 (180–207)	200 (181–225)	195 (180–210)	0,405
Intraoperative blood loss volume, ml	800 (500–1000)	700 (500–800)	600 (400–800)	0,221
Drains blood loss volume, ml	435 (370–490)	450 (385–410)	240 (190–270)	<0,0001
Total blood loss volume, ml	1261 (1000–1530)	1135 (970–1305)	865 (740–1060)	0,001

\* Statistical analysis to check the equality of the several samples medians using the Kruskal-Wallis test..

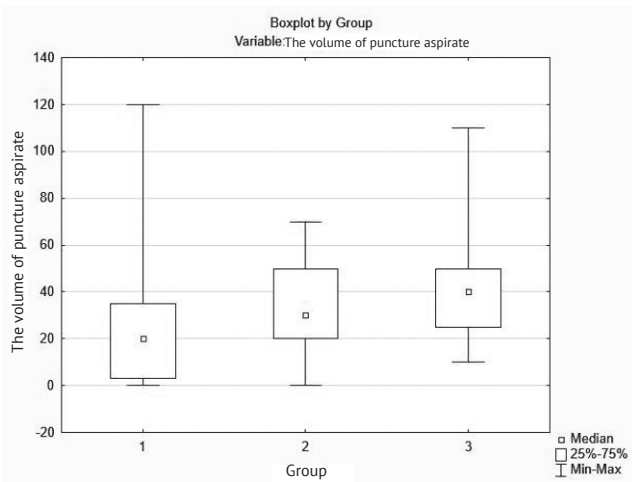


Figure 1. The volume of puncture aspirate in the study groups

These trends were also confirmed by the results of the correlation analysis of the studied indicators. In particular, it was found that there was a strong reliable negative correlation ( $CC -0.712$ ;  $p < 0.05$ ) of the modified tactics with a decrease in the volume of drainage blood loss, as well as the average strength of the negative relationship with respect to total blood loss ( $CC -0.451$ ;  $p < 0.05$ ). In addition, a medium-strength reliable positive relationship was revealed ( $CC 0.342$ ;  $p < 0.05$ ) between the applied tactics of perioperative management and the volume of aspirate obtained as a result of punctures of the operated joint. At the same time, the delayed start of pharmacological thromboprophylaxis in combination with a short drainage period allowed to significantly ( $p < 0.01$ ) reduce the need for transfusion: on average, one dose of allogeneic blood and fresh-frozen plasma (Table 4).

Table 4

**The volume of blood components transfusion in the groups**

Parameter	Group I, Me (IQI)	Group II, Me (IQI)	Group III, Me (IQI)	<i>p</i> *
Volume of transfused allogeneic blood, ml	600 (300–638)	300 (0–600)	275 (0–300)	0,004
Volume of transfused plasm, ml	600 (550–765)	300 (0–580)	275 (0–515)	0,0007

\* Statistical analysis to check the equality of the several samples medians using the Kruskal-Wallis test.

According to the results of clinical examination and ultrasound examination of the lower extremities veins, no data for deep vein thrombosis were found in all patients, regardless of the thromboprophylaxis regimen used.

The frequency of the chronic infectious process relapses in the hip joint was comparable and amounted to 13% ( $n = 4$ ) in group I and 10% ( $n = 3$ ) each in groups II and III. There were no differences in the effectiveness of PPI treatment between the groups ( $p > 0.05$ ). One patient in group I was diagnosed with the infectious process relapse 10 days after surgery. After 3 weeks, despite the treatment, the patient developed disseminated intravascular coagulation syndrome (DIC-syndrome) and sepsis. The septic process was stopped, but the patient was discharged with a fistula and the appointment of suppressive antibacterial therapy.

In the remaining clinical cases, patients were discharged on days 12–14 after the sutures removal and the formation of a post-operative scar. A relapse of the infectious process developed on average 95 days (IQI 72–108) after discharge. In 4 patients (two from group I, one from group II, one from group III), a fistula was formed in the post-operative scar area. The remaining 5 patients (one from group I, two from group II, two from group III) showed local signs of an infectious process, which was confirmed by bacteriological analysis before the 2nd stage of treatment. Thus, the effectiveness of the 1st stage of treatment was 89%.

Among 80 patients with remission of the infectious process, 75 (93.8%) patients

underwent the 2nd stage of treatment. Contraindications for stage-by-stage surgical treatment due to concomitant pathology were established in 5 patients (two from group I, one from group II, two from group III). A year after the debridement, a relapse of PPI developed in 1 observation (group II) out of 75 cases, which required repeated hospitalization to the purulent surgery department. The effectiveness of the second stage of treatment was 99%.

### Discussion

The effectiveness of the two-stage method of chronic hip PPI treatment varies in a wide range — from 80 to 95% [2, 6, 20]. The success of treatment is determined by many factors: the somatic status, the pathogen, the number and quality of previous surgeries, the condition of soft tissues. In addition, special attention is currently being paid to the strategy of perioperative management of patients undergoing orthopedic surgery on large joints of the extremities. The concept of fast track surgery implies a reduction in the duration of inpatient treatment by improving the protocol of anesthesia, thromboprophylaxis, blood conservation, drainage and rehabilitation [21, 22].

There is a working group that develops and updates national clinical guidelines for the prevention of VTE [11, 23, 24].

However, all developments in this area relate to aseptic cases of primary and revision arthroplasty. To date, the protocol of patients with PPI perioperative management does not differ from that of standard total hip arthroplasty. At the same time, the

dosages of anticoagulants and hemostatics in patients undergoing surgery for hip joint PPI are designed for standard conditions and do not take into account risk factors from an infected wound with corresponding violations of local hemostasis. In the study of B.G. Ziatdinova et al. found that patients with hip joint PPI have a significantly higher tendency to hypercoagulation and thrombocytosis than patients with coxarthrosis, which requires a longer regimen of prevention of PAT relative to aseptic revision [25]. The proposed scheme of perioperative management has shown its effectiveness, despite the delayed start and the standard duration of thromboprophylaxis for conventional arthroplasty up to 35 days after surgery.

To date, there is no single view on the need and timing of a postoperative wound drainage in patients with hip joint PPI. H. Xu et al. analyzed the results of treatment of 13,000 patients after primary arthroplasty of the knee and hip joints. They came to the conclusion that the routine use of drainage systems leads to a higher frequency of blood transfusions and a longer stay in the hospital, and therefore recommended to abandon this technique [26].

According to R.M. Tikhilov et al., the refusal to use drainage systems after primary total hip joint arthroplasty in combination with the modification of the thromboprophylaxis system allowed to reduce intraoperative blood loss and the need for allogeneic hemotransfusion by 2.2 times [27]. However, in the conditions of the infectious process in PPI, the refusal to drain the postoperative wound has no scientific justification. The possibility of carrying debridement without drainage is not sufficiently covered in the scientific literature.

The proposed tactics of perioperative management contributed to blood conservation and reduced the need for transfusion, without increasing the frequency of infection relapses, despite the shortened period of drainage of the postoperative wound (pat-

ent for the invention RU 2739684 C1). This fact is significant, because the long-term hip joint chronic infectious process, especially in elderly patients, inhibits hematopoiesis, which is confirmed by the data we have obtained. In our study, 43% (n = 39) of patients had anemia of varying severity before surgery. A negative correlation of average strength between age and the degree of anemia indicates a higher risk of developing anemia against the background of PPI in elderly and senile patients. Some foreign researchers claim that preoperative anemia is a significant factor in the development of PPI after primary arthroplasty [28, 29, 30], which suggests that this parameter may increase the risk of PPI recurrence. This assumption requires the further research.

#### *Limitations of the study*

The limitation of this study is the small size of clinical groups. The statistical methods used for processing the results were carried out taking into account this factor and the absence of a normal distribution. For the analysis, nonparametric criteria were used that correspond to this type of data distribution. The presence of the patient with sepsis in group I could influence the results of the analysis. During the treatment, 4200 ml of allogeneic blood and 6600 ml of fresh-frozen plasma were transfused to this patient, which significantly exceeded the median values in all groups. It should be noted that an additional statistical analysis was carried out with the exception of hemotransfusion indicators in this patient. As a result, the median values without quartiles did not differ from those presented in Table 4.

#### **Conclusion**

The proposed tactics of perioperative management of patients with hip joint PPI allowed to reduce blood loss and reduce the need for transfusion of blood components in the absence of the risk of thromboembolic complications and recurrence of PPI. A posi-

tive result of treatment allows us to recommend the proposed scheme for a wider clinical application.

### Informed consent

The patients gave their voluntary informed consent to participate in the study.

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AUTHORS' INFORMATION:

*Andrei A. Kochish* — Orthopaedic Surgeon, Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 kochishman@gmail.com  
<https://orcid.org/0000-0001-8573-1096>

*Svetlana A. Bozhkova* — Dr. Sci. (Med.), Head of the Research Department of Wound Infection Prevention and Treatment, Head of the Clinical Department of Clinical Pharmacology, National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 clinpharm-rniito@yandex.ru  
<https://orcid.org/0000-0002-2083-2424>

*Vasilii A. Artyukh* — Cand. Sci. (Med.), Head of Septic Surgery Department, Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 artyukhva@mail.ru  
<https://orcid.org/0000-0002-5087-6081>

*Vitaly N. Liventsov* — Cand. Sci. (Med.), Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 vnliventsov@yandex.ru  
<https://orcid.org/0000-0001-8748-2134>

*Alexander V. Afanas'ev* — Orthopaedic Surgeon, Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 avafanasev@rniito.ru  
<https://orcid.org/0000-0002-3097-7846>

*Sergei S. Toropov* — Orthopaedic Surgeon, Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia  
 doctoropovss@yandex.ru  
<https://orcid.org/0000-0002-9451-1834>

**Authors' contributions:**

*Kochish A.A.* — collection and processing of material, statistical processing, text preparation

*Bozhkova S.A.* — development of the concept and design of the study, interpretation and analysis of the obtained data, editing of the obtained data, editing

*Artyukh V.A.* — collection and processing of material, conducting research

*Liventsov V.N.* — collection and processing of material, conducting research

*Afanasyev A.V.* — collection and processing of material, conducting research

*Toropov S.S.* — collection and processing of material, conducting research

All authors made a significant contribution to the research and preparation of the article and read and approved the final version before its publication. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Competing interests:** the authors declare that there are no competing interests.