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The First Step of Two-Stage Hip Revision: What Affects the Result?

Svetlana A. Bozhkova, Yuliya V. Oleinik, Vasilii A. Artyukh, Alexander P. Antipov, Sergei S. Toropov

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

Abstract

Background. The most common method of treatment of chronic periprosthetic joint infection (PJI) is considered to be a two-stage revision arthroplasty. The efficacy of this technique is largely determined by the results of infection management after the first (debridement) stage, which may depend on many factors. At the same time, the widespread tendency to reduce the duration of patients' hospital stay brings to the forefront the problem of long wait for the results of preoperative microbiological examination.

***Aims of the study*:** 1) to retrospectively evaluate the efficacy of the debridement stage of chronic periprosthetic hip joint infection in 2021 depending on the availability of preoperative microbiological examination results; 2) to determine the factors influencing the treatment outcome.

Methods. Patients (n = 86) with chronic PJI of the hip were allocated into two groups depending on the presence or absence of results of the microbiological examination of preoperative biomaterials (aspirate and/or tissue biopsy) at the time of performing the first stage of the two-stage revision arthroplasty.

Results. The availability of final results of the microbiological examination (MBE) of joint aspirate at the time of surgery had no significant effect on the efficacy of infection management (p = 0.536; OR = 1.53, 95% CI 0.43-5.45). There was a significant reduction of the risk when the results of preoperative and intraoperative MBE coincided (p = 0.024; OR = 0.121, 95% CI 0.015-0.990). An increased risk of adverse outcome of the debridement stage of treatment was observed in the case of types 2C (p = 0.042; OR = 6.66; 95% CI 1.26-35.2) and 3B (p = 0.078; OR = 8.1, 95% CI 1.015-64.8) acetabular defects, type 3A femoral defects (p = 0.021; OR = 6.57, 95% CI 1.49-29.01), and connective tissue diseases (p = 0.062; OR = 5.25, 95% CI 1.05-26.2). The presence of microbial associations (p=0.02; OR = 6.75, 95% CI 1.36-33.44) and the presence of Gram-negative bacteria in them (p = 0.058; OR = 4.2, 95% CI 1.02-17.20) significantly worsened the treatment prognosis. As the number of patient's risk factors increased, the probability of an unfavorable outcome increased significantly (p<0.001).

Conclusions. Polymicrobial infection, presence of Gram-negative bacteria in microbial associations, connective tissue diseases, types 2C and 3B acetabular defects, type 3A femoral bone defects, and total number of risk factors in one patient had a significant negative impact on the outcome of debridement surgery. Apparently, the results of the microbiological examination of preoperatively sampled biomaterials are much more important as a diagnostic criterion for suspected periprosthetic infection than as a criterion for the drug choice for etiotropic antibacterial therapy. However, this assumption should be studied on a larger sample of patients.

Keywords: chronic periprosthetic joint infection, PJI, microbiological examination, initial antibiotic treatment, risk factors for recurrence of PJI.

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✉ *Yuliya V. Oleinik*; e-mail: hamster715@gmail.com

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Санирующий этап лечения пациентов с хронической перипротезной инфекцией тазобедренного сустава: от чего зависит результат?

С.А. Божкова, Ю.В. Олейник, В.А. Артюх, А.П. Антипов, С.С. Торопов

ФГБУ «Национальный медицинский исследовательский центр травматологии и ортопедии им. Р.Р. Вредена» Минздрава России, г. Санкт-Петербург, Россия

Реферат

Актуальность. Самым распространенным методом лечения хронической перипротезной инфекции (ППИ) считается двухэтапное реэндопротезирование. Эффективность данной методики во многом определяют результаты купирования инфекции после первого (санирующего) этапа, что может зависеть от множества различных факторов. При этом повсеместная тенденция к уменьшению продолжительности госпитализации профильных пациентов выводит на передний план проблему длительного ожидания результатов дооперационного микробиологического исследования.

***Цели исследования*:** 1) ретроспективно оценить эффективность санирующего этапа лечения хронической перипротезной инфекции тазобедренного сустава за 2021 г. в зависимости от наличия результатов дооперационного микробиологического исследования; 2) определить факторы, влияющие на исход лечения.

Материал и методы. Пациенты (n = 86) с хронической ППИ тазобедренного сустава были распределены на две группы в зависимости от наличия или отсутствия результатов микробиологического исследования дооперационных биоматериалов (аспират и/или тканевой биоптат) на момент выполнения первого этапа двухэтапного ревизионного эндопрпотезирования.

Результаты. Наличие окончательных результатов микробиологического исследования (МБИ) суставного аспирата на момент выполнения операции не оказывало значимого влияния на эффективность купирования инфекционного процесса (p = 0,536; ОШ = 1,53; 95% ДИ 0,43–5,45). Установлено значимое снижение риска при полном совпадении результатов МБИ до- и интраоперационных материалов (p = 0,024; ОШ = 0,121; 95% ДИ 0,015–0,990). Увеличение риска неблагоприятного исхода санирующего этапа лечения наблюдалось при наличии дефектов вертлужной впадины типов 2С (p = 0,042; ОШ = 6,66; 95% ДИ 1,26–35,2) и 3В (p = 0,078; ОШ = 8,1; 95% ДИ 1,015–64,8), дефектов бедренной кости типа 3А (p = 0,021; ОШ = 6,57; 95% ДИ 1,49–29,01), а также заболеваний соединительной ткани (p = 0,062; ОШ = 5,25; 95% ДИ 1,05–26,2). Значимо ухудшало прогноз лечения наличие микробных ассоциаций (p = 0,02; ОШ = 6,75; 95% ДИ 1,36–33,44), а также присутствие в их составе грамотрицательных Гр(-) бактерий (p = 0,058; ОШ = 4,2; 95% ДИ 1,02–17,20). С увеличением количества факторов риска у пациента значительно возрастала вероятность неблагоприятного исхода (p<0,001).

Заключение. Значимое негативное влияние на результат санирующей операции имели полимикробная инфекция, наличие грамотрицательных бактерий в составе микробных ассоциаций, заболевания соединительной ткани, дефекты вертлужной впадины типов 2С и 3В, дефекты бедренной кости типа 3А, а также совокупное количество факторов риска у одного пациента. По-видимому, результаты микробиологического исследования дооперационно взятых биоматериалов имеют гораздо большее значение как диагностический критерий при подозрении на перипротезную инфекцию, чем как критерий выбора препаратов для этиотропной антибактериальной терапии. Однако это предположение должно быть исследовано на большей выборке пациентов.

Ключевые слова: хроническая перипротезная инфекция, микробиологическое исследование, стартовая антибактериальная терапия, факторы риска рецидива перипротезной инфекции.

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Олейник Юлия Владимировна; e-mail: hamster715@gmail.com

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BACKGROUND

Periprosthetic joint infection (PJI) is considered one of the most devastating complications of total hip arthroplasty (THA), which worsens the quality and overall life expectancy of patients [1, 2]. At the same time, the risk of treatment failure remains rather high, and according to some scientific publications, it reaches 10-29% after performing a two-stage revision arthroplasty, which is still considered the gold standard [3, 4]. The high recurrence rate is determined by various factors starting from the somatic status of patients [5, 6] and hypoalbuminemia [7, 8] to the impossibility of prolonged oral antimicrobial therapy [9].

One of the most important parameters significantly affecting the treatment efficacy is the etiology of the infectious process, i.e. the type of microbial pathogen and its antibiotic sensitivity [6]. The results of preoperative microbiological examinations (MBE) should determine the type of etiotropic antibacterial therapy in the postoperative period, but the peculiarities of PJI pathogenesis, including the presence of bacterial depots in the patient's organism and biofilm formation [10], predetermine a significant share of disagreement of the results of MBE of preoperative aspirate and intraoperatively taken materials and thus require correction of previously prescribed antibacterial therapy (ABT) [11]. Moreover, the widespread tendency to decrease the duration of hospital stay in orthopedic clinics often forces to stop waiting for preoperative MBE results and to prescribe initial empirical antibiotic therapy before surgery.

Aim of the study is to retrospectively evaluate the efficacy of the debridement stage of treatment of chronic periprosthetic hip joint infection depending on the results of preoperative microbiological examination, as well as to determine the risk factors for an unfavorable outcome.

METHODS

Study design

This retrospective study is based on the treatment outcomes of patients with chronic PJI of the hip in the department of septic osteology from January to December 2021.

Inclusion criterion for the study was the performed stage 1 of a two-stage revision hip arthroplasty for chronic PJI of the hip.

Exclusion criteria:

1) sepsis, systemic inflammatory response syndrome, bacteremia on admission;

2) no data on MBE performed before and/or after surgery;

3) history of infectious diseases of the musculoskeletal system before primary hip arthroplasty;

4) total removal of the femur during debridement stage.

A total of 130 patients with chronic PJI of the hip were treated during this period, 86 of them meeting the inclusion and exclusion criteria. The share of men was 51.2% (44/86) with a median age of 64 years (IQR 53-71), while the share of women was 48.8% (42/86) with a median age of 68 years (IQR 64-72). The median of BMI reached 27.1 kg/m^2 (24.2-71.7).

In the preoperative period, in those cases when aspirate obtaining was impossible, tissue biopsy samples were taken from within the fistula according to the original technique (Russian Federation patent RU 2698175 C1).

The patients were divided into two groups depending on the presence (Group 1) or absence (Group 2) of the results of MBE of preoperative biomaterials (aspirate and/or tissue biopsy) at the time of surgery. Group 1 included 39 patients, Group 2 – 47 patients.

Surgical intervention in all patients consisted of implant removal, debridement and radical surgical treatment of an osteomyelitis focus, insertion of an antimicrobial spacer and drainage of the joint cavity. The final etiology of the infectious process was determined on the basis of MBE results of intraoperative materials: five tissue biopsy samples, synovial fluid and removed prosthetic components. From the day of surgery the patients, whose final results of preoperative MBE were not ready, received empirical ABT (vancomycin + cefoperazone/sulbactam or vancomycin + levofloxacin) according to the local protocol of treatment of patients with chronic PJI of the hip. Patients with a previously known etiology of the infectious process were treated according to these data. The final results of MBE of intraoperative materials having been received, a clinical pharmacologist was consulted for

correction of therapy and prescription of drugs for the outpatient stage.

Using the data from the arthroplasty registry of the Vreden National Medical Research Center of Traumatology and Orthopedics, the database of the microbiological laboratory and the data extracted from the medical records, a database of patients was formed in Microsoft Office Excel 365 spreadsheets. It included gender, age, BMI, concomitant diseases, waiting period for MBE results, results of examination of pre- and intraoperative materials, anamnesis data (duration of infection, number of debridement surgeries), local status: bone defects, laboratory tests (WBC, Hb, total protein, CRP) at the time of admission and discharge. The degree of bone mass loss was determined according to the W.G. Paprosky classifications for the acetabulum and femur [12, 13]. ABT duration at the inpatient and outpatient stages was also taken into account.

Treatment outcomes were determined by a phone interview of patients: a favorable outcome was considered to be the absence of signs of infection recurrence at a follow-up period of at least 24 months from the time of surgery.

Statistical analysis

IBM SPSS Statistics v.26 software was used for statistical analysis. Normality of distribution of quantitative variables was tested using the Shapiro-Wilk and Kolmogorov-Smirnov tests. The median (Me) was used to describe quantitative variables and the lower (Q1) and upper (Q3) quartiles (25-75% IQR) were used as measures of dispersion. Comparisons within the study groups were performed using the Mann-Whitney and Kruskal-Wallis tests. Nominative data were described with absolute values and percentages (n, %), the presence or absence of significant differences was tested by two tests: Pearson's χ^2 and Fisher's exact test. Differences between groups were considered statistically significant at $p<0.05$. An odds ratio (OR) with 95% confidence interval (95% CI) was calculated to quantify the relationship between the probability of outcome (recurrence) and the presence of a risk factor. A subanalysis of treatment outcomes in groups was performed depending on the number of risk factors identified in each patient during the study. Discriminant analysis was performed to determine the relationship between the probability of developing an unfavorable outcome and the number of risk factors identified. Discriminant function equation:

$$y = a_1x_1 + a_2x_2 + \ldots + a_nx_n + a_0,$$

where y — value of discriminant function; x — independent indicators (factors); a_1, a_n — coefficients; a_0 — constant.

Statistically significant differences between groups when comparing the mean values of the discriminant function in both groups were established using Wilks' λ statistic.

RESULTS

The share of patients with chronic hematogenous infection in Group 1 was 48.1% (n = 24), in Group 2 — 51.9% (n = 27), p = 0.658. The average time from the primary arthroplasty to the infectious process onset in both groups was about two years (Table 1). The duration of the infectious process in Group 1 was 12 months, in Group 2 — 10 months (p = 0.53).

Table 1

Medical history data

Parameter	Group 1, Me (IQR)	Group 2, Me (IQR)	p
Time from arthroplasty to PJI onset, mos.	24.3 (3–73)	24.3 (2.5–73.0)	0.879
Time from PJI onset to index surgery, mos.	12.0 (3.1–34.5)	10.0 (3.8–24.0)	0.530

There were no previous interventions for PJI of the hip in Group 1 — 48.7% (n = 19) of patients, in Group 2 — 61.7% (n = 29), p = 0.278. Among patients with recurrent PJI, 3 or more operations were performed in 45% (n = 9) and 22.2% (n = 4) of patients (p = 0.075) in groups 1 and 2, respectively. The share of patients with a draining fistula was 46.2% (n = 18) in Group 1 and 76.6% (n = 36) in Group 2 (p = 0.007). The preoperative MBE result of tissue biopsy samples from the fistulae was obtained in an average of 9 days (IQR = 8-11) from sampling, while the result of hip synovial fluid examination was ready in an average of 6.5 days (IQR = 6-7). The hospital stay duration in Group 1 was 15 days (IQR = 12-18), (IQR = 14-21) in Group 2 — 17 days.

Cardiovascular and gastrointestinal diseases accounted for more than 70% of cases in Group 1

and 85% in Group 2 (Table 2). Anemia of varying severity at the time of admission was diagnosed in 25.6% (n = 10) and 40.4% (n = 19) of patients, respectively. Group 1 patients were almost 5 times more likely to have renal and urinary diseases (p = 0.038) and 2.5 times more likely to have hepatic and biliary diseases (p = 0.129). Connective tissue diseases had a significant impact on the outcomes of chronic PJI treatment, increasing the risk of recurrence of the infectious process more than 5-fold (p = 0.062, OR = 5.25, 95% CI 1.05-26.20).

No intergroup differences were found between the laboratory parameters at the time of admission and in the postoperative period (p>0.05). At the same time, all patients included in the study showed significant negative dynamics of pre- and postoperative hemoglobin, total protein and albumin levels (p<0.001). Hemoglobin in patients by the time of discharge decreased by 20 g/L, total protein and albumin – by 13 and 9 g/L, respectively (Table 3).

No significant differences were obtained when analyzing perioperative parameters: the median of the blood loss in both groups was 700 ml (p = 0.737). The surgery duration was 175 min (IQR = 149-208) and 165 min (IQR = 137-192) in groups 1 and 2, respectively (p = 0.248). Blood transfusion was administered to 3 (7.7%) patients in Group 1 and to 6 (12.0%) in Group 2 (p = 0.464).

Table 2

Concomitant diseases

Disease	Group 1, Me (IQR)	Group 2, Me (IQR)	p
Essential hypertension	28 (71.8)	42 (89.4)	0.052
Gastrointestinal diseases	29 (74.4)	40 (85.1)	0.279
Coronary heart disease	18 (46.2)	25 (53.2)	0.665
Chronic heart failure	16 (41.0)	15 (39.1)	0.449
Anemia	10 (25.6)	19 (40.4)	0.174
Diabetes mellitus	9 (23.1)	9 (19.1)	0.791
Renal and urinary diseases	8 (20.5)	2 (4.2)	0.038
Hepatic and biliary diseases	8 (20.5)	4 (8.5)	0.129
Cardiac arrhythmia	7 (17.9)	14 (29.8)	0.221
Respiratory diseases	6 (15.4)	11 (23.4)	0.422
Smoking	3 (7.7)	8 (17.0)	0.331
Hepatitis C	4 (10.3)	3 (6.4)	0.697
Connective tissue diseases	2 (5.1)	6 (12.8)	0.283
Anticoagulant intake	3 (7.7)	4 (8.5)	1.0
Other diseases	3 (7.7)	5 (10.6)	>0.05

Table 3

Pre- and postoperative laboratory parameters

Laboratory parameters	Before surgery, Me (IQR)	After surgery, Me (IQR)	p
Hb, g/L	117.5 (106.0-130.0)	97 (91.0-105.0)	<0.001
CRP, mmol/L	33.9 (16.3-53.7)	37.4 (23.8-65.0)	0.164
WBC, 109/L	8.0 (6.5-9.7)	7.8 (6.6-9.5)	0.121
Total protein, g/L	74.8 (71.0-79.2)	61.7 (57.0-67.0)	<0.001
Albumin (n = 79), g/L	40.2 (37.4-42.0)	33.3 (30.5-35.5)	<0.001

Types 2A and 2B acetabular defects were prevalent in both groups (Fig. 1). Type 3A defect was diagnosed only in 2.6% (n = 1) of cases in Group 1 and 25.5% (n = 12) in Group 2 (p = 0.005). Significant differences (p = 0.013) were found when analyzing the effect of the acetabular bone loss on the outcomes of PJI treatment: type 2C defects increased the risk of recurrence 6.7-fold (p = 0.042; OR = 6.66, 95% CI 1.26-35.20) and type 3B defects 8-fold (p = 0.078; OR = 8.1, 95% CI 1.015-64.800).

In both groups, in the vast majority of cases, femoral defects formed during the debridement surgery corresponded to type 2 (Fig. 2). There were no significant intergroup differences by femoral defect type, but the risk of unfavorable outcome was significantly lower in patients with type 2 femoral defects (p = 0.06; OR = 0.24, 95% CI 0.07-0.90). In contrast, type 3A defects increased the risk of recurrence 6.6-fold (p = 0.021; OR = 6.57, 95% CI 1.49-29.01).

According to the results of preoperative MBE, the pathogen growth in Group 1 was absent in 12.8% (n = 5) of cases, and in 17.9% (n = 7) the microbial associations were isolated with 42.8% (n = 3) including Gram-negative bacteria. Staphylococci predominated in the spectrum of pathogens isolated from preoperative material (Fig. 3), with a cumulative proportion of 76.3%. The share of methicillin-resistant strains was 11.1% among *S. aureus* (MRSA) and 69.2% among *S. epidermidis* (MRSE).

In the postoperative period, no bacterial growth was obtained from intraoperative materials from only one (2.6%) patient in Group 1, and the infection was considered culture-negative. Polybacterial infection was diagnosed in 48.7% (n = 19) of Group 1 patients and in 42.6% (n = 20) of Group 2 patients (p = 0.448). The incidence of microbial associations with Gram-negative pathogens was 36.8% (n = 7) and 30.0% (n = 6) (p = 0.556), respectively. It was found that the polybacterial infection unlike the monobacterial one increased the risk of adverse outcome more than 6.7-fold (p = 0.02; OR = 6.75, 95% CI 1.36-33.44), and the presence of Gram-

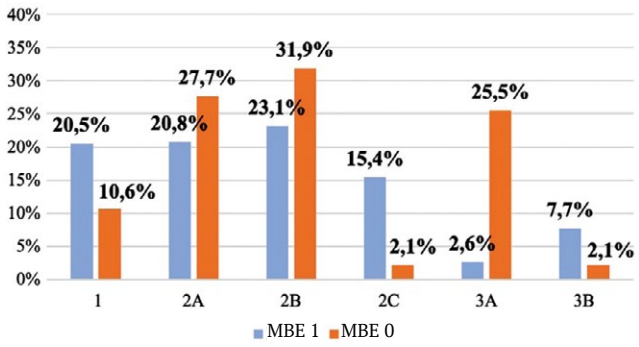

Fig. 1. Acetabular bone defects

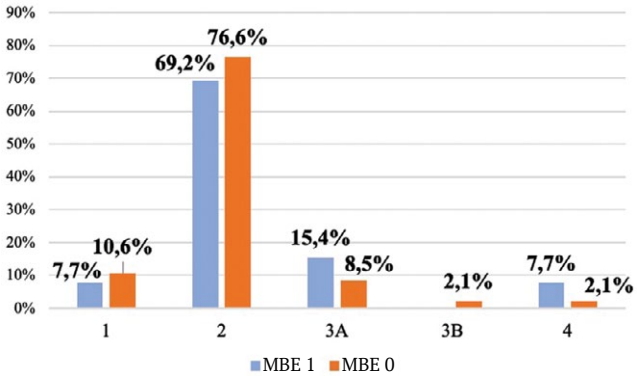

Fig. 2. Femoral фbone defects

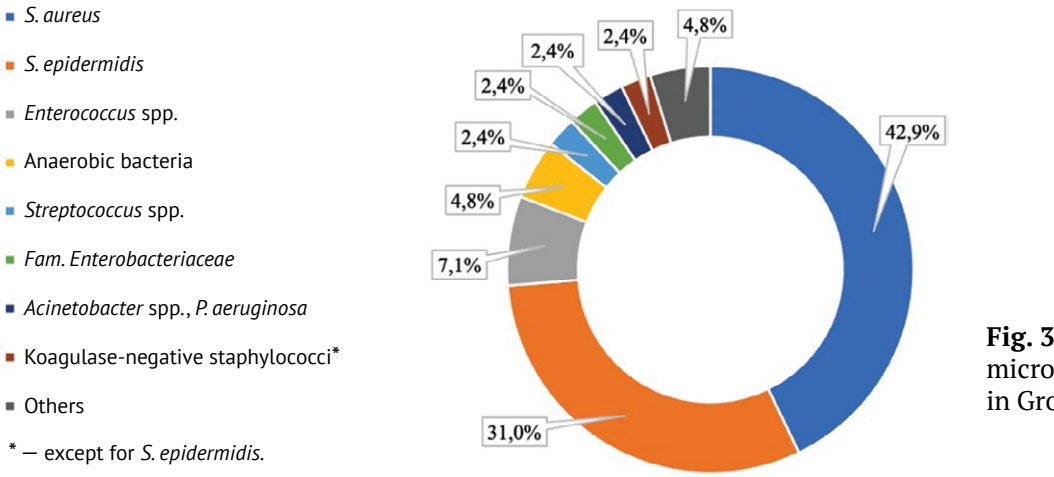

Fig. 3. Preorerative microbiology spectrum in Group 1

negative bacteria in microbial associations increased the risk of unfavorable treatment outcome 4-fold (p = 0.058; OR = 4.2, 95% CI 1.02-17.20).

An intragroup analysis of the concordance between the MBE results of pre- and intraoperative samples in Group 1 showed complete disagreement in 17.9% of cases (n = 7) and partial agreement in 41.05% (n = 16). In the remaining 41.05% (n = 16) of cases, the MBE results of pre- and intraoperative materials were the same. Statistical analysis revealed that complete agreement of the MBI results of pre- and intraoperative samples more than 8-fold reduced the risk of PJI recurrence (p = 0.024; OR = 0.121, 95% CI 0.015-0.990). Despite some differences in MBE results, staphylococci prevailed in the microbial spectrum postoperatively, with the total share of staphylococci in Group 1 reaching 80% (Table 4). In Group 2, they accounted for only 57.3% of the microbial spectrum, and in comparison with Group 1, streptococci were 6 times more frequent, and anaerobic pathogens and representatives of the *Enterobacteriaceae* were 2.6 times more frequent.

Intravenous antibiotic therapy in all patients was started on the day of surgery after biomaterial sampling for microbiological examination. On average, its duration in the studied cohort of patients was 8 days (IQR = 7-11) and did not differ between the groups (p>0.05). Empirical antibiotic therapy was administered to 38.5% of patients (n = 15) who had preoperative MBE results, as the isolated pathogens were within the spectrum of antibiotic activity defined by the local protocol for initial therapy. In Group 2 in 48.9% of cases (n = 23) empirical antibiotic therapy was administered as well. Initial therapy in the remaining 51.1% of patients included antibiotics against the strains of pathogens most often characterized by a high level of resistance, which were isolated during the previous debridement surgeries. It took an average of 5 days (IQR = 3-6) until the final correction of therapy. Etiotropic intravenous antibacterial therapy from the moment of its administration lasted 4 days (IQR = 1-7) with subsequent change to oral drug forms. Correction of antibacterial therapy was carried out not in all patients (Table 5).

Table 4

Microbial spectrum in groups according to postoperative examination, %

Pathogen	Group 1	Group 2
S. aureus	351.40	25.30
S. epidermidis	32.30	21.30
Coagulase-negative staphylococci	12.30	10.70
Anaerobic bacteria	4.60	12.00
Enterobacteriaceae	3.10	8.00
Acinetobacter spp., *P. aeruginosa*	3.10	4.00
Streptococcus spp.	1.50	9.30
Enterococcus spp.	1.50	5.30
Other pathogens	6.20	4.00

* — except for *S. epidermidis*.

Table 5

Correction of antibiotic therapy in groups

Correction of antibiotic therapy	Group 1		Group 2	
	n (%)	n (%) of recurrences	n (%)	n (%) of recurrences
No correction	17 (43.6)	1 (5.9)	15 (31.9)	0 (0)
Partial correction (1 drug)	12 (30.8)	3 (25.0)	12 (25.5)	1 (8.3)
Complete correction	10 (25.6)	2 (20.0)	20 (42.6)	4 (20.0)

Complete or partial change of antibacterial drugs was performed in 56.4% (n = 22) and 68.1% (n = 32) of cases in groups 1 and 2, respectively. Complete change of intravenous therapy was performed 1.7 times more often in Group 2. Despite the absence of statistical significance (p>0.05), in both groups there was a tendency to increase the frequency of recurrences depending on the need to change antibiotic therapy (see Table 5). At the outpatient stage all patients were administered oral antibiotics for 8 weeks. The maximum period of administration was 4 weeks in case of linezolid prescription only in accordance with the instructions for medical use of the drug, since longer administration is associated with a high incidence of adverse effects.

The share of patients with an unfavorable outcome of PJI treatment at 2-year follow-up in the groups with presence or absence of an MBE result at the time of surgery was 15.4% (n = 6) and 10.6% (n = 5), respectively (p = 0.536; OR = 1.53, 95% CI 0.43-5.45).

The following factors statistically significantly worsening treatment outcomes were included in further subanalysis: microbial associations, presence of Gram-negative bacteria in microbial associations, connective tissue diseases, types 2C and 3B acetabular defects, and type 3A femoral defects.

It was found that in all 18 patients (44.2%) enrolled in the study who did not have the considered risk factors, persistent suppression of infection was achieved. The share of such patients in Group 2 was 1.9 times higher than in Group 1 (Table 6). The presence of a single risk factor for recurrence was found in 35.9% and 27.7% of cases in groups 1 and 2, respectively (n = 14; n = 13), leading to recurrences in 14.3% and 7.7% of observations, respectively (n = 2; n = 1). Patients with a combination of two or more factors were more numerous in Group 1. Adverse outcomes were more frequent in Group 2 (44.4%) than in Group 1 (33.3%).

Discriminant analysis revealed a statistically significant positive correlation between the number of risk factors identified during the study and unfavorable treatment outcome (p<0.001). The sensitivity of the model was 72.7%, the specificity was 82.7%.

Table 6

Number of risk factors in groups

Number of factors	Group 1		Group 2	
	n (%)	n (%) of recurrences	n (%)	n (%) of recurrences
0	13 (33.3)	0 (0.0)	25 (53.2)	0 (0.0)
1	14 (35.9)	2 (14.3)	13 (27.7)	1 (7.7)
2 and more	12 (30.8)	4 (33.3)	9 (19.1)	4 (44.4)

DISCUSSION

In the studied cohort of patients, the efficacy of the management of chronic PJI of the hip after debridement stage was 87.2% (n = 75), despite a high share of patients with polymicrobial infection (45.3%), which, according to the scientific literature, is a significant risk factor for PJI recurrence [24]. The achieved results are comparable with the data of Russian and foreign authors. F. Li et al. in their meta-analysis describe favorable outcomes after two-stage revision arthroplasty in 79.6% of patients [14]. In a multicenter study by B.J. Kildow et al. this parameter amounted to 88.2% [15]. According to the data of V.Y. Murylev et al. eradication of infection after debridement stage of the two-stage revision arthroplasty was achieved in 92.1% of cases [16]. A.A. Kochish et al. reported effective treatment of PJI in 89% of cases as a result of the use of the modified tactics of perioperative management of profile patients [17].

According to some researchers, the impossibility to start etiotropic antibacterial therapy from the day of surgery negatively affects the treatment outcomes [9]. However, the intergroup analysis of efficacy in our study showed no significant differences depending on the presence or absence of MBE results at the time

of surgery: this parameter was 84.6% (n = 33) and 89.4% (n = 42), respectively (p = 0.535). It should be noted that the clinical profile of patients in the comparison groups differed: patients with an identified etiology of the infectious process were more likely to have urinary infection, multiple debridement interventions in the history, and significant defects of the bones forming the hip. At the same time, 38.5% and 48.9% of patients in groups 1 and 2, respectively, received initial empiric therapy. The need for a broad-spectrum initial therapy is determined by the significant differences in pre- and intraoperative MBE results reported previously [11]. In our study in Group 1, complete matching of pre- and intraoperative MBE results was observed in only 41% of cases (n = 16). At the same time, the share of polymicrobial infection increased 2.7-fold: from 17.9% preoperatively (n = 7) to 48.7% postoperatively (n = 19). In our opinion, such discrepancies are caused by the peculiarities of the pathogenesis of the infectious process associated with orthopedic implants: formation of sessile forms of bacteria as part of biofilms [18], intracellular location of microorganisms, as well as colonization of osteocyte-lacunar tubules, proved in relation to *S. aureus* [19, 20]. In Group 1, this pathogen accounted for 35.4% of the microbial spectrum, in Group 2 — only 25.3%.

The COVID-19 pandemic made a certain contribution to the shortening of the preoperative period, when the terms of preoperative examination of trauma and orthopedic patients were universally reduced in order to decrease the risk of coronavirus infection outbreak among the hospitalized patients [21]. As a consequence, it was often not possible to postpone surgical intervention until the final results of MBE were available. The lack of data on the etiology of the infectious process determines the need to prescribe empiric antibacterial therapy to patients in the postoperative period according to the educated guess principle [22], which requires regular microbiological monitoring of the spectrum of leading pathogens and their antibiotic resistance [23]. The study showed that the necessity to change parenteral antibacterial therapy was accompanied by an increase in the incidence of PJI recurrence.

Regardless of the presence or absence of MBE results at the time of surgery, a number of factors had a statistically significant impact on patients' treatment outcomes. First of all, the presence of microbial associations in a patient 6.7 times increased the risk of PJI recurrence, and the presence of Gram-negative bacteria in their composition — 4 times. Our earlier studies showed a similar trend: extremely low rate of polymicrobial infection management — only 27.8% (p<0.0001). At the same time, the presence of Gram-negative pathogens in microbial associations significantly increased the risk of recurrence (p=0.07) [24].

Other risk factors identified in this study leading to unfavorable outcome of PJI treatment have also been reported in the relevant literature. In Group 1, 45% of patients (n = 9) with recurrent infection had a history of 3 or more debridement interventions. In the study of H. Abdelaziz et al. this factor more than 4-fold increased the risk of reinfection (p<0.005) [25]. Type 3A femoral defects, which were more common in patients with the identified etiology of PJI (15.4%; n = 6), increased the probability of an unfavorable outcome 6.6 times (p = 0.021). According to P.A. Slullitel et al. a similar loss of bone mass was associated with a 13.5-fold greater risk of PJI recurrence (p<0.003) [26]. According to A.A. Kochish et al. data, a long-term course of type III chronic hematogenous PJI is often associated with the formation of extensive defects of the acetabulum [27]. In our study, types 2C and 3B were also more frequently observed in Group 1 – 15.4% of patients (n = 6) and 7.7% of patients (n = 3) than in Group 2 – 2.1% of cases each (n = 1), increasing the risk of recurrence 6.7 and 8 times, respectively.

Discriminant analysis showed that the unfavorable outcome of debridement stage of treatment of PJI of the hip statistically significantly (p<0.001) depends on the number of risk factors in a patient. At that, among the cohort of patients with 2 and more risk factors the unfavorable outcome of debridement stage was observed in 38% of cases, with one risk factor – in 11,1%. In the absence of risk factors, persistent suppression of the infectious process was achieved in all patients.

Limitation of the study

Small size of the study groups is considered to be a limitation of the study, which has been taken into account when choosing statistical methods. Also, such factors as the time from arthroplasty and

infection onset to primary surgical care, creation and benefits of a local depot of antibiotics have not been considered in this study.

CONCLUSIONS

To date, no similar analysis of the impact of the presence or absence of microbiological examination results at the time of debridement surgery has been performed in the scientific literature, and the principle of the necessity to obtain these results before surgical intervention has not been questioned. The study showed that the availability of data on the causative agent isolated from aspirate and/or tissue biopsy samples from the peri-implant fistula in the preoperative period had no significant effect on the efficacy of treatment of chronic periprosthetic hip joint infection. However, the probability of an unfavorable outcome increased significantly ($p<0.001$) with an increase in the number of identified risk factors in a patient ($p<0.001$). Apparently, the results of microbiological examination of preoperatively taken biomaterials are much more relevant as a diagnostic criterion for suspected periprosthetic infection than as a criterion for the choice of drugs for etiotropic antibacterial therapy. Nevertheless, this assumption requires further studies on a larger sample of patients.

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Authors' information

✉ *Yuliya V. Oleinik*
Address: 8, Akademika Baykova str., St. Petersburg, 195427, Russia
http://orcid.org/0009-0001-1654-1536
e-mail: hamster715@gmail.com

Svetlana A. Bozhkova — Dr. Sci. (Med.), Professor
http://orcid.org/0000-0002-2083-2424
e-mail: clinpharm-rniito@yandex.ru

Vasily A. Artyukh — Dr. Sci. (Med.)
https://orcid.org/0000-0002-5087-6081
e-mail: artyukhva@mail.ru

Denis I. Astakhov
https://orcid.org/0009-0007-7129-1553
e-mail: denmail_69@mail.ru

Alexander P. Antipov
https://orcid.org/0000-0002-9004-5952
e-mail: a-p-antipov@ya.ru

Sergey S. Toropov
https://orcid.org/0000-0002-9451-1834
e-mail: doctoropovss@yandex.ru