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Periprosthetic Knee and Hip Infection — Is It Possible to Compare Treatment Outcomes?

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Abstract

Background. It is known that the outcomes of patients treatment with periprosthetic joint infection (PJI) are significantly influenced by the state of the patient's body, the nature of the pathogen, the state of tissues in the area of the infectious focus and the treatment tactics. However, topographic and anatomical features of the blood supply to the knee and hip joints, as well as the volume of soft tissues, can affect the spectrum of pathogens, manifestations of the infectious process and, as a consequence, the effectiveness of treatment.

The aim of the study was to conduct a comparative analysis of the somatic status of patients, the etiology of the infectious process and the effectiveness of treatment of PJI depending on its localization.

Methods. A single-center retrospective study was conducted. The cases of 337 patients were studied — 119 patients with knee and 218 patients with hip PJI who underwent treatment with a two-stage technique during the period from 2007 to 2017. A comparative analysis of the PJI pathogens structure and concomitant pathology between patients with hip and knee PJI was carried out. The frequency of infection relief in the groups following the first stage was counted.

Results. Recurrence was diagnosed four times more frequently in patients with hip PJI compared to knee PJI. Risk factors for recurrence were gram-negative pathogens, microbial associations, and fistulous forms of the infectious process. Localization of the infectious process in the hip area was associated with a statistically significant greater volume of blood loss during the prolonged debridement surgery.

Conclusions. Recurrences of PJI occur more frequently in the hip area compared to the knee joint. Further analysisof critical factors in recurrence development is necessary for potential intervention.

Keywords: periprosthetic joint infection, hip arthroplasty, knee arthroplasty, comorbidity, etiology.

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Перипротезная инфекция коленного и тазобедренного суставов — можно ли сравнивать результаты лечения?

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Реферат

Актуальность. Известно, что на исходы лечения пациентов с перипротезной инфекцией (ППИ) значимое влияние оказывают состояние организма пациента и тканей в области инфекционного очага, характер возбудителя, тактика проведенного лечения. Однако топографо-анатомические особенности кровоснабжения коленного и тазобедренного суставов, а также объема мягких тканей также могут влиять на спектр возбудителей, проявления инфекционного процесса и, как следствие, на эффективность лечения.

Цель исследования — провести сравнительный анализ соматического статуса пациентов, этиологии инфекционного процесса и эффективности лечения перипротезной инфекции в зависимости от ее локализации.

Материал и методы. Проведено когортное ретроспективное исследование. Изучены истории болезни 337 пациентов: 119 с ППИ после эндопротезирования коленного сустава (КС) и 218 — после эндопротезирования тазобедренного сустава (ТБС), прошедших лечение с применением двухэтапной методики с 2007 по 2017 г. Проведен сравнительный анализ структуры возбудителей ППИ и сопутствующей патологии между пациентами с ППИ КС и ТБС, определена частота купирования инфекции в обеих группах после первого этапа лечения.

Результаты. Рецидив диагностировали в 4 раза чаще у пациентов с ППИ ТБС относительно ППИ КС. Факторами риска рецидива были грамотрицательные возбудители, микробные ассоциации и свищевые формы инфекционного процесса. Локализация инфекционного процесса в области ТБС ассоциирована со статистически значимо большим объемом кровопотери на фоне более длительной операции санирующего этапа.

Заключение. Рецидивы перипротезной инфекции чаще происходят в области тазобедренного сустава по сравнению с коленным суставом. Необходим дальнейший анализ критически важных факторов развития рецидива с целью возможного воздействия на них.

Ключевые слова: перипротезная инфекция, эндопротезирование тазобедренного сустава, эндопротезирование коленного сустава, коморбидность, этиология.

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BACKGROUND

Periprosthetic joint infection (PJI) following arthroplasty is one of the most serious complications. It consistently ranks among the top three most common reasons for revision surgery, along with dislocations and aseptic instability [1, 2]. The frequency of PJI remains high, and its absolute numbers are increasing, leading to substantial financial burdens associated with its treatment [3, 4]. High recurrence rates, coupled with the rising prevalence of difficult-to-eradicate (DTE) pathogens, compel surgeons to continue using the two-stage treatment method, which involves debridement with the placement of an antimicrobial spacer, followed by rearthroplasty [5, 6]. Despite being the established method for treating chronic PJI, the recurrence rate remains high, ranging from 10% to 30% [7, 8].

Currently, risk factors related to patients, such as obesity, chronic liver and kidney diseases, systemic illnesses, and dependencies, are actively being studied [9, 10, 11]. However, the influence of the localization of the infectious process, i.e., an anatomical factor, has not been adequately explored. The knee joint and hip joint have unique topographic and anatomical features in terms of blood supply and soft tissue volume in the surgical access area. Their proximity to the organs of the pelvis for hip and a thin layer of connective tissue for knee could potentially affect the spectrum of PJI pathogens and the frequency of fistula formation.

A review of the literature on the research topic revealed a limited number of publications dedicated to the comparative analysis of risk factors for PJI recurrence based on its localization. New data regarding the characteristics of infectious processes in different locations and their impact on outcomes could improve the effectiveness of treatment for this patient population.

The aim of this study — to conduct a comparative analysis of the somatic status of patients, the etiology of the infectious process, and the effectiveness of treatment for chronic PJI based on its localization.

METHODS

Study design

A retrospective cohort study was conducted based on the analysis of medical records and telephone interviews of 337 patients with PJI following primary arthroplasty. This included 119 patients with knee PJI and 218 patients with hip PJI who underwent treatment at Vreden National Medical Research Center of Traumatology and Orthopedics from 2007 to 2017.

Inclusion criteria: Newly diagnosed PJI with subsequent debridement surgery and the placement of an antimicrobial spacer.

Exclusion criteria: revisions in the patient's medical history, systemic inflammatory response at admission, and the use of a tourniquet during knee joint debridement.

PJI diagnosis was made based on the criteria of the Consensus Meeting on Periprosthetic Joint Infection (2018) [12]. Patients were divided into two groups based on the localization of the infectious process: group 1 — knee infection and group 2 — hip infection. Both groups were assessed for hospitalization duration, duration of debridement surgery, volume of blood loss, spectrum of PJI pathogens, comorbidity index [13], infection type according to W. Zimmerli, the proportion of patients with fistulous infection forms, and the effectiveness of PJI control.

Microbiological examination results of tissue biopsies and sonicated fluid samples from removed constructs were considered for analyzing the spectrum of pathogens. Infection type was determined based on W. Zimmerli's classification, which is based on the time of infection manifestation after primary arthroplasty [14]. Three infection types were identified: early (manifesting within less than 3 months), delayed (manifesting between 3 to 12 months), and late (manifesting after 12 months).

To obtain a cumulative comorbidity score, the frequency of pathologies that could influence treatment outcomes was analyzed. The comorbidity score was determined by summing the scores for all pathologies according to their severity [13].

The effectiveness of eradicating chronic infection was assessed upon the patients' admission for the second stage of surgical treatment. The mean follow-up period for patients after the first stage was 180 days (IQR 150-95). Eradication of infection was defined as the absence of clinical and laboratory signs of the infectious process, as well as no recurrence data between treatment stages. Eleven patients

with knee PJI were excluded from the treatment effectiveness analysis due to their unavailability during the study.

Statistical analysis

The collected data were analyzed using the StatSoft STATISTICA 10. The comparison of the frequencies of qualitative characteristics (gender, PJI type, treatment effectiveness) was conducted using the chi-squared (χ^2) and Pearson methods. Median (Me) and interquartile range (IQR) (Q1-Q3; 25-75%) were used for quantitative variables. When analyzing differences in quantitative data (age, duration of hospitalization and surgery, total comorbidity score) between the study groups, the Mann-Whitney U test was employed. Differences were considered statistically significant at $p < 0.05$. To assess the risk of recurrence, the relative risk (RR) with a 95% confidence interval (CI) was calculated following evidence-based medicine rules.

RESULTS

The study revealed a prevalence of females over males in the overall cohort of patients included in the study (Table 1). The proportion of females among patients with knee PJI was significantly higher ($p = 0.03$) than the corresponding figure in the hip PJI group. The age of patients ranged from 22 to 87 years, with a median (Me) of 62 years and an interquartile range (IQR) of 53–69 years. Patients with knee infection were significantly older than those with hip PJI ($p = 0.004$).

Irrespective of the localization of the infectious process, the prevailing infection type (51.6%) was late-onset infection, with symptoms manifesting a year or more after arthroplasty. Fistulous infection (FI) was observed in half of all cases (50.7%), but comparative analysis established its statistically significant prevalence among patients with infection localized in the hip area ($p < 0.05$).

The comorbidity index ranged from 5 to 12 points (Table 2). Patients with knee PJI had, on average, a higher level of this indicator than the group with hip PJI ($p = 0.01$).

In contrast, the duration of surgery ($p = 0.00$), the volume of intraoperative blood loss ($p = 0.00$), and the length of hospitalization ($p = 0.02$) were significantly higher among patients with hip infection.

Table 1

Characteristics of patients in the study groups, % (*n*)

Characteristic	Total, n = 337	Knee group, n = 119	Hip group, n = 218	p
Male	39.8 (134)	32.0 (38)	44.0 (96)	0.03
Female	60.2 (203)	**68.0 (81)**	56.0 (122)	
Age, years	62 (53–69)	**64 (58–69)**	61 (50–70)	0.004
PJI type:				
early	24.6 (83)	26.7 (32)	23.4 (51)	>0.05
delayed	23.7 (80)	26.0 (31)	22.5 (49)	>0.05
late	51.6 (174)	47.0 (56)	54.1 (118)	>0.05
PJI form:				
fistulous	50.7 (171)	27.7 (33)	**63.3 (138)**	0.00
non-fistulous	49.3 (166)	**72.3 (86)**	36.7 (80)	0.00

* Statistically significant values are shown in bold.

Table 2

Study parameters in study groups

Parameter	Knee group	Hip group	p
Comorbidity index	**9 (7–12)**	8 (5–11)	0.01
Hospitalization duration, days	23 (19–27)	**25 (21–31)**	0.02
Surgery time, min	165 (135–190)	**190 (160–220)**	0.000
Blood loss, ml	650 (400–900)	**800 (500–1100)**	0.001

* Statistically significant values are shown in bold.

The effectiveness of controlling PJI after the debridement stage in the overall patient cohort was 83.8% (Table 3). Of note is the statistically significant predominance of adverse treatment outcomes among patients with hip infection compared to the knee nfection (p = 0.002).

Among the leading pathogens causing PJI in both patient groups, *staphylococci* (54.2%) were predominant (Table 4). Among patients with knee infection, *Staphylococcus epidermidis* slightly prevailed, while *Staphylococcus aureus* prevailed in the hip group. No significant differences in the frequency of microorganisms were found between the groups, except for *Propionibacterium* sp. This pathogen was significantly more frequently isolated from the biomaterial of patients with knee PJI (p = 0.04).

Further analysis of pathogen structure focused on studying the frequency of PJI recurrence in patients with infections of different localizations (Table 5). It was found that monobacterial infection caused by Gram-positive (Gram(+)) bacteria significantly recurred more frequently (p < 0.05) when the infectious process was localized in the hip area. In patients with knee PJI, the isolation of Gram-negative (Gram(-)) pathogens increased the risk of recurrence by 7 times (RR — 7.3; 95% CI 1.2–45.9) compared to Gram(+) infection.

Microbial associations were predominantly found in patients with hip PJI, with the participation of (Gram(-) bacteria increasing the risk of recurrence by more than 2 times (RR — 2.3; 95% CI 0.7–7.3).

Table 3

Outcomes before the second stage of treatment, % (n)

Outcome	Total	Knee group	Hip group	p
Recurrence	16.2 (49)	5.0 (5)	**21.8 (44)**	0.002
Remission	83.8 (254)	95.0 (96)	78.2 (158)	>0.05
Total	100 (303)	100 (101)	100 (202)	n/a

* Statistically significant values are shown in bold; n/a – not applicable.

Table 4

Structure of PJI pathogens in groups

Pathogen	Knee group, % (n)	Hip group, % (n)	p
Staphylococcus epidermidis	29.2 (40)	28.1 (74)	>0.05
Staphylococcus aureus	27.0 (37)	33.4 (88)	>0.05
Enterococcus sp.	8.8 (12)	7.2 (19)	>0.05
Propionibacterium sp.	7.3 (10)	1.9 (5)	0.04*
Enterobacteriaceae family	6.6 (9)	4.2 (11)	>0.05
Coagulase-negative staphylococci	5.1 (7)	4.6 (12)	>0.05
Streptococcus sp.	4.4 (6)	6.1 (16)	>0.05
Non-fermenting Gram-negative bacteria	4.4 (6)	6.5 (17)	>0.05
Others	4.4 (6)	4.9 (12)	>0.05
Corynebacterium sp.	2.9 (4)	1.9 (5)	>0.05
Candida sp.	0.0 (0)	1.5 (4)	>0.05
Total microorganisms	100 (137)	100 (263)	>0.05

* Statistically significant values are shown in bold. Coagulase-negative *staphylococc*i (except *S. epidermidis*); Enterobacteriaceae family – including *Escherichia coli*, *Klebsiella pneumoniae, Enterobacter cloacae*; Non-fermenting Gram(-) negative bacteria: *Ps. Aeruginosa, Acinetobacter* sp.

Table 5

Recurrence rate in patients with mono-/polymicrobial forms of PJI in groups, % (n / N)

PJI cases	Recurrence		p
	Knee group	Hip group	
Monomicrobial form Gram(+)	3.0 (2/66)	22.2 (30/135)	0.002
Monomicrobial form Gram(-)	22.2 (2/9)	23.1 (3/13)	>0.05
Polymicrobial form Gram(+)	6.7 (1/15)	15.4 (4/26)	>0.05
Polymicrobial form: Gram(+) and Gram(-)	0.0 (0/3)	35.7 (5/14)	n/a
No growth	0.0 (0/6)	10.0 (1/10)	n/a
Fungi	0.0 (0/2)	25.0 (1/4)	n/a
Total	5.0* (5/101)	21.8* (44/202)	0.002

n – number of patients with PJI recurrence; N – number of patients with a specific PJI form;
* — average recurrence rate in the group.
Statistically significant values are shown in bold; n/a – not applicable.

DISCUSSION

Stage revision arthroplasty remains a competitive treatment method for PJI despite promising results of single-stage surgical strategies in recent years. Authors of several meta-analyses describe the advantages of single-stage revision arthroplasty and gradually expand its indications based on data showing comparable infection eradication effectiveness. However, they still emphasize the significant role of the two-stage algorithm. For patients with complex somatic status, obesity, the presence of fistulas, and the presence of multi-drug resistant pathogens, staged revision arthroplasty is preferable. Given that a significant proportion of patients fall into these categories, this strategy remains relevant.

The prevalence of osteoarthritis of the hip and knee is higher in women than in men, and the incidence increases during menopause due to cartilage volume reduction and bone loss. This fact is reflected in the patient population undergoing primary hip and knee replacement.

A similar gender distribution is observed among patients with hip and knee PJI, as confirmed by the data from our study. However, the proportion of males in the structure of patients with infectious complications becomes more significant. This may be related to the fact that male gender, according to scientific publications, is an independent risk factor for PJI.

S. Xu et al have shown that one of the predisposing factors for the development of fistulous forms of PJI is the localization of the infectious process. According to their data, the development of PJI after hip arthroplasty was significantly more often accompanied by fistula formation (25.4%) compared to the localization of the infectious process in the knee joint (18.5%). According to our study, the majority of patients with knee PJI had the presence of fistulas (63.5%), which was statistically significantly higher than in similar studies by foreign colleagues; a similar indicator among patients with hip PJI was comparable with international statistics at 27.7%.

The total comorbidity index score in both groups in our study corresponded to an average risk of recurrence. Despite a higher comorbidity score, the effectiveness of the debridement stage was higher in patients with hip PJI. This might be related to the higher frequency of fistulous forms in patients with knee PJI, which are often associated with significant soft tissue inflammation, or possibly other risk factors. For example, our study found a significantly longer duration of debridement surgery with spacer implantation and associated higher intraoperative blood loss, which are predisposing risk factors for PJI recurrence.

An analysis of treatment outcomes in patients with knee PJI revealed a significant

negative impact of microbial associations with Gram(-) bacteria on the effectiveness of the first stage of surgical treatment. The presence of such pathogens increased the risk of failure by more than 2 times, confirming the results of earlier studies.

Staphylococci were the leading pathogens of PJI in both study groups, which can be attributed to their ability to form microbial biofilms. Despite the similar species structure of pathogens, except for the more frequent isolation of *Propionibacterium* sp. from patients with knee infection (p = 0.04), microbial associations more frequently caused knee PJI.

Negative effects of Gram(-) pathogens on the effectiveness of the sanitation stage of monobacterial hip PJI were also observed. The risk of recurrence was 7 times higher compared to Gram(+) pathogens. When monobacterial infection was localized in the knee joint, such a dependency was not found. A similar negative trend of Gram(-) pathogens' involvement in the etiology of PJI was also identified by B. Zmistowski et al, with the frequency of infection recurrence caused by Gram(-) and Gram(+) pathogens being 48% and 31%, respectively.

Limitations of the sudy

This study has limitations due to its retrospective nature and an uneven number of patients in the comparison groups. However, this limitation was mitigated by strict inclusion criteria in the study and adequate statistical data processing methods.

CONCLUSIONS

The study showed significant differences in the effectiveness of the debridement stage of two-stage treatment for patients with newly diagnosed PJI depending on the localization of the infectious focus. Infection in the knee joint was characterized by a higher recurrence rate compared to the hip joint. Prognostically unfavorable factors included the involvement of Gram-negative pathogens and microbial associations in the etiology of the infection, the presence of fistulas, and consequently, longer surgery duration and increased blood loss.

Further research is needed to identify the full range of the most significant risk factors for the development of recurrent infectious processes and to develop measures for their possible modification or mitigation of their negative effects depending on the localization of PJI.

DISCLAIMERS

Author contribution

Bozhkova S.A. — research concept and design, manuscript writing and editing, data analysis and interpretation.

Preobrazhensky P.M. — data analysis and interpretation, manuscript writing.

Kochish A.A. — data collection and analysis, data statistical processing, manuscript writing.

Tikhilov R.M. — research concept, drafting the article.

Artyukh V.A. — data analysis and interpretation, manuscript editing.

Klitsenko O.A. — data statistical processing, drafting the article.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the study to ensure proper consideration and resolution of all possible issues related to the correc-tness and reliability of any part of the work.

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Consent for publication. The authors obtained written consent from patients to participate in the study.

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