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Comorbidity Index as a Risk Factor of Knee PJI Recurrence After Spacer Implantation

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Background. Patient-related risk factors for periprosthetic joint infection (PJI) are currently investigated in detail. However, the influence of those factors on PJI recurrence and their confounding effect was not investigated. Identifying factors that influence PJI recurrence and establishing the role of each risk factor are important.

The study aimed to analyze the comorbidity structure in patients with knee PJI and create, based on obtained data, a rating scale that allows predicting the probability of PJI recurrence after spacer implantation.

Methods. A single-center study was conducted based on retrospective data of 161 patients with PJI after primary total knee arthroplasty treated with staged reimplantation from January 2007 to January 2017. To clarify comorbidity structure and the most important risk factors, all patients were divided into two groups: patients with PJI recurrence after spacer implantation (group 1, n = 48) and patients who successfully passed spacer implantation (n = 113, group 2). Based on the obtained data, the frequency of comorbidities was analyzed. The list included 17 points that characterized the presence and severity of different comorbidities. Then, we conducted a logistic regression analysis to identify the significance of each factor and thresholds for the comorbidity index (CI) for the interpretation of the final score. With the presented scale, spacer implantation in the compared groups was analyzed.

Results. The most significant comorbidities were anemia, chronic kidney disease, obesity, and cardiovascular pathology. The CI thresholds were calculated, which allowed interpretation of the obtained score. The distribution of patients by risk categories within each group was also analyzed, and differences between groups were determined. The CI value corresponding to the minimal risk of PJI recurrence was more common ($p<0.0001$) in group 1. Moreover, more than half of the patients with failed spacer implantation had a high risk of PJI recurrence according the CI value, and only 6.2% of patients who had successful treatment had CI high value ($p<0.0001$).

Conclusions. The multivariate analysis of the presence and severity of concomitant pathologies enabled the development of a comorbidity scale with the calculation of an integral indicator (comorbidity index) and establishment of its threshold values. The proposed CI could be the basis for a combined relapse risk calculator and an algorithm for choosing the surgical treatment strategy in patients with knee PJI, which requires further investigation.

Keywords: periprosthetic joint infection, knee, recurrence, comorbidity, risk factors.

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Расчет индекса коморбидности как фактора риска рецидива перипротезной инфекции после установки спейсера коленного сустава

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Актуальность. В настоящее время подробно изучены связанные с пациентом факторы, повышающие риск возникновения перипротезной инфекции (ППИ), однако влияние тех же факторов на риск развития рецидива инфекции, а также кумулятивный эффект нескольких заболеваний на риск рецидива изучены недостаточно.

Цель исследования — проанализировать структуру сопутствующей патологии у пациентов с ППИ коленного сустава и на основании полученных данных создать оценочную шкалу, позволяющую прогнозировать вероятность развития рецидива инфекции после санирующего этапа операции.

Материал и методы. Ретроспективное одноцентровое когортное исследование основано на полученных из медицинской документации сведениях о 161 пациенте с ППИ после первичного эндопротезирования коленного сустава, прошедшего этапное лечение за период с января 2007 г. по январь 2017 г., собранных в ходе диссертационного исследования. С целью уточнения структуры коморбидности и наиболее важных факторов риска рецидива ППИ пациентов разделили на две группы: группа 1 — пациенты с рецидивами ППИ после выполнения первого этапа лечения — 48 человек; группа 2 — пациенты с ППИ, успешно прошедшие первый этап (имплантация спейсера) — 113 человек. При выполнении диссертационного исследования первого автора (П.М.П.) был сформирован перечень сопутствующей патологии, состоящий из 17 пунктов, характеризующих наличие и выраженность различных сопутствующих заболеваний. В дальнейшем при помощи мультифакторного статистического анализа с использованием метода классификационных деревьев определяли значимость каждой патологии, пороговые значения для суммарного балла по сформулированной шкале коморбидности (индекса коморбидности) для интерпретации полученных результатов.

Результаты. Наибольшая значимость среди прочих факторов принадлежит хронической железодефицитной анемии, заболеваниям почек, ожирению и патологии сердечно-сосудистой системы. Установлены значения пороговых критериев индекса коморбидности, позволяющие трактовать полученный результат. Проанализировано распределение пациентов по категориям риска внутри каждой группы и определены межгрупповые различия. Значение индекса, соответствующее минимальному риску рецидива инфекции, чаще встречалось в группе пациентов без рецидива ППИ (p<0,0001). Более половины пациентов с неудачными попытками санации очага инфекционного воспаления имели высокий риск, по сравнению с пациентами без рецидива ППИ.

Заключение. Проведение многофакторного анализа наличия и выраженности сопутствующей патологии позволило разработать шкалу коморбидности с расчетом интегрального показателя (индекса коморбидности) и установить его пороговые значения. Предложенный индекс коморбидности может лечь в основу объединенного калькулятора риска рецидива и алгоритма тактики выбора хирургического лечения у пациентов с ППИ коленного сустава, что требует дальнейших исследований.

Ключевые слова: перипротезная инфекция, коленный сустав, рецидив, коморбидность, факторы риска.

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Background

Over the past decade, periprosthetic joint infection (PJI) has steadily become one of the most common reasons for revision interventions after knee arthroplasty [1, 2]. Given the increasing number of PJI cases caused by difficult-to-treat pathogens and a significant proportion of complicated PJI cases (such as undetected pathogens, fistulous forms of PJI, and massive bone defects), staged re-endoprosthetics remains one of the preferred surgical approaches [3, 4, 5]. The treatment of PJI is associated with significantly higher costs and a greater number of complications than arthroplasty for aseptic reasons [6, 7]. According to Lum et al., the mortality rate varies from 1.7% to 34.0%, and its causes can be both the severity of the infectious process and decompensation of concomitant pathology [8].

Currently, patient-related factors that increase the PJI risk have been studied in detail, which include the presence of systemic diseases, liver and kidney pathologies, immunodeficiency states, obesity, peripheral vessel pathologies, etc. [9]. However, the influence of these factors and the cumulative effect of several diseases on the risk of recurrence are less investigated. Thus, not only identifying the factors that influence the risk of relapse but also establishing the degree of this influence is important. Considering that several patient-related risk factors are modifiable, the identification of key pathologies will help the patient be more prepared at the preoperative stage for the upcoming surgical intervention, reducing the probability of PJI recurrence and lethal outcomes.

This study aimed to analyze the comorbidities in patients with knee PJI and, based on the data obtained, to create an assessment scale for predicting the probability of infection recurrence after the sanitizing stage.

Methods

Study design

A retrospective single-center cohort study was conducted based on the medical records of 161 patients with PJI after primary knee replacement who underwent staged treatment from January 2007 to January 2017, collected during the thesis research of the first author* [*P M. Preobrazhensky, Ways to Optimize Revision Knee Arthroplasty in Patients with Periprosthetic Infection, Ph.D. (Medicine) thesis work, Saint Petersburg (2017)]. The average follow-up period was 5.6 (2.4–7.2) years.

The criteria for exclusion from the study were previous revision interventions on the knee joint and signs of a systemic inflammatory response.

Diagnostics of the knee PJI was performed based on the criteria of the International Consensus Meeting [10]. The PJI type was determined based on the timing of its manifestation after primary arthroplasty, that is, early (<3 months after arthroplasty), delayed (3–12 months after arthroplasty), and late (>12 months after arthroplasty) [11].

To clarify the structure of comorbidities and the most important risk factors for PJI recurrence, patients were distributed into two comparison groups:

- Group 1 included patients with PJI relapse after stage 1 of treatment (n = 48);
- Group 2 consisted of patients with PJI whose spacer implantation was successful (n = 113) (Fig. 1).

In the comparison groups, known risk factors for the occurrence of infectious complications were analyzed, namely, initial diagnoses; identification of the pathogens in the puncture sample preoperatively or diagnostically significant pathogens from the intraoperative material; presence and severity of cardiovascular, respiratory, liver and biliary duct, and urinary disorders; diabetes mellitus; systemic, hematological, and malignant diseases; coagulation disorders; and intake of anticoagulants.

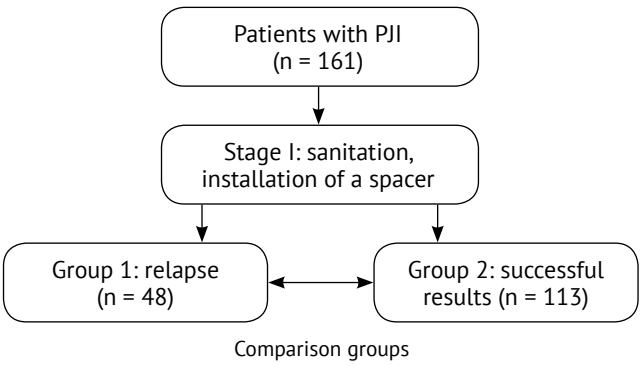

Fig. 1. Study flowchart

To determine the degree of the estimated risk of PJI recurrence, we created a list of comorbidities, consisting of 17 items characterizing the presence and severity of various comorbidities. Each item, depending on the degree of disease manifestation, was assigned 0–3 points: 0, no manifestations; 1, minor manifestations or their absence, and no permanent therapy is required; 2, presence of clinical manifestations, but with a controllable patient condition, and constant therapy is required; and 3, moderate and severe manifestations despite treatment (Table 1).

Subsequently, in the multivariate analysis using the classification tree method, we determined the significance of each factor and threshold values for the total score according to the formulated comorbidity scale, that is, the comorbidity index for interpreting the results obtained. This scale was used to analyze the treatment outcomes of all study patients.

In this study, all patients underwent a sanitizing surgery, including arthrotomy, removal of the components of the endoprosthesis and cement mantle, if any, debridement of soft and bone tissues involved in the infectious process, abundant lavage of the joint cavity using Lavasept solution (at least 5 L), and further implantation of an antimicrobial articulating or block-shaped cement spacer [4].

Stage 1 of surgical treatment was considered successful if the patient had no clinical or laboratory signs of PJI recurrence upon admission for revision arthroplasty. Repeated sanitizing interventions between sanitation stages were interpreted as a poor outcome.

Statistical analysis

The clinical results obtained were analyzed using the StatSoft STATISTICA 10 software system. Frequency characteristics (sex, PJI type, comorbidities, and outcomes) of qualitative indicators were compared using nonparametric χ^2 methods, Pearson's χ^2, and Fisher's test. The median was used as the central characteristic, and the lower (Q1) and upper (Q3) quartiles (25%–75% of the interquartile range) were used as measures of dispersion. Quantitative parameters (such as age, duration of hospitalization, surgery duration, and blood loss volume) in the study groups were compared using the Mann–Whitney test. Differences between the groups were considered significant at $p < 0.05$. The classification tree method was used to determine the significance of factors and threshold values in the proposed comorbidity scale.

Results

The infectious process was possible to be arrested in 113 of 161 study patients after the first stage of sanitizing surgery. Stage 2 was revision arthroplasty. Thus, the efficiency of the sanitation stage was 70.1%.

The general characteristics of both the study cohort and comparison groups are presented in Table 2. The distribution of patients by sex and age in the comparison groups was comparable with a slight predominance of women. The average age of the patients in the comparison groups was 60.5 (29–77) years. A hematogenous route of generalized infection in which symptoms manifest later than 12 months was the most common in both groups. In the majority of the study patients, primary arthroplasty was performed for idiopathic gonarthrosis, that is, in 70.2% of patients without PJI recurrence and 50.0% of patients with relapses. Posttraumatic gonarthrosis occurred significantly more often ($p = 0.05$) in patients with PJI relapses, and systemic diseases as the cause of primary arthroplasty occurred with a comparable frequency.

As regards PJI pathogens in patients who completed successfully the two-stage treatment, Staphylococcus *epidermidis* was the most common, whereas in patients with relapses of infection, *S. aureus* was the most common pathogen. Moreover, 40% of *S. aureus* isolates in patients with relapses were resistant to methicillin, surpassing more than twice ($p = 0.086$) that in patients without relapses (17.7%). In addition, the frequency of methicillin-resistant strains of epidermal staphylococcus in the comparison groups was comparable. Representatives of *Corynebacterium* spp. and *Enterobacteriaceae* were more frequently isolated from patients with poor treatment outcomes (Table 3).

Polymicrobial infection was also diagnosed two times more often in recurrent PJI, that is, in 22.6% of the cases compared with 10.6% of patients who had successful surgery ($p = 0.05$).

The most common somatic pathologies in both groups were cardiovascular diseases (coronary heart disease, arterial hypertension, and heart fail-

Table 1

List of comorbidities

Disease	0 points	1 point	2 points	3 points
Ischemic heart disease	No	Constant therapy is not required	Use of therapy, the condition is compensated, and/or a history of infarction	Decompensation: unstable angina, acute coronary syndrome, acute myocardial infarction
Congestive heart failure	No	CHF-I	CHF-II (A and B)	CHF-III
Cardiac arrhythmia	No	Constant therapy is not required	Permanent or paroxysmal form of arrhythmia, use of constant therapy; the condition is compensated	Newly detected untreated arrhythmia and decompensation during therapy
Arterial hypertension	No	Constant therapy is not required	Use of constant therapy; the condition is compensated	Decompensation: hypertensive crisis
Peripheral vascular disease: obliterating atherosclerosis, varicose veins, endarteritis	No	Initial signs, constant therapy is not required	Moderate signs; therapy is required	Surgical treatment is required
Diabetes mellitus	No	Diet	Use of therapy; the condition is compensated	Subcompensation and decompensation
Respiratory system diseases: COPD and chronic bronchitis, bronchial asthma	No	Initial signs, constant therapy is not required	Moderate signs; therapy is required	Severe respiratory failure
Malignant neoplasms, including hematological	No	History, no recurrence	Stabilization during antitumor treatment	With distant metastases, progression during treatment
Pathology of the liver and BD	No	Initial signs, constant therapy is not required	Use of therapy; the condition is compensated	Hepatic cirrhosis, severe signs of liver failure
GIT pathology	No	Initial signs, constant therapy is not required	History of gastrointestinal ulcer; therapy is required	Acute erosive gastritis, acute ulcer, and bleeding from the GIT
Systemic connective tissue diseases: RA, SLE, scleroderma, etc.	No	Initial signs, constant therapy is not required	Use of therapy; the condition is compensated	Decompensation during therapy
Anemia of any etiology	No	Mild: ≥90 g/l	Moderate: 70–90 g/L	Severe: <70 g/L
Coagulation system disorders: thrombophilia, thrombocytopenia, etc.	No	Without hypo- or hypercoagulation	Clinical and laboratory manifestations of hypo- or hypercoagulation	History of venous thrombosis or PAE
Intake of anticoagulants	No	For orthopedic indications	For cardiological indications; without hypocoagulation	For cardiological indications; there are clinical and laboratory manifestations of hypocoagulation
HIV/AIDS	No	Constant therapy is not required	Use of therapy; the condition is compensated	Development of an infectious process associated with HIV/AIDS
Diseases of the kidneys and UT: CRF associated with glomerulonephritis, diabetes, etc., chronic infections of the kidneys and UT	No	Kidney disease without CRF; history of acute infection	Initial or moderate CRF, remission of chronic disease	Severe CRF or dialysis, exacerbation of infection
Metabolic status: entry of height and weight, automatic calculation of BMI and assignment of the required number of points	Normal	Overweight (BMI 26.0–27.9)	Obesity I–II (BMI 31.0–40.9)	Obesity III–IV (BMI 36–41), anorexia (BMI < 17.5)

CHF – chronic heart failure; COPD – chronic obstructive pulmonary disease; GIT – gastrointestinal tract; BD – biliary ducts; RA – rheumatoid arthritis; SLE – systemic lupus erythematosus; PAE – pulmonary artery thromboembolism; UT – urinary tract; CRF – chronic renal failure; BMI –, body mass index.

Table 2

Characteristics of patients in the study groups

Parameter	Total, *n* = 161 *n* (%)	Group 1, *n* = 48, *n* (%)	Group 2, *n* = 113, *n* (%)	*p*
Gender				
Men	41 (25.5)	17 (35.4)	24 (21.2)	0.075
Women	120 (74.5)	31 (64.6)	89 (78.8)	0.075
PJI type				
Early	46 (28.5)	13 (27.1)	33 (29.2)	0.850
Delayed	48 (29.9)	14 (29.8)	34 (30.1)	1.000
Late	67 (41.6)	21 (43.7)	46 (40.7)	0.730
Initial pathology				
Idiopathic gonarthrosis	103 (64.0)	24 (50.0)	**79 (70.2)**	0.010
Posttraumatic gonarthrosis	37 (23.0)	**16 (33.3)**	21 (18.5)	0.050
Rheumatoid arthritis	21 (13.0)	8 (16.7)	13 (11.3)	0.400

Statistically significant values are given in bold.

Table 3

Structure of PJI pathogens in both groups

Pathogens	Group 1 *n* (%)	Group 2 *n* (%)	*p*
Staphylococcus epidermidis	15 (23.1)	**48 (37.5)**	0.05
Staphylococcus aureus	20 (30.8)	42 (32.8)	0.87
CNS	6 (9.2)	14 (10.9)	0.81
Streptococcus sp.	1 (1.5)	3 (2.4)	1.00
Enterobacteriaceae	**9 (13.9)**	3 (2.4)	0.01
Enterococcus spp.	6 (9.3)	6 (4.7)	0.22
NGNB	0 (0)	3 (2.4)	0.55
Corynebacterium spp.	**4 (6.1)**	1 (0.7)	0.04
Propionibacterium spp.	1 (1.5)	4 (3.1)	0.66
Candida sp.	0 (0)	1 (0.7)	1.00
Other	3 (4.6)	3 (2.4)	0.40
Total	65 (100)	128 (100)	–

CNS – coagulase-negative staphylococci (except for *S. epidermidis*); *Enterobacteriaceae,* including *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae*; NGNB – nonfermentative gram-negative bacteria. Significant values are given in bold.

ure). Moreover, this pathology was detected significantly more often in patients with PJI relapses ($p < 0.001$) (Fig. 2).

Peripheral vascular disease, as a risk factor for PJI occurrence and recurrence and tends to progress in case of repeated surgical interventions, occurred in 48% of the patients in group 1 compared with 24.8% of the patients in group 2 ($p < 0.001$). Similar differences in the incidence were found for liver and biliary duct, gastrointestinal tract, and kidney and urinary tract diseases ($p < 0.0001$). Iron deficiency anemia, which develops in the course of a chronic infectious process, was also significantly more often ($p < 0.0001$) detected during preoperative laboratory examination in group 1. The rest of the indicators included in the analysis did not show significant differences in the comparison groups.

In the multivariate statistical analysis, each indicator used in the comorbidity scale was assigned with its degree of significance depending on the influence of this factor on the final result (Table 4).

Among other factors, hematological diseases (chronic iron deficiency anemia), kidney diseases, obesity, and cardiovascular diseases (arterial hypertension and coronary heart disease) were significant.

The total score obtained when completing the scale for each patient is called the comorbidity index. Later, based on the statistical analysis, the values of the threshold criteria for the comorbidity index were determined, which allow interpretation of the results obtained. In the study patients, the number of points corresponding to each category of results was calculated (Fig. 3). The distribution of patients by risk category within each group was also analyzed, and intergroup differences were determined Table 5).

The index value corresponding to the minimum risk of infection recurrence was more common ($p < 0.0001$) in the group without PJI recurrence (group 2; 51.3%). Moreover, more than half of the patients with unsuccessful attempts to sanitize the infectious inflammation foci (group 1) had a high risk of recurrence (58.3%), which was significantly higher ($p < 0.0001$) than that in patients without PJI recurrence (6.2%). The final average values of the comorbidity index in the group without and with PJI recurrence were 7.4 (3–14) and 13.0 (6–21), respectively.

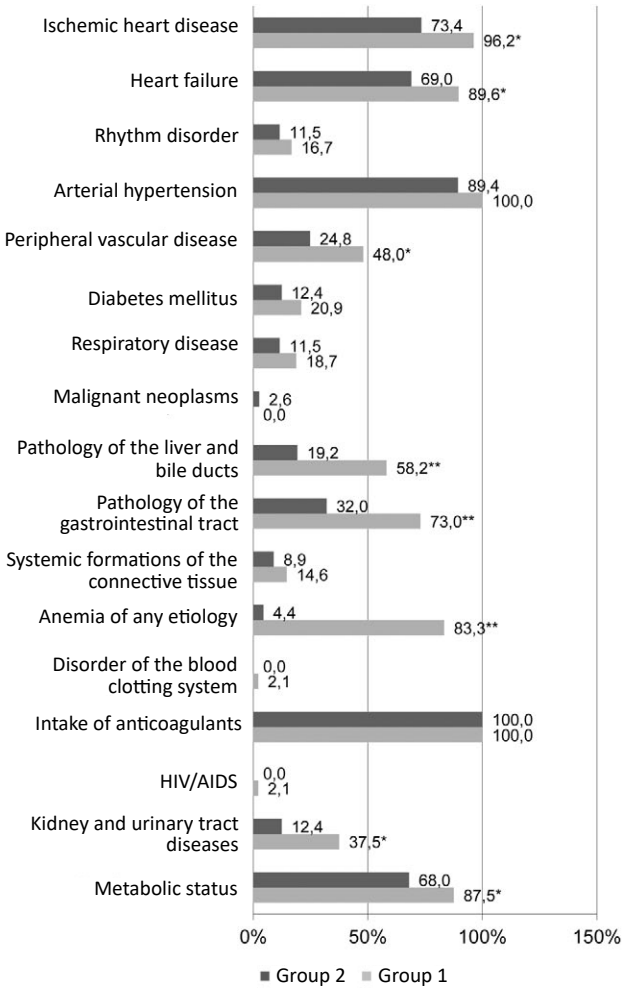

Fig. 2. Occurrence of concomitant pathology in groups 1 and 2;
*p<0.001; ** p<0.0001 compared with group 2

Table 4

Significance of indicators of the comorbidity scale

Indicators	Significance of the factor by strength	Place
Anemia of any etiology	100	1
Kidney and urinary tract diseases	86	2
Arterial hypertension	80	3
Metabolic status	78	4
Ischemic heart disease	71	5
Diabetes mellitus	40	6
Heart failure	39	7
Pathology of the gastrointestinal tract	37	8
Pathology of the liver and bile ducts	34	9
Rhythm disorders	24	10
Respiratory system diseases	23	11
Peripheral vascular diseases	20	12
Intake of anticoagulants	16	13
Systemic connective tissue diseases	9	14
Malignant neoplasms	6	15
Blood coagulation disorders	5	16
HIV/AIDS	2	17

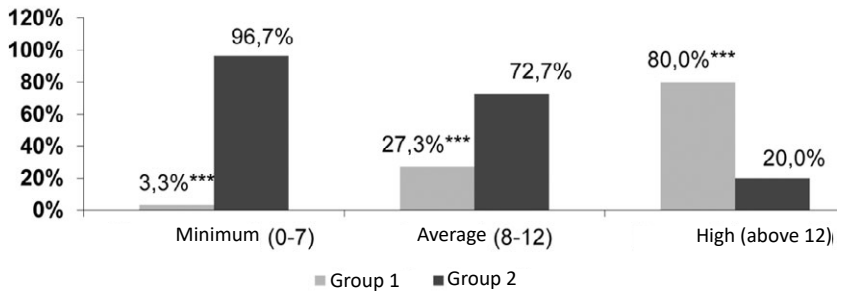

Fig. 3. Distribution of patients in groups 1 and 2 depending on the risk calculated by the comorbidity index,
*** p<0.0001 compared with group 2

Table 5

Distribution by risk categories within both groups, %

Risk	Group 1	Group 2	*p* (between groups)
Minimum	4.2	51.3	0.0001
Medium	37.5	42.5	0.3000
High	58.3	6.2	0.0001
Total	100	100	–

Discussion

The development of relapse after spacer implantation and further attempts of staged surgical treatment are known to result in the aggravation of comorbidity and an increased risk of lethal outcomes [12]. Thus, identification of the key risk factors for recurrence, their mutually aggravating effect, and, if possible, correction at the preoperative stage can both increase the efficiency of repeated endoprosthetics and reduce the mortality of patients postoperatively.

Preoperative anemia in patients undergoing primary arthroplasty more than double (from 2.0% to 4.2%) the risk of PJI manifestation, as established by Greenky et al. after analyzing complications in 15,707 patients. Nearly half of the patients (44%) with preoperative anemia required donor blood transfusion; while in the absence of this risk factor, this indicator was 13.4% [13]. Although allogeneic blood transfusion increases the risk of PJI, Newman et al. did not reveal a relationship between this method of hemoglobin correction and the recurrence of infectious complications [14].

By using the classification tree method, we revealed that anemia in a patient with PJI at the preoperative stage most affects the risk of relapse. However, this risk factor is modifiable, and timely correction of the hemoglobin level will increase the efficiency of the first stage of surgical treatment.

According to our data, kidney and urinary tract diseases increase the risk of failure of sanitizing interventions in patients with PJI; their frequency in patients with PJI recurrence reached 37.5%, significantly exceeding ($p < 0.001$) the same indicator in group 1 (12.4%). McCleery et al. came to similar conclusions, having proved a significant increase in the relative risk of development of both early PJI (RR 1.52; $p = 0.002$) and late hematogenous infection (RR 2.22; $p = 0.001$) in patients with chronic kidney disease after primary arthroplasty [15]. An even greater risk of infectious complications is typical for patients with end-stage chronic kidney disease, who receive hemodialysis (RR 4.40; $p = 0.001$) [16].

In our study, another significant risk factor for recurrence was being overweight among patients with PJI. The influence of this factor is also confirmed by international publications. Katakam et al. reported a higher failure rate in patients with obesity who underwent sanitation of the infectious site with preservation of the endoprosthesis components (57.9%) than in patients without obesity (36.8%; $p = 0.035$). Watts et al. demonstrated a significantly lower efficiency of the sanitation stage in patients with PJI receiving staged surgical treatment, that is, 22% of relapses in case of morbid obesity compared with 4% in the comparison group ($p < 0.01$) [17, 18].

Understanding the significance of the influence of the cumulative effect of various pathologies on the life expectancy of patients resulted in the development of various calculators that predict both the potential life expectancy of a patient and the risk of upcoming surgical intervention. Charlson et al., based on patient age and presence of concomitant pathologies (cardiovascular, lung, liver, urinary system, neurological, and oncological diseases and diabetes mellitus), created a calculator to predict the 10-year survival of patients [19]. The disease severity on this scale was taken into account only for liver pathology, diabetes mellitus, and oncological diseases, whereas for the other included pathologies, only their presence matters.

Subsequently, the Charlson scale was validated to predict early mortality (3 months, 1 year, and 5 years) in older patients hospitalized with an exacerbation of chronic pathology [20]. This

scale was also used in assessing the risk of survival in patients with end-stage kidney disease, who receive hemodialysis, and patients with prostate cancer, depending on the type of prostate-specific antigen detected [21, 22]. A modified Charlson scale also enabled assessing the 30-day mortality in patients with bacteremia caused by *S. aureus* [23].

A correlation was also established between scores obtained on the American Society of Anesthesiologists (ASA) scale, which is used to predict the risk of surgery, and the probability of PJI. Namba et al. revealed that patients who scored >3 points on the ASA scale belong to the group with a high risk of infectious complications [24].

The combination of modifiable and nonmodifiable risk factors is known to affect the probability of PJI. An analysis of 64 factors, performed by Tan et al., led to the development of a calculator that computes the probability of infectious complications. However, such a calculator enables computation only of the risk of PJI manifestation, and it is not applicable for predicting the risk of recurrence of an infectious process due to the structure of risk factors [25].

To predict the outcomes of sanitation of the infectious inflammation focus with the preservation of the components of the endoprosthesis (debridement, antibiotics, and implant retention [DAIR] procedure), based on the presence of certain pathologies, underlying diseases leading to the development of gonarthrosis, and the level of C-reactive protein, two groups of researchers created two different calculators. The KLIC scale predicts the success rate of the DAIR procedure, regardless of the term of PJI manifestation, and the CRIME80 scale is used for a similar surgical intervention in acute hematogenous infection [26, 27].

Based on the analysis of 56 risk factors in 293 patients with PJI, Klemt et al. found that the strongest predictors of recurrence are attempts of sanitation interventions with the preservation of endoprosthesis components, obesity, bad habits, and detection of an inveterate pathogen (*Enterococcus* sp.). Moreover, the authors did not conduct a detailed analysis of comorbidity, limiting themselves to determining the presence of the most known pathologies that increase the risk of PJI [28].

The calculation of the comorbidity index, which we have developed, showed that for 58% of patients with PJI relapses, a score of >12 points corresponded to a high risk of PJI relapse. Only 6.2% ($p < 0.0001$) of the patients in the group without relapses had a high risk of relapse, which indicates a high sensitivity of the developed scale for calculating the risk of PJI recurrence.

Study limitations

The limitations of this study were the noninclusion of factors not related to comorbidity (initial diagnosis, pathogen type, duration of hospitalization, previous surgeries, and spacer type) in the analysis and the lack of approbation of the proposed comorbidity index on a prospective cohort of patients, which is planned to be performed in the future.

Conclusions

A multivariate analysis of the presence and severity of concomitant pathology enabled us to develop a comorbidity scale that allows the calculation of an integral indicator (comorbidity index) and set its threshold values. A high score on the proposed index (>12 points) increases significantly the risk of PJI recurrence. The proposed comorbidity index can form the basis of a combined recurrence risk calculator and an algorithm for choosing surgical treatment in patients with knee joint PJI, but this requires further research.

Disclaimers

Authors' contributions

Preobrazhensky P.M. — the concept and design of study, data collection, analysis and interpretation of the obtained data, statistical data processing, writing of the manuscript.
Bozhkova S.A. — the concept and design of the study, writing and editing of the manuscript, interpretation the obtained data.
Kazemirsky A.V. — the concept and design of the study, writing and editing of the manuscript.

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 correctness and reliability of any part of the work.

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