UDC 616.726.3-089.844-002.828 **ORIGINAL ARTICLE**

Laboratory tests in the diagnosis of periprosthetic joint infection after total knee arthroplasty

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Abstract

Aim. To investigate changes in blood leukocyte and neutrophil counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin levels in patients with varying degrees of severity of periprosthetic joint infection following total knee arthroplasty, and to assess their diagnostic significance.

Methods. The study included patients with periprosthetic joint infection that developed following total knee arthroplasty and who underwent comprehensive clinical and laboratory evaluation. A comparative analysis of laboratory parameters was performed according to the severity of the infectious process. Blood leukocyte count, relative neutrophil percentage, ESR, CRP, and procalcitonin levels were determined. In addition, leukocyte count and relative neutrophil percentage in synovial fluid were assessed.

Results. The main laboratory parameters reflecting the inflammatory process increased with increasing severity of periprosthetic joint infection. The neutrophil percentage increased from 72.7 ± 5.9–74.5 ± 6.2% in mild cases to 88.6 ± 6.4–89.1 ± 6.2% in severe cases. ESR also increased with disease severity, reaching 75.2 ± 17.6–76.2 ± 17.7 mm/h in severe cases. CRP levels increased from 34.9 ± 14.9–35.2 ± 15.4 mg/L in mild cases to 142.3 ± 45.3–159.4 ± 47.9 mg/L in severe cases. In the main group, the mean procalcitonin level was 0.29 ± 0.12 ng/mL in mild cases, 0.88 ± 0.37 ng/mL in moderate cases, and 2.12 ± 0.88 ng/mL in severe cases ($p < 0.001$).

Conclusion. The observed changes in leukocytosis, neutrophilia, ESR, CRP, and procalcitonin according to the severity of periprosthetic joint infection indicate that these laboratory parameters can be used for a comprehensive assessment of the severity and activity of the infectious process. In particular, elevated procalcitonin and CRP levels may provide additional diagnostic value in identifying severe infectious inflammation.

Keywords: *knee joint; periprosthetic joint infection; infectious inflammation; laboratory diagnosis; C-reactive protein; procalcitonin; total knee arthroplasty.*

MAIN TEXT

Introduction

Total knee arthroplasty is one of the effective surgical methods in modern orthopedics that makes it possible to restore the motor function and improve the quality of life of patients with severe degenerative-dystrophic and post-traumatic diseases. However, periprosthetic infectious inflammation (PJI) developing after arthroplasty is one of the most serious complications of this procedure and is of particular importance due to the complexity and prolonged duration of treatment and the increased need for revision surgical interventions [1–5].

The clinical course and severity of periprosthetic infectious inflammation vary among patients, and early detection of the infectious process, as well as objective assessment of its activity and severity, is of great importance in determining treatment tactics. Therefore, identification of reliable laboratory criteria reflecting the systemic and local manifestations of the infectious process and investigation of their diagnostic significance is one of the current areas of modern orthopedics and reconstructive surgery [6–10].

The results of the study revealed a consistent increase in leukocytosis and neutrophilia in the blood with increasing severity of periprosthetic infectious inflammation. In addition, a significant increase in ESR and C-reactive protein levels from mild to severe disease indicated an increase in the activity of the inflammatory process in the body. In particular, an increase in procalcitonin levels from 0.29±0.12 ng/mL in mild cases to 0.88±0.37 ng/mL in moderate cases and 2.12±0.88 ng/mL in severe cases demonstrated the additional significance of this biomarker in assessing the severity of the infectious process [11, 12].

At the same time, since each of these laboratory parameters individually cannot serve as an absolutely specific criterion for periprosthetic infectious inflammation, their comprehensive assessment is considered important. Analysis of leukocyte and neutrophil counts, ESR, C-reactive protein, and procalcitonin values in combination with the clinical course of the disease and other diagnostic criteria makes it possible to assess the activity and severity of the infectious process more objectively [13–19].

In this regard, comprehensive investigation of changes in the main blood inflammatory markers and procalcitonin values depending on the severity of the disease in periprosthetic infectious inflammation developing after total knee arthroplasty, determination of their diagnostic and prognostic significance, and development of approaches aimed at improving treatment tactics are of important scientific and practical significance.

The aim of the study was to improve methods for the early diagnosis and objective assessment of the severity of the disease based on a comprehensive assessment of various degrees of severity of periprosthetic infectious inflammation developing after total knee arthroplasty, determination of the diagnostic significance of leukocyte and neutrophil counts, erythrocyte

sedimentation rate, C-reactive protein and procalcitonin in the blood, as well as leukocyte and neutrophil values in synovial fluid.

Material and Methods

For this study, 112 patients with periprosthetic infectious inflammation observed after total knee arthroplasty who were treated in the clinical setting of the Republican Specialized Scientific and Practical Medical Center of Traumatology and Orthopedics during 2015–2026 were included. They were divided into two groups: the main group – 52 patients and the comparison group – 60 patients. Clinical and laboratory examinations were performed in patients with periprosthetic infectious inflammation observed after total knee arthroplasty in order to comprehensively assess the characteristics and severity of the infectious process. Particular attention was paid to identifying changes in hematological and synovial fluid parameters associated with the inflammatory process in the body at different degrees of disease severity.

The quantitative parameters of leukocyte count (×10⁹/L), neutrophil percentage (%), erythrocyte sedimentation rate (ESR, mm/h), C-reactive protein (CRP, mg/L), and procalcitonin (ng/L) were determined in the blood test. The obtained laboratory data were grouped according to the severity of periprosthetic infectious inflammation, and the differences between them were statistically analyzed. This approach made it possible to comparatively assess the degree of systemic and local manifestations of infectious inflammation [20].

Results

At the first stage of the study, the leukocyte count in the blood of patients with different degrees of severity of periprosthetic infectious inflammation was analyzed. This parameter was assessed as one of the main hematological parameters reflecting the activity of the infectious-inflammatory process. The obtained results were compared according to disease severity and evaluated based on statistical analysis (Table 1).

Table 1. Analysis of leukocyte counts in the comparator groups (×10⁹/L)

Severity Degree	Comparator groups				p
	Main gr. (n=60)		Comparison gr. (n=52)		
	Abs.	M±SD	Abs.	M±SD	
Mild degree (n=29)	13	9,7±1,9	16	9,2±2,1	<0.05*
Moderate severity degree (n=56)	31	12,6±2,4	25	13,2±2,2	<0.01**
Severe degree (n=27)	16	16,4±3,3	11	15,9±2,9	<0.001***

Note. ≥0.05 – statistically non-significant results; ≤0.05 – conventional level of statistical significance; ≤0.01** – high level of statistical significance; ≤0.001*** – very high level of statistical significance.*

Analysis of the data presented in Table 1 showed that the level of leukocytosis in the comparison groups increased proportionally with increasing severity of periprosthetic infectious inflammation. In particular, mild leukocytosis was recorded in a total of 29 patients in both groups, moderate leukocytosis in 56 patients, and severe leukocytosis in 27 patients. Comparative analysis between the groups revealed that mild leukocytosis occurred at a slightly higher frequency in the comparison group than in the main group – 16 and 13 patients, respectively (P<0.05*). Moderate leukocytosis, in contrast, was observed more frequently in the main group, accounting for 31 patients, while it was recorded in 25 patients in the comparison group (P<0.01**). Severe leukocytosis also predominated in the main group and was identified in 16 and 11 patients, respectively (P<0.001***). Thus, the obtained results showed that as periprosthetic infectious inflammation progressed, higher levels of leukocytosis were more common in patients in the main group. The identified differences between the groups were statistically significant, indicating that leukocyte count is one of the important laboratory parameters for assessing disease severity.

Continuing the above study, the neutrophil count in the blood (%) was studied as the second parameter in order to assess blood inflammatory markers.

The results are presented in Figure 1.

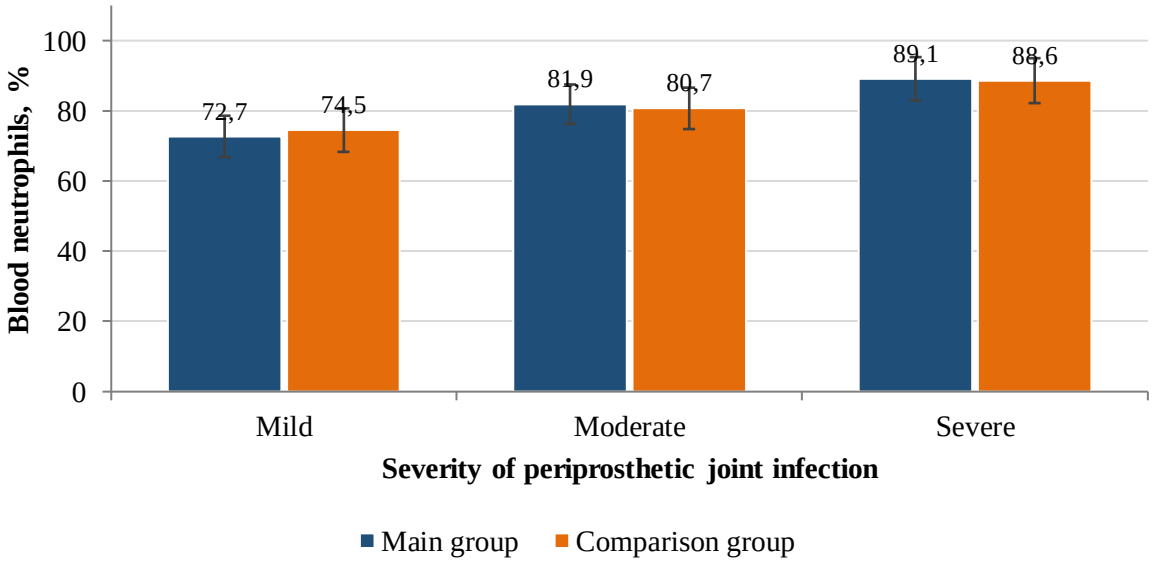


Figure 1. Relative blood neutrophil count (mean ± SD) by severity of periprosthetic joint infection in the main and comparison groups.

Analysis of the data in the above table showed that neutrophilia parameters also increased progressively with increasing severity of periprosthetic infectious inflammation. In patients with mild neutrophilia, the mean blood neutrophil count was 72.7±5.9% (n=16) in the main group and 74.5±6.2% (n=16) in the comparison group. A statistically significant difference was identified between these values, with the result in the comparison group being higher than that in the main group (P<0.001***). In moderate neutrophilia, the proportion of neutrophils in the blood was

higher in patients in the main group than in the comparison group. Specifically, this parameter was 81.9±5.6% (n=31) in the main group and 80.7±5.9% (n=25) in the comparison group. The difference between the groups was assessed as statistically significant (P<0.01**). In severe neutrophilia, a higher result was also recorded in the main group: the mean neutrophil count was 89.1±6.2% (n=16), while this parameter was 88.6±6.4% (n=11) in the comparison group. This difference was also of high statistical significance and was found to be significant at P<0.001***. Overall, the obtained results showed that the proportion of neutrophils in the blood tended to increase consistently with increasing severity of periprosthetic infectious inflammation. In particular, higher neutrophilia values were observed in patients in the main group in moderate and severe infectious processes.

The process of periprosthetic infectious inflammation induces a systemic inflammatory response in the body. In this process, increased erythrocyte aggregation due to an increase in the levels of acute-phase proteins, particularly fibrinogen, accelerates their sedimentation rate. In this regard, an increase in the erythrocyte sedimentation rate (ESR) is recorded in the general blood test. High ESR values reflect the activity of the inflammatory process in the body and are of importance as an additional laboratory criterion in the comprehensive assessment of the severity of periprosthetic infectious inflammation.

The results are presented in Figure 2.

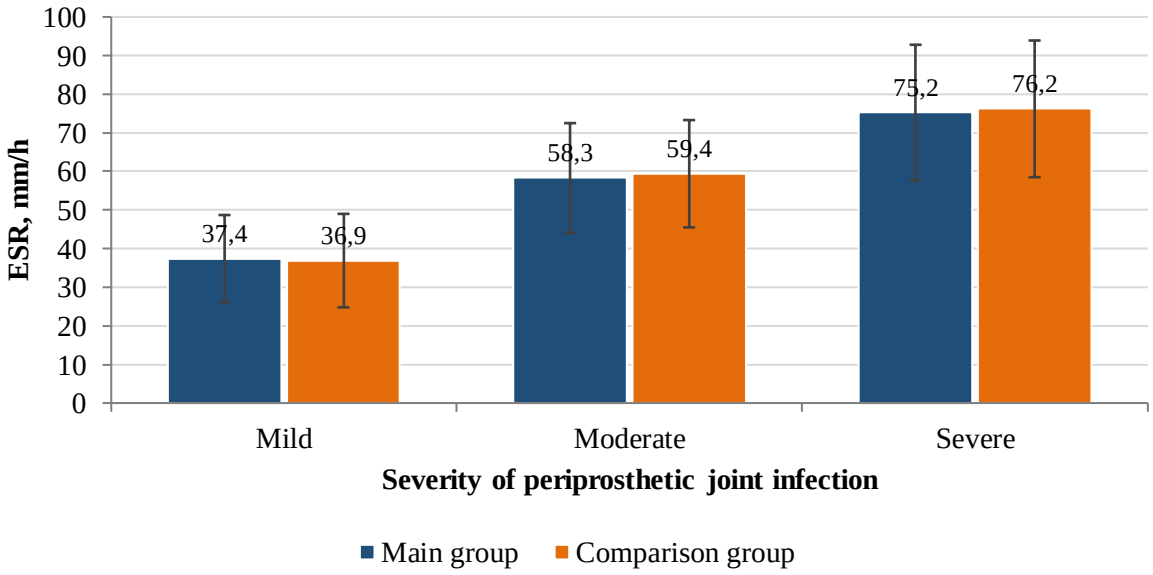


Figure 2. Erythrocyte sedimentation rate (mean ± SD) by severity of periprosthetic joint infection in the main and comparison groups.

The erythrocyte sedimentation rate (ESR) values demonstrated characteristic changes at different degrees of severity of periprosthetic infectious inflammation. In patients with a mild infectious process, the mean ESR was 37.4±11.3 mm/h in the main group and 36.9±12.1 mm/h in the comparison group. The value in the main group was slightly higher than that in the comparison

group, and the difference between the groups was statistically significant (P<0.001***). In moderate periprosthetic infectious inflammation, a higher ESR value was recorded in patients in the comparison group. Specifically, the ESR was 59.4±13.9 mm/h in the comparison group and 58.3±14.2 mm/h in the main group. The difference between these groups was statistically significant, with P<0.001***. In a severe infectious process, the ESR value was also higher in patients in the comparison group, amounting to 76.2±17.7 mm/h and 75.2±17.6 mm/h, respectively. The difference between the groups was statistically significant and was assessed as significant at P<0.01**. Overall, the obtained results showed a tendency toward a significant increase in the ESR value with increasing severity of periprosthetic infectious inflammation. At the same time, ESR is an important laboratory parameter for assessing the activity of the inflammatory process in the body, and it is advisable to interpret it in conjunction with other inflammatory markers.

At the next stage, the C-reactive protein (CRP) parameter was studied in order to assess the activity of periprosthetic infectious inflammation. CRP is one of the acute-phase proteins reflecting the systemic inflammatory response in the body. In cases where an infectious-inflammatory process develops around the prosthesis following total knee arthroplasty, its blood level may increase. However, an increase in CRP does not specifically confirm the presence of infection; therefore, its results should be assessed comprehensively together with clinical data, other laboratory parameters, and instrumental examinations. The results of the CRP study are presented in Table 2.

Table 2. Analysis of C-reactive protein results in the comparison groups (mg/mL)

Severity Degree	Comparator groups				p
	Main gr. (n=60)		Comparison gr. (n=52)		
	Abs.	M±SD	Abs.	M±SD	
Mild degree (n=29)	13	34,9±14,9	16	35,2±15,4	<0.001***
Moderate severity degree (n=56)	31	94,6±32,8	25	99,7±33,1	<0.001***
Severe degree (n=27)	16	159,4±47,9	11	142,3±45,3	<0.001***

Note. ≥0.05 – statistically non-significant results; ≤0.05 – conventional level of statistical significance; ≤0.01** – high level of statistical significance; ≤0.001*** – very high level of statistical significance.*

Analysis of the C-reactive protein (CRP) values showed that its blood level increased consistently with increasing severity of periprosthetic infectious inflammation. At the same time, certain differences between the main and comparison groups were recorded at each degree of disease severity. In mild periprosthetic infectious inflammation, the mean CRP level was slightly higher in patients in the comparison group than in the main group. Specifically, this parameter was 35.2±15.4 mg/L in 16 patients in the comparison group, while in 13 patients in the main group it

was 34.9±14.9 mg/L. The difference between the groups was found to be statistically significant (P<0.001***). In cases of moderate periprosthetic infectious inflammation, the CRP level was also found to be relatively higher in the comparison group. Its mean value was 99.7±33.1 mg/L in 25 patients in the comparison group, whereas it was 94.6±32.8 mg/L in 31 patients in the main group. This difference was also noted to be statistically significant at a high level of significance (P<0.001***). When the results of 27 patients with severe periprosthetic infectious inflammation were analyzed, the CRP level was higher in the main group than in the comparison group. In 16 patients in the main group, the mean CRP value was 159.4±47.9 mg/L, whereas in 11 patients in the comparison group this parameter was 142.3±45.3 mg/L. The difference between the groups was statistically significant at a high level of significance and was P<0.001***. Thus, analysis of CRP values according to disease severity demonstrated an increase in inflammatory activity as the infectious process became more severe. The highest CRP values were recorded in severe periprosthetic infectious inflammation, indicating that this parameter can be used as an important laboratory criterion in the comprehensive assessment of the activity of the infectious-inflammatory process.

Among the laboratory parameters studied, procalcitonin is of particular importance, as it is considered a biomarker reflecting the systemic inflammatory response of the body, mainly to bacterial infection. In cases of periprosthetic infectious inflammation, changes in procalcitonin levels are of additional diagnostic significance in assessing the systemic nature of the infectious process and its clinical severity. From this perspective, in the present study, blood procalcitonin levels were determined in patients, and the obtained results were comparatively analyzed according to different degrees of severity of periprosthetic infectious inflammation. The results of the study are presented in Table 3 [21, 22].

Table 3. Analysis of procalcitonin results in patients in the main group (ng/mL)

Severity Degree	Comparator groups Main gr. (n=60)		p
	Abs.	M±SD	
Mild degree (n=29)	13	0,29±0,12	<0.001***
Moderate severity degree (n=56)	31	0,88±0,37	<0.001***
Severe degree (n=27)	16	2,12±0,88	<0.001***

Note. ≥0.05 – statistically non-significant results; ≤0.05 – conventional level of statistical significance; ≤0.01** – high level of statistical significance; ≤0.001*** – very high level of statistical significance.*

Analysis of the procalcitonin values showed that the level of this biomarker also increased consistently with increasing severity of periprosthetic infectious inflammation. In 13 patients in the main group with mild periprosthetic infectious inflammation, the mean procalcitonin value was 0.29±0.12 ng/mL. This result was characterized by a statistically significant difference at a high level of significance (P<0.001***). In moderate periprosthetic infectious inflammation, the mean procalcitonin level in 31 patients included in the main group was 0.88±0.37 ng/mL. This parameter was higher than that in mild cases, and the difference was found to be statistically significant (P<0.001***). In 16 patients with severe periprosthetic infectious inflammation, the highest procalcitonin values were observed, with a mean value of 2.12±0.88 ng/mL. This result was also statistically significant at a high level of significance, with P<0.001***. Thus, the study results showed that procalcitonin levels tended to increase with increasing severity of periprosthetic infectious inflammation. The highest procalcitonin values were recorded in patients with a severe infectious process.

In addition to the leukocyte count and erythrocyte sedimentation rate results obtained in the general clinical blood test, it is necessary to assess carbohydrate metabolism in the patient's body based on the determination of blood glucose levels and glycated hemoglobin – HbA1c, i.e., a parameter formed as a result of the binding of glucose in the blood to erythrocyte hemoglobin (Tables 4 and 5).

Table 4. Analysis of blood glucose levels at different degrees of severity of periprosthetic infectious inflammation

Parameter and groups (n=112)		Mild PJI (n=13/16)	Moderate PJI (n=31/25)	Severe PJI (n=16/11)	p
		M±SD	M±SD	M±SD	
Fasting glucose (mmol/L)	Main gr. (n=60)	5,8±0,9	7,1±0,6	8,2±1,2	<0.05*
	Compar. gr. (n=52)	5,5±0,7	6,4±0,6	8,4±1,1	<0.01**
Median (IQR)	Main gr.. (n=60)	5,6 (4,9-6,2)	6,9 (6,5-7,7)	8,0 (7,2-8,6)	<0.05*
	Compar. gr. (n=52)	5,3 (4,8-5,9)	6,2 (5,9-6,8)	8,2 (7,5-8,9)	<0.01**

Note. ≥0.05 – statistically non-significant results; ≤0.05 – conventional level of statistical significance; ≤0.01** – high level of statistical significance; ≤0.001*** – very high level of statistical significance.*

When periprosthetic infectious inflammation is diagnosed after total knee arthroplasty, determination of fasting blood glucose in patients makes it possible to predict the course of the pathological process, the general condition of the patient, the condition of the knee joint, and the viability of the endoprosthesis, and makes it possible to select treatment tactics or introduce various

modifications. According to the data presented in Table 4, analysis of morning fasting blood glucose levels in patients of both comparison groups showed a direct correlation between worsening of the pathological process and an increase in blood glucose levels ($p<0.05$*-0.01**). In 13 patients with mild PJI inflammation, the blood glucose level was 5.8±0.9 mmol/L, the lowest and highest values ranged from 4.9 to 6.2 mmol/L, while in 16 patients in the comparison group diagnosed with the same degree of severity, the blood glucose level was 5.5±0.7 mmol/L, and the lowest and highest values ranged from 4.8 to 5.9 mmol/L ($p<0.05$*-0.01**) [23, 24].

In 31 patients in the main group diagnosed with moderate PJI inflammation, the blood glucose level was 7.1±0.6 mmol/L, and the lowest and highest values ranged from 6.5 to 7.7 mmol/L, whereas in 25 patients in the comparison group diagnosed with the same degree of severity, the blood glucose level was 6.4±0.6 mmol/L, and the lowest and highest values ranged from 5.9 to 6.8 mmol/L ($p<0.05$*-0.01**).

In 16 patients with severe PJI inflammation, the blood glucose level was 8.2±1.2 mmol/L, while the lowest and highest values ranged from 7.2 to 8.6 mmol/L, whereas in 11 patients in the comparison group diagnosed with the same degree of severity, the blood glucose level was also 8.4±1.1 mmol/L, and the lowest and highest values ranged from 7.5 to 8.9 mmol/L ($p<0.05$*-0.01**).

As noted above, in developing indications for total joint arthroplasty or increasing prosthesis viability after surgical procedures, blood glucose levels or the presence of diabetes mellitus in the patient, particularly an increase in glycated hemoglobin levels in the blood as a result of the chronic course of the disease in the patient, are among the main factors. The glycemic status in the blood is assessed as follows: <5.7% – normal range; 5.7–6.4% – prediabetes range; 6.5–6.9% – diabetes range, normal, relatively good control; 7.0–7.9% – inadequate glycemic control; 8.0–8.9% – marked uncontrolled hyperglycemia; ≥9.0% – very poor glycemic control [25];

In the present study, blood glycated hemoglobin levels were studied in patients in the main group (Table 5).

Table 5. Analysis of blood glycated hemoglobin (HbA1c, %) levels at different degrees of severity of periprosthetic infectious inflammation in patients in the main group

HbA1c (%) (n=60)	Mild PJI (n=13/21,7%)		Moderate PJI (n=31/51,7%)		Severe PJI (n=16/26,6%)		Total 60/100%	
	n	%	n	%	n	%	n	%
<5,7	0	0	0	0	0	0	0	0
5,7-6,4	3	5%	0	0	0	0	3	5%
6,5-6,9	2	3,4%	7	11,7%	3	5%	12	20,1%
7,0-7,9	3	5%	10	16,7%	5	8,3%	18	30%
8,0-8,9	5	8,3%	8	13,3%	5	8,3%	18	30%
≥9,0	0	0	6	10%	3	5%	9	15%

According to the data in Table 5, in patients in the main group (n=60), the blood glycated hemoglobin – HbA1c level increased with increasing severity of periprosthetic infectious inflammation. This does not mean that an increase in blood glycated hemoglobin levels causes worsening of the disease or that an increase in blood glycated hemoglobin aggravates the disease. It only indicates whether blood glucose control is adequate or has not been corrected. Among the 60 patients in the main group diagnosed with periprosthetic infectious inflammation, no patients with blood glycated hemoglobin levels within the normal range were identified, and only a prediabetic condition was detected in 3 (5%) patients diagnosed with mild PJI. Of the total 60 patients, 12 (20.1%) had a well-controlled diabetic condition, 18 (30%) had inadequate glycemic control, 18 (30%) had marked uncontrolled hyperglycemia, and in the remaining 9 (15%) clinical cases, patients had very poor glycemic control.

Conclusion

1. With increasing severity of periprosthetic infectious inflammation, changes in hematological parameters indicative of inflammation in the blood became more pronounced. In particular, the progressive increase in leukocytosis and neutrophilia indicated increased activity of the infectious process.

2. The laboratory markers of inflammation, erythrocyte sedimentation rate - ESR and C-reactive protein - CRP, increased proportionally with disease severity. ESR increased from 36.9 ± 12.1–37.4 ± 11.3 mm/h in mild cases to 75.2 ± 17.6–76.2 ± 17.7 mm/h in severe cases, while CRP increased from 34.9 ± 14.9–35.2 ± 15.4 mg/L in mild cases to 142.3 ± 45.3–159.4 ± 47.9 mg/L in severe cases. These parameters are of significant importance for the comprehensive assessment of the activity of periprosthetic infectious inflammation.

3. Procalcitonin levels demonstrated a pronounced association with the severity of periprosthetic infectious inflammation. In patients in the main group, the mean procalcitonin level was 0.29 ± 0.12 ng/mL in mild cases, 0.88 ± 0.37 ng/mL in moderate cases, and 2.12 ± 0.88 ng/mL in severe cases ($P < 0.001$). In addition, the progressive increase in procalcitonin levels indicates its importance as an additional laboratory criterion for assessing the systemic nature and severity of the infectious process.

4. From a practical perspective, regular assessment of blood glucose and HbA1c in patients who have undergone total knee arthroplasty and developed PJI is advisable for the comprehensive assessment of the course of the infectious process, timely detection of concomitant diabetes mellitus or uncontrolled hyperglycemia, individualization of treatment strategies, and reduction of the risk of postoperative complications.

Additional information

Author contributions. All authors contributed to the compilation and layout of this material.

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