Original Article
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Diagnosis of Late Periprosthetic Joint Infection. Which Diagnostic Algorithm to Choose?

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Abstract

Background. Nowadays, according to the foreign and native registers data, the number of patients with periprosthetic infection (PJI) tends to increase. The early PJI diagnostics allows to provide timely effective treatment. Several widely used PJI diagnostic algorithms PJI exist. ***The objective of the study*** is comparative analysis of diagnostic value, accuracy and specificity of contemporary diagnostic algorithms. ***Materials and methods.*** A post-hoc analysis of 242 patients undergoing revision arthroplasty in 2018, held at FSFI FCTOE, was carried out. According to the study design, 127 patients were included in this study. PJI was diagnosed according to three known algorithms: ICM (International Consensus Meeting 2018), WAIOT (The World Association against Infection in Orthopedics and Trauma), EBJIS (The European Bone and Joint Infection Society 2018). Diagnostic sensitivity, specificity and total accuracy of each algorithm was carried out. The evaluation of ICM diagnostic algorithm was made with 2 variants: "not convincing = no infection", "not convincing = infection". The presence of infection was confirmed by bacteriological examination of synovial fluid aspirate, intraoperative biopsy of materials and sonification of explanted components. ***Results.*** The highest value of common accuracy was achieved in ICM 2018 algorithm — "not convincing = infection" was 91.3%, with sensibility and specificity — 89.3% and 93.0% respectively. The best specificity was shown by the algorithms WAIOT and ICM ("not convincing = no infection) – 95.8%, with sensibility and common accuracy — 80.4% and 89.0% respectively. The sensibility and specificity of EBJIS algorithm was 87.5% and 84.5%, respectively, the common accuracy — 85.8%. ***Conclusion.*** All included in investigation diagnostic algorithms showed high specificity values in diagnostics of hip and knee PJI without significant differences. Patients with subclinical PJI and low virulent pathogens have the biggest difficulties in PJI diagnostics. It seems that the selection of analyzed algorithms doesn't play an important role, however PJI diagnostics requires complex approach with the use of different clinical and laboratory values.

Keywords: periprosthetic joint infection, revision surgery, diagnostic algorithm, ICM 2018, EBJIS 2018, WAIOT.

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Introduction

Currently, joint arthroplasty is a highly effective method for many diseases and joint injuries consequences treatment [1]. However, domestic and foreign data indicate the growing problem of *periprosthetic joint infection* (PJI). This is caused by a widespread increase in the number of primary arthroplasty as well as a high percentage of chronization of process during infection developme [2, 3]. The treatment of such patients is associated with significant financial, physical and emotional expenses. The implementation of PJI diagnostic algorithm allows choosing the correct treatment tactics for the patient and reducing the risk of recurrence [4, 5, 6]. A significant part of the infection is caused by low-virulent pathogens with a characteristic subclinical course of the infectious process [7]. The greatest difficulty for diagnosis in the preoperative period is a PJI without identified pathogen, as well as an infection associated with a biofilm (type IV infection by the Coventry–Tsukayama classification). In these cases the diagnosis of PJI is made only on the basis of a positive bacteriological study of intraoperative biopsy specimens and of the explanted endoprosthesis [8, 9, 10]. Each case with pain in the area of the endoprosthesis should be considered as a potential infectious complication until proven otherwise [11, 12, 13]. Thus, taking into account the general trend towards an increase in the absolute number of patients with PJI, it became necessary to select an algorithm for PJI detecting with high diagnostic accuracy.

The purpose of this study was to conduct a comparative assessment of the diagnostic value, accuracy and specificity of modern diagnostic algorithms.

Materials and Methods

The study design

This was a retrospective single-center study.

The study included the patients undergone revision hip or knee arthroplasties at the Federal Center of Traumatology, Orthopedics and Arthroplasty, Barnaul, Russia, in 2018.

Inclusion criteria: the presence of clinical and radiological signs of aseptic or septic instability of hip or knee endoprosthesis components before the surgery.

Exclusion criteria: insufficient examination volume to fill in the diagnostic algorithms, systemic disease (rheumatoid arthritis, systemic lupus erythematosus, gout), revisions for periprosthetic fracture or recurrent dislocation, revision shoulder and elbow arthroplasty, 2nd stage of two-stages revision arthroplasty.

127 patients of 242, undergone surgery in 2018, met the inclusion criteria: 47 men (mean age 57.1 years), 80 women (mean age 63.9 years). Knee joints were 43, hip joint — 84. The characteristics of the operated patients are shown in Figure 1.

The result of bacteriological examination was taken as the reference criterion for the presence or absence of PJI when one of the conditions was met:

– the growth of strains with the same antibiotic susceptibility profile from 2 or more biomaterial samples: aspirate, tissue biopsies, sonicated fluid from removed components of the endoprosthesis;

– the growth of a highly virulent microorganism (gram-negative microorganism or *S. aureus*) from one sample of biomaterial [6].

Positive growth of a low-virulent pathogen from a single biomaterial sample or from an explanted component of the endoprosthesis after sonication was considered contamination.

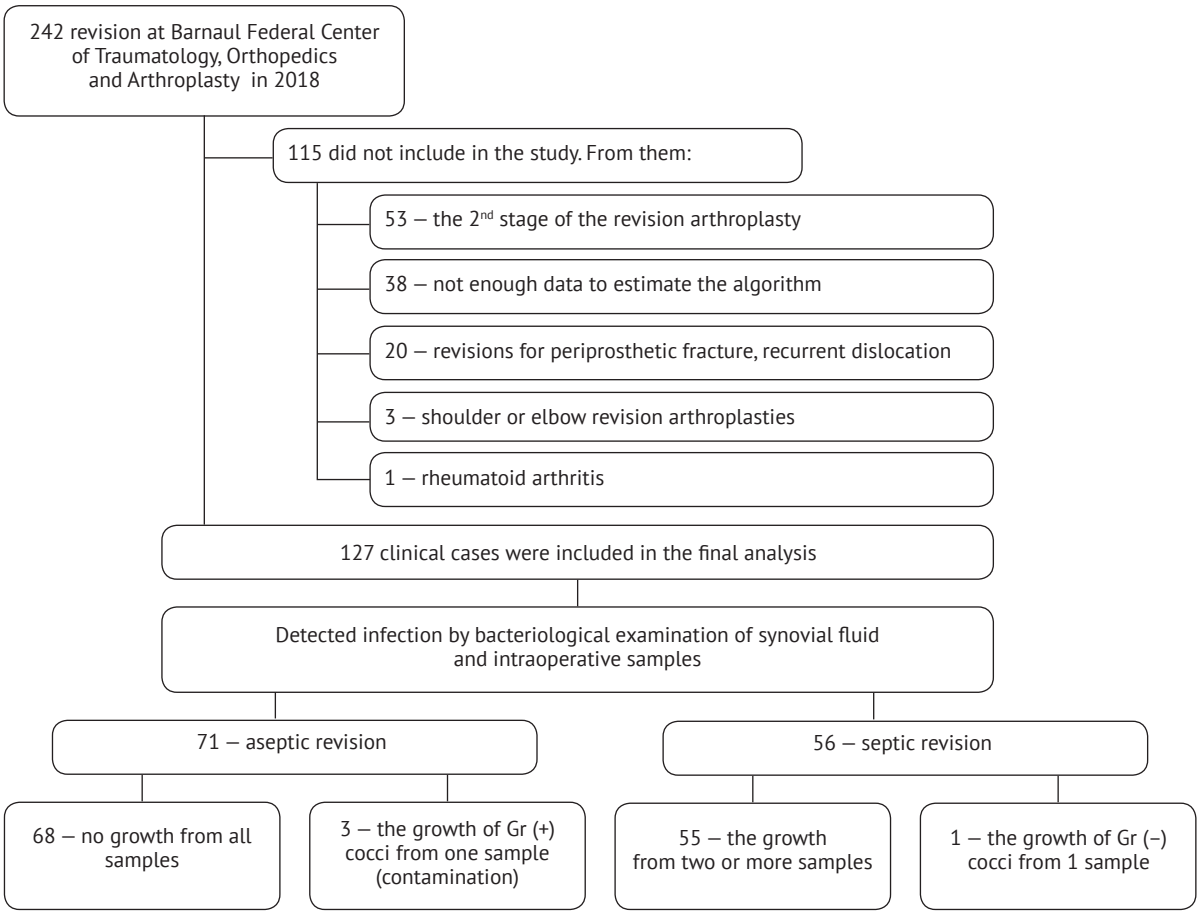

Figure. A patient flowchart

All the patients were examined for PJI in the preoperative period using the diagnostic algorithms by *International Consensus Meeting 2018* (ICM) [14], the *World Association against Infection in Orthopedics and Trauma* (WAIOT) [15], the *European Bone and Joint Infection Society 2018* (EBJIS) [16] (Table 1).

The ICM 2018 diagnostic algorithm has the option "unconvincing", and therefore two conditions were considered to assess its diagnostic significance: "unconvincing = no infection" and "unconvincing = infection". The WAIOT diagnostic algorithm does not rule out infection until the results of the bacteriological examination of intraoperative samples are obtained. The sum of points below zero is considered as: a) no infection, b) biofilm form of PJI, c) contamination. To assess the diagnostic significance of the algorithm, the sum of points below zero was regarded as "no infection".

PJI definition

The following clinical and laboratory parameters were used in this study to diagnose PJI:

– the presence of a fistulous communication with the joint cavity;

– visible soft tissues suppuration around the endoprosthesis;

– visible endoprosthesis in the wound;

– increased blood ESR level;

– increase in the level of CRP in the blood serum;

– cytological examination of the joint aspirate with the percentage of neutrophils determination;

– bacteriological examination of the joint aspirate.

Table 1

Diagnostic algorithms

Algorithm characteristics	ICM	WAIOT	EBJIS
Assessment system	1 of 2 large criteria OR small criteria score: ≥6 infection 3-5 unconvincing (consider further diagnostics such as next generation sequencing) <3 no infection * * Proceed with caution: adverse tissue reactions, crystal deposition diseases, slow growing organisms	The sum of the criteria points: <0 no infection, contamination, infection, associated with biofilm * ≥0 mild infection ≥1 severe infection * In such cases, the diagnosis can be confirmed after surgery on the basis of histological and bacteriological examination of intraoperative samples (with the use of prolonged bacteriological examination, antibiofilm technique)	≥1 Positive criterion
Criteria	Large criteria: Fistula communicating with the joint cavity, or visible endoprosthesis in the wound Growth of an identical microorganism from two or more material samples obtained by standard bacteriological methods Small criteria: A) increased CRP (>100 mg/L for acute infection; >10 mg/L for chronic infection) or D-Dimer (unknown threshold for acute infection; >860 μg/L for chronic infection) (2 points) B) rise in ESR (does not matter for acute infection; > 30 mm/h for chronic infection) (1 point) C) increased number of leukocytes in the joint fluid (>10.000 cells/ml for acute infection; > 3.000 cells/ml for chronic infections) OR leukocyte esterase (++ for acute and chronic infection) (2 points) D) increase in the proportion of neutrophils in the joint fluid (>90% for acute, >70% for chronic infection) (2 points) E) the growth of a microorganism from one biomaterial sample (2 points) F) positive histological examination (3 points) G) visible intraoperative suppuration (3 points)	Infection confirmation criteria (specificity> 90%): Each positive test +1 point Each negative test 0 points Suppuration or functional fistula or endoprosthesis visible in the wound Increased number of leukocytes in the joint fluid > 3000 cells/ml Growth of microorganisms from synovial fluid Leukocyte esterase ++ Infection exclusion criteria (sensitivity> 90%): Each negative test -1 point Each positive test is 0 points 1. The rise of ESR> 30 mm/h 2. Increase in CRP> 10 mg/L 3. The number of leukocytes in the joint fluid <1500 cells/ml (Allows the inclusion of new tests or procedures, provided that they meet the minimum required sensitivity and specificity, without the need to change the definition structure)	1. Visible suppuration around the joint or a functioning fistula 2. Increased number of leukocytes in the joint fluid (>2000 cells/ml or> 70% neutrophils) 3. Positive histological examination 4. Growth of microorganisms from synovial fluid or ≥2 * biopsies or from sonic fluid (>50 ** CFU/ml) *for highly virulent (gram-negative microorganisms, S. aureus) or in patients on the background of antibiotic therapy, growth from one biological sample is sufficient ** against the background of antibiotic therapy, for S. aureus and anaerobes it can be <50 CFU/ml

Laboratory indicators

The ESR examination was performed from venous blood by the Westergren method using a Westerlight 1230 analyzer (Dixion, Russia). Blood serum CRP was measured by immunoturbodimetry in an extended concentration range by the Dimension Xpand analytical system (Siemens, Germany). The synovial fluid examination included the nucleated cell elements count and the smear stained by Romanovsky–Giemsa for the proportion of the neutrophilic leukocytes study. The cell counting was performed by the Carl Zeiss binocular microscope (Germany) using plastic slide plates for the biological fluids cellular elements count. The synovial fluid for this purpose was diluted 20 times with 0.3% NaCl solution.

The bacteriological examination of synovial fluid and intraoperative samples. The joint puncture was performed by the surgeon under aseptic conditions. The hip joints were punctured under US guidance. After receiving the 1st portion of the aspirate, the syringe was replaced with a sterile to reduce the risk of contamination. After it, the main portion of the aspirate was taken. The obtained samples were sent to the laboratory n their native state within 10 to 15 minutes. The bacteriological examination of each sample included primary inoculation onto the Columbia agar plates with 5% lamb's blood and thioglycol medium, aerobic and anaerobic vials for the VersaTrek analyzer (Trek Diagnostic, USA). The synovial fluid was inoculated without preliminary preparation, biopsies were prehomogenized, and prosthetic components in sterile bags were sonicated for 5 minutes in 0.9% NaCl solution using an Elmasonic S10H ultrasonic bath (Elma, Germany) with the operating frequency of 37 kHz and the power of 60 W. The primary cultures were incubated at 35°C for 14 days. When the microorganisms growth was detected, the pathogens identification and their sensitivity determination were performed by the automatic bacteriological analyzer Walk Away (Siemens, Germany).

Statistical analysis

Registration, systematization of primary data and visualization of the obtained results were performed using Microsoft Office Excel 2010 spreadsheets. The statistical analysis was carried out using the MedCalc 15.8 software. In the case of quantitative indicators description, a check for normality of distribution was done according to the Kolmogorov-Smirnov test. In the case of normal distribution, the obtained data were described using arithmetic means and the boundaries of the 95% confidence interval (95% CI). The nominal data were reported using absolute values and percentages. The comparison of nominal data was performed using Pearson's chi-square test, corrected for Yates continuity. The critical level of significance (P) is assumed to be less than 0.05. The confidence interval (CI) for categorical data was determined based on frequency distributions. The quantitative dependence of an outcome probability on the presence of a factor was calculated using the odds ratio with a 95% confidence interval. The assessment of the diagnostic significance of the algorithms for PJI was carried out using formulas for calculating the sensitivity, specificity, overall accuracy, predictive value of a positive and negative result, likelihood ratio for a positive and negative result.

Results

The PJI was confirmed in 56 (44.1%) cases, 71 (55.9%) cases were regarded as no infection thus confirming the aseptic instability of the endoprosthesis components (Table 2).

In 4 clinical cases, growth was determined in one biomaterial sample, including 3 cases of conditionally pathogenic gram-positive bacteria (coryneforme bacteria, Staphylococcus epidermidis, micrococcus), which were regarded as contamination. In the 4th case, a strain of gram-negative bacillus, Burkholderia cepacia, was isolated, which was regarded as an infection.

According to the ICM diagnostic algorithm, infection was excluded in 72 cases, in 48 cases the convincing data were obtained for PJI. In 17 patients, the diagnosis could be made based on the presence of a large criterion (fistula) and in 31 — according to small criteria. In 7 cases the obtained result was assessed as "unconclusive". The efficiency was assessed according to 2 options: "unconvincing = no infection" and "unconvincing = infection". The use of the WAIOT diagnostic algorithm excluded infection in 79 cases at the preoperative stage, allowed the diagnosis of PJI in 48 cases, of which 37 cases corresponded to a high-grad infection and 11 — to the low-grade PJI. According to the criteria of the EBJIS diagnostic algorithm, the infection was diagnosed in 60 cases, its absence — in 67 clinical cases. The results of calculating the indicators of the compared algorithms diagnostic significance are presented in Table 3.

Further, 23 clinical cases with false results according to at least one of the algorithms were allocated to a separate group, of which 11 cases were with a false-positive result and 12 — with a false-negative one (Table 4).

Table 2

The characteristics of the patients in study groups

Indicator	Infection	No infection	p
Age, years, average/(95% CI)	59.3/(35–81)	63.1/(37.2–80.4)	0.051
Gender, n (%), M/F	30 (53.6)/26 (46.4)	17 (23.9)/54 (76.1)	0.0012/0.0012
Joint, n (%), Hip/Knee	36 (64.3)/20(35.7)	48 (67.6)/23 (32.4)	0.8386/0.8386
Functioning fistula, n (%)	16(28.6)	1(1.4)	<0.001
Preoperative laboratory test, n (%)			
ESR >30 mm	37 (66.1)	2 (2.8)	<0.0001
CRP >10 mg/L	38 (67.9)	4 (5.6)	<0.0001
Cytosis <1500 cells/ml	9 (16.1)	55 (77.5)	<0.0001
Cytosis >2000 cells/ml	43 (76.8)	11 (15.5)	<0.001
Cytosis >3000 cells/ml	41 (73.2)	5 (7.0)	<0.0001
Neutrophils >70%	39 (69.6)	3 (4.2)	<0.0001
Microorganism was isolated from the aspirate, n (%)	40/56 (71.4)	2/71 (2.8)	<0.0001
Hip	23/36 (63.8)	1/48 (2.1)	<0.0001
Knee	17/20 (85.0)	1/23 (4.3)	<0.0001

Table 3

The comparison of algorithms diagnostic significance

Indicators	ICM 2018 unconvincing = infection	ICM 2018 unconvincing = no infection	WAIOT	EBJIS
Reliably positive	50	45	45	49
Reliably negative	66	68	68	60
False positive	5	3	3	11
False negative	6	11	11	7
Sensitivity,% (CI)	89.3 (0.84–0.95)	80.4 (0.73–0.87)	80.4 (0.73–0.87)	87.5 (0.82–0.93)
Specificity,% (CI)	93.0 (0.89–0.97)	95.8 (0.92–0.99)	95.8 (0.92–0.99)	84.5 (0.78–0.91)
Overall accuracy,% (CI)	91.3 (0.86–0.96)	89.0 (0.84–0.94)	89.0 (0.84–0.94)	85.8 (0.80–0.92)
Positive predictive value	91 (0.86–0.96)	94 (0.90–0.98)	94 (0.90–0.98)	82 (0.75–0.89)
Negative predictive value	92 (0.87–0.97)	86 (0.80–0.92)	86 (0.80–0.92)	90 (0.85–0.95)
Positive result likelihood ratio	12.7	19.0	19.0	5.6
Negative result likelihood ratio	0.12	0.21	0.21	0.15

Table 4

Difficult diagnostic cases

Clinical case No	Criteria						Diagnostic algorithms			Growth from biopsies (number of samples out of 6)	Growth from sonicated fluid (number of components)
	FVS	ESR, mm/h	CRP, mg/L	Cytosis, cells/ml	PMNL, %	JABE	ICM	WAIOT	EBJIS		
False-negative clinical cases											
FN 1	–	18	6	800	72	–	–	–	+	CNS (3)	CNS (4)
FN 2	–	7	4	220	0	–	–	–	–	CNS (2)	CNS (3)
FN 3	–	27	15	2200	82	–	U/c	–	+	CNS (1)	CNS (3)
FN 4	–	25	2	1800	55	–	–	–	–	Negative	CNS (4)
FN 5	+	27	11	1200	36	–	+	–	+	CNS (2)	CNS
FN 6	–	25	2	44	0	–	-	–	–	Negative (2)	CNS (2)
FN 7	–	11	5	24000	97	–	U/c	–	+	Negative (6)	CNS (2)
FN 8	–	51	34	44	0	–	U/c	–	–	CNS(2)	EF(4)
FN 9	–	81	34	44	0	–	U/c	–	–	Negative (2)	CNS (4)
FN 10	–	9	13	264	0	–	–	–	–	EF (6)	EF (4)
FN 11	–	16	4	88	0	–	–	–	–	CNS (2)	CNS (1)
FN 12	–	2	29	2200	51	SE	U/c	+	+	Negative	B(P)c (1)
False-positive clinical cases											
FP 1	–	3	1	5800	47	–	U/c	–	+	–	–
FP 2	–	17	2	300	70	–	–	–	+	–	–
FP 3	–	19	26	23000	90	CB	+	+	+	–	–
FP 4	–	18	8	5200	40	–	U/c	–	+	–	–
FP 5	–	31	7	2400	47	–	–	–	+	–	–
FP 6	+	11	2	5200	73	–	+	+	+	–	–
FP 7	–	18	5	2200	62	–	–	–	+	–	–
FP 8	–	14	1	2400	8	–	–	–	+	–	–
FP 9	–	3	1	2400	62	–	–	–	+	–	–
FP 10	–	9	5	2400	71	SE	+	+	+	–	–
FP 11	–	18	1	2400	51	–	–	–	+		–

ABBREVIATIONS: B(P)c – Burkholderia (Pseudomonas) cepacia; CB – Coryneform bacteria; CNS – Coagulase-negative staphylococcus; CRP – C-reactive protein; EF – Enterococcus faecium; ESR – Erythrocyte sedimentation rate; FN – False-negative; FP – False-positive; FVS – Fistula with visible suppuration; JABE – Joint aspirate bacteriological testing; PMNL – Polymorphonuclear leucocytes; SE – Staphylococcus epidermidis; U/c – Unconvincing.

Discussion

Around the world, the search for new methods and procedures for detecting PJI continues [17, 18, 19, 20, 21, 22]. The greatest diagnostic accuracy is achieved by a combination of clinical and laboratory criteria. This is confirmed by our study. The analysis of scientific publications in the eLIBRARY showed that our study was the first in Russia providing the direct comparative assessment of PJI leading diagnostic algorithms effectiveness. In addition, we demonstrated the dependence of diagnostic accuracy of the algorithms on the quality of the examination for each criterion [23, 24, 25].

First of all, the diagnostic value of the aspirate examination directly depends on the quality of the joint puncture. As a rule, the knee joint puncture is not difficult, which cannot be said about the hip joint puncture. According to various authors, the sensitivity and specificity of hip joint aspirate bacteriological examination is 59 to 79% and 91 to 96% [8, 26, 27, 28, 29]. This is comparable to our results: 64% and 98%, respectively.

Further, indicators of cytosis and the proportion of polymorphonuclear cells in the joint aspirate also depend on the methods of counting, the duration of transportation, and the prevention of clot formation in the material. The strict adherence to the rules of biomaterial samples delivery, processing and testing is required to obtain the reliable results.

Lastly, the reliability of PJI diagnostic criteria depends on the concomitant pathology. According to the study design, the patients with gout and rheumatoid arthritis were not included in the study. The data on concomitant pathology were entered into the medical record on the basis of the submitted medical documentation. No additional examination before revision arthroplasty was performed. In this regard, we do not exclude the possibility of participation in the study of the patients with undetected gout or rheumatoid arthritis.

The largest number of false negative results was found employing the WAIOT algorithm. In 9 out of 11 cases, the causative agent of the infection was coagulase-negative staphylococcus, which is a low-virulent pathogen with a pronounced ability to form microbial biofilms [7, 8, 9, 10, 30]. The difficulty of diagnosis lies in the characteristic subclinical course of PJI caused by a low-virulent pathogen [8, 10, 30]. In our study, the WAIOT diagnostic algorithm comprised 3 inclusion and exclusion criteria. It seems that it is possible to increase the diagnostic value of this algorithm by including additional criteria without changing the structure of the algorithm [15] or by changing the interpretation of the sum of points below zero to the option “biofilm form of PJI” instead of “no infection”, as we adopted, but this requires further analysis. In addition, it is possible to consider a modification of the WAIOT algorithm by the inclusion of the “large” criteria, for example, “the presence of a fistulous tract communicating with the joint cavity”. It should be noted that a good outflow of pathological discharge through the fistula in some cases does not allow obtaining the aspirate from the joint, and if present, it usually reduces the reliability of cytosis and the level of leukocyte enzymes (esterase and alpha-defensin). Because of this, the instruction for the use of the test system for determining alpha-defensin does not recommend this technique in the patients with fistulous tracts due to the risk of obtaining a false-negative result.

The largest number of false-positive results was obtained using the EBJIS algorithm, according to which the cytosis of the aspirate of more than 2000 cells/mL and/or the proportion of neutrophils of more than 70% was a confirmation of the PJI. This explains the greater number of false-positive results in comparison with other algorithms. The rise of the cytosis threshold value to 3000 cells/mL in our study increased the specificity/overall

accuracy from 84.5/85.8% to 93.0/90.6%, respectively, with the constant sensitivity result of 87.5%.

Due to the fact that our study was retrospective, the diagnostic significance of the ICM algorithm was assessed in two versions: "unconvincing = infection" and "unconvincing = no infection". The former option showed the greatest overall accuracy. In clinical practice, the result "unconvincing" requires additional or repeated examinations, which will increase the diagnostic value of the algorithm.

Despite the high indicators of the diagnostic significance of all the algorithms used, the clinical cases, when the interpretation of the preoperative examination results did not provide the unambiguous confirmation or exclusion of the infection, remained a "gray area". As a rule, these are the patients with increased blood levels of CRP and/or ESR, which are nonspecific signs of any inflammatory process, and without pronounced cytosis and growth of microorganisms in the aspirate. The coagulase-negative staphylococci were isolated from intraoperative materials in most cases of false negative results. The pathogenicity factor of these microorganisms is characterized by the ability to form microbial biofilms [7]. This largely explains the absence of pronounced signs of infection in the joint fluid. In our opinion, the patient with such inconclusive results before surgery should be considered in clinical practice as "conditionally infected". In such a case the intraoperative express diagnostics should be planned using histological examination of frozen sections, repeated tests for leukocyte esterase or alpha-defensin, besides taking tissue biopsies and removed components of endoprosthesis for microbiological examination. In addition, it seems rational, if it is impossible, to perform express diagnostics during the operation, the prescription of empirical wide spectrum antibacterial therapy (with mandatory activity against methicillin-resistant staphylococci) until the final results of bacterial examination of intraoperative samples are obtained.

The study limitations. Firstly, due to the absence of the histological examination data of the tissues from the area of the operated joint, our adopted reference criterion was the result of bacteriological examination of intraoperatively obtained tissue samples and removed components. As it is know, 2 positive cultures with an identical strain of one type of pathogen are considered as the confirmation of PJI in all algorithms used [14, 15, 16]. This gave us the right to use this rule as the "gold standard". However, like other diagnostic criteria, any bacteriological study, cultivation of intraoperative biopsies and of the explanted endoprosthesis also has its limitations [21] and not in all cases of infection can give a positive result. So, according to the standard criterion which we established, 3 clinical cases (FP3, FP6, FP10) were attributed to false positive results due to the absence of microorganism growth from the explanted endoprostheses and 6 biopsy specimens, despite the presence of a fistula communicating with the joint cavity (FP6), increased cytosis and high neutrophils count of the aspirate, as well as the growth of opportunistic pathogens in the preoperative aspirate (FP3, FP10). This leads to a 2nd limitation characteristic for the retrospective studies. The cross-sectional nature of the study made it difficult to determine the influence of individual factors on the final result. Although our study can serve as a starting point for further research.

Conclusion

All diagnostic algorithms included in this study are characterized by high level of diagnostic power for detecting knee or hip PJI without significant differences. The ICM algorithm in the "unconvincing = infection" variant showed a higher overall accuracy rate of 91.3%, diagnostic sensitivity and specificity were 89.3% and 93.0%, respectively. The best specificity was shown by the WAIOT and ICM algorithms (unconvincing = no in-

fection): 95.8%, with sensitivity and overall accuracy of 80.4% and 89.0%, respectively. The sensitivity and specificity of the EBJIS algorithm were 87.5% and 84.5%, respectively, and the overall accuracy — 85.8%. The greatest difficulties were experienced making PJI diagnosis in the subclinical cases caused by low-virulent pathogens. Thus, the diagnosis of PJI requires an integrated approach with employment of various clinical and laboratory methods. Probably, the choice of one or another diagnostic algorithm does not play a fundamental role. However, it seems important to develop local protocols for the diagnosis and management of the patients with suspected or apparent PJI in every healthcare facility which provides medical care to the patients with joint implants.

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