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Emergency histological examination in diagnosis of periprosthetic joint infection in revision total knee arthroplasty

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Abstract

Introduction Diagnostic algorithms are used for detection of periprosthetic joint infection (PJI) including sampling for histological evaluation (HE). The purpose was to assess the diagnostic significance of emergency HE of fresh-frozen intraoperative biomaterial as part of preoperative PJI screening of patients undergoing revision total knee arthroplasty (RTKA). **Material and methods** The prospective study included 83 patients who were admitted to two trauma and orthopaedic centers for RTKA. The European Bone and Joint Infection Society 2021 (EBJIS21) algorithm was used to detect PJI of the knee joint. The diagnostic value of screening PJI with/without regard to the results of an emergency HE was compared with the results of a microbiological study (MBI) of all types of biomaterials obtained from each patient. Subanalysis was additionally performed in patients with aseptic instability and antimicrobial spacer. **Results** Pathomorphological examination of freshly frozen and paraffin-embedded tissues showed the difference of 7.2 %, which did not significantly affect the interpretation of the results ($p > 0.05$). Diagnostically significant pathogens were identified in 83.3 % of cases with PJI confirmed by emergency HE ($p < 0.001$). A positive emergency HE result increased the chances of isolating diagnostically significant organisms by 34 times (95 % confidence interval (CI): 4.721 – 244.859) as compared with negative HE cases. The proportion of detected cases with emergency HE included in the screening increased from 2.4 to 8.4 %. The inclusion of emergency HE in the screening improved the diagnostic value both in the general cohort of patients and in the subanalysis of comparison groups due to a two-fold increase in sensitivity. **Conclusion** Relevance of the emergency HE results and the PJI criteria should be considered as a significant prognostic factor for an infectious process, however, this technique should be used only in a complex algorithm for PJI detection. Poor outcomes in 18.2 % of cases of probable PJI necessitated a change in the approach to managing this cohort of patients.
Keywords: knee joint, revision arthroplasty, periprosthetic joint infection, latent PJI, histological evaluation, frozen tissues

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INTRODUCTION

Many diagnostic modalities have been investigated in an attempt to accurately identify patients with aseptic instability of endoprosthetic components and periprosthetic joint infection (PJI), in the latency, in particular. International professional communities (WAIOT [1], MSIS [2], AAOS [3], EBJIS [4]) undertake to develop and improve diagnostic algorithms with one of the criteria for verifying the diagnosis using histological examination (HE) of intraoperative biological material. However, the timing of obtaining the results of HE of paraffin-embedded tissues allows for the diagnosis of PJI to be confirmed or ruled out in a retrospective manner. The diagnostic value of the HE of a fixed biomaterial is comparable to the HE of freshly frozen tissues with the results ranging from 0 to 2.4 % [5-8]. HE of freshly frozen sections of intraoperative material has a significant advantage of obtaining the result within 20 minutes (Order of the Ministry of Health of the Russian Federation dated March 24, 2016 No. 179n "On the rules for conducting pathological and anatomical studies", M., 2016) which would allows identification of the treatment option and postoperative management of a PJI in combination with preoperative findings. However, there is a paucity of foreign publications reporting the diagnostic value of HI of fresh frozen tissues in the detection of PJI or the recurrence in patients undergoing revision total knee arthroplasty (reTKA) for various reasons, and there are no Russian works on this topic, which determined the purpose of our study.

The objective was to evaluate the diagnostic role of urgent HE of fresh frozen intraoperative biological material as part of preoperative screening of patients admitted for reTKA in identification of PJI or its recurrence.

MATERIAL AND METHODS

Study cohort of patients

The prospective study included 83 patients admitted to two centers between October 2020 and September 2022 for reTKA due to aseptic instability of the endoprosthetic components or for the second stage of PJI treatment. Depending on the primary diagnosis, patients were divided into comparison groups: group 1 (n = 50) included patients who were diagnosed with aseptic instability of endoprosthetic components who were hospitalized for reTKA, and group 2 (n = 33) consisted of patients who were admitted for the second stage of PJI treatment to have the spacer removed and endoprosthesis reimplanted.

Patients of group 1 underwent reTKA, removal of the endoprosthetic components and the cement mantle, if any, and washing of the joint cavity with isotonic sodium chloride solution (at least 5 liters). Patients of group 2 underwent removal of the spacer and cement mantle, debridement of the bone and surrounding soft tissues, followed by abundant lavage of the joint cavity with a polyhexanide solution (at least 5 liters) and reimplantation of the endoprosthesis. Debridement, one-stage reTKA or spacer implantation was performed in case of PJI detected in group 1 or recurred in group 2. Revision endoprosthesis or articulating spacer (if a decision was made to implant it) was fixed using antibiotic-containing bone cement (Refobacin bone cement or DePuy CMW 3 bone cement). The decision to change intraoperative strategy in case of PJI was made by the operating surgeon.

Medicated and non-medicated prophylaxis of venous thromboembolic complications was administered for the patients postoperatively. A 3-day course of antibiotics (cephalosporins of I-II generations) was administered for Group 1 according to the approved local protocol. Patients of group 2 received a 7-to-10-day course of parenteral antimicrobial therapy approved by a clinical pharmacologist, in accordance with pathogen identified at debridement or in preoperative aspirates to be followed by oral antibacterial drugs administered for 1-2 months. Antimicrobial therapy could be corrected with HE and microbiological examination (MBE) of the intraoperative samples.

Research methods

Preoperative physical examination and laboratory testing including CBC, ESR and serum CRP levels, and knee aspiration were performed for the patients. The aspirate was referred to MBE; a cytological examination (CE) was additionally performed in the absence of blood admixture in the aspirate.

Joint aspiration was performed intraoperatively prior to arthrotomy after a skin incision and, if aspirate was available it was sent for bacteriological examination; with absent blood admixture, it was referred for CE in a vial if not performed earlier. The endoprosthetic components or the spacer removed were sent in a sterile polyethylene container to the laboratory for ultrasonic treatment and subsequent MBE of the sonic fluid. At least 5 samples of periprosthetic tissue biopsies were obtained for MBE from different sites and delivered to the laboratory in sterile tubes. Clinical isolation was performed using methods approved at the clinics of the centers in accordance with international Standards for microbiology investigations. Species identification was performed by MALDI-TOF-MS using the FlexControl system and MBT Compass 4.1 software (Bruker Daltonics, Germany), Score ≥ 2.0 and a Micro Scan Walk Away 96 Plus analyzer (Beckman Coulter., USA). Antibiotic sensitivity was determined in accordance with the clinical guidelines "Determination of the sensitivity of microorganisms to antimicrobial drugs" (2021) (www.antibiotic.ru/minzdrav/category/clinical-recommendations). MBE results were accepted as diagnostically significant with a pathogenic strain of bacteria isolated from one sample [9] or identical strains of an opportunistic pathogen with an identical antibiotic susceptibility profile from ≥ 2 samples of biomaterials. At least 3 samples of the periprosthetic membrane were obtained intraoperatively at the endoprosthetic components for urgent and elective HE. The biomaterial was immediately sent to the pathology department using a polyethylene container without p urgent reservatives. The EBJIS21 algorithm was used to identify PJI in the cohort of patients [4, 10]. The impact of urgent HE on the diagnostic value of screening for PJI including solely preoperative results, was compared with the MBE results of all types of biomaterials obtained from each patient.

Pathological study

One to three sections were obtained from a tissue biopsy for urgent HE using a semi-automatic microtome-cryostat MCM-2850 (Mtpoint Technology, RF) or NM 525 NX (Thermo Fisher Scientific, USA) at a working temperature of minus 25-28 °C, dehydrated in alcohol and stained with hematoxylin and eosin. The material was examined by a pathologist using a biomedical microscope Eclipse 50i (Nikon, Japan) or Primo Star (Carl Zeiss, Germany). The result of the study was immediately reported to the operating trauma and orthopaedic surgeon. The biomaterial was fixed in 10 % formalin (pH 7.4) for elective HE, dehydrated

in alcohols of increasing concentration using a Microm STR-120 (Micron Technology, USA) or Carousel STP-120 material, and embedded in paraffin using a modular Tissue-Tek TEC5 (Sacura, Japan) or MPS/P2 (SLEE Medical, Germany) paraffin embedding station. Sections 5-7 μm thick were obtained using a Leica sledge microtome (Germany) or Microm HM 430 (Thermo Fisher Scientific, USA). Staining was produced with hematoxylin and eosin according to the manufacturers' instruction (Bio-Vitrum, Russia) using an automatic linear stainer Raffaelo Advanced (DIAPATH, S.p.A., Italy). Microscopic examination and photographic documentation were produced using an EVOS XL Core microscope (Thermo Fisher Scientific, USA) outfitted with a highly sensitive color CMOS camera ×400 magnification and a Levenhuk D870T trinocular microscope (Levenhuk, USA) outfitted with a Levenhuk C800 NG digital camera (Levenhuk, USA) .

Polymorphonuclear neutrophils (PNN) were counted in 10 fields of view as recommended by Feldman D. et al. (1995) [11], who offered microscopy of histological slides following the rules to minimize sampling errors: granulation tissue to be analyzed with two or more samples; the fields of view to be identified with the greatest cell infiltration of PNN; PNN to be counted at a higher magnification (x400); PNN with clearly defined cytoplasmic boundaries to be counted. The infectious process was verified in the presence of 5 or more PNNs in at least 5 fields of view (Fig. 1a). A suspected PJI included cases with 5 or more PNNs detected in 1-4 visual fields. With PNNs being less than 5 in all fields of vision, PJI was ruled out (Fig. 1b). All samples were interpreted blindly by the pathologist in relation to preoperative findings.

Treatment outcomes were assessed with the modified Delphi technique [12] based on the results of an examination or a telephone survey of the patient. A successful outcome was considered to be the absence of: a) fistulous tract, non-healing wound or recurrence of infection caused by a pathogen; b) an unintended surgical intervention; c) death for any reason; d) refusal of reimplantation. The median follow-up was 18 months (interquartile range of 9-22).

Statistical analysis

Data of the patients were imported into the Microsoft Excel electronic database. Statistical analysis was performed using the StatTech v. 3.0.6 (LLC "Stattech", Russia). Quantitative variables were assessed for compliance with the normal distribution using the Shapiro-Wilk test (the number of subjects less than 50) or the Kolmogorov-Smirnov test (the number of subjects 51 and over). Quantitative variables with a normal distribution were described using arithmetic means (M) and the 95 % confidence interval (95 % CI). Quantitative data were presented using the median (Me) and interquartile interval (IQI) in the absence of a normal distribution. Categorical data were described as absolute values and percentages. The Student's t-test was used to compare two groups in terms of a quantitative variable having a normal distribution with variances being equal. The Mann-Whitney U-test was used to compare two groups in terms of a quantitative variable with the distribution being different from the normal. The Fisher's exact test (for expected values less than 10) or the Pearson's chi-square test (for expected values of 11 and over) were used to compare percentages in the analysis of four-field cross tables.

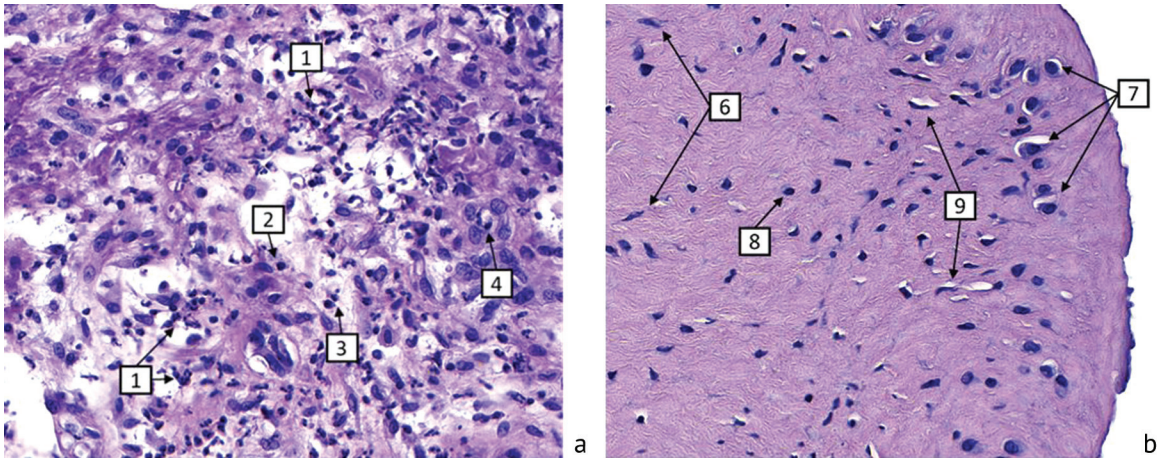

Fig. 1 Microphoto of histological preparations of periprosthetic membranes stained with hematoxylin and eosin. Magnification ×400: (a) connective tissue with inflammatory infiltration showing a large number of neutrophilic polymorphonuclear granulocytes and formation of clusters (significantly more than 5 in the field of view) (1), a small number of lymphocytes (2) and plasma cells (3), small vessels with large endotheliocytes (4); (b) small-celled connective tissue with rare fibroblasts and fibrocytes (6), with poor cellular infiltration - histiocytes (7), single lymphocytes (8), rare small thin-walled vessels with flattened endotheliocytes (9)

The odds ratio (OR), defined as the ratio of the probability of an event occurring in a group exposed to a risk factor to the probability of an event occurring in the control group was used as a quantitative measure of the effect comparing relative parameters. The limits of 95 % CI were calculated to project the OR values to the study cohort. Based on the data obtained, the significance of the relationship between the outcome and the factor was considered proven if the confidence interval was found outside the border of no effect, taken as 1.

RESULTS

The median age of patients in the cohort was 68 years (IQR of 61-72). Most of the patients were females (77.1 %). The comparison groups were comparable in terms of age and gender (Table 1).

The preoperative median ESR and leukocyte count showed no significant differences between groups 1 and 2 (Table 2). The blood CRP level of patients with spacers was 2.2 times higher than in the comparison group on admission (p = 0.022). The preoperative CRP level was ≥ 10 mg/L in 18 % and 24.2 % patients of groups 1 and 2, respectively. The proportion of patients with a combined increase in CRP and ESR There was an increase in both CRP and ESR in 6.1 % patients of group 1 and 6.0 % of group 2.

Preoperative aspirate for MBE showed negative results in the majority of patients (97 % and 96 % in groups 1 and 2, respectively). MSSE and *Staphylococcus caprae* were isolated in two cases of group 1, and *Staphylococcus lugdunensis* was isolated in one case of group 2. The aspirate was inappropriate for CI in almost half of the patients (43.4 %, n = 36). Normal aspiration cytology was observed in most cases (92 % in group 1 and 90.9 % in group 2) (Table 3). The results met the criteria for infection in all other cases.

Preoperative evaluation using the EBJIS21 algorithm, demonstrated 3.6 % of cases out of the cohort who met the criteria for PJI including 1-2 patients in group and 1 patient in group 2 (Table 4). The infection was likely to be detected in another 2.4 % of cases, and the rest of the cases were regarded as aseptic instability of the components or arrest of PJI after the first stage of surgical treatment.

Table 1

Analysis of the sex and age in the comparison groups

Description	Group 1, n = 50	Group 2, n = 33	p
Age, years (95 % CI)	65.2 (62.3-68.1)	67.3 (64.4-70.1)	> 0.05
Female, n (%)	42 (84.0)	22 (66.7)	> 0.05
Male, n (%)	8 (16.0)	11 (33.3)	

Table 2

Analysis of levels of serum markers in comparison groups

Description	Groups	Me	IQR	n	p
ESR (mm/h)	Group 1	13.0	8.2-19.0	50	> 0.05
	Group 2	16.0	10.0-25.0	33	
CRP (mg/L)	Group 1	2.5	1.4-5.3	50	0.022
	Group 2	5.5	2.3-9.2	33	
leukocytes (*10^9/L)	Group 1	6.9	5.9-8.3	50	> 0.05
	Group 2	7.0	5.7-8.1	33	

Table 3

CE results of preoperative aspirate in patients of comparison groups

Description	Status	Number of patients, n (%)		p
		Group 1	Group 2	
Leukocytes (c/mL)	≤ 1500	23 (92.0)	10 (90.9)	> 0.05
	> 1500 ≤ 3000	–	–	
	> 3000	2 (8.0)	1 (9.1)	
PNN (%)	≤ 65 %	18 (90.0)	7 (87.5)	> 0.05
	> 65 % ≤ 80 %	–	–	
	> 80 %	2 (10.0)	1 (12.5)	
Esterase activity	none/+	23 (92.0)	10 (90.9)	> 0.05
	++/+++	2 (8.0)	1 (9.1)	

Table 4

Preoperative screening for the presence of PJI of comparison groups using the EBJIS21

Description	Comparison groups		p
	Group 1	Group 2	
PJI is improbable	47 (94.0)	31 (94.0)	> 0.05
PJI is probable	1 (2.0)	1 (3.0)	
PJI is confirmed	2 (4.0)	1 (3.0)	

MBE of the intraoperative samples showed the growth of a microorganism obtained from one or more samples in 19.3 % of cases (n = 16/83). Coagulase-negative staphylococci (CNS) were most common microorganisms isolated from intraoperative samples detected in 62.5 % (n = 10/16) with MRSE (5/10) observed in 50 % regardless of the group (Fig. 2). Diagnostically significant microorganisms were isolated more often in group 2 (12.1 %, n = 4/33) than in group 1 (10 %, n = 5/50). The pathogen was not isolated from intraoperative samples in 10 % of patients (n = 1/10) with PJI confirmed by other criteria.

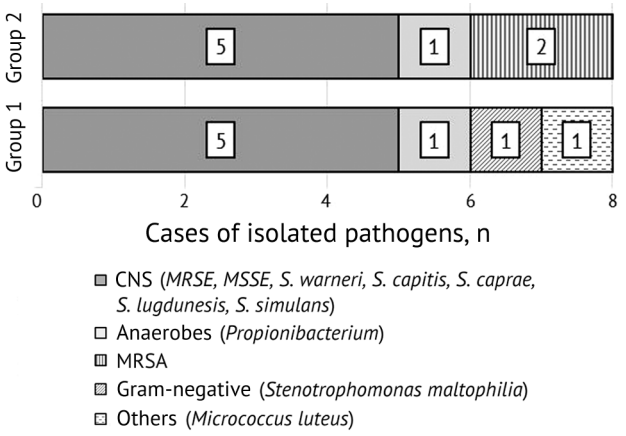

Fig. 2 Pathogens isolated from intraoperative biomaterial in comparison groups

The diagnostic significance of MBE for PJI verification was most influenced by tissue biopsy ($p < 0.001$) with the results being significant in the majority of cases (88.9 %). Other materials (aspirates, sonic fluid) were used to detect infection in 11.1 % (n = 1/9) of observations (Fig. 3).

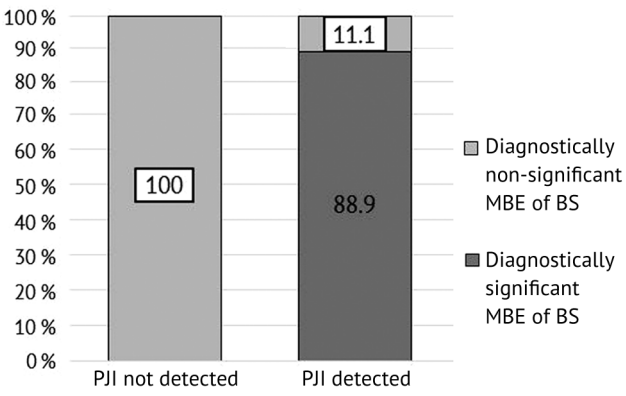

Fig. 3 Effect of MBE of biopsy specimens (BS) on PJI verification

PJI was detected in 7.2 % (n = 6) of cases in HE of fresh frozen periprosthetic tissues with the results meeting the criterion of probable infection in 6 % of cases (n = 5). The urgent and elective HE showed higher ($p > 0.05$) proportion of patients with probable and histologically confirmed PJI in the group of patients with spacers measuring 18.2 and 15.2 %, respectively. The parameter was 10 and 12 % in patients of group 1, respectively. There was 7.2 % of discrepancies in the results of pathomorphological examination of freshly frozen and paraffin-fixed tissues and had no significant impact on the interpretation of the results ($p > 0.05$) (Table 5).

Diagnostically significant pathogens were identified ($p < 0.001$) in the majority of cases (83.3 %) with PJI confirmed using urgent histology. A positive result of an urgent HE increased the chances of isolating diagnostically significant microorganisms by 34 times (95 % CI: 4.721 – 244.859) as compared with cases of a negative HE result. Conformity of the urgent HE and the probable PJI increased the odds of pathogen isolation by 19.8 times (95 % CI: 0.744 – 527.260).

Table 5

Results of urgent and elective histological examination of intraoperative samples in comparison groups

Description	PJI	Comparison groups		p
		Group 1, n = 50	Group 2, n = 33	
Urgent HE	improbable	45 (90.0)	27 (81.8)	> 0.05
	probable	2 (4.0)	3 (9.1)	
	confirmed	3 (6.0)	3 (9.1)	
Elective HE	improbable	44 (88.0)	28 (84.8)	> 0.05
	probable	2 (4.0)	2 (6.1)	
	confirmed	4 (8.0)	3 (9.1)	

Preoperative screening of the cohort of patients showed PJI confirmed in 3 cases at the time of surgical intervention. The inclusion of an urgent HE in the screening programme allowed identification of 7 cases of PJI (8.4 %) with 4 detected in addition to the results of preoperative screening. PJI was confirmed in the 7 cases with a comprehensive postoperative assessment using the EBJIS21 algorithm. The proportion of cases detected with urgent HE included in the screening increased from 2.4 % to 8.4 %. PJI was diagnosed postoperatively in two more cases (2.4 %) using the MBE. Introduction of urgent HE into the screening increased the rate of detected cases of PJI from 4 % (n = 2) to 8 % (n = 4) of patients in group 1. Comprehensive postoperative evaluation using the EBJIS21 algorithm showed the presence of infection in 12 % of patients (n = 6) with a primary diagnosis of aseptic instability of implant with one case of false-negative result of HE. The HE results were consistent with probable infection in the absence of other positive PJI criteria in another patient.

Urgent HE in combination with other EBJIS21 criteria increased the proportion of infectious cases with spacers confirmed at the time of surgery from 3 % (n = 1) to 9.1 % (n = 3). Comprehensive postoperative assessment using the EBJIS21 algorithm showed the persistent infectious process in 12.1 % of patients (n = 4) with a false negative result of HE in one case. The overall diagnostic value of preoperative screening for the study cohort was rather low due to low sensitivity regardless of the study group or when evaluating the cases included in the study (Table 6). The inclusion of urgent HE in the screening improved the diagnostic value in the general cohort of patients and in sub-analysis of comparison groups due to an increase in sensitivity by 2 or more times and an insignificant change in other parameters.

A probable PJI identified at preoperative screening using urgent HE ($p < 0.001$) at the time of revision TKA and with comprehensive postoperative assessment using the EBJIS21 algorithm ($p = 0.001$) was a significant risk factor for treatment failure (Table. 7).

Table 6

Diagnostic value of preoperative evaluation for PJI in the general cohort of patients and in comparison groups as compared to the results of MBE of the samples

Description	Patients	Sensitivity	Specificity	Accuracy	PPV	NPV
Screening	Total	44.4	98.6	92.8	80	93.6
	Group 1	40	100	94	100	93.8
	Group 2	25	96.6	87.9	50	90.3
Screening + eHE	Total	77.8	90.5	89.2	50	97.1
	Group 1	80	93.3	92	57.1	97.7
	Group 2	75	86.2	84.8	42.9	96.2

Notes: screening, preoperative examination of ESR, CRP, CE and MBE of the aspirate; screening + eHE, screening and an urgent HE of an intraoperative sample; PPV, positive predictive value; NPV, negative predictive value

Table 7

Correspondence of the results of pre- and postoperative assessment for the presence of PJI using the EBJIS21 algorithm and the outcomes of specific patients using the modified Delphi criteria

Stage of diagnosis	Outcome as outlined in the history	With criteria of EBJIS21 P			p
		improbable	probable	confirmed	
Preoperative screening and HE	successful	72 (88.9)	3 (3.7)	6 (7.4)	< 0.001
	failure	0 (0.0)	2 (100.0)	0 (0.0)	
Postoperative comprehensive evaluation	successful	62 (76.5)	9 (11.1)	10 (12.3)	0.001
	failure	0 (0.0)	2 (100.0)	0 (0.0)	

DISCUSSION

A recent study based on data from the National Joint Registry and the New Zealand registry found PJI rates for all revision knee arthroplasties to be 23.6 % (n = 21894) [13] and 51.6 % (n = 349) [14]. The recurrence rate is reported as high as 12.7 % [15] after implantation of the endoprosthesis in cases of one-stage surgical treatment of PJI of the knee and 16.2-24 % after two-stage management [15, 16], and the frequency of PJI manifestation is 2.94 % after revision procedures due to aseptic instability of endoprosthetic components. The probability of PJI manifestation increases by 6 times and reaches 18.45 % with an "unexpected" PJI detected in 3.75-10 % of cases of reTKA [17] as growth of pathogens from the intraoperative samples of patients who had

undergone reTKA for "aseptic" reasons [18]. Increased proportion of patients with PJI after reTKA and the high rate of relapses can be caused by inadequate diagnostic screening for PJI and patients with probable infection are not detected and approaches to treatment strategy are not changed. Intraoperative HE of fresh frozen samples as a method for diagnosing infection was first reported by Charosky C. et al. (1973) who concluded that the presence of acute inflammatory changes or chronic inflammation in tissues in rEP can be associated with a probable PJI [19]. HE of a biological sample is included in modern algorithms for detecting PJI, since the presence of acute inflammatory cells in tissue is highly specific for the infectious process [5, 20-22]. Two to three biological specimens to be collected from the periprosthetic bone-graft interface, synovial membrane, pseudocapsule, or other "suspicious" tissue would have a role because of the inflammatory infiltrate being unevenly distributed in the joint [11, 23]. Modern diagnostic algorithms recommend examining at least 5 fields of view with a magnification of ×400, however, infection can be suspected if at least one of the fields of view contains 5 or more PNNs [4].

There are single studies reporting HE of frozen samples in a comprehensive postoperative assessment using the MSIS/ICM18 algorithm [6, 8, 24]. However, we did not find studies evaluating the impact of urgent HE on the diagnostic value of preoperative screening for the presence of PJI using the EBJIS21 algorithm for diagnosing infection at the second stage of PJI treatment and during reimplantation due to instability of endoprosthetic components. In our series, we compared HE of frozen section with the EBJIS21 criteria and assessed the impact of the results on the diagnostic value of PJI screening. Parvizi J. et al. (2011) suggested that the HE findings may be different between different morphologists exploring biomaterial [25], which would lead to inadequate results of urgent and elective HE. Examination of patients at the stage of debridement and at the stage of endoprosthetic reimplantation demonstrated the cumulative share of the concordance between the results of urgent and elective HE measuring 97.7 % [26], which was comparable to the results of our series measuring the concordance of 92.8 %. Data on the sensitivity of frozen sections for the diagnosis of PJI varies greatly in different publications ranging between 18.2 % and 100 % with the specificity demonstrating a smaller range of differences between 89.5 % and 100 % [5-8, 12, 27-31].

Our series showed that HE of frozen section appeared to be of limited use to rule out PJI due to its low sensitivity being very useful for detecting PJI due to high specificity, which is consistent with the results reported [6, 8, 24]. Borrego F. et al. (2007) reported the sensitivity and specificity of urgent HE of periprosthetic tissues in reTKA measuring 66.7 % and 89.7 %, respectively [24], which was consistent with our findings of 77.8 % and 90.5 %, respectively. Coagulase-negative staphylococci and C. acnes (Propionibacterium) can reduce the diagnostic value of the research method [22] with the bacteria dominating in the spectrum of microorganisms isolated from biological samples in both groups we explored. The concordance of the results of urgent HE with the criteria for the presence of PJI in our series was a significant prognostic factor for the isolation of a diagnostically significant pathogen (OR 34 (95 % CI: 4.721–244.859)) and was in compliance with the data reported (OR 54.7 (95 % CI 31.2-95.7)) [32]. J. Qiao et al. (2021) suggested that a positive frozen section at reimplantation was independently associated with subsequent failure and earlier reinfection, despite normal ESR and CRP levels pre-reimplantation [33]. We found that the presence of a probable infection identified during preoperative screening including urgent HE was a significant ($p < 0.001$) factor for a poor outcome: 2 of 3 patients had a poor outcome that necessitated treatment of the patients as those diagnosed with PJI. A comprehensive examination of patients including intraoperative HE of freshly frozen periprosthetic tissues can increase the proportion of PJI cases [4] and allow timely changes in treatment strategy. Two-stage reimplantations reported by Insall J. et al. (1983) remains the "gold standard" for the treatment of PJI [34]. Göksan S. et al. (1995) suggested that one-stage reimplantation was a reasonably reliable procedure for the management of a loose infected prosthesis [35]. One-stage reimplantation can be an alternative to the two-stage technique in the chronic PJI.

More surgeons are opting for a single-stage change instead of debridement antibiotics implant retention (DAIR) with the proportion of two-stage and multi-stage revisions being significant. In 2008, 20.28 % of the PJI patients were treated with the DAIR approach in Germany [36], whereas 36.95 % of the patients underwent a single-stage change. 42.77 % cases were managed with a two- or multi-stage change. In 2018, however, DAIR procedures decreased to 11.41 %, whereas the single-stage change as the chosen treatment strategy increased to 42.55 % of all PJI cases, and a two- or multi-stage change was performed in 46.04 % of revisions due to infection. Despite the fact that more researchers come to the conclusion that one-stage

exchange arthroplasty can be considered as an effective method for the treatment of PJI, there is no consensus on the indications for its use [37-38].

In our series, PJI was diagnosed in 10 patients with 3 cases having a false-negative result based on comprehensive postoperative assessment using the EBJIS21 and the MBE of samples,. It was the operating surgeon who chose treatment strategy in each case of identified PJI. Three patients were treated with debridement and implantation of an articulating spacer, one-stage reTKA was performed for the rest cases. A successful treatment result was achieved in the 10 cases. The treatment strategy did not change in 11 cases with the results of a comprehensive postoperative examination corresponding to the criteria for a probable PJI. One patient was diagnosed with PJI at 18 months of reTKA. Another case was fatal and interpreted as a treatment failure according to the modified Delphi criteria. Poor outcomes were noted in 18.2 % of cases (2 out of 11)with the results meeting the criteria for probable infection. Both poor outcomes were seen in patients diagnosed with probable PJI based on preoperative screening, which confirmed the assumption that this cohort of patients should be managed similarly to cases of confirmed infection. No signs of PJI were detected in the cases where infection was unlikely during the observation period (Me, 18 months; MKE, 9-22).

Our study had a number of limitations. There was a lack of consensus on the "gold standard" for confirming or eliminating PJI. Bacteriological examination of the samples was used in our series to detect PJI. There was a small sample size leading to greater confidence intervals of diagnostic parameters with limited reproducibility, relatively short follow-up periods, with may-be different outcomes in increased treatment periods. Antibiotic regimens could differ from case to case in the postoperative period, and the effect on failure rates was not considered in the series.

CONCLUSION

Inclusion of urgent HE of frozen periprosthetic tissues in the algorithm of perioperative examination of patients allowed for a greater detection rate of PJI at the time of reTKA. The concordance of the results of urgent HE and the criteria for the presence of PJI should be considered as a significant prognostic factor for an infectious process, whereas the presence of 3 false-negative results of the HE necessitated the technique to be used in a complex algorithm for diagnosing PJI, for example, EBJIS21. Timely detection of the infectious process facilitated the adjustment of treatment strategy of reTKA patients and a successful treatment outcome regardless of the cause of reTKA. Poor outcomes noted in 18.2 % of cases of probable PJI indicated the need for a similar change in the approach to managing the patients. In general, urgent HE of freshly frozen periprosthetic tissues included in the screening for the presence of PJI resulted in increased diagnostic sensitivity and a slightly decreased specificity, which amounted to 80 % and 93.3 % in patients with unstable endoprosthetic components, and 75 % and 86.2 % in the spacer group, respectively.

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