International Orthopaedics (2019) 43:1303–1308
https://doi.org/10.1007/s00264-018-4227-x

ORIGINAL PAPER

Intra-operative diagnosis of periprosthetic joint infection can rely on frozen sections in patients without synovial fluid analyses

Chi Xu[1] · Heng Guo[1,2] · Ji-Ying Chen[1]

Received: 15 August 2018 / Accepted: 30 October 2018 / Published online: 10 November 2018

Abstract

Background The purpose of this study was to determine whether frozen sections can increase diagnostic values of serological tests for the assessment of periprosthetic joint infection (PJI) in patients without synovial fluid analyses.

Methods A retrospective review of 128 revision arthroplasties (79 hips and 49 knees) from January 2016 to December 2017 was performed. Diagnosis of PJI was based on the Musculoskeletal Infection Society criteria for infection. Three diagnostic models for PJI, with model 1 including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), model 2 including model 1 plus frozen sections > 5 polymorphonuclear neutrophil (PMN)s per high-power field (HPF), and model 3 including model 1 plus frozen sections > 10 PMNs per HPF, were developed. Then receiver operating characteristic (ROC) curves were generated, and the areas under the ROC curves (AUCs) were compared.

Results The AUC of model 1, model 2, and model 3 was 79.40% [95% confidence interval (CI), 69.84 to 86.64%], 89.30% (95% CI, 82.93 to 93.92%), and 85.52% (95% CI, 78.44 to 91.4%), respectively. The AUC of model 1 was significantly lower than that of model 2 ($p = 0.002$) and model 3 ($p = 0.039$). Although the result was not significant ($p = 0.132$), there was a trend toward a higher AUC of model 2 than model 3.

Conclusions This study reveals that intra-operative frozen sections significantly increased the performance of serum ESR and CRP in the diagnosis of PJI. The combination of serological tests and frozen sections for the assessment of PJI may be reliable in patients without synovial fluid analyses.

Keywords Periprosthetic joint infection · Frozen section histology · Sedimentation rate · C-reactive protein

Introduction

Periprosthetic joint infection (PJI) after total joint arthroplasty (TJA) is a rare but dreaded complication that is associated with an increased risk of morbidity and mortality [1, 2]. Therefore, the timely and accurate diagnosis of PJI is crucial. As lack of "gold standard" for the diagnosis of PJI, the Musculoskeletal Infection Society (MSIS) has developed criteria to standardize the definition of PJI, which was modified by the International Consensus Meeting (ICM) in 2013 [3, 4]. These definitions are based on the combination of clinical findings, microbiological cultures, serological tests, joint aspiration analyses, and histological features.

The intra-operative frozen section histology is a timely and cost-effective tool in the diagnosis of PJI. However, its diagnostic value remains controversial [5–10]. The major concern is the discrepancy comparing frozen and paraffin section, which has been suggested that tissue samples were insufficiently representative of cytohistology by using frozen section [5, 6]. Another issue is that the frozen section can be false negative in certain low-grade infection [7–9] or false positive in patients with periprosthetic fracture [7, 10]. Additionally, the optimal diagnostic thresholds of polymorphonuclear neutrophil (PMN) per high-power field (HPF) have conflicting results in the literature, while the MSIS for PJI recommended five PMNs per HPF [3, 11–14].

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00264-018-4227-x) contains supplementary material, which is available to authorized users.

✉ Ji-Ying Chen
jiying_chen301@163.com

[1] Department of Orthopaedic Surgery, General Hospital of People's Liberation Army, No. 28 Fuxing Road, Haidian District, Beijing 100853, China

[2] Department of Orthopaedic Surgery, Beijing Mentougou District Hospital, Beijing, China

Table 1 Patient characteristics

	Total ($n = 128$)	Septic ($n = 48$)	Aseptic ($n = 80$)	p value
Gender (n, %)				0.112
Female	78 (60.94)	25 (52.08)	53 (66.25)	
Male	50 (39.06)	23 (47.92)	27 (33.75)	
Age (year)	59.84 ± 14.69	61.85 ± 11.96	58.64 ± 16.06	0.232
BMI (kg/m^2)	25.37 ± 4.34	25.33 ± 2.94	25.39 ± 5.01	0.936
Joint (n, %)				0.004
Hip	79 (62.20)	22 (45.83)	57 (72.15)	
Knee	49 (38.28)	26 (54.17)	23 (28.75)	
Diabetes mellitus (n, %)	18 (14.06)	11 (22.92)	7 (8.75)	0.035
Rheumatoid arthritis (n, %)	3 (2.34)	1 (2.08)	2 (2.50)	1.000
Malignance (n, %)	10 (7.81)	4 (8.33)	6 (7.50)	1.000

It is important to differentiate between septic and aseptic revisions since the managements of those two are entirely different. Despite the undoubted diagnostic value of synovial fluid analyses, it may be not routinely obtained in some circumstances, especially before presumed aseptic revision. Additionally, prior studies showed that a "dry tap" may occur in almost half of joint aspirations while radiological guidance was used [15, 16]. For patients without synovial fluid analyses, intra-operative decision-making process mainly relies on serological tests involving erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and frozen sections. However, to our best knowledge, there has been no study on the performance of the combination of serum ESR, CRP, and frozen sections for the assessment of PJI.

Therefore, the purposes of this study were (1) to assess the association between frozen section results and PJI; (2) to determine whether frozen sections can increase diagnostic values of serological tests in the assessment of PJI; and (3) to compare the accuracy of five and ten PMNs per PHF as the threshold. Our hypothesis was that the combination of serological tests and frozen sections in the diagnosis of PJI would be satisfactory. It was also hypothesized that there was no difference in the diagnostic performance between five and ten PMNs per PHF as the threshold.

Table 2 Organism profile

Microorganism	
Staphylococcus aureus	5 (10.4)
Coagulase-negative staphylococci	20 (41.7)
Methicillin-resistant organism	3 (6.2)
Enterococcus spp.	2 (4.2)
Streptococcus spp.	6 (12.5)
Polymicrobial organism	6 (12.5)
Culture negative	16 (33.3)

Methods

Patients

After institutional review board approval, we retrospectively reviewed our institutional revision database, which consisted of 331 revisions (201 hips and 130 knees) from January 2016 to December 2017. One hundred and sixty-two cases with missing data for intra-operative frozen sections were excluded. Patients with a prior two-stage exchange arthroplasty, a megaprosthesis, a diagnosis of periprosthetic fracture or dislocation, or those with missing criteria data were also excluded. After the aforementioned criteria, 128 revisions including 79 hips and 49 knees were included in the final analysis.

Data collection

Serum ESR and CRP were routinely obtained for every patient before revision arthroplasty in our institution. Other clinical records were reviewed manually in detail to extract pertinent information that included gender, age, body mass index (BMI), joint of interest, diabetes mellitus, and rheumatoid arthritis. Prior studies have shown that coagulase-negative staphylococci (CNS) can cause a PJI with a decreased PMN infiltration rate [7–9]. Therefore, the cultured organism was also reviewed.

Three to five samples of tissues to be analyzed were obtained during surgery from the periprosthetic membrane and other periprosthetic tissues in which infection was suspected. Each sample was gathered in a separate clean specimen bag and was promptly referred to the pathology department in a sterile transport to avoid cross-contamination. All samples were stained using haematoxylin and eosin (H&E) and analyzed based on Feldman et al.'s criteria [17]. Multiple sections from each sample were classified by two experienced pathologists, and the number of PMNs per HPF (× 400) was

Table 3 Association between frozen sections and PJI

Frozen section histology	Num. of septic revisions (%)	Num. of aseptic revisions (%)	OR, 95% CI	
			Non-adjusted	Adjusted
≤ 5 PMNs per PHF	8 (16.67)	59 (73.8)	Ref.	Ref.
5–10 PMNs per PHF	14 (29.17)	14 (17.5)	7.37 (2.59, 20.99)	10.29 (2.58, 41.09)
> 10 PMNs per PHF	26 (54.17)	7 (8.8)	27.39 (8.99, 83.49)	29.16 (6.81, 124.76)

determined in 5–10 separate microscopic fields. The average was calculated as the result of frozen section.

Definition of PJI

Diagnosis of PJI was based on the MSIS criteria for infection [3]. PJI was defined when the following occur:

1. Two positive periprosthetic cultures grew phenotypically identical organisms, or
2. A sinus tract communicating with the joint existed, or
3. Three of the following five criteria were met:

   (1) Elevated serum ESR and CRP
   (2) Elevated synovial fluid white blood cell count or 2+ change on leukocyte esterase test strip
   (3) Elevated synovial fluid polymorphonuclear neutrophil percentage
   (4) Positive histologic analysis of periprosthetic tissue
   (5) A single positive culture

Statistical analysis

Categorical variables were presented as frequencies and percentages, and continuous variables as means and standard deviation. The clinical characteristics between groups were compared with the use of the independent *t*-test or Mann–Whitney test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

Both univariate and multivariable logistic regression analyses were performed to assess the relationship between frozen section results and PJI. In the multivariable model, we adjusted for gender, age, BMI, joint of interest, diabetes mellitus, rheumatoid arthritis, and CNS. Unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were reported. For this analysis, frozen section results were first modeled as a categorical variable (≤ 5, 5–10, or > 10 PMNs per HPF). Additionally, the 3 original categories were also modeled as a continuous variable to test for a liner trend in a dose-response analysis (*p* for trend).

Three diagnostic models of PJI were constructed using logistic multivariable regression models, with model 1 including serum ESR and CRP, model 2 including model 1 plus frozen sections > 5 PMNs per HPF, and model 3 including model 1 plus frozen sections > 10 PMNs per HPF. Then, the nomograms of the three models were developed. Receiver operating characteristic (ROC) curves were generated using bootstrap resampling (times = 500) to determine the diagnosed value of the three models. The area under the ROC curve (AUC) with 95% CI was used as a measure of diagnostic accuracy, and all models were compared by using the DeLong method [18]. A *p* value less than 0.05 was considered significant. All of the statistical analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solution, Inc., Boston, MA).

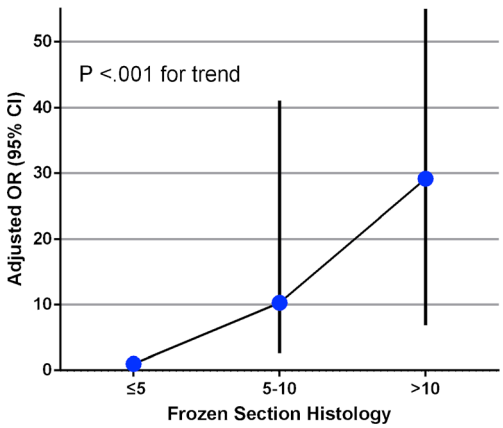

Fig. 1 Dose-response analysis

Results

According to the MSIS criteria for PJI, 48 patients were confirmed septic and 80 aseptic. The patient characteristics were shown in Table 1. No difference in gender, age, and BMI was observed between the PJI and aseptic groups. The organism profile of patients with PJI was shown in Table 2.

Patients with 5–10 and more than 10 PMNs per PHF had significantly higher unadjusted odds of PJI compared to those with less than 5 PMNs per PHF (Table 3). In the multivariable analysis, patients with 5–10 PMNs per PHF had significantly higher adjusted odds (adjusted OR, 10.29; 95% CI, 2.58 to

Table 4 Formulas of the three models

Model	Formula
Model 1	− 1.80380 + 0.19664 ∗ CRP + 0.03849 ∗ ESR
Model 2	− 3.43866 + 0.36659 ∗ CRP + 0.03123 ∗ ESR + 2.77662 ∗ (if frozen section > 5 PMNs per PHF is 1; or is 0)
Model 3	− 2.29445 + 0.21087 ∗ CRP + 0.03230 ∗ ESR + 2.27651 ∗ (if frozen section > 10 PMNs per PHF is 1; or is 0)

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

41.09) of PJI than those with no more than 5 PMNs per PHF, and the association was stronger for patients with more than 10 PMNs per PHF (adjusted OR, 29.16; 95% CI, 6.81, 124.76). In a separate dose-response analysis (Fig. 1), the odds of the diagnosis of PJI increased significantly with an increasing number of PMNs per PHF ($p < 0.001$ for trend).

The formulas of the three diagnostic models were present in Table 4, and the nomograms of models were shown in Supplementary Figure. Model 2 (81.25%) had the highest accuracy among the three models (model 1, 76.56%; model 3, 79.69%; Table 5). The AUC of model 1, model 2, and model 3 was 79.40% (95% CI, 69.84 to 86.64%), 89.30% (95% CI, 82.93 to 93.92%), and 85.52% (95% CI, 78.44 to 91.4%), respectively (Fig. 2). The AUC of model 1 was significantly lower than that of model 2 ($p = 0.002$) and model 3 ($p = 0.039$). Although the result was not significant ($p = 0.132$), there was a trend toward a higher AUC of model 2 than that of model 3. Additionally, the sensitivity of model 2 (85.42%) was higher than that of model 3 (81.25%) without decreasing specificity (78.75%).

In total, 63 (78.8%) cases in the aseptic group and 18 (37.5%) cases in the septic group had a dry tap or no synovial fluid analysis. In the 30 PJI cases (62.5%) with synovial fluid WBC counts (SFWBC), 26 cases (86.7%, 26/30) had a SFWBC more than 3000 cells/μ. Of them, 80.8% (21/26) were considered as infection in model 1, 92.3% (24/26) in model 2, and 88.5% (23/26) in model 3.

Discussion

Intra-operative frozen section histology for diagnosis of PJI is widely used to assist surgeons deciding whether to implant definitive prostheses (a one-stage exchange arthroplasty) or to insert an antibiotic cement spacer followed by reimplantation after a course of antibiotics in the revision arthroplasty (a two-stage exchange arthroplasty). In current literature, there is a lack of data on the histopathology for the diagnosis of PJI but more interests in exploring new serological and synovial tests, such as D-dimer and synovial alpha-defensin. There may be an explanation that frozen sections are not routinely obtained in several institutions due to no pathologist available, lack of communication between surgeons and pathologists, and limited knowledge of histological techniques and importance on the significance of diagnosis established with histology by surgeons.

To our best knowledge, this is the first study to evaluate the combination of serological tests and frozen sections for assessment of PJI. The results revealed that frozen section could significantly increase diagnostic values of serum ESR and CRP with the AUC of almost 90%. Additionally, although the results were not significant, the threshold of 5 PMNs per PHF had higher sensitivity and diagnostic accuracy than that of 10 PMNs per PHF without decreasing specificity.

Serum ESR and CRP remain as first-line screening tests in PJI literature due to the high sensitivity and routine accessibility, even in patients with inflammatory conditions [19]. Prior studies have reported the sensitivity of serum ESR and CRP ranges from 42 to 94% and 74 to 94%, respectively [19–22]. However, as their modest specificity, they should not be utilized solely but a combination with other tests, involving synovial fluid analyses and histology in the diagnosis of PJI.

While joint aspiration was a simple and critical tool in the diagnosis of PJI, it may be not routinely obtained in patients who underwent an intended revision arthroplasty. Additionally, a "dry tap" may occasionally encounter, especially in hip procedures. For patients without pre-operative aspiration results but with equivocal serological tests, the decision-making process may be based on intra-operative

Table 5 Performance of the three models

	Cutoff	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Model 1	− 0.9564	81.25	73.75	65.00	86.76	76.56
Model 2	− 0.3089	85.42	78.75	70.69	90.00	81.25
Model 3	− 1.0040	81.25	78.75	69.64	87.50	79.69

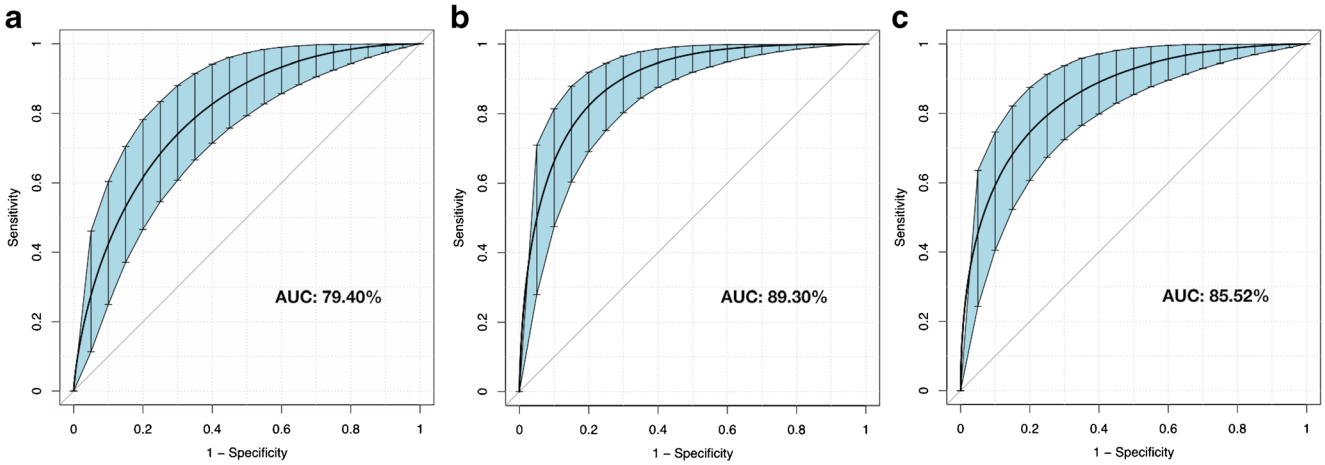

Fig. 2 Receiver operating characteristic curves (ROCs) for the three models; (**a**) model 1, (**b**) model 2, and (**c**) model 3. Blue shading shows the bootstrap-estimated 95% CI with the area under the ROC curve (AUC)

frozen sections. Moreover, negative results for both serum ESR and CRP do not exclude the diagnosis of periprosthetic joint infection (PJI). Our results revealed that the combination of serological tests and frozen section may be reliable in the assessment of PJI.

Our results reveal that frozen sections performed well in predicting PJI. Furthermore, there was an apparent dose-response effect between frozen section results and PJI. There have been a large number of studies over the past forty years which showed that the presence of PMN infiltrates in periprosthetic tissues is associated with the diagnosis of PJI. The importance of histology in the assessment of PJI has been reflected by its inclusion in the MSIS criteria for PJI that has been widely accepted worldwide [23]. The histology techniques involved intra-operative frozen sections and post-operative permanent paraffin sections. Compared with paraffin sections for final assessment, frozen sections mainly help surgeons diagnose or rule out PJI and decide the following management in the operation. The diagnostic values of frozen section in PJI have been inconsistent in the literature with sensitivity and specificity being reported to vary from 18 to 100% [7, 24–28]. Tsaras and his colleagues conducted a systematic review and meta-analysis using twenty-six studies involving 3269 patients undergoing revision hip or knee arthroplasty [28]. The pooling data showed that frozen sections had a pooled diagnostic OR of 54.7, a likelihood ratio of a positive test of 12.0, and a likelihood ratio of a negative test of 0.23 for the diagnosis of PJI, which was similar with our results.

The best thresholds of frozen sections remain controversial [11, 23, 28]. A meta-analysis by Tsaras et al. compared the diagnostic OR and likelihood ratios of five and ten PMNs per PHF as the threshold and did not find any difference in diagnostic performance between the two cutoff points [28]. Another meta-analysis by Zhao et al. suggested that although there was no difference in sensitivity or diagnostic OR, specificity was significantly higher for ten than for five PMNs per PHF as the threshold for diagnosing PJI solely [11]. They explained that the different results from Tsaras et al. were because Tsaras et al. failed to use sensitivity/specificity as the indexes. However, most studies enrolled in both two meta-analyses were limited due to high heterogeneity among included studies (e.g., differences in the inclusion and exclusion criteria, tissue sampling bias, and technique of the pathologists) and a non-standardized definition of PJI. Inconsistent with our hypothesis, the current results revealed a higher sensitivity without decreasing specificity for five than ten PMNs per HPF when combining with serum ESR and CRP in the diagnosis of PJI. Therefore, we recommend a cut-off value of five PMNs per PHF as the threshold in diagnosing PJI.

Several limitations should be considered. First, the study was retrospective in nature and thus was subject to its inherent limitations and biases. Second, the results were from a single institution and the sample size was not large. However, bootstrap resampling ($n = 500$), an internal validation method, was performed in the present study. Third, the numbers of frozen section samples taken were different among patients that range from 3 to 5, which may affect the resection results. Fourth, the diagnostic accuracy may be underestimated as only patients who were deemed to have a moderate or high risk of infection may have frozen section results. Therefore, we believed a better performance of the combination of serum tests and frozen sections for the assessment of PJI in a consecutive cohort. Lastly, although MSIS criteria are the preferred standard for PJI, the accuracy is not 100% [29].

Conclusions

This study reveals that intra-operative frozen sections significantly increased the performance of serum ESR and CRP in the diagnosis of PJI. The combination of serological tests and frozen sections for the assessment of PJI may be reliable in patients

without synovial fluid analyses. A threshold of five PMNs per PHF had greater sensitivity without decreasing specificity. These findings should keep in borne when diagnosing or ruling out PJI intra-operatively, especially for patients without joint aspiration analyses. Further prospective studies with larger cohorts are required to validate these results.

Acknowledgements The authors would like to thank all staff from the participating departments and clinics.

Compliance with ethical standards

Competing interests On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Perfetti DC, Boylan MR, Naziri Q et al (2017) Have periprosthetic hip infection rates plateaued? J Arthroplast 32:2244–2247. https://doi.org/10.1016/j.arth.2017.02.027
2. Kurtz SM, Lau EC, Son M-S et al (2018) Are we winning or losing the battle with periprosthetic joint infection: trends in periprosthetic joint infection and mortality risk for the Medicare population. J Arthroplast. https://doi.org/10.1016/j.arth.2018.05.042
3. Parvizi J, Zmistowski B, Berbari EF et al (2011) New definition for periprosthetic joint infection: from the workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res 469:2992–2994. https://doi.org/10.1007/s11999-011-2102-9
4. Parvizi J, Gehrke T (2014) Definition of periprosthetic joint infection. J Arthroplast 29:1331. https://doi.org/10.1016/j.arth.2014.03.009
5. Pandey R, Drakoulakis E, Athanasou NA (1999) An assessment of the histological criteria used to diagnose infection in hip revision arthroplasty tissues. J Clin Pathol 52:118–123
6. Tohtz SW, Müller M, Morawietz L et al (2010) Validity of frozen sections for analysis of periprosthetic loosening membranes. Clin Orthop Relat Res 468:762–768. https://doi.org/10.1007/s11999-009-1102-5
7. Athanasou NA, Pandey R, de Steiger R et al (1995) Diagnosis of infection by frozen section during revision arthroplasty. J Bone Joint Surg Br 77:28–33
8. Bori G, Soriano A, García S et al (2006) Low sensitivity of histology to predict the presence of microorganisms in suspected aseptic loosening of a joint prosthesis. Mod Pathol 19:874–877. https://doi.org/10.1038/modpathol.3800606
9. Bori G, Soriano A, García S et al (2009) Neutrophils in frozen section and type of microorganism isolated at the time of resection arthroplasty for the treatment of infection. Arch Orthop Trauma Surg 129:591–595. https://doi.org/10.1007/s00402-008-0679-6
10. Muñoz-Mahamud E, Bori G, García S et al (2013) Usefulness of histology for predicting infection at the time of hip revision for the treatment of Vancouver B2 periprosthetic fractures. J Arthroplast 28:1247–1250. https://doi.org/10.1016/j.arth.2012.12.016
11. Zhao X, Guo C, Zhao G-S et al (2013) Ten versus five polymorphonuclear leukocytes as threshold in frozen section tests for periprosthetic infection: a meta-analysis. J Arthroplast 28:913–917. https://doi.org/10.1016/j.arth.2012.10.015
12. Parvizi J, Tan TL, Goswami K et al (2018) The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplast. https://doi.org/10.1016/j.arth.2018.02.078
13. Francés Borrego A, Martínez FM, Cebrian Parra JL et al (2007) Diagnosis of infection in hip and knee revision surgery: intraoperative frozen section analysis. Int Orthop 31:33–37. https://doi.org/10.1007/s00264-005-0069-4
14. Banit DM, Kaufer H, Hartford JM (2002) Intraoperative frozen section analysis in revision total joint arthroplasty. Clin Orthop Relat Res:230–238
15. Partridge DG, Winnard C, Townsend R et al (2018) Joint aspiration, including culture of reaspirated saline after a "dry tap", is sensitive and specific for the diagnosis of hip and knee prosthetic joint infection. Bone Joint J 100-B:749–754. https://doi.org/10.1302/0301-620X.100B6.BJJ-2017-0970.R2
16. Roberts P, Walters AJ, McMinn DJ (1992) Diagnosing infection in hip replacements. The use of fine-needle aspiration and radiometric culture. J Bone Joint Surg Br 74:265–269
17. Feldman DS, Lonner JH, Desai P, Zuckerman JD (1995) The role of intraoperative frozen sections in revision total joint arthroplasty. J Bone Joint Surg Am 77:1807–1813
18. DeLong ER, DeLong DM, Clarke-Pearson DL (1988) Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 44:837–845
19. Saleh A, George J, Faour M et al (2018) Serum biomarkers in periprosthetic joint infections. Bone & Joint Research 7:85–93. https://doi.org/10.1302/2046-3758.71.BJR-2017-0323
20. Greidanus NV, Masri BA, Garbuz DS et al (2007) Use of erythrocyte sedimentation rate and C-reactive protein level to diagnose infection before revision total knee arthroplasty: a prospective evaluation. J Bone Joint Surg Am 89:1409–1416. https://doi.org/10.2106/JBJS.D.02602
21. McArthur BA, Abdel MP, Taunton MJ et al (2015) Seronegative infections in hip and knee arthroplasty: periprosthetic infections with normal erythrocyte sedimentation rate and C-reactive protein level. Bone Joint J 97-B:939–944. https://doi.org/10.1302/0301-620X.97B7.35500
22. Yi PH, Cross MB, Moric M et al (2014) The 2013 Frank Stinchfield award: diagnosis of infection in the early postoperative period after total hip arthroplasty. Clin Orthop Relat Res 472:424–429. https://doi.org/10.1007/s11999-013-3089-1
23. Zmistowski B, Della Valle C, Bauer TW et al (2014) Diagnosis of periprosthetic joint infection. J Arthroplast 29:77–83. https://doi.org/10.1016/j.arth.2013.09.040
24. Kwiecien G, George J, Klika AK et al (2017) Intraoperative frozen section histology: matched for Musculoskeletal Infection Society criteria. J Arthroplast 32:223–227. https://doi.org/10.1016/j.arth.2016.06.019
25. Bori G, McNally MA, Athanasou N (2018) Histopathology in periprosthetic joint infection: when will the morphomolecular diagnosis be a reality? Biomed Res Int 2018:1–10. https://doi.org/10.1155/2018/1412701
26. Abdul-Karim FW, McGinnis MG, Kraay M et al (1998) Frozen section biopsy assessment for the presence of polymorphonuclear leukocytes in patients undergoing revision of arthroplasties. Mod Pathol 11:427–431
27. Della Valle CJ, Bogner E, Desai P et al (1999) Analysis of frozen sections of intraoperative specimens obtained at the time of reoperation after hip or knee resection arthroplasty for the treatment of infection. J Bone Joint Surg Am 81:684–689
28. Tsaras G, Maduka-Ezeh A, Inwards CY et al (2012) Utility of intraoperative frozen section histopathology in the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am 94:1700–1711. https://doi.org/10.2106/JBJS.J.00756
29. Parvizi J, Tan TL, Goswami K et al (2018) The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplast 33:1309–1314. e2. https://doi.org/10.1016/j.arth.2018.02.078