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Preoperative Aspiration Culture for Preoperative Diagnosis of Infection in Total Hip or Knee Arthroplasty

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This meta-analysis evaluated preoperative aspiration culture for diagnosing prosthetic joint infection (PJI) in total hip arthroplasty (THA) and total knee arthroplasty (TKA). The pooled sensitivity and specificity were 0.72 (95% confidence interval, 0.65 to 0.78) and 0.95 (0.93 to 0.97), respectively. Subgroup analyses revealed nonsignificant worse diagnostic performance for THA than for TKA (sensitivity, 0.70 versus 0.78; specificity, 0.94 versus 0.96). Preoperative aspiration culture has moderate to high sensitivity and very high specificity for diagnosing PJI.

Prosthetic joint infection (PJI) is a common and challenging complication for both patients and surgeons (1–4). The incidence of PJI after total joint arthroplasty (TJA) is 1 to 12% (5, 6). A multitude of preoperative tests are available to clinicians for diagnosing PJI, including preoperative laboratory testing and radiological examination (7). However, the limited sensitivity and specificity of these tests pose difficulties in distinguishing between PJI and other causes of joint failure, such as aseptic loosening (1, 8). Guidelines by the American Academy of Orthopaedic Surgeons (AAOS) and Infectious Diseases Society of America (IDSA) strongly recommend preoperative aspiration culture for assessment for PJI (9, 10). In recent years, several studies have assessed the diagnostic value of preoperative aspiration culture for PJI. However, the sensitivities (range, 0 to 1) and specificities (range, 0.54 to 1) among studies are inconsistent (7, 11–43). We therefore performed a meta-analysis for evaluating the detection validity of preoperative aspiration culture in the diagnosis of PJI.

We searched Medline, Embase, and Ovid from 1 January 1990 through 1 May 2013 with combined search terms using medical subject headings (MeSH) or free-text words: (i) "aspiration," "aspirate," or "synovial fluid" and (ii) "joint prosthesis," "prosthesis infection," "septic loosening," "aseptic loosening," "replacement," or "arthroplasty." We also manually searched related review articles and the reference lists of eligible studies. The reviewers independently evaluated the selected studies using the following inclusion criteria: (i) accuracy of preoperative aspiration culture, in comparison with visible purulence of the surgical site, presence of a sinus tract (fistula) communicating with the prosthesis, acute inflammation in histopathology sections of periprosthetic tissue, or simultaneously obtained microbiologic cultures from at least two periprosthetic tissue samples (the reference standard), for the diagnosis of joint infection; (ii) sufficient data to allow us to calculate the true-positive (TP), false-negative (FN), false-positive (FP), and true-negative (TN) values; and (iii) $\geq$10 patients with data extraction using a standardized data collection form (X.Q., Z.Z., and C.W.). If different studies included the same patients, we used the one that was the most detailed. Discrepancies were resolved by discussion with other investigators and consulting the original articles (Z.Z. and K.D.).

We estimated the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and area under the curve (AUC) of summary receiver-operating characteristic curves to evaluate the capability of preoperative aspiration culture assays in diagnosing PJI. For each study, we constructed a 2-by-2 contingency table consisting of TP, FN, FP, and TN results. We then calculated sensitivity as TP/(TP + FN), specificity as TN/(FP + TN), DOR as (TP $\times$ TN)/(FP $\times$ FN), PLR as sensitivity/(1 $-$ specificity), and NLR as (1 $-$ sensitivity)/specificity. We performed subgroup analyses to assess potential heterogeneity using the following stratification: type of arthroplasty (total hip arthroplasty versus total knee arthroplasty), publication year ($<$2002 versus $\geq$2002), geographical location (United States versus Europe), number of patients ($<$100 versus $\geq$100), study design (prospective versus retrospective), patient enrollment (consecutive versus not provided). We also constructed Deeks' funnel plot asymmetry test to evaluate potential publication bias. All statistical analyses were performed using STATA version 11 (StataCorp, College Station, TX, USA). *P* values of $<$0.05 were considered statistically significant.

We scanned 2,179 titles and abstracts, of which we excluded 1,970 studies during the first phase of our selection strategy. During the second phase (full-text review), we excluded 175 studies. A total of 34 articles, comprising 3,332 patients, fulfilled all inclusion criteria and were subjected to analysis (see Table S1 in the supplemental material). Twenty-one studies detected PJI in total hip

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arthroplasty (THA), 4 in total knee arthroplasty (TKA), and 9 in both THA and TKA. Thirteen studies enrolled patients prospectively. Patient enrolments were consecutive in 11 studies and were not documented in 23. We found significant heterogeneity for all test performances.

The pooled sensitivity, specificity, PLR, NLR, DOR, and AUC estimates for the detection of PJI using preoperative aspiration culture were 0.72 (95% confidence interval [CI], 0.65 to 0.78), 0.95 (95% CI, 0.93 to 0.97), 15.3 (95% CI, 10.6 to 22.1), 0.29 (95% CI, 0.23 to 0.38), 52 (95% CI, 31 to 86), and 0.94 (95% CI, 0.92 to 0.96), respectively (Fig. 1A). The Deeks' funnel plot asymmetry test found no evidence of a small-study effect for preoperative aspiration culture ($P = 0.12$) (Fig. 1B). In subgroup analyses, test performances varied by the type of arthroplasty, publication year, geographical location, patient number, study design, and patient enrollment (Table 1). The sensitivity and specificity of THA were 0.70 (95% CI, 0.59 to 0.79) and 0.94 (95% CI, 0.91 to 0.96), and those of TKA were 0.78 (95% CI, 0.60 to 0.90) and 0.96 (95% CI, 0.70 to 1.00), respectively. Prospective studies revealed a nonsignificantly lower sensitivity of 0.69 (95% CI, 0.58 to 0.78) compared to retrospective studies.

This meta-analysis showed that preoperative aspiration culture had moderate to high sensitivity (72%) and very high specificity (95%) for diagnosing PJI, which is acceptable for clinical practice (Fig. 2).

The diagnosis of PJI after TJA remains a challenge (1, 7, 10). Of the numerous preoperative tests available—including white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels—no test has perfect sensitivity and specificity (1, 7, 10, 44). However, their diagnostic ability is not entirely reliable; a recent meta-analysis showed that the sensitivity and specificity of WBC count, ESR, and CRP levels were 45%, 75%, and 88% and 87%, 70%, and 74%, respectively (44). While fluorodeoxyglucose positron emission tomography (FDG-PET) (sensitivity, 82%; specificity, 87%) and antigranulocyte scintigraphy with ^{99m}Tc-labeled monoclonal antibodies (sensitivity, 83%; specificity, 80%) show good diagnostic capabilities (45, 46), these tests are expensive, complex, and need special operators, limiting their clinical application.

Moreover, we must highlight that with a joint aspiration sample, culture and leukocyte counts and percentages of neutrophils can be realized. Several studies have assessed the diagnostic value of preoperative aspiration leukocyte count and percentages of neutrophils for PJI. The sensitivity of aspiration leukocyte count ranges from 36% to 100%, with specificity from 60% to 99% (35, 47–50). And the sensitivity of aspiration percentages of neutrophils ranges from 71% to 98%, with specificity from 62% to 98% (35, 47, 48, 51, 52). Furthermore, low-grade infections caused by low-virulent microorganisms usually have normal values of inflammatory markers. So it is important to perform preoperative aspiration culture if there is a high suspicion of PJI even though values of inflammatory markers are normal.

Guidelines by the AAOS and IDSA strongly recommend preoperative aspiration culture for detecting PJI. Our results demonstrate that preoperative aspiration culture is a diagnostic method with very high specificity, in agreement with the AAOS and IDSA guidelines. However, the true diagnostic ability of preoperative aspiration cultures depends on whether bacteria are accurately recovered from synovial fluid aspirate (8, 53), which is influenced by various factors, including synovial fluid volume, antibiotic use, and specimen contamination. Therefore, occasional false-positive results may induce a moderate sensitivity.

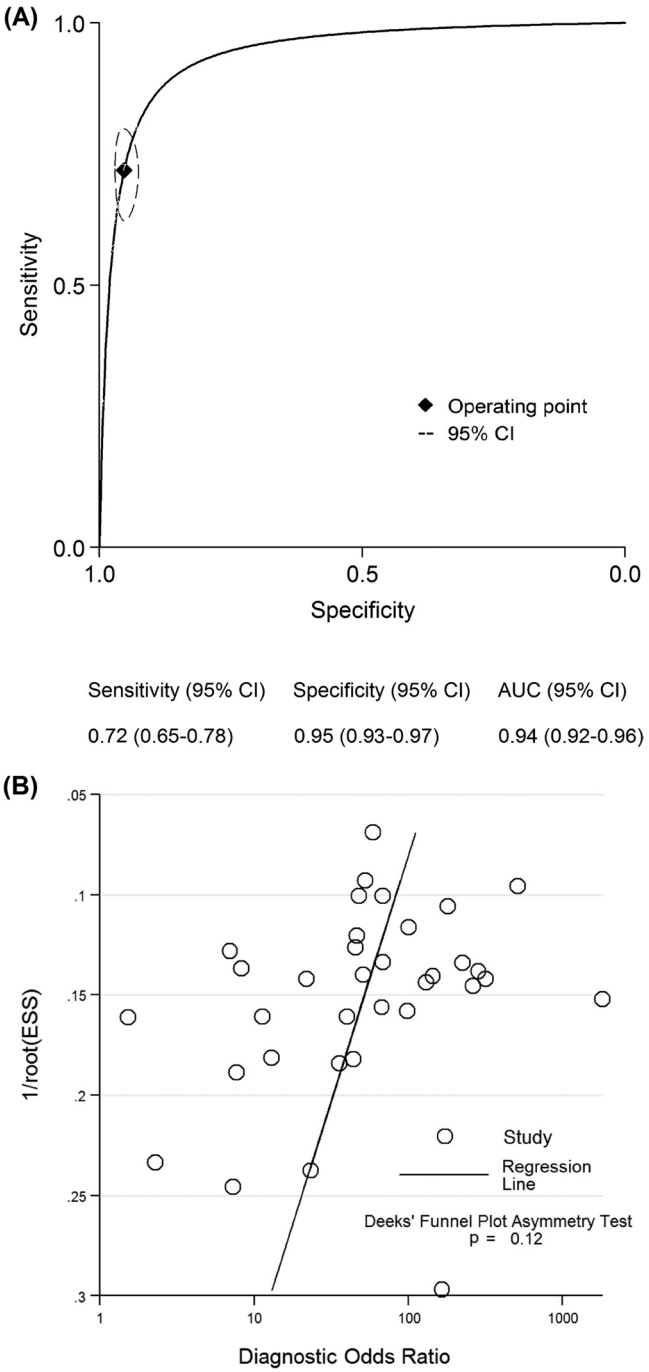

FIG 1 Summary ROC curves (A) and funnel plots (B) for preoperative aspiration culture. Curves include a summary operating point for sensitivity and specificity on the curve and a 95% confidence contour ellipsoid.

Our study has certain limitations. First, the reference standards in the included studies varied, with no established gold standard. Misclassification bias resulting from imperfect reference standards may affect the estimates of diagnostic accuracy of a tested method (45). Second, 13 studies were prospectively designed. Study design was assessed as a potential source of heterogeneity;

TABLE 1 Accuracy estimates from subgroup analyses

Targeted study characteristic	No. of studies	No. of patients	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR
Overall studies	34	3,332	0.72 (0.65–0.78)	0.95 (0.93–0.97)	0.94 (0.92–0.96)	15.3 (10.6–22.1)	0.29 (0.23–0.38)	52 (31–86)
Type of arthroplasty								
Total hip arthroplasty	21	2,134	0.70 (0.59–0.79)	0.94 (0.91–0.96)	0.94 (0.91–0.95)	11.3 (7.7–16.7)	0.32 (0.23–0.45)	35 (19–66)
Total knee arthroplasty	4	332	0.78 (0.60–0.90)	0.96 (0.70–1.00)	0.90 (0.88–0.93)	21.9 (1.8–262.1)	0.22 (0.11–0.47)	97 (5–2010)
Publication year								
<2002	17	1,613	0.74 (0.60–0.84)	0.95 (0.93–0.96)	0.96 (0.93–0.97)	14.3 (9.7–21.1)	0.28 (0.18–0.44)	51 (25–104)
≥2002	17	1,719	0.71 (0.63–0.78)	0.96 (0.92–0.98)	0.90 (0.87–0.92)	17.1 (8.2–35.8)	0.30 (0.23–0.40)	56 (23–136)
Geographical location								
United States	10	1,264	0.73 (0.57–0.85)	0.96 (0.92–0.98)	0.96 (0.93–0.97)	19.2 (9.5–38.6)	0.28 (0.17–0.47)	69 (26–178)
Europe	20	1,776	0.73 (0.65–0.80)	0.95 (0.92–0.97)	0.93 (0.91–0.95)	15.1 (9.0–25.6)	0.28 (0.21–0.37)	54 (27–108)
No. of patients								
<100	21	1,261	0.70 (0.59–0.79)	0.95 (0.92–0.97)	0.94 (0.91–0.95)	14.7 (8.5–25.5)	0.31 (0.22–0.45)	47 (21–102)
≥100	13	2,071	0.76 (0.67–0.83)	0.95 (0.92–0.97)	0.95 (0.92–0.96)	15.9 (10.1–25.0)	0.26 (0.19–0.35)	62 (36–107)
Study design								
Prospective	13	1,285	0.69 (0.58–0.78)	0.96 (0.92–0.98)	0.93 (0.90–0.95)	15.8 (8.6–28.9)	0.33 (0.23–0.45)	49 (23–104)
Retrospective	15	1,421	0.71 (0.56–0.83)	0.96 (0.92–0.98)	0.95 (0.93–0.97)	17.6 (8.7–35.6)	0.30 (0.19–0.49)	58 (21–161)
Patients enrollment								
Consecutive	11	1,356	0.71 (0.52–0.85)	0.94 (0.91–0.96)	0.95 (0.92–0.96)	11.6 (7.3–18.6)	0.31 (0.17–0.55)	38 (15–97)
Not provided	23	1,967	0.72 (0.65–0.78)	0.96 (0.93–0.98)	0.91 (0.89–0.93)	18.3 (10.2–32.8)	0.29 (0.23–0.37)	63 (31–127)

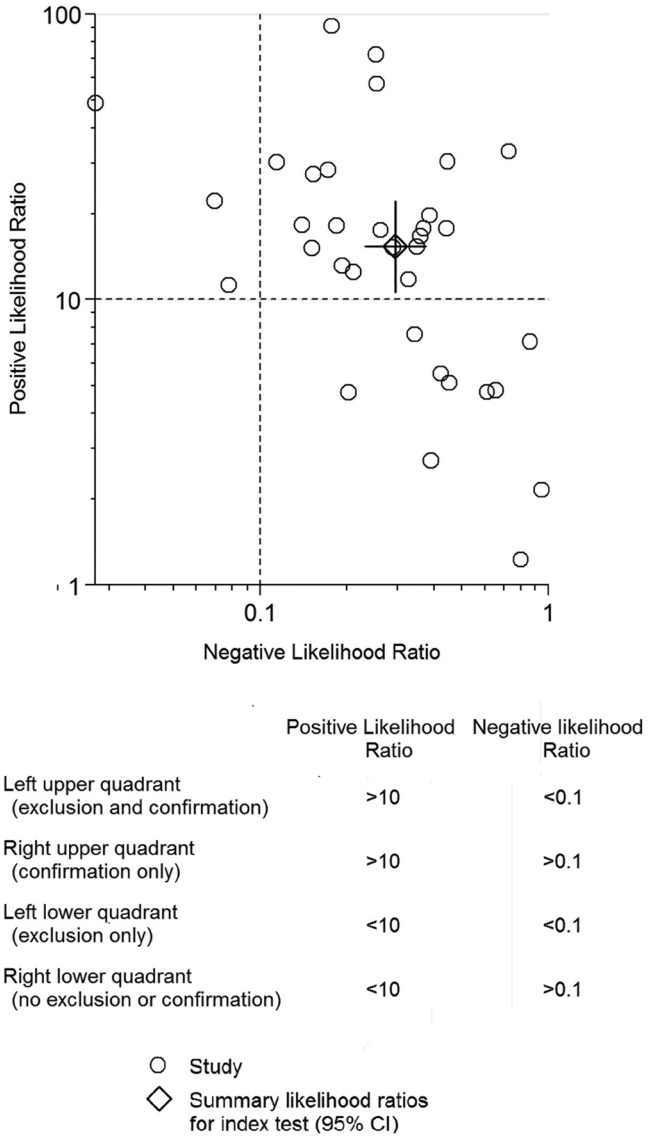

FIG 2 Likelihood ratio scattergram for preoperative aspiration culture. The likelihood ratio profile shows that preoperative aspiration culture is a potent tool for ruling out PJI in this patient population.

however, subgroup analysis showed that prospective study design did not significantly influence the sensitivity. Third, the summary results of this meta-analysis had high statistical heterogeneity. Although thorough subgroup analyses were included to investigate possible sources of heterogeneity, no causes of heterogeneity were revealed. These issues may reduce the strength of the conclusions drawn from this meta-analysis.

In conclusion, the meta-analysis indicates that preoperative aspiration culture may play a role in the diagnosis of PJI; however, identifying the optimal combination of diagnostic tests for PJI needs further studies.

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