REVIEW ARTICLE

Diagnostic Accuracy of the Synovial Fluid α-Defensin Lateral Flow Test in Periprosthetic Joint Infection: A Meta-analysis

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Objectives: There is a controversy on the diagnostic reliability and accuracy of synovial fluid α-defensin in periprosthetic joint infection (PJI). We performed this meta-analysis to evaluate the diagnostic accuracy of the α-defensin lateral flow test in PJI.

Methods: PubMed, Embase, and the Cochrane library were systematically searched, and articles (up to January 2020) on the diagnosis of hip and knee PJIs using the α-defensin Synovasure lateral flow test were included. The diagnostic accuracy of the α-defensin lateral flow test in PJI was evaluated using meta-analysis. The pooled sensitivity, specificity, accuracy, positive and negative likelihood ratio, diagnostic odds ratio, and post-test probabilities were calculated.

Results: Seventeen studies including 1443 cases were included. Meta-analysis showed the pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and a diagnostic odds ratio was 0.83 (95% *CI* 0.77, 0.88), 0.95 (95% *CI* 0.93, 0.97), 16.86 (95% *CI* 11.67, 24.37), 0.17 (95% *CI* 0.13, 0.24) and 85.30 (95% *CI* 47.76, 152.35), respectively. The area under the hierarchical summary receiver operating characteristic curve was 0.97 (95% *CI* 0.95, 0.98). Subgroup analysis also confirmed the high efficiency of α-defensin Synovasure lateral flow test in diagnosing PJIs, irrespective of ethnicity. Fagan's nomogram analysis there was a high positive post-test probability of 94% and a low negative post-test probability of 15%.

Conclusions: We indicated that the α-defensin lateral flow test had a high accuracy for diagnosing PJI. Large-scale studies are needed to validate its significance in PJI diagnosis.

Key words: Arthroplasty; Periprosthetic joint infection; Systematic review; α-defensin lateral flow test

Introduction

Periprosthetic joint infection (PJI) is an inevitable and catastrophic complication after total joint arthroplasty. The morbidity of PJI post primary total knee and hip arthroplasty is approximately 1%–4% and 1% within 2 years, respectively[1,2]. It increases by more than two-fold times after revision total hip and knee arthroplasty[3–5]. In addition, PJI is the most common cause for revision total joint arthroplasty, accounting for approximately 20%–47% of early or late revisions[6–8]. Although the incidence of PJI is relatively low, it causes

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profound health, financial, and socioeconomic burdens on patients and reduces the quality of life. The accurate and timely preoperative diagnosis of PJIs post arthroplasty surgeries is important to manage the catastrophic complication.

Some studies have shown the concordance between patient-related risk factors and the incidence of PJI. There is much evidence showing that comorbid conditions and medical risk factors including morbid obesity, malnutrition, hyperglycemia, malnutrition, hyperglycemia, cardiovascular disorders, and preoperative anemia associate with an increased adjusted risk of PJI[2,3,9,10]. The most common organisms identified in the infected joints include *Staphylococcus aureus* (*S. aureus*), methicillin-sensitive *S. aureus* (MRSA), and *S. epidermidis*[2,5,11]. Biomarkers including synovial fluid cell count[12], C-reactive protein (CRP)[13], interleukin-6 (IL-6), and α-defensin[12,14] have potential efficacy in diagnosing PJI. Accordingly, the diagnostic criteria as defined by the Musculoskeletal Infection Society (MSIS) included pathogen isolation, serum CRP, synovial leucocytes, and neutrophils[15], which has been regarded as the reference standard for diagnosing PJI.

Since the publication of MSIS criteria, there is tremendous evidence that shows the potential to improve the accuracy in PJI diagnosis. Alpha-defensin is a small (30–50 arginine-rich amino acid), cationic, and non-oxidative antimicrobial peptide that is mainly synthesized and secreted by polymorphonuclear lymphocytes including neutrophils (1, 2, 3, and 4 subtypes) and Paneth cells (5 and 6 subtypes) of the ileum in response to pathogens[16–20]. Alpha-defensin is naturally released by neutrophils into the synovial fluid in response to pathogens[16,21,22]. It induces rapid death of the microorganisms by promoting depolarization of the cell membrane *via* interacting with or binding to the negatively charged membranes[16,21,22]. Recent evidence shows that Alpha-defensin might be an ideal biomarker for PJI[14,23]. Ahmad *et al.*[14] proved that laboratory-based α-defensin ELISA test showed a higher ever reported accuracy in PJI diagnosis compared with Synovasure lateral flow test. In 2018, Han *et al.*[23] indicated that laboratory-based α-defensin ELISA test has a higher pooled sensitivity, specificity, and accuracy than the α-defensin lateral flow test (sensitivity: 0.96 *vs* 0.86; specificity: 0.97 *vs* 0.96; accuracy: 0.99 *vs* 0.95, respectively). However, some studies showed the higher accuracy of the α-defensin lateral flow test in PJI diagnosis than the MSIS criteria including CRP and erythrocyte sedimentation rate (ESR), and polymorphonuclear lymphocytes[2,24]. Accordingly, α-defensin protein has been recommended to be included in the diagnostic algorithm in the future[12,14,23]. Before that, the accuracy of the α-defensin lateral flow test in PJI should be fully analyzed.

Several studies focusing on the intraoperative performance of the α-defensin lateral flow test in PJI diagnosis have been published during the past 2 years[25–27]. The reanalysis of the performance of the α-defensin lateral flow test in PJI diagnosis is necessary. Therefore, the purpose of this study was to evaluate the diagnostic reliability and accuracy of the α-defensin lateral flow test in PJI.

Materials and Methods

Ethics Statement

This study was a systematic review and meta-analysis to evaluate the accuracy of the α-defensin lateral flow test in

TABLE 1 The study inclusion criteria (PICOS-criteria) used in this current study

Parameter	Inclusion criteria
Population	Patients have hip and knee PJIs after total hip/knee arthroplasty; without restrictions on sex, race, and age
Intervention	α-defensin lateral flow test (Synovasure™) was used to assess PJIs
Comparison	Without interventions before diagnosis of PJIs. Other diagnostic methods could be used as comparisons
Outcome	Diagnostic accuracy of PJI using α-defensin lateral flow test; The false-negative, false-positive, true positive, and true negative data were included.
Study design	Retrospective, prospective, and cohort studies published in English

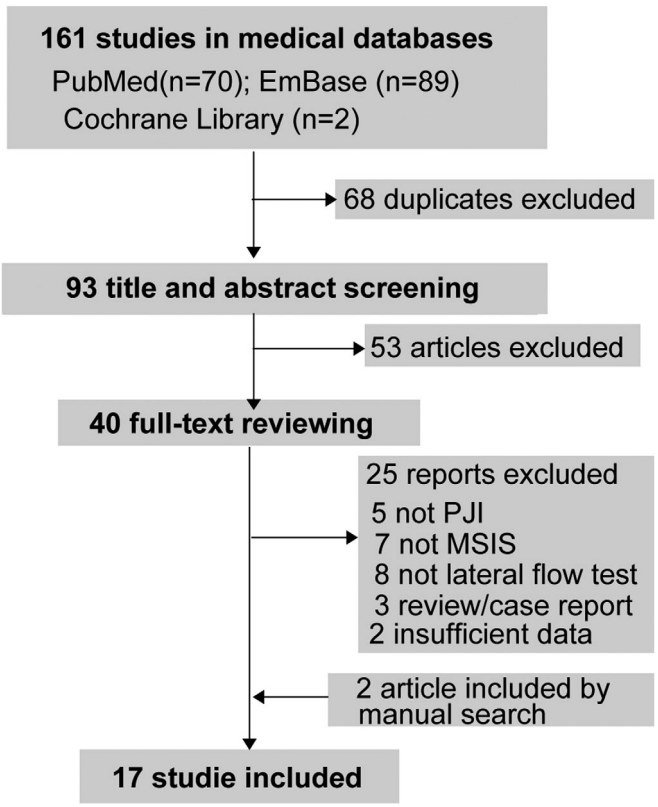

Fig. 1 Flow chart of selection process for eligible studies.

TABLE 2 The characteristics of the 17 included studies

Study	Year	Study design	Region	Participants	Median age (range, yrs)	Detection method	Assay platform	Gold standard	TP	FP	FN	TN
Kasparek *et al.*[31]	2016	retrospective	USA	40	71 (41–91)	Lateral flow test	Synovasure (CD Diagnostics)	MSIS	8	2	4	26
Suda *et al.*[32]	2017	prospective	Germany	28	67.7 (39–88)	Lateral flow test	Synovasure™ PJI Test (Zimmer, Warsaw, IN)	MSIS	10	3	3	14
Sigmund *et al.*[33]	2017	prospective	Austria	49	65 (20–89)	Lateral flow test	Synovasure	MSIS	9	2	4	34
Vincent *et al.*[34]	2018	prospective	France	39	NA (35–78)	Lateral flow test	Synovasure™, (Zimmer, Warsaw, IN)	MSIS	8	3	1	29
Scholten *et al.*[35]	2018	prospective	Netherlands	37	66 (51–81)	Lateral flow test	Synovasure™, (Zimmer, Warsaw, IN)	MSIS	1	0	4	29
Gehrke *et al.*[36]	2018	prospective	Germany	191	NA	Lateral flow test	Synovasure kit	MSIS	70	0	6	119
Sigmund *et al.*[37]	2018	retrospective	Germany	71	70 (41–85)	Lateral flow test	Synovasure kit (Zimmer Biomet)	MSIS	48	1	12	22
Riccio *et al.*[38]	2018	retrospective	Italy	72	68.7 (57–79)	Lateral flow test	Synovasure (CD Diagnostics)	MSIS	34	1	6	32
Renz *et al.*[39]	2018	prospective	Germany	167	70 (41–94)	Lateral flow test	Synovasure kit (Zimmer Biomet)	MSIS	38	1	7	33
Kuiper *et al.*[25]	2020	cohort	Netherlands	52	72 (9.2)	Lateral flow test	Synovasure (CD Diagnostics)	MSIS	6	5	0	41
Balato *et al.*[40]	2017	prospective	Italy	52	63 (48–79)	Lateral flow test	Synovasure (CD Diagnostics)	MSIS	14	1	2	34
Ding *et al.*[27]	2019	retrospective	Singapore	70	67	Lateral flow test	Synovasure kit (Zimmer Biomet)	MSIS	14	4	5	47
Plate *et al.*[41]	2018	prospective	Switzerland	109	63(48–85)	Lateral flow test	Synovasure(Zimmer Biomet, Winterthur, Switzerland)	MSIS	18	7	2	82
Sigmund *et al.*[26]	2019	prospective	Austria	101	71(22–91)	Lateral flow test	Synovasure (Zimmer Inc., Warsaw,IN, USA)	MSIS	21	4	9	67
Stone *et al.*[15]	2018	retrospective	USA	183	65.7 (34–91)	Lateral flow test	Synovasure (CD Diagnostics)	MSIS	30	6	7	140
Bingham *et al.*[42]	2014	retrospective	USA	61	64.2	Lateral flow test	Synovasure (CD Diagnostics Inc., Wynnewood, PA,USA)	MSIS	21	2	0	38
Berger *et al.*[43]	2017	cohort	Belgium	121	63.5 (36–88)	Lateral flow test	Synovasure (PJI lateral flow; Zimmer Biomet, Warsaw, Indiana)	MSIS	33	3	1	84

FN, false negative; FP, false positive; MSIS, Musculoskeletal Infection Society; NA, not applicable; TN, true negative; TP, true positive.

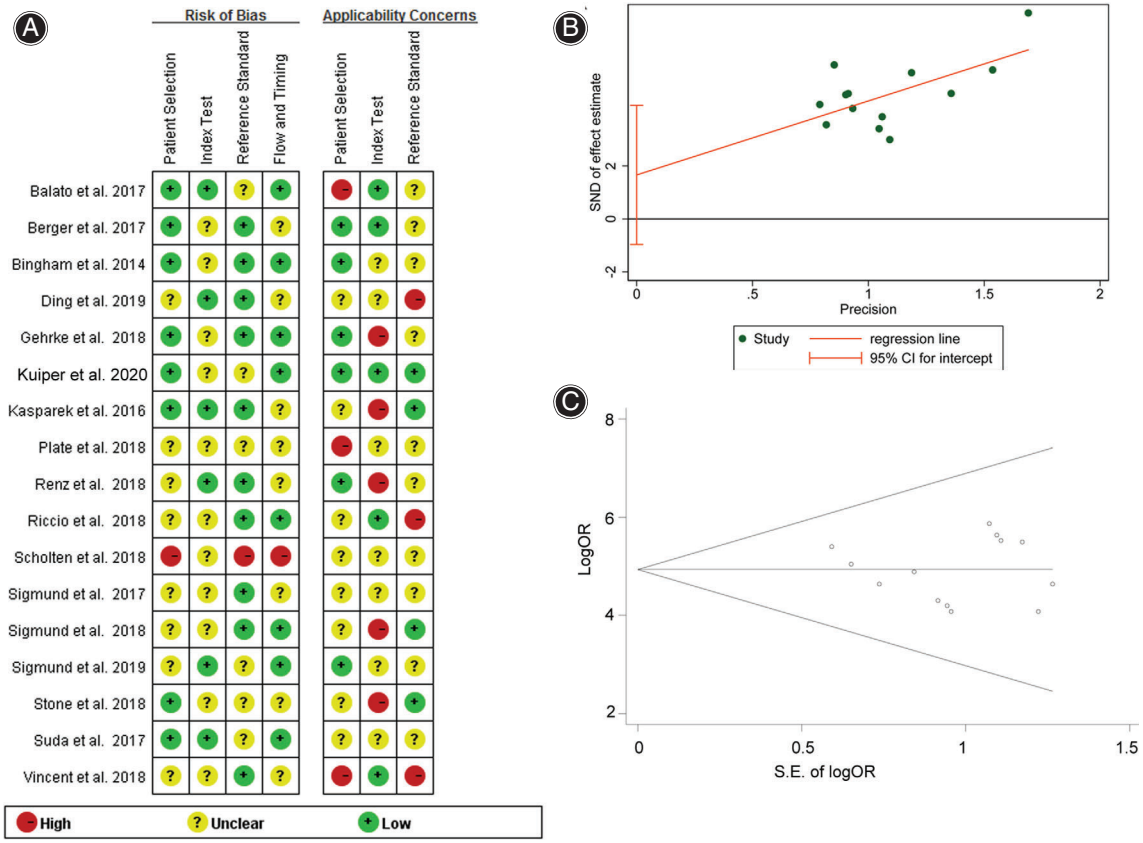

Fig. 2 Assessment of study quality and publication bias. (A) Quality assessment of included studies using QUADAS-2 tool. (B) The Egger's regression chart of published bias analysis. (C) The Begg's funnel for bias analysis. OR, odds ratio; CI, confidential interval.

diagnosing PJI. This study was performed according to the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses[28]. This systematic review did not include animal and human experiments, and the ethics committee approval was not applicable accordingly.

Search Strategy

Studies that were published up to January 2020 were searched in medical databases (PubMed, Embase, and the Cochrane library) using the keywords "periprosthetic joint infection," "prosthesis-related infections," "synovial α-defensin," "synovial alpha defensin" and "synovial defensin." The search strategy was "periprosthetic joint infection [Title/Abstract]) OR periprosthetic joint infection [MeSH Terms] OR prosthesis-related infections[Title/Abstract] OR prosthesis-related infections [MeSH Terms]" AND "α-defensin [MeSH Terms] OR α-defensin [Title/Abstract] OR alpha defensing [Title/Abstract] OR alpha defensing [MeSH Terms] OR defensing [Title/Abstract] OR defensin [MeSH Terms]" AND "sensitivity and specificity OR specificity* OR accuracy OR predictive value* OR ROC OR likelihood ratio*." Eligible studies were manually searched from the reference lists of the review articles and included studies.

Study Selection

Studies were independently selected by two authors. The inclusion criteria were: (i) studies that evaluate the diagnostic accuracy of PJI using α-defensin lateral flow test; (ii) studies did not put restrictions on sex, race, and age; (iii) English articles; (iv) PJIs were diagnosed according to the recommended criteria by MSIS or modified criteria by International Consensus Meeting; and (v) studies with complete clinical data (diagnosis criteria, assay platform, and the number of patients with true positive, false positive, true negative, and false negative PJI) that could be used for the sensitivity and specificity. The inclusion criteria are shown in Table 1. Patients with true-positive PJIs were defined as suspected PJIs by α-defensin test and final diagnosis by culture-positive microbiology investigation of preoperative aspirates and intraoperative samples of synovial fluid. False-positive was defined as: the α-defensin test showed positive reactions, but aspirates were culture-negative. True negatives were defined when the α-defensin test was negative and aspirates were

culture-negative, while false-negatives were defined when the α-defensin test was positive, but aspirates were culture-positive.

Studies were excluded if they were: (i) with incomplete data; (ii) duplicated articles (articles using the same study cohort); (iii) contained patients with infection of sites or organs outside the periarticular prosthesis; and (iv) reviews, animal studies, comments or conference paper without complete clinical data.

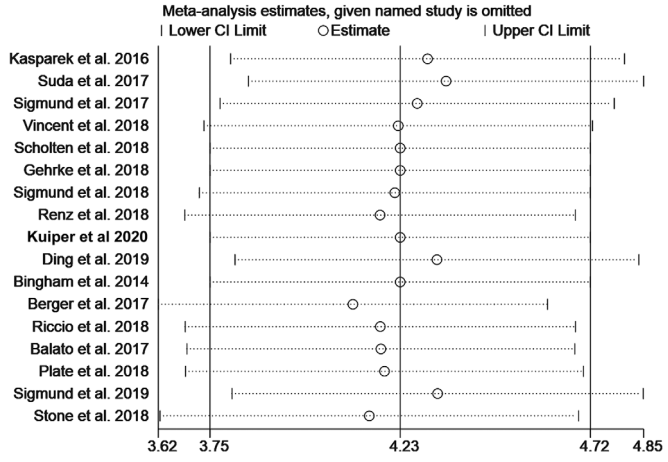

Fig. 3 Sensitivity analysis of the included studies.

Data Extraction and Quality Assessment

The false negative, false positive, true positive, and true negative data in each article were extracted. Article quality was evaluated independently by two reviewers using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) quality appraisal tool, which consists of four domains: patient selection, index test, reference standard, and flow and timing[29]. The risk of bias and applicability concerns of included studies was assessed. A discussion was required to resolve disagreements, and adjudication was made by a third reviewer.

Statistical Analysis

Data were processed and analyzed using the Stata 15.1 and RevMan5.2 software. A mixed-effect model for bivariate meta-analysis of diagnostic test accuracy studies was used to calculate the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio[24]. A hierarchical summary receiver operating characteristic curve (HSROC) was calculated. The heterogeneity of data across studies was statistically assessed by the Q test and I-square

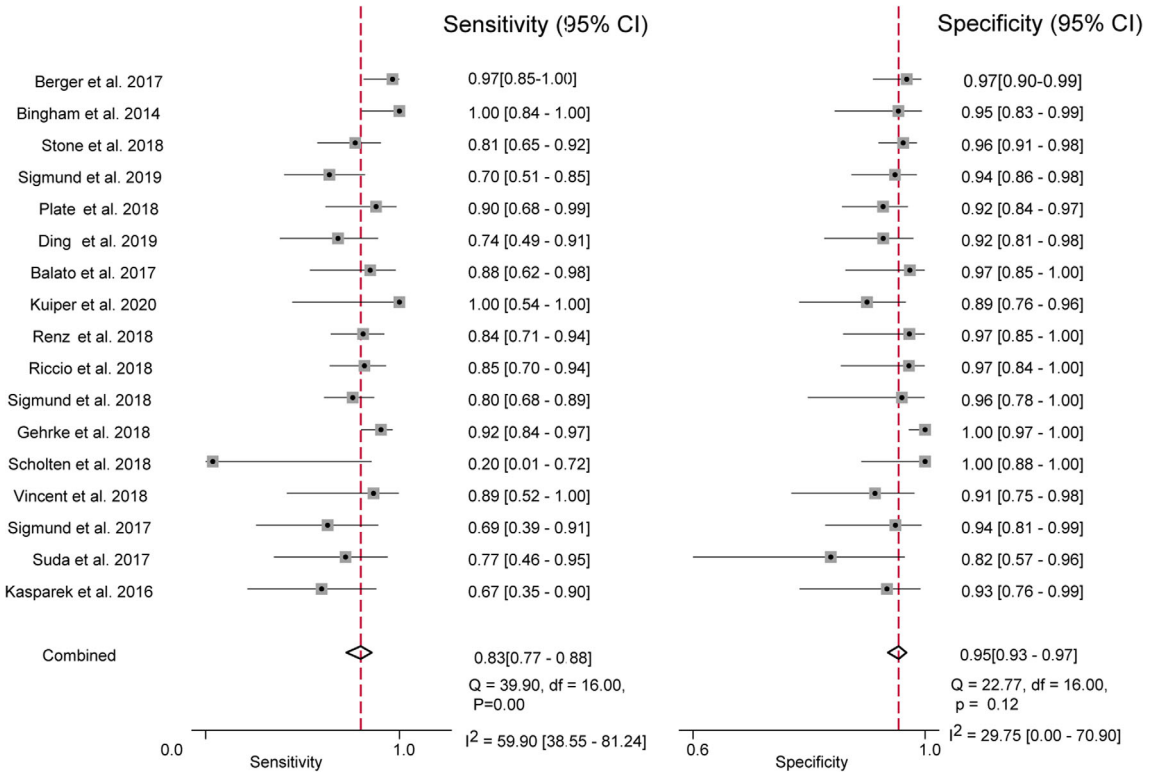

Fig. 4 Pooled sensitivity and specificity for the diagnostic efficiency of periprosthetic joint infection using the α-defensin lateral flow test. *CI*, confidence interval.

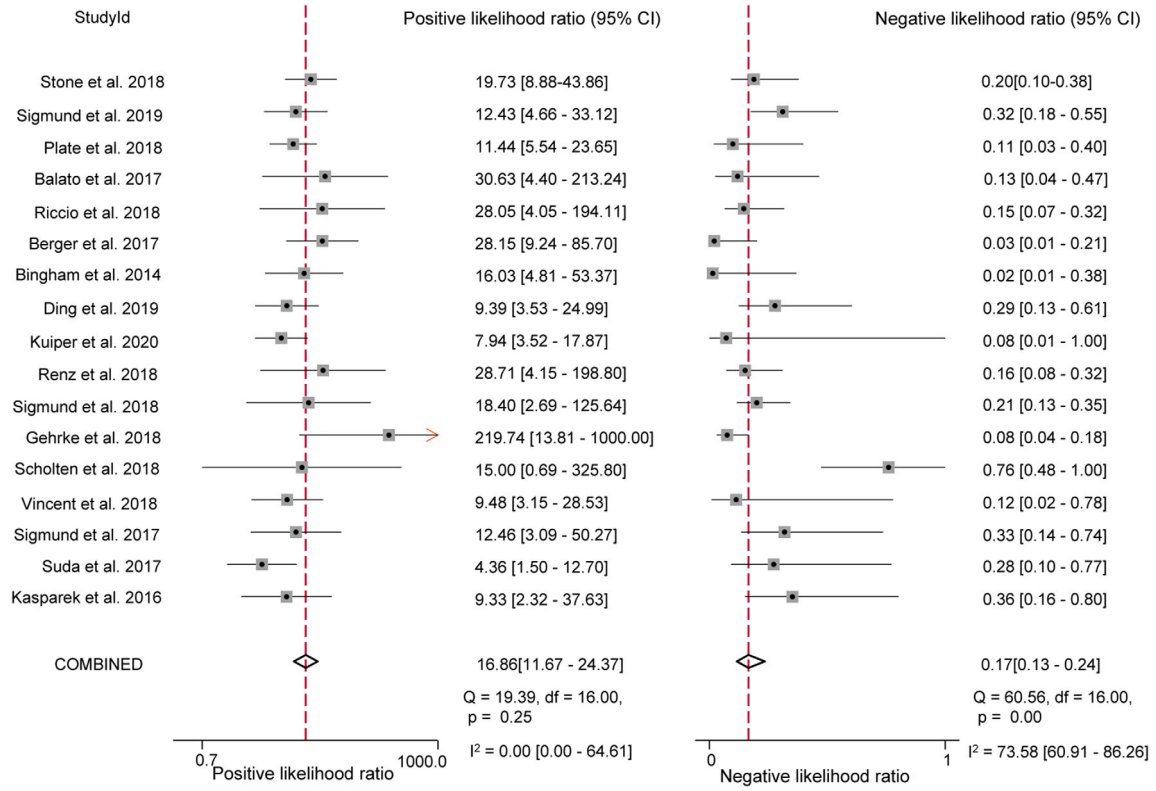

Fig. 5 Pooled positive and negative likelihood ratio for the diagnostic efficiency of periprosthetic joint infection using α-defensin lateral flow test. *CI*, confidence interval.

(I^2) statistic test. $P < 0.10$ and $I^2 > 50\%$ was defined as significant heterogeneity, or otherwise ($P > 0.10$ and $I^2 < 50\%$) significant homogeneity. Sensitivity analysis was performed to examine the source of heterogeneity. Publication bias was assessed using Egger's and Begg's tests. $P < 0.05$ was regarded as significant publication bias. Pre- and post-test odds were calculated using Fagan's nomogram[30]. Pre-test odds = pre-test probability/(1-pre-test probability), and post-test odds = post-test probability/(1- post-test probability).

Results

Study Selection

Medical databases included 161 studies that related to the keywords. After removing 68 duplicated articles, 93 publications were screened based on title and abstract. After the full-text screening, 17 studies[15,25–27,31–43] were included according to the predetermined inclusion and exclusion criteria (Fig. 1 and Table 1).

Study Characteristics

All the 17 studies[15,25–27,31–43] evaluated the diagnostic accuracy of the α-defensin lateral flow test in PJI (Table 2). In total, 1443 cases who underwent hip or knee arthroplasty surgeries were included. All studies included the number of patients with false negative, false positive, true positive, and true negative PJI. Among the 17 included studies, nine were prospective studies[26,32–36,39–41], six were retrospective studies[15,27,31,37,38,42], and two were cohort studies[25,43]. Also, 13 studies were performed in European countries, including Germany[32,36,37,39], France[34], Netherlands[25,35], Italy[38,40], Switzerland[41], Belgium[43], and Austria[26,33], three in the USA[15,31,42], and one in Singapore[27], and two in. All studies were published between 2014 and 2020.

Quality Assessment

There was a low risk of bias and applicability concerns based on the QUADAS-2 quality appraisal tool (Fig. 2A). Egger's (t = 1.39, 95% *CI* −0.96, 4.30, P = 0.191; Fig. 2B) and Begg's test (z = 1.95, Pr > |z| = 0.059, continuity corrected; Fig. 2C) indicated that there was no evidence of significant publication bias in the 17 included studies. Sensitivity analysis showed that the results of true positive were relatively stable and reliable (Fig. 3).

Meta-Analysis for the Diagnostic Efficiency of PJI Using the α-Defensin Lateral Flow Test

Meta-analysis indicated that the α-defensin lateral flow test had a pooled sensitivity of 0.83 (95% *CI* 0.77, 0.88; I^2 = 59.90%) and a pooled specificity of 0.95 (95% *CI* 0.93,

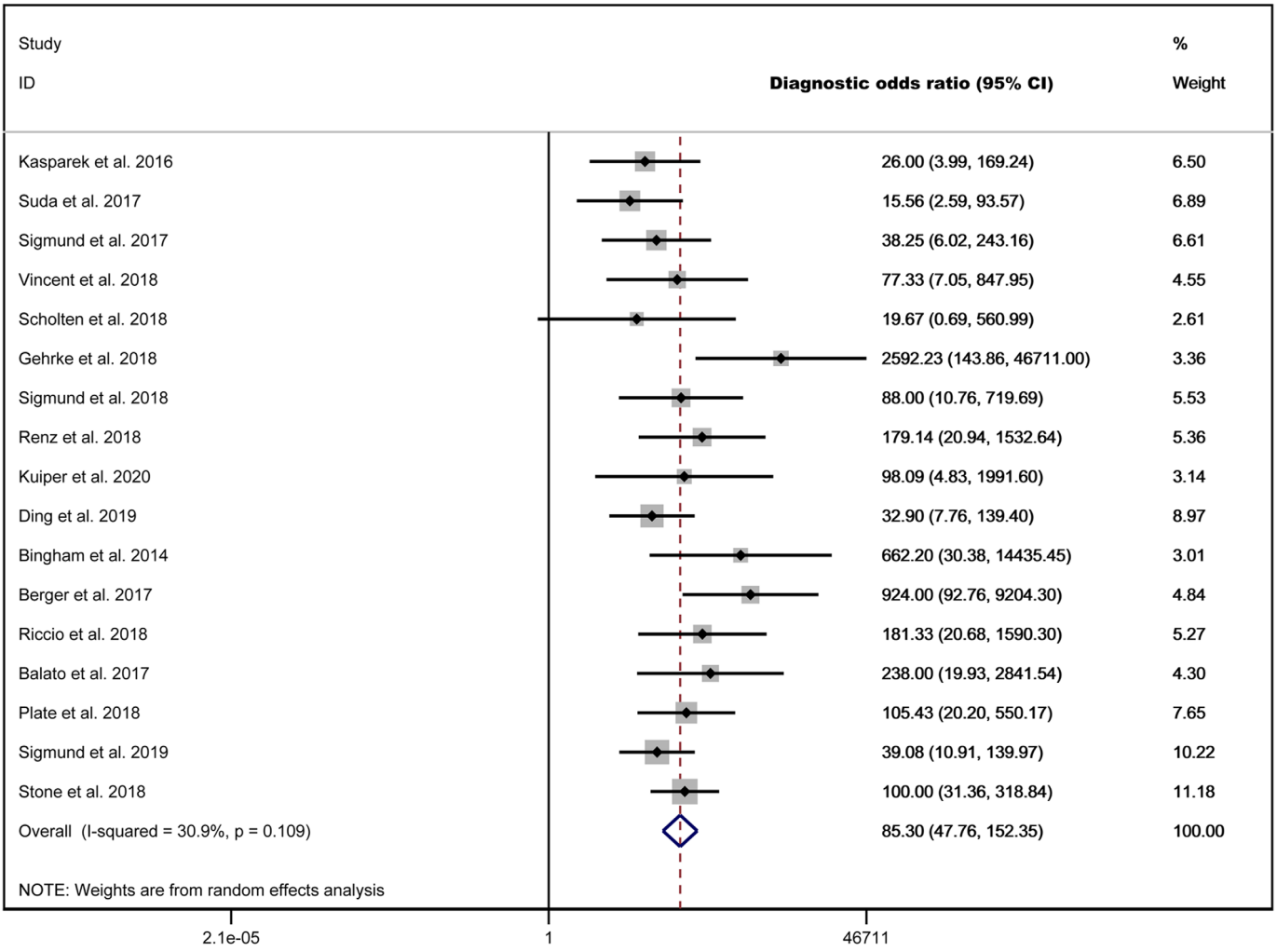

Fig. 6 The diagnostic odds ratio for the diagnostic efficiency of periprosthetic joint infection using the α-defensin lateral flow test. *CI*, confidence interval.

0.97; I^2 = 29.75%) in diagnosing PJIs (Fig. 4). The pooled positive likelihood ratio was 16.86 (95% *CI* 11.67, 24.37, I^2 = 0%), pooled negative likelihood ratio was 0.17 (95% *CI* 0.13, 0.24, I^2 = 0%; Fig. 5), with a pooled diagnostic odds ratio of 85.30 (95% *CI* 47.76, 152.35; I^2 = 30.9%; Fig. 6).

Subgroup Analysis for the Diagnostic Efficiency of PJI

Subgroup analysis was performed to analyze the regional difference in diagnostic efficiency of PJI using the α-defensin lateral flow test. We found the diagnostic sensitivity of the α-defensin lateral flow test for PJI was 0.81 (95% *CI* 0.67, 0.90) and 0.85 (95% *CI* 0.78, 0.90) in patients from Europe countries (n = 11)[25,32,34–41,43] and others (n = 6)[15,26,27,31,33,42], respectively, and the specificity was 0.96 (95% *CI* 0.92, 0.97) and 0.95 (95% *CI* 0.91, 0.97), respectively (Table 3). Besides, the α-defensin lateral flow test had a sensitivity of 0.82 (95% *CI* 0.76, 0.87) and 0.85 (95% *CI* 0.75, 0.91), and an equivalent specificity of 0.95 (95% *CI* 0.92, 0.97) in diagnosing PJI based on the retrospective experience and prospective/cohort experience, respectively (Table 3).

Accuracy and Validation

The area under the HSROC curve (AUC) was 0.97 (95% *CI* 0.95, 0.98), with a high sensitivity of 0.83 (95% *CI* 0.77, 0.88) and specificity of 0.95 (95% *CI* 0.93, 0.97; Fig. 7A). Based on the Fagan's nomogram analysis, we found there was a high positive post-test probability of 94% and a low negative post-test probability of 15% (Fig. 7B). These data showed that the α-defensin lateral flow test had high accuracy in diagnosing PJI. Subgroup analysis also confirmed that the AUC value of the α-defensin lateral flow test in PJI diagnosis were 0.97 (95% *CI* 0.95, 0.98) and 0.96 (95% *CI* 0.94, 0.97) in patients from Europe and other countries, respectively (Table 3), and were 0.96 (95% *CI* 0.94, 0.97), and 0.97 (95% *CI* 0.95, 0.98) based on the retrospective experience and prospective/cohort experience, respectively.

TABLE 3 The subgroup analysis for the efficiency of using α-defensin lateral flow test for periprosthetic joint infection

	Characteristic	No. of Study	Sensitivity (95%*CI*)	Specificity (95% *CI*)	Diagnostic *OR* (95% *CI*)	AUC (95% *CI*)	LRP (95% *CI*)	LRN (95% *CI*)
Pooled	All studies	17	0.83 (0.77,0.88)	0.95 (0.93,0.97)	97 (53, 176)	0.97 (0.95, 0.98)	16.9 (11.7,24.4)	0.17 (0.13,0.24)
Subgroup								
Study design	Retrospective	6	0.82 (0.76,0.87)	0.95 (0.92,0.97)	87 (47,162)	0.96 (0.94, 0.97)	16.5 (10.2,26.7)	0.19 (0.14,0.26)
	Prospective/cohort	11	0.85 (0.75,0.91)	0.95 (0.92,0.97)	115 (47,285)	0.97 (0.95, 0.98)	18.5 (10.3,33.2)	0.16 (0.09,0.28)
Region	North America/Others	6	0.81 (0.67,0.90)	0.95 (0.91,0.97)	74 (29,191)	0.96 (0.94, 0.97)	15.1 (8.9,25.6)	0.20 (0.11,0.37)
	Europe	11	0.85 (0.78,0.90)	0.96 (0.92,0.97)	121 (53,274)	0.97 (0.95, 0.98)	19.2 (10.8,34.0)	0.16 (0.10,0.24)

AUC, area under the hierarchical summary receiver operating characteristic curve; *CI*, confidential interval; LRN, likelihood ratio-negative; LRP, likelihood ratio-positive; *OR*, odds ratio.

Discussion

The diagnostic reliability and accuracy of α-defensin in PJI has been widely evaluated during the past few years[12,24,27,36,39,42], and some studies have confirmed that α-defensin is highly accurate for diagnosing PJI[27,36,39,42,44]. While some indicate that the α-defensin lateral flow test is less sensitive and may be used as a confirmatory test for PJI[23,39]. This systematic review and meta-analysis of 17 studies indicated that the α-defensin lateral flow test had a pooled sensitivity, specificity, and AUC of 0.83 (95% *CI* 0.77, 0.88), 0.95 (95% *CI* 0.93, 0.97), and 0.97 (95% *CI* 0.95, 0.98), respectively. The current study showed that the synovial fluid α-defensin test is a valuable indicator for PJIs post total knee/hip arthroplasty, which was consistent with that previously reported by others[14,23].

Neutrophil defensins are capable of inhibiting MRSA and regulating the production of cytokines including IL-1β and IL-8 and inflammatory responses[18,19,45]. Wehkamp *et al.*[18] indicated that α-defensin expression was increased in paneth cells of the ileum in patients in response to inflammation. Alpha-defensin is elevated in aspirates culture-positive for *Propionibacterium acnes*[44] and is effective and capable of inhibiting the survival of MRSA and *S. aureus*[45]. Some clinical studies showed that α-defensin was effective in predicting pathogen-positive cultures[44]. Accordingly, α-defensin has been identified as an effective predictor of PJI.

When it comes to the diagnostic reliability and accuracy of α-defensin in PJI, there is a general agreement that the laboratory-based α-defensin ELISA test has a higher accuracy than the lateral flow test in diagnosing PJI[23]. The α-defensin lateral flow test has a sensitivity ranging from 67% to 100% and a specificity ranging from 89% to 100%[15,25,26,33,36,37,39,40,42], and the laboratory-based α-defensin ELISA test has a sensitivity ranging from 85% to 100% and a similar specificity and accuracy[14,23,37,46]. Our present study showed that the α-defensin lateral flow test had a pooled sensitivity of 0.83 (95% *CI* 0.77, 0.88), a pooled specificity of 0.95 (95% *CI* 0.93, 0.97), a pooled accuracy of 0.97 (95% *CI* 0.95, 0.98), a pooled positive likelihood ratio of 16.86 (95% *CI* 11.67, 24.37), a pooled negative likelihood ratio of 0.17 (95% *CI* 0.13, 0.24), and a pooled diagnostic odds ratio of 85.30 (95% *CI* 47.76, 152.35). Subgroup analysis showed its high sensitivity, specificity, and accuracy was not race related. These results were similar to the results reported by Han *et al.*[23] and Ahmad *et al.*[14] Taken together these results indicated that the laboratory-based α-defensin ELISA test might have higher diagnostic reliability and accuracy in PJI diagnosis than the α-defensin lateral flow test.

In comparison with MSIS criteria, however, the α-defensin lateral flow test had similar or higher diagnostic accuracy in diagnosing PJI[40]. Balato *et al.*[40] found that the α-defensin lateral flow test presented higher sensitivity (84.5%) and negative predictive value (94.4%) than CRP and ESR combination (81.3% and 90.6%, respectively),

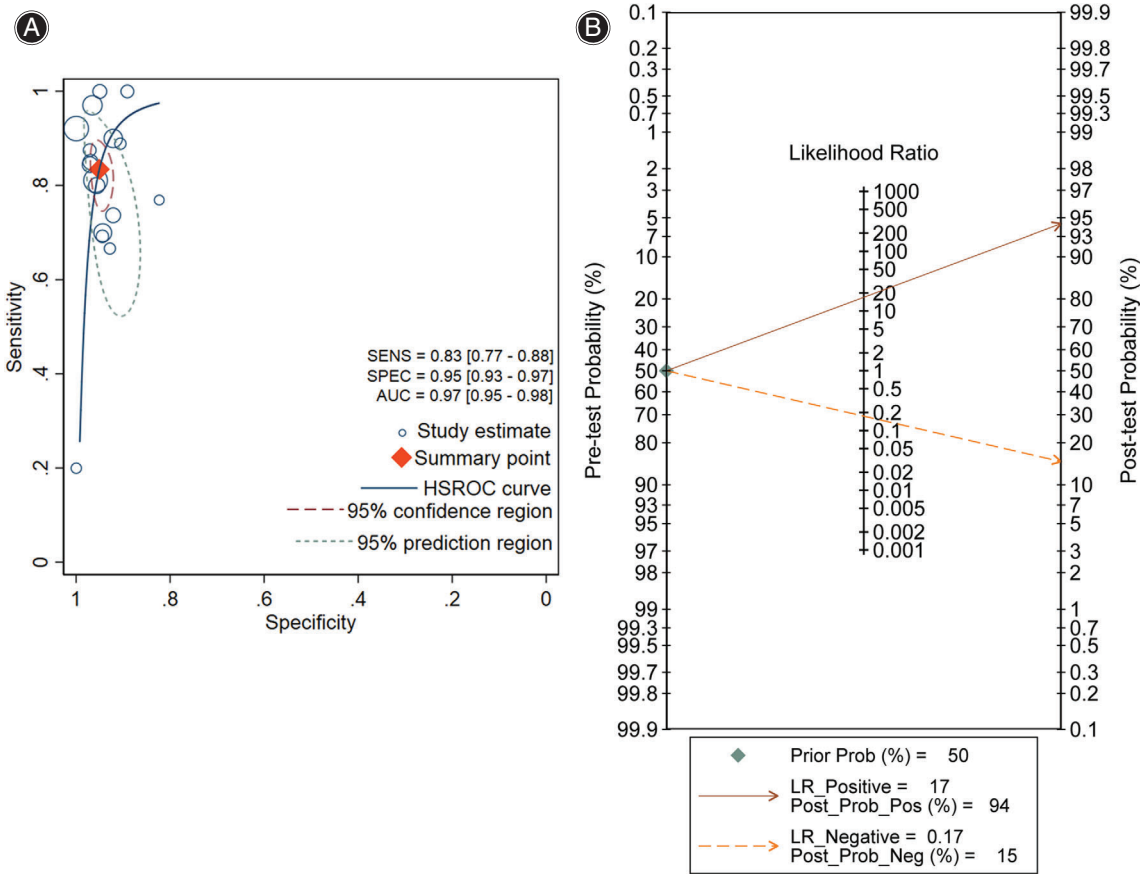

Fig. 7 The hierarchical summary receiver operating characteristic (HSROC) curve A and Fagan's nomogram (B) for the diagnostic accuracy of periprosthetic joint infection using α-defensin lateral flow test. SENS, sensitivity; SPEC, specificity; AUC, area under the HSROC curve.

synovial fluid white blood cell count (75.0% and 88.9%), two positive periprosthetic cultures (75.0% and 89.7%), sinus tract communicating with the prosthesis (25% and 74.5%) and synovial fluid polymorphonuclear percentage > 80% (75.0% and 89.5%). Ahmad *et al.*[14] showed that CRP has a similar sensitivity (0.86, 95% *CI* 0.81, 0.91) and specificity (0.90 95% *CI* 0.86, 0.93) to the Synovasure™ test (0.78, 95% CI 0.66, 0.87; and 0.89, 95% *CI* 0.78, 0.95) in diagnosing PJI. These results suggested the high reliability of the α-defensin lateral flow test in diagnosing PJI and should be in conjunction with other MSIS criteria for PJI. Besides, the α-defensin lateral flow test had a significantly shorter examination period compared with the ELISA test. The result of the lateral flow test is available within 10 minutes. Therefore, the lateral flow test is commonly used by surgeons for the intraoperative diagnosis and prompt treatment for PJI. For the preoperative diagnosis of PJI, however, the α-defensin lateral flow test is inferior to laboratory-based the α-defensin ELISA test in consideration of the accuracy and expense.

This current study included limitations. Firstly, a gold standard for diagnosing PJI is lacking. The MSIS statement is a reference standard and is commonly used in clinical practice. A patient must fulfill a single major criterion or at least four of the six minor criteria to be diagnosed with PJI. There is increasing evidence that shows the MSIS criteria including CRP, ESR and polymorphonuclear percentage were less accurate than α-defensin[38,40]. Diagnosing PJI remains challenging due to the emerging of more available diagnostic test methods. Secondly, there was potential publication bias and heterogeneity across the 17 included studies. Thirdly, most studies were published with short follow-up for diagnosing potential PJIs. Hence, the false-negative values as well as the sensitivity and accuracy of the α-defensin lateral flow test might be misrepresentations. The latter two limitations might influence the reliability of the results in this current study.

Conclusions

In this study, the diagnostic reliability and accuracy of the α-defensin lateral flow test in PJI was confirmed. It was found to have a relatively high performance for diagnosing PJI. The lateral flow test had a high sensitivity (0.83, 95% CI 0.77, 0.88), specificity (0.95, 95% CI 0.93, 0.97), and accuracy (0.97, 95% CI 0.95, 0.98) in diagnosing PJI after total joint

arthroplasty. We propose that the α-defensin lateral flow test be included in the clinical diagnostic criteria for PJI. More and large-scale studies are needed to validate the significance and accuracy of the α-defensin lateral flow test in PJI diagnosis.

Authors' contributions

Conception and design of the research: Yuqing Zeng. Acquisition, analysis and interpretation of data: Xingyang Zhu, Wenjun Feng, Xiaobo Sun, Jiangchun Zeng and Shu Deng. Statistical analysis: Yuqing Zeng, and Haitao Zhang. Drafting the manuscript: Yuqing Zeng and Shu Deng. Literature mining: Yuqing Zeng and Shu Deng. Manuscript revision for important intellectual content: Yirong Zeng. All authors have read and approved the manuscript.

Declarations

Ethical Approval

This article does not contain any studies with human participants performed by any of the authors.

Consent for Publication

Not applicable.

Availability of Data and Material

All data generated data during the analysis are included in this published article.

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