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Diagnostic arthroscopy for periprosthetic shoulder arthroplasty infections: a systematic review and meta-analysis

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Background: Periprosthetic joint infection of the shoulder (PJI) is a devastating complication with a reported incidence of 1%-15.4% and is often difficult to diagnose with current diagnostic tools including serologic tests and arthrocentesis. This systematic review evaluates the reliability and validity of arthroscopic biopsy in the current literature for the diagnosis of shoulder PJI.

Methods: MEDLINE, Scopus, Web of Sciences, Google Scholar, and Cochrane databases were queried electronically from inception to June 2022 for publications reporting diagnostic accuracy of shoulder arthroscopic biopsy for detecting infection after anatomic total shoulder arthroplasty, shoulder hemiarthroplasty, or reverse total shoulder arthroplasty. This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Results: After exclusion, our meta-analysis consisted of 7 articles with a total of 112 patients. The estimated pooled sensitivity and specificity of arthroscopic biopsy for confirmation of shoulder periprosthetic infection were 0.87 (95% confidence interval [CI]: 0.73-0.95) and 0.79 (95% CI: 0.67-0.88), respectively. The pooled positive likelihood ratio and negative likelihood ratio were 4.15 (95% CI: 2.57, 6.70) and 0.17 (95% CI: 0.08, 0.36), respectively. The aggregate positive predictive value was 73.58% (95% CI: 63.29%-81.82%), and aggregate negative predictive value was 89.83% (95% CI: 80.59%-94.95%). The diagnostic odds ratio of arthroscopic biopsy was 19.92 (95% CI: 4.96-79.99).

Conclusion: Arthroscopic biopsy in patients suspected of shoulder PJI has good diagnostic accuracy, with high sensitivity and specificity. Given the various biopsy protocols (such as devices, numbers, locations, etc.), further prospective studies are necessary to define the future role of arthroscopic biopsy in diagnosis and treatment.

The incidence of primary and revision shoulder arthroplasty is growing considerably, with a projected increase in volume by 232.2% in the United States alone by 2025.[36] Due to this tremendous rise in popularity, the growth rate of shoulder arthroplasty is expected to exceed that of both hip and knee arthroplasties by 2040.[19] Periprosthetic joint infection of the shoulder (PJI) can be a devastating complication, with a reported incidence of 1%-15.4% in the literature,[3,4,10,20,23,30] amounting to at least 6000 cases of PJI yearly.[9,18] PJI of the shoulder presents a challenge to surgeons, as it is often difficult to diagnose or rule out with current diagnostic tools in patients with pain/poor function following shoulder arthroplasty.[20] While validated algorithms have been established for detecting PJI of hip and knee implants, these algorithms do not display similar reliability and validity for shoulder implants.[6] Furthermore, PJI often does not present with pathognomonic signs of infection including draining sinuses (present in 44% of cases), erythema (present in 35% of cases), fever (present in 21% of cases), night sweats (present in 9% of cases), and chills (present in 9% of cases).[7,22,29,33] These diagnostic difficulties may be attributed to the high prevalence of low-virulence microorganisms including *Cutibacterium acnes* (38.9%) and coagulase-negative *Staphylococcus* including *S epidermidis* (14.0%).[25,28] The most common bacteria responsible for shoulder PJI, *C. acnes*, is different from other PJI-causing organisms joints due to its high colonization rate of the skin and dermis of the shoulder girdle[25,27,32] and its fastidious nature,

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making detection and eradication difficult.[22] Thus, serologic testing (serum white blood cells, erythrocyte sedimentation rate, and C-reactive protein) that has high diagnostic utility in hip and knee PJIs has a significantly lower sensitivity (SN) and negative predictive value (NPV) in patients with shoulder PJI.[28] Furthermore, the poor SN of other biomarkers including serum IL-6 (14%) in shoulder PJI limits its clinical utility, although it is reasonably specific (94%).[35]

Thus, shoulder PJI often cannot be excluded based on serologic tests, and therefore, additional workup may be warranted. Arthrocentesis, which is diagnostic of knee and hip PJI, may not be a reliable tool in shoulder PJI due to a high rate of dry taps from the glenohumeral joint (approximately 50%) as well as difficulty culturing low virulence, fastidious organisms like *C. acnes*.[6,24,33] Therefore, the International Consensus Meeting on Orthopaedic Infections (ICM) proposed that synovial tissue sampling, rather than aspirated fluid, may be a more reliable method to identify fastidious organism. The ICM recommended obtaining 5 separate deep specimens from various aspects of the shoulder, with debate regarding open vs. arthroscopic sampling.[11,12]

Arthroscopic biopsy remains an attractive option due to less soft tissue damage, minimal invasiveness, rapid recovery, and better visualization of the synovial membrane and components.[1,15,26] Additionally, arthroscopy allows for simultaneous treatment of underlying pathologies including stiffness due to postoperative adhesion, rotator cuff tears following anatomic total shoulder arthroplasty, loose glenoid components, and biceps tendon injuries.[16,26] The most common indication for shoulder arthroscopy after arthroplasty is pain or loss of motion with no clear pathologic cause.[17] The aim of this study was to perform a systematic review and meta-analysis of the existing literature to evaluate studies that report on the use of arthroscopy for the diagnosis of shoulder PJI and to report its efficacy.

Methods

Protocol and registration

We systematically searched previously published papers investigating the diagnostic accuracy of shoulder arthroscopic biopsy for detecting periprosthetic infection. This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline.

Literature search

The MEDLINE, Scopus, Web of Sciences, Google Scholar, and Cochrane databases were queried electronically from inception to June 2022. Two independent reviewers screened all titles, abstracts, and full texts. No filters were placed on article type, written language, and full-text articles. The references of all relevant articles were manually assessed to ensure that all possible articles were considered. Duplicate titles were excluded. The inclusion criteria were as follows: an arthroscopic biopsy was performed as a separate procedure prior to potential revision shoulder arthroplasty procedure in patients who had previously undergone anatomic total shoulder arthroplasty, shoulder hemiarthroplasty, or reverse total shoulder arthroplasty in all evidence levels without restriction in sex and ages. Studies including patients with gross signs of periprosthetic infection such as wound dehiscence, secretion, erythema, sinus tract, severely elevated laboratory markers, and implant loosening, prior to diagnostic arthroscopy were excluded. Studies were also excluded if the sample size was fewer than five patients.

Data extraction

Data were collected by two independent reviewers and characteristics of the studies (the first author, the country where the study was performed, publication date, the journal, the level of evidence, sample size) were extracted (Table I).

Assessment of methodological quality

The quality of the methods of each included article was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2), a validated instrument to assess for susceptibility to bias. The four domains assessed by the QUADAS-2 tool were patient selection, index test, reference standard, and flow and timing. If the answers to all signaling questions in a domain are “yes” then the “low” risk grade is given. If the answer to any signaling question is “no” then a “high” risk grade is given. The “unclear” category was only used where the reported data were insufficient to permit a judgment (Table II).

Outcomes reporting

Revision surgery was performed as a separate surgery following the arthroscopic tissue biopsy and cultures were obtained intraoperatively. The primary outcomes were the true positive (TP), true negative (TN), false negative (FN), and false positive (FP) of arthroscopic biopsy for periprosthetic joint infection. Revision surgery biopsy result was considered the gold standard, with any single positive intraoperative biopsy considered a positive test. Hierarchical Summary Receiver Operating Characteristic (HSROC) curve values were calculated to show pooled test accuracy accounting for the SN, specificity (SP), and likelihood ratio (LR) of laboratory values for classifying positive arthroscopic biopsy and positive cultures at the time of revision surgery. Area under the HSROC curve demonstrates test discrimination, with values >0.8 representing excellent discrimination between SN and SP. Each arthroscopic biopsy associated with a positive infection was regarded as a TP, while each negative arthroscopic biopsy was considered a TN, and each arthroscopic test result which not confirmed by intraoperative biopsy was considered as false data. A meta-analysis of all data detailing the results of diagnostic arthroscopic biopsy as a stand-alone procedure was conducted with aggregate data from each study reporting the results of intraoperative cultures at the time of revision surgery to calculate SN, SP, negative likelihood ratio, and positive likelihood ratio for arthroscopic biopsy. Diagnostic odds ratio was calculated according to the formula: DOR = (TP/FN)/(FP/TN) to determine the odds of a positive arthroscopic biopsy in those with shoulder PJI relative to the odds of a positive arthroscopic biopsy in patients without shoulder PJI. DOR values > 10 were considered representative of strong association. Forest plots were created as a visual representation.

Data synthesis

Meta-DiSc version 1.4 (Meta-DiSc, Hospital Ramon y Cajal Universidad Complutense de Madrid, Madrid, Spain) software and Comprehensive Meta-analysis software version 3

Table I
Characteristics of the studies.

Study	Year	Journal	Journal of Bone and Joint Surgery level of evidence	Technique	Number of samples	Revision surgery
Akgün et al[2] (Germany)	2019	*Arthroscopy*	3	Abnormal appearance tissue	≥3	Y
Dilisio et al[6] (USA)	2014	*Journal of Bone and Joint Surgery - American Volume*	1	Abnormal appearance tissue	≥3	Y
Doherty et al[8] (UK)	2019	*J Shoulder Elbow Surg*	4	Different positions within the joint	5	Y
Guild et al[14] (USA)	2020	*Arthroscopy*	4	Abnormal appearance tissue	5	Y
Mederake et al[21] (Germany)	2021	*Archives of Orthopaedic and Trauma Surgery*	Not mentioned	Synovial lining of the joint zones	5 microbiological, 5 histological	Y
Pruijn et al[31] (Netherlands)	2021	*Journal of Shoulder and Elbow Surgery*	3	Different positions within the joint	6	Y
Tashjian et al[34] (USA)	2017	*Journal of Shoulder and Elbow Surgery*	3	Random fashion	At least 2	Y

Y, yes.

Table II
Tabular presentation for QUADAS-2 results.

Study	Risk of bias			Flow and timing	Applicability concerns		
	Patient selection	Index test	Reference standard		Patient selection	Index test	Reference standard
Tashjian et al[34] (USA)	□	□	□	□	■	□	□
Akgün et al[2] (Germany)	□	□	□	□	□	□	□
Dilisio et al[6] (USA)	□	□	□	□	□	□	□
Doherty et al[8] (UK)	□	□	□	□	?	□	□
Guild et al[14] (USA)	□	□	□	□	?	□	□
Mederake et al[21] (Germany)	□	□	□	□	□	□	□
Pruijn et al[31] (Netherlands)	□	□	□	□	□	□	□

QUADAS-2, quality assessment of diagnostic accuracy studies-2.
□, low risk; ■, high risk; ?, unclear risk.

(Comprehensive Meta-Analysis, Englewood, NJ, USA) were used for statistical analysis. The heterogeneity among the included studies was investigated using Q-statistic and I^2 index. If the value of I^2 was higher than 50% or *P* value was less than .05, the random model was used to estimate the SN and SP of shoulder arthroscopic biopsy to detect periprosthetic infection. Alternatively, if the value of I^2 was less than 50% and *P* value was higher than .05, the SN and SP of arthroscopic biopsy were calculated using a fixed model.

Results

Search

A total of 2136 studies were screened in our preliminary search. After the removal of duplicates, abstracts of the remaining 1633 studies were assessed by two independent reviewers (P.J. and A.K.). The full text of 93 articles was evaluated for eligibility and 86 articles were excluded according to the exclusion criteria. Finally, 7 articles evaluating 112 patients were included in our meta-analysis (11, 30-33, 35, 36). Details of the database searches are presented in Figure 1.

Study characteristics

The characteristics of the 7 included studies such as authors, title, year and journal of publication, and level of evidence are detailed in Table I. Studies were performed between 2014 and 2021, with the sample sizes ranging from 7 to 23 subjects. Most studies were level III or IV evidence.

Meta-analysis: diagnostic accuracy indices

The estimated pooled SN and SP of arthroscopic biopsy for confirmation of shoulder periprosthetic infection were 0.87 (95% confidence interval [CI]: 0.73-0.95) and 0.79 (95% CI: 0.67-0.88), respectively (Figs. 2 and 3). The pooled positive likelihood ratio and negative likelihood ratio were 4.15 (95% CI: 2.57, 6.70) and 0.17 (95% CI: 0.08, 0.36), respectively. The aggregate positive predictive value (PPV) was 73.58% (95% CI: 63.29%-81.82%), and aggregate NPV was 89.83% (95% CI: 80.59%-94.95%). Furthermore, the diagnostic odds ratio of arthroscopic biopsy was 19.92 (95% CI: 4.96-79.99) (Fig. 4). The area under the HSROC revealed an appropriate accuracy of 0.934 (Fig. 5).

Discussion

The key finding from this systematic review is that arthroscopic biopsy can be a useful diagnostic modality for assessing possible shoulder periprosthetic infection in a painful shoulder arthroplasty without clear evidence of infection. Using tissue obtained during revision surgery for culture as the gold standard, the estimated pooled SN and SP of arthroscopic biopsy to confirm shoulder periprosthetic infection were 0.87 and 0.79, respectively. The considerable odds ratio (19.92) and appropriate accuracy (0.934) of arthroscopic biopsy in shoulder PJI diagnosis make arthroscopic tissue sampling a highly effective adjunct for the diagnosis of shoulder PJI.

There is no general agreement on the best approach for diagnosing periprosthetic shoulder infection.[5,8,17,25,27,32,34] However, the literature seems to support that specimens obtained from

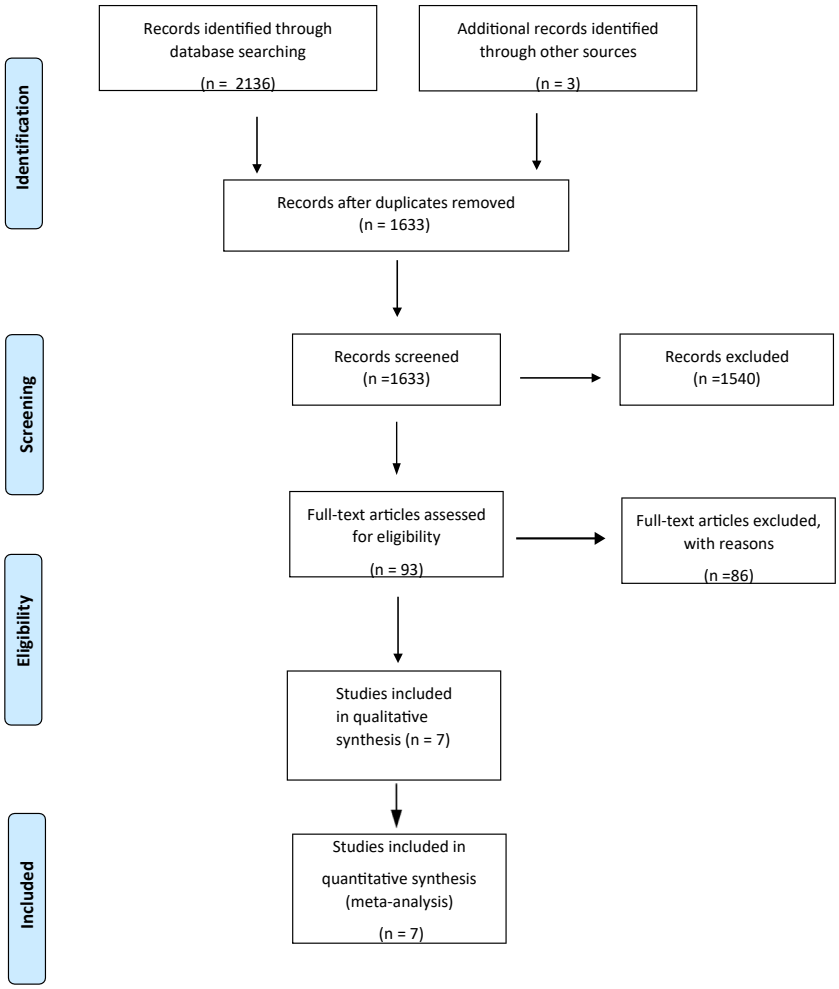


Figure 1 PRISMA flow diagram of search results. *PRISMA*, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

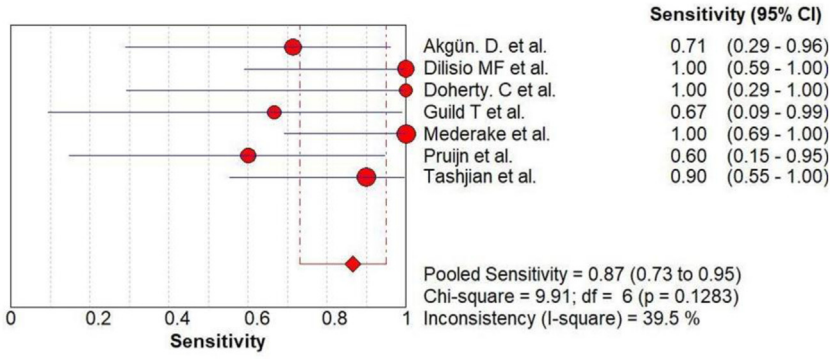


Figure 2 Pooled sensitivity.

arthroscopic tissue biopsy are significantly more accurate at diagnosing periprosthetic shoulder infection than glenohumeral aspiration.[6,21,31]

Dilisio et al demonstrated that arthroscopic shoulder biopsy is a dependable method for diagnosing periprosthetic infection and the causative organism. All arthroscopic biopsy culture results were consistent with the open biopsy results obtained intraoperatively, yielding 100% SN, SP, PPV, and NPV. In contrast, glenohumeral aspiration under fluoroscopic guidance yielded a SN of 16.7%, SP of 100%, PPV of 100%, and NPV of 58.3%.[6]

Mederake performed a retrospective study on 56 patients who underwent revision shoulder arthroplasty. Twenty-two of the cases had arthroscopic biopsy before revision surgery. They hypothesized that preoperative arthroscopic biopsy would have the greatest diagnostic accuracy, which was corroborated, with a SN of 90% and a SP of 83%.[21]

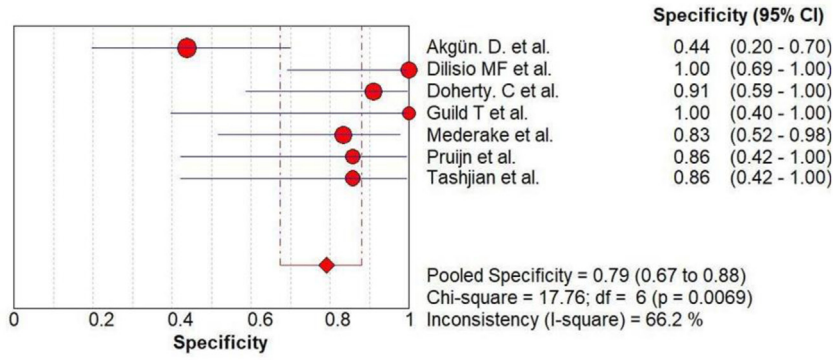


Figure 3 Pooled specificity.

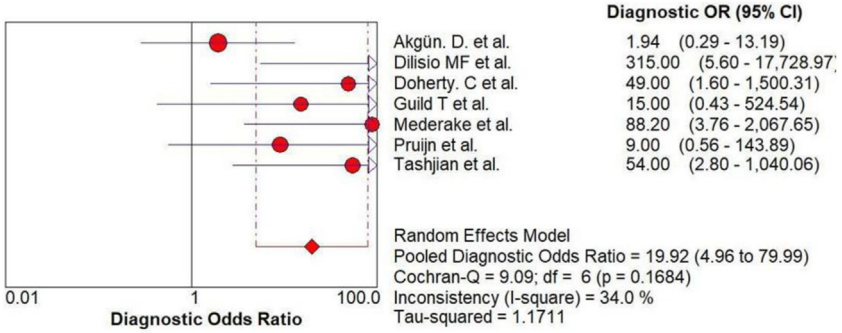


Figure 4 Pooled diagnostic odds ratio.

Pruijn et al compared the accuracy of shoulder needle aspiration with arthroscopic and mini-open surgery biopsy cultures. This study demonstrated the diagnostic advantage of arthroscopic biopsies over sterile aspiration for diagnosing shoulder infections. Although in this study, arthroscopic biopsy cultures showed moderate SN and SP of 60.0% and 85.7%, these values were similar or greater than those of sterile aspiration, with a low SN (20.0%) but high SP (90.6%).[31]

The aspiration results in this study are consistent with Grosso et al. They reported a SN of 18.8% and SP of 94.7% for diagnosing periprosthetic shoulder infection. The variation in shoulder PJI definitions, biopsy techniques, tissue sample quantities, and even culture techniques can profoundly affect study results.[13,31]

Finally, Akgün et al mentioned how the SN of arthroscopic biopsy declined from 100% to 80%, while the SP increased from 39% to 94.4% when considering periprosthetic shoulder infection based on at least two cultures positive for the same microorganism instead of just one.[2]

Shoulder arthroscopy after arthroplasty is not only used as a diagnostic tool but also for procedures such as rotator cuff repairs, subacromial decompression, adhesions release, capsular release, and loose body removal.[14,26] Guild et al performed a study of 13 patients treated with arthroscopy following painful shoulder arthroplasty. They successfully treated 46% of patients with arthroscopic procedures, preventing the need for revision arthroplasty. Arthroscopic biopsy culture results had a 100% correlation with intraoperative culture results.[14]

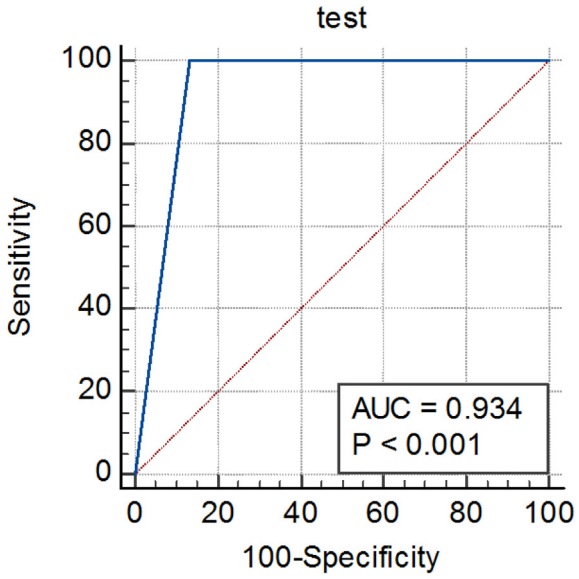
Conclusion

Periprosthetic shoulder infections can be challenging to detect routinely. *C. acnes* has a notably slow growth pattern and can often be present in patients with normal laboratory tests for infection and negative glenohumeral aspiration cultures. In a patient with unexplained pain following shoulder arthroplasty and normal lab tests, a diagnostic arthroscopic biopsy may help clarify which patients are harboring a PJI.

Limitations

Although this meta-analysis is comprehensive in its analysis of the available literature, with quality assessment via the QUADAS-2 tool, several limitations exist. This study is subject to the limitations of most systematic review studies. First, there is a possibility of search bias due to the difficulty of screening for every possible study assessing the subject of interest. Second is the possibility of publication bias, due to significant results being published over nonsignificant results. Third, most of the studies were retrospective and, because of the small sample size, likely had some component of selection bias. Fourth, the studies included in the analysis may lack uniformity due to varying protocols including number of tissue samples collected per case, length of time the cultures were held per case, the gold standard definition of PJI in each study, and the definition of a positive arthroscopic biopsy in each study. Fifth, there was not a standardized definition of PJI across all the studies, and therefore, we considered any single positive intraoperative biopsy result as a standard positive test though this may not be standard practice. Finally, most studies (except for two) only compared the outcome of arthroscopic biopsy to intraoperative biopsy as the gold standard and did not utilize other tests for further comparison like arthrocentesis.

Because of these differences, this study is unable to outline a specific protocol for arthroscopic biopsy for detecting periprosthetic shoulder infection.



Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.934
Standard Error [a]	0.0207
95% Confidence interval [b]	0.871 to 0.972
z statistic	20.958
Significance level P (Area=0.5)	<0.0001

Figure 5 Hierarchical Summary Receiver Operating Characteristic Curve (HSROC) outlining discrimination of diagnostic arthroscopy for periprosthetic joint infection.

A prospective multicenter study or randomized controlled trial evaluating the diagnostic accuracy of arthroscopic biopsy for detecting periprosthetic shoulder infections may allow for further evaluation of its utility.

Conclusion

Arthroscopic biopsy has strong diagnostic accuracy for shoulder PJI, with relatively high SN and SP. Given the heterogeneity of biopsy protocols in this study (including various PJI definitions, number and location of samples, etc.), further prospective studies are necessary to define the future role of arthroscopic biopsy in diagnosis and treatment.

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Conflicts of interest: Albert Lin is a paid consultant for Arthrex and Wright Medical, Inc., not related to this study. The other authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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