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The role of sonication in the diagnosis of periprosthetic joint infection in total shoulder arthroplasty

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An increased sensitivity of sonication compared to periprosthetic tissue cultures in the diagnosis of periprosthetic joint infection (PJI) of hip and knee arthroplasty has been reported. The goal of this study was to determine if there is also an added value of implant sonication in the diagnosis of PJI in total shoulder arthroplasty (TSA). A retrospective analysis of patients who underwent removal of their TSA combined with sonication of the implant for suspicion of PJI between April 2009 and August 2017 was performed. The diagnosis of PJI was based on the major criteria described by Parvizi. We calculated sensitivity, specificity, predictive values, likelihood ratios and diagnostic accuracy for sonication cultures in comparison with periprosthetic tissue cultures. Data from 41 patients were analysed. Standard synovial fluid cultures combined with intraoperative periprosthetic tissue cultures had a sensitivity of 95%, specificity of 95% and total accuracy of 95%. Sonication cultures had a sensitivity of 91%, specificity of 68% and total accuracy of 80%. Six patients had negative standard cultures but positive sonication cultures. In patients with only one positive standard culture, the pathogen of the sonication culture corresponded to the pathogen of the positive soft tissue culture. We found a possible added value of sonication of TSA in the diagnosis of PJI in conjunction with standard intraoperative cultures. In some patients with suspicion of low-grade TSA infection, sonication could identify a possible causal microorganism despite negative standard cultures.

Keywords: Total shoulder arthroplasty, periprosthetic joint infection, sonication, *cutibacterium acnes*.

INTRODUCTION

The use of total shoulder arthroplasty (TSA) is steadily increased over the last years and so is the absolute number of complications requiring revision surgery[1]. One of the most frequent complications of TSA is periprosthetic joint infection (PJI). The incidence of PJI in primary TSA is 1-2% and up to 15 % in revision TSA[2-4]. Identification of the responsible microorganism is essential for a correct antibiotic treatment of patients with PJI. Synovial fluid and intraoperative periprosthetic tissue cultures are considered to be the golden standard for the diagnosis of PJI and identification of the responsible microorganis[5]. However, Akgün et al. reported only a sensitivity of 61% for these cultures in TSA based on the definition of PJI from the International Consensus Meeting on Orthopaedic infections[6,7].

PJI is frequently caused by *staphylococcus aureus* or *coagulase-negative staphylococcus*. Gram-negative bacteria and fungi can also rarely cause PJI[8]. However, *cutibacterium acnes* (*c. acnes*) is the causal microorganism in 71% of PJI in TSA[6]. Because of the low virulence, resulting in often subtle clinical signs and strong adherence of *c. acnes* to arthroplasty surfaces, PJI due to *c. acnes* is especially challenging to diagnose[9]. In PJI, biofilms formed by microorganisms can attach to the surface of the arthroplasty. A biofilm consists of microorganisms enclosed in a glycocalyx matrix which seals the microorganisms from the effects of antibiotics[10,11]. Analysis of the implants attached biofilm might contribute to the diagnosis of PJI. One way of analysing biofilms is sonication of the removed implant[12,13]. Sonication uses ultrasound for the disintegration of the biofilm from the arthroplasty. Cultures of the obtained sonication fluid can identify a possible causal microorganism of PJI[14]. This technique has improved the sensitivity of microbial cultures from implant biofilms[15,16].

Piper et al. found sonication cultures to be more sensitive than standard tissue cultures for detection of PJI in TSA[15]. However, some recent studies questioned

the role of sonication in the diagnosis of PJI of TSA[6,17,18]. In view of the costs, the time-consuming preparation protocol and the required infrastructure associated with sonication, further determination of the role of sonication in diagnosing of PJI in TSA seems to be justified. Therefore, the aim of this study was to confirm our hypothesis that sonication has an added value in diagnosing PJI in TSA.

MATERIALS AND METHODS

The study was approved by the Medical Ethics Committee UZ / KU Leuven (S61302).

We retrospectively analysed the records of all patients who underwent revision or removal of a TSA for suspicion of PJI between April 2009 and August 2017 in our institution. Only patients whose arthroplasty underwent the sonication protocol combined with the standard periprosthetic tissue cultures were included. Patients with less than 6 different culture samples were excluded[16,19].

The diagnosis of PJI was based on the two major criteria described by Parvizi et al. (Appendix 1)[20]. (1) the presence of a sinus tract communicating with the prothesis and (2) the same pathogen isolated by culture from two or more separate tissue or fluid samples obtained from the affected prosthetic joint. Based on these criteria patients were divided in a PJI-group and a non-PJI group. We collected general data from each patient: gender, age, affected side, the indication and date of the primary arthroplasty and the symptoms, type of and period to revision arthroplasty. The biochemical follow-up in terms of serum c-reactive protein (CRP), sedimentation and white blood cell (WBC) count of patients with negative tissue cultures but positive sonication cultures a time of revision TSA was further analysed. To further determine the possible value of positive sonication cultures we compared tissue cultures obtained during later revision TSA procedure to the initial sonication cultures for this patient group. Patients with all negative synovial and soft tissue cultures but positive sonication cultures belonged to group A. Patients with only one positive synovial or soft tissue culture and positive sonication cultures belonged to group B.

Synovial fluid and intraoperative periprosthetic tissue samples were processed for aerobic and anaerobic incubation for 14 days. For the sonication protocol the prosthetic components were transferred in a sterile measuring cup from the operating room to the laboratory. At the laboratory, the components were covered with ringer solution at a temperature of 20°C and subjected to sonication with a power density of 0.22+-0.04W/cm² (40 kHz) for 3 minutes. The obtained liquid was transfused into a conical tube in a sterile manner in a vortex mixer for another 5 minutes. Afterwards, the liquid was drained, 5 ml of Tryptic soy broth was added, and the substance went in the vortex mixer for the last time. The sonication fluid was plated onto 5 different agar plates (blood, MacConkey, mannitol salt, thioglycolate and trypticase soy agar) and incubated for a minimum of 14 days. A cut-off value of 5 colonies from the same organism was used to differentiate between infection and contamination.

Statistical analysis was performed with Microsoft Excel and SPSS 25[21]. Descriptive statistics were used to describe the demographic and clinical data, PJI diagnosis and the microorganisms involved. Sensitivity, specificity, predictive values, likelihood ratios, and diagnostic accuracy were determined for both standard and sonication cultures. Diagnostic accuracy measures the ability of a test to detect a condition when it is present and detect the absence of a condition when it is absent. The diagnostic accuracy was determined by the sum of true positives and true negatives compared with the definition of PJI described by Parvizi et al. divided by the total of patients. Finally, formal significance testing for sensitivity and specificity between the two types of cultures was done by the McNemar's test.

RESULTS

We reviewed a total of 80 patient files and excluded 39 patients because they did not meet the inclusion criteria. The patient profiles are outlined in Table I. The most common primary indications for TSA implantation were proximal humerus fracture (n=25), rotator cuff tear arthropathy (n=7) and shoulder osteoarthrosis (n=9). The most common symptom before extraction was chronic pain in 29 patients. Other signs were swelling (n=2), redness (n=2), a sinus tract and/or wound problems (n=7). We found increased pre-operative sedimentation, white blood cell count or CRP

Table I. — Patient characteristics.

Number	41
Age (y), mean (range)	70y (39-91y)
Male/Female ratio	46% (19 vs 22)
Original arthroplasty	23 rTSA, 13 aTSA, 5 HA
Time to explantation (months), mean (range)	46 (2-210)

rTSA, reverse total shoulder arthroplasty; a*TSA*, anatomic total shoulder arthroplasty; *HA*, hemiarthroplasty.

in 30 patients. We identified loosening of the glenoid component on radiographic imaging in 1 patient. 54% (22/41) patients belonged to the PJI group (20), the other 46% (19/41) formed the no-PJI group. In the PJI group 11 of the 22 (50%) patients had *c. acnes* as the responsible microorganism. In 10 of these patients, *c. acnes* was identified in synovial fluid, tissue cultures and sonication cultures. One patient had only positive synovial fluid and tissue cultures with *c. acnes* with negative sonication culture. Other common pathogens in the PJI-group were *s. aureus* in 8 (36%) and *s. epidermis* in 10 (45%) patients.

Standard synovial fluid combined with intraoperative periprosthetic tissue cultures had a sensitivity and specificity of 95%. Sonication cultures had a sensitivity of 91% (p= 1) and a specificity of 68% (p= 0.063). The total accuracy of both tests was 95% and 80% respectively (Table II). When standard synovial fluid and periprosthetic tissue cultures were compared with sonication cultures, 20 patients had both positive standard and sonication cultures, 13 patients had negative standard and sonication cultures, two patients had positive standard cultures and negative sonication cultures and six patients had the opposite, positive sonication and negative standard cultures (Figure 1). The two patients with positive standard and negative sonication cultures had 8 out of 8 and 5 out of 7 positive synovial fluid and tissue cultures. The responsible pathogen was *s. aureus* and *c. acnes* respectively. The one patient who belonged to the non-PJI group although standard and sonication cultures were positive had two positive synovial fluid and tissue cultures, but from two different pathogens. The detected microorganisms were *c. acnes* and *corynebacterium.* The one patient with negative synovial fluid and soft tissue cultures and positive sonication cultures belonged to the PJI group due to the presence of a sinus tract.

Table II. — Performance of standard cultures and sonication cultures.

	Standard cultures	Sonication cultures	P-value
Sensitivity	95% (21/22)	91% (20/22)	1
Specificity	95% (18/19)	68% (13/19)	0.063
PPV	95% (21/22)	77% (20/26)	-
NPV	95% (18/19)	87% (13/15)	-
LR+	0.05	2.89	-
LR-	0.05	0.13	-
Accuracy	95% (39/41)	80% (33/41)	-

PPV, positive predictive value; *NPV*, negative predictive value; *LR+*, positive likelihood ratio; *LR-*, negative likelihood ratio.

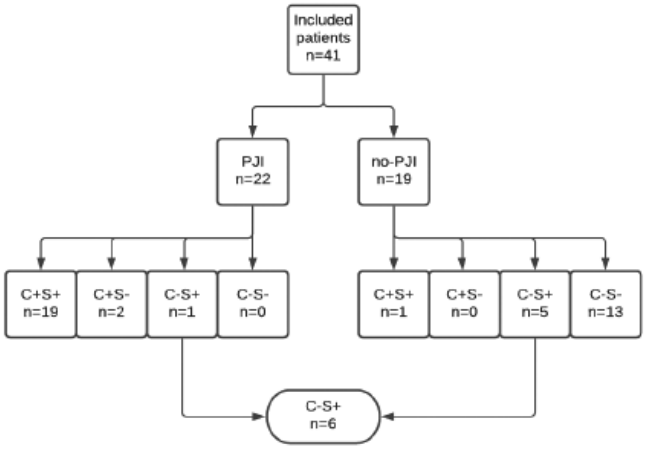

Figure 1 — Flowchart patient results
N, number of patients; PJI, periprosthetic joint infection; C+/-, positive/negative synovial fluid and tissue cultures; S+/-, positive/negative sonication cultures.

Table III. — Culture details of six patients with negative synovial fluid or tissue cultures and positive sonication.

		Initial synovial fluid and tissue cultures		Sonication cultures		Later synovial fluid and tissue cultures
		Result	Pathogen	Result	Pathogen	Pathogen
Group A	Patient 1	7/7 negative	/	Positive	*c. acnes*	*c. acnes*
	Patient 2	12/12 negative	/	Positive	*c. acnes*	(All later cultures negative)
	Patient 3	12/12 negative	/	Positive	*c. acnes*	(Died short after surgery)
Group B	Patient 4	1/10 positive	*c. acnes*	Positive	*c. acnes*	*s. haemolyticus, s. epidermidis, corynebacterium*
	Patient 5	1/9 positive	*c. acnes*	Positive	*c. acnes*	*c. acnes, s. epidermidis*
	Patient 6	1/9 positive	*s. aureus*	Positive	*s. aureus*	(All later cultures negative)

c. acnes, cutibacterium acnes; s. haemolyticus, staphylococcus haemolyticus; s. epidermidis, staphylococcus epidermidis; s. aureus, staphylococcus aureus
Patients with all negative synovial and soft tissue cultures but positive sonication cultures belonged to group A. Patients with only one positive synovial or soft tissue culture and positive sonication cultures belonged to group B.

We further analysed the patients with negative synovial fluid and tissue cultures but positive sonication (n=6). The results and corresponding pathogens of their cultures are summarized in Table III. Patients with all negative synovial and soft tissue cultures but positive sonication culture (group A) were treated as infected, with antibiotic treatment based on the antibiogram the sonication culture. In group B, one patient was treated based on the antibiogram of sonication, one based on the antibiogram of the soft tissue culture and the last one was based on both the antibiogram of sonication and the one positive tissue culture. All six patients had a good biochemical evolution based on CRP, sedimentation and white blood cell (WBC) count after final revision TSA.

DISCUSSION

Implant sonication has proven its added value in the diagnosis of PJI of hip or knee arthroplasty, especially in patients who received antibiotics the last 14 days before surgery [14,16]. However, the role of sonication in the diagnosis of PJI in TSA remains controversial[6,15,17,18]. The aim of this study was to determine if there is an added value of implant sonication in the diagnosis of PJI of TSA.

Piper et al. found an added value of sonication cultures with a sensitivity of 68% versus 55% for standard tissue cultures[15]. However, Grosso et al., Torrens et al. and Akgun et al. found a lower sensitivity for sonication compared to tissue cultures[6,17,18]. We found no significant difference in sensitivity between standard soft tissue and fluid cultures and sonication cultures. Due to a different definition used for diagnosis of PJI, direct comparison of these results is difficult. Piper et al. and Akgun et al. only excluded patients if less than two periprosthetic tissue specimens were submitted for culture during TSA explantation. In contrast to Grosso et al. and Torrens et al. who used a cut off of at least four samples[6,15,17,18]. In this study we excluded patients with less than six different cultures.

This comparison showed that we always adhered to the strictest conditions in terms of minimum number of cultures needed for diagnosing PJI and inclusion in our study. This makes our study less sensitive to false negative and false positive diagnosis of PJI. All these methodological differences make it difficult to obtain an overall conclusion on the sensitivity of implant sonication in het diagnosis of PJI in TSA.

In our cohort, one patient with an active sinus tract had negative standard cultures, but we were able to identify the causal microorganism with the sonication culture. Furthermore, in two patients with negative standard cultures but positive sonication cultures on time of TSA explantation, the same pathogen was re-cultured in standard cultures during later revision surgery. According to these results, sonication is able to detect or confirm the causal microorganism of PJI for some patients where an infection is suspected but in the absence of positive tissue cultures. Also, patients with just one positive tissue culture were considered as no-PJI group. In 5 out of the 6 patients with positive sonication culture but negative standard cultures, *c. acnes* was the identified microorganism by the sonication culture. Sonication can play a key role in the diagnosis of low-grade TSA PJI with *c. acnes*. This can be explained by the low number of microorganisms associated with *c. acnes* infections and the biofilm formation making them difficult to culture and detect[19]. However, sonication can also give false negative results like in the two patients with positive standard and negative sonication cultures (9%). That is why we believe that sonication of retrieved TSA implants is a useful adjuvant in the diagnosis of PJI in TSA rather than a diagnostic tool on its own. In addition, sonication requires a decent cost, a time-consuming preparation protocol and the necessary infrastructure. Based on the results of this study, the additional accuracy and sensitivity that sonication culture can yield in the diagnosis of PJI is the main reason why implant sonication remains standard practice in our hospital for patients who undergo revision or removal of a TSA for suspicion of PJI.

A weakness of this study is the small population size. Other studies we compared with in this article had a sample size between 34 and 252 patients. Larger studies could further confirm our findings in the future.

CONCLUSION

This study could prove an added value of sonication of TSA in the diagnosis of PJI, especially in patients with no or just one positive synovial or intraoperative soft tissue culture. We think that standard tissue cultures should remain the golden standard for diagnosis of shoulder PJI, although sonication could contribute to earlier detection and correct antibiotic treatment in selected cases.

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APPENDIX 1

Definition of periprosthetic joint infection (PJI)

Based on the proposed criteria, a definite PJI exists when:

1) **There is a sinus tract communicating with the prothesis; or**
2) **A pathogen is isolated by culture from two or more separate tissue or fluid samples obtained from the affected prosthetic joint; or**
3) **When four of the following six minor criteria exist**:
    a. Elevated serum erythrocyte sedimentation rate (ESR) and serum c-reactive protein (CRP) concentration,
    b. Elevated synovial white blood cell (WBC) count,
    c. Elevated synovial polymorphonuclear percentage (PMN%),
    d. Presence of purulence in the affected joint,
    e. Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
    f. Greater than five neutrophils per high power field in 5 high power fields observed from histological analysis of periprosthetic tissue at 400 times magnification.

Please note that a PJI may be present if less than 4 of these criteria are met. The panel also acknowledged that in certain low-grade infections (e.g., c. acnes), several of these criteria may not be routinely met despite the presence of PJI.