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

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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. 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. 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 microorganisms. 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.

PJI is frequently caused by staphylococcus aureus or coagulase-negative staphylococcus. Gram-negative bacteria and fungi can also rarely cause PJI. However, cutibacterium acnes (c. acnes) is the causal microorganism in 71% of PJI in TSA. 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. 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. Analysis of the implants attached biofilm might contribute to the diagnosis of PJI. One way of analysing biofilms is sonication of the removed implant. Sonication uses ultrasound for the disintegration of the biofilm from the arthroplasty. Cultures of the obtained sonication fluid can identify a possible causal microorganism despite negative standard cultures.

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

INTRODUCTION

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.
the role of sonication in the diagnosis of PJI of TSA\textsuperscript{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\textsuperscript{16,19}.

The diagnosis of PJI was based on the two major criteria described by Parvizi et al. (Appendix 1)\textsuperscript{19}, (1) the presence of a sinus tract communicating with the prosthesis 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 or CRP and/or wound problems (n=7). We found increased pre-

The most common primary indications for TSA 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-

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

rTSA, reverse total shoulder arthroplasty; aTSA, anatomic total shoulder arthroplasty; HA, hemiarthroplasty.
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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

| 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.

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

<table>
<thead>
<tr>
<th>Initial synovial fluid and tissue cultures</th>
<th>Sonication cultures</th>
<th>Later synovial fluid and tissue cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A Patient 1</td>
<td>7/7 negative</td>
<td>Positive c. acnes</td>
</tr>
<tr>
<td>Group A Patient 2</td>
<td>12/12 negative</td>
<td>Positive c. acnes</td>
</tr>
<tr>
<td>Group A Patient 3</td>
<td>12/12 negative</td>
<td>Positive c. acnes</td>
</tr>
<tr>
<td>Group B Patient 4</td>
<td>1/10 positive</td>
<td>Positive c. acnes, s. haemolyticus, s. epidermidis, corynebacterium</td>
</tr>
<tr>
<td>Group B Patient 5</td>
<td>1/9 positive</td>
<td>Positive c. acnes</td>
</tr>
<tr>
<td>Group B Patient 6</td>
<td>1/9 positive</td>
<td>Positive s. aureus</td>
</tr>
</tbody>
</table>

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. However, the role of sonication in the diagnosis of PJI in TSA remains controversial. 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. However, Grosso et al., Torrens et al. and Akgun et al. found a lower sensitivity for sonication compared to tissue cultures. 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. 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 the 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. 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.

REFERENCES

### 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 prosthesis; 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.