Two-stage revision remains the gold standard for successful treatment of chronic periprosthetic joint infection after total knee arthroplasty (TKA). This technique was first described by Insall et al.\(^1\) and Haleem et al.\(^2-6\) To determine the correct time for TKA reimplantation, a reliable diagnostic method to detect persistent periprosthetic joint infection is essential, but no reliable method has been identified.\(^7-9\) For the serologic infection parameters erythrocyte sedimentation rate and C-reactive protein level, the most common currently used diagnostic method to identify persistent periprosthetic joint infection before TKA reimplantation is synovial aspiration of the knee joint.\(^10,11\)

The current study investigated the diagnostic validity of synovial spacer aspiration to detect persistent periprosthetic joint infection during 2-stage septic revision TKA.

abstract

Despite the lack of validation, synovial aspiration remains a common practice during 2-stage septic revision total knee arthroplasty (TKA). The goal of this study was to investigate the diagnostic validity of synovial polymethylmethacrylate (PMMA) spacer aspiration of temporary knee arthrodesis to detect persistent periprosthetic joint infection before TKA reimplantation. This retrospective cohort study included 73 consecutive patients who underwent 2-stage septic revision TKA according to a standard protocol. After explantation surgery, including temporary arthrodesis with an intramedullary stabilized PMMA spacer, all patients had synovial aspiration 2 weeks before reimplantation to exclude persistent periprosthetic joint infection. Patients had a 2-week antibiotic holiday before aspiration. Sensitivity and specificity of the synovial PMMA spacer joint aspiration for the detection of periprosthetic joint infection were determined and referenced against intraoperative microbiologic and histologic samples obtained at second-stage surgery. Sensitivity of the synovial PMMA spacer aspiration was 21%. Because of poor diagnostic validity, synovial PMMA spacer aspiration cannot be recommended for routine exclusion of persistent periprosthetic joint infection before TKA reimplantation. Therefore, exclusion of persistent periprosthetic joint infection should be supplemented by other diagnostic methods, and it is not necessary to delay TKA reimplantation for PMMA spacer aspiration. [Orthopedics. 2017; 40(4):231-234.]

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During this retrospective diagnostic study, 73 consecutive patients who underwent standard 2-stage septic revision TKA from 2010 to 2011 were analyzed (level of evidence III). Institutional review board approval was obtained before the study was performed. Periprosthetic joint infection was classified according to the criteria of Zimmerli et al and Parvizi et al. All patients underwent 2-stage septic revision TKA according to the standard protocol described later. Synovial spacer aspiration was performed 2 weeks before second-stage surgery, after a 2-week antibiotic-free interval. All microbiologic samples were incubated for 14 days.

Exclusion criteria included incomplete data sets, lack of microbiologic results from synovial spacer aspiration, and antimicrobial therapy within 2 weeks before the acquisition of microbiologic samples. Patients whose treatment deviated from the standard protocol were excluded as well. Based on the exclusion criteria, 11 cases were excluded, leaving 62 cases for analysis.

In the study department, the standard surgical technique for first-stage surgery includes synovial aspiration before capsulotomy, acquisition of 5 periprosthetic tissue samples, sampling of the periprosthetic membrane for histologic analysis, complete synovectomy, debridement of osseous surfaces, and lavage of the joint space with 0.04% polymixin (Serasept; Serag-Wiessner KG, Naill, Germany). Temporary knee arthrodesis was performed with a customized gentamicin-loaded polymethylmethacrylate (PMMA) spacer reinforced with 2 steel tubes, allowing for intramedullary femoral and tibial fixation, with a standard technique that was published previously. After intraoperative acquisition of microbiologic samples, intraoperative antibiotic prophylaxis was initiated with 2 g cefazolin and continued postoperatively with intravenous administration of 3 g sultamicillin 3 times daily. Treatment was then adapted according to the results of the resistance test after first-stage surgery.

The temporary arthrodesis was maintained for 8 weeks and supplemented with systemic antimicrobial therapy during the first 6 weeks. After a 2-week antibiotic-free interval, synovial spacer aspiration was performed. When no fluid could be aspirated, intra-articular injection of 3 mL sterile saline was performed and reaspirated. The collected fluid was cultivated for 14 days to ensure detection of slow-growing bacterial species. The definitive diagnosis of persistent periprosthetic joint infection was made according to the results of intraoperatively acquired microbiologic and histologic samples at second-stage surgery. Patients with persistent periprosthetic joint infection, as detected by synovial spacer aspiration, underwent repeat debridement and had an extended course of antimicrobial therapy. Patients who underwent TKA reimplantation and had positive intraoperative cultures had an extended course of antimicrobial therapy for a minimum of 6 weeks, depending on the species isolated and the corresponding resistance pattern. For patients whose microbiologic samples obtained during second-stage surgery had negative results, antibiotic prophylaxis was discontinued after 2 weeks.

Sensitivity, specificity, negative predictive value, and positive predictive value for the detection of persistent periprosthetic joint infection were calculated for synovial aspiration and serum C-reactive protein level at first-stage surgery, synovial spacer aspiration, and second-stage surgery (Table 1).

### Results

This study included 27 men and 35 women. Average age was 68 years (±11 years). In 7 cases, persistent periprosthetic joint infection was detected with synovial spacer aspiration before second-stage surgery (Table 2). Patients underwent additional debridement and exchange of the PMMA spacer supported by an extended course of antibiotic therapy for an additional 6 weeks. In 27 cases, the synovial spacer aspiration showed false-negative results in reference to the intraoperative samples of the second-stage surgery. Sensitivity and specificity of the microbiologic samples of synovial spacer aspiration are shown in Table 1.

The positive bacterial isolations obtained at explantation, synovial spacer aspiration, and second-stage surgery for the 7 cases of persistent periprosthetic joint infection detected with synovial spacer aspiration are shown in Table 2. In 4 of the 7 cases of culture-positive synovial spacer aspiration, the bacterial species detected were concordant with the bacterial species found during explantation. These included *Staphylococcus epidermidis* (patient 1), *S aureus* (patient 3), *Enterococcus faecalis* (patient 5), and *Candida albicans* (patient 6), indicating a true persistent periprosthetic joint infection that was identified with synovial spacer aspiration, despite previous debridement and antibiotic therapy. In the 3 other cases of persistent periprosthetic joint infection, bacterial species detected with synovial spacer aspiration were different from those found during first-stage surgery. These included *S epidermidis* (patient 2),

### Materials and Methods

#### Table 1

<table>
<thead>
<tr>
<th>Diagnostic Performance of Synovial Spacer Aspiration for Detection of Persistent Periprosthetic Joint Infection</th>
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<tbody>
<tr>
<td>Parameter</td>
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<tr>
<td>Sensitivity</td>
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<td>Specificity</td>
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<td>Positive predictive value</td>
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<td>Negative predictive value</td>
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#### Table 2

| Parameter | Value |
|---|
| Sensitivity | 21% |
| Specificity | 100% |
| Positive predictive value | 100% |
| Negative predictive value | 51% |
E faecalis (patient 4), and Propionibacterium acnes (patient 7).

In all cases of persistent periprosthetic joint infection detected with synovial spacer aspiration, no gentamicin-sensitive species were found. This was also the case for all bacterial species isolated during second-stage surgery.

**DISCUSSION**

Despite the lack of validation, synovial aspiration during 2-stage revision TKA is a common clinical practice before prosthesis reimplantation.11 In the current study, synovial spacer aspiration for detection of persistent periprosthetic joint infection during 2-stage septic revision TKA showed sensitivity of only 21%.

This study showed that synovial spacer aspiration is not sufficient to exclude persistent periprosthetic joint infection. The very low sensitivity of 21% for detection of persistent periprosthetic joint infection with synovial spacer aspiration is a clear indication that synovial spacer aspiration has insufficient diagnostic validity for routine clinical use. The reason for its poor performance is likely the low number of planktonic bacteria present in the synovia in persistent periprosthetic joint infection.16-18 In the case of periprosthetic joint infection, the causative bacterial species are present in the form of a biofilm, with few bacteria present in the synovia.16-18 For other joints, such as the hip, large variations in the sensitivity of synovial aspiration have been reported, with sensitivity ranging from 12% to 100% for synovial aspiration.18,19 Risk factors associated with synovial aspiration, such as contamination during the procedure, should be considered and make the practice of synovial spacer aspiration during septic 2-stage revision TKA less attractive.

The authors reisolated the microorganisms from the index procedure 4 times, and newly isolated bacteria were found in 3 cases (Table 2). There are 3 possible explanations for this finding. The first is that the patients had polymicrobial periprosthetic joint infection and the additional species were not detected during first-stage surgery.20-22 The other 2 possibilities are that the additional species represent contamination either during synovial spacer aspiration or intraoperatively. In 1 case of polymicrobial periprosthetic joint infection, 1 of the 2 index microorganisms was detected during second-stage surgery, suggesting a true persistent periprosthetic joint infection (patient 1). In addition, a single case of fungal infection with C albicans persisted beyond revision surgery (patient 6).

**Limitations**

One limitation of this study was that the study design most likely was not ideal for culture-based detection of gentamicin-sensitive bacterial species during second-stage surgery (independent of reimplantation or repeat debridement). Because gentamicin was added to the PMMA spacer, the concentration of gentamicin in situ at the time of synovial spacer aspiration affected the diagnostic culture findings. No gentamicin-sensitive species were detected with synovial spacer aspiration after local gentamicin elution from the PMMA spacer. Further, analysis of the resistograms of all isolated bacteria for gentamicin sensitivity showed no newly developed resistance to gentamicin over the course of the study, suggesting that the concentration and duration of treatment were sufficient to eradicate the initially detected bacterial species.

**CONCLUSION**

The current findings suggest that parameters other than microbiologic results from synovial spacer aspiration should be used to determine the correct timing of TKA reimplantation. A possible solution to this dilemma is the use of non–culture-based parameters, such as alpha-defensin or synovial C-reactive protein level, to confirm the eradication of periprosthetic joint infection before reimplantation. A second possible solution that does not require culture is the use of intraoperative.
frozen tissue sections, which have shown good diagnostic performance for predicting culture-positive infection during the explantation stage of 2-stage septic total hip arthroplasty and revision TKA.23 However, diagnostic performance for excluding culture-positive infection was poor.23 Evidence for the use of frozen tissue sections to exclude periprosthetic joint infection before TKA reimplantation is even worse, with reported sensitivity of 25% to 33%.24,25

In light of the study findings, the authors no longer perform synovial spacer aspiration before second-stage surgery. After temporary arthrodesis and continuous antibiotic therapy are maintained for a minimum of 6 weeks, TKA reimplantation is performed if serum infection findings (C-reactive protein level and erythrocyte sedimentation rate) are normal and if the knee does not show clinical signs of persistent infection (effusion, calor, and rubor). The greatest advantage of eliminating synovial spacer aspiration from the treatment protocol is that antibiotic therapy can be continued from the time of explantation until second-stage surgery without interruption because there is no need for an antibiotic holiday before synovial spacer aspiration.

REFERENCES