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Complications - Infection

Puncture Protocol in the Diagnostic Work-Up of a Suspected Chronic Prosthetic Joint Infection of the Hip

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ABSTRACT

Background: Diagnosing a chronic prosthetic joint infection (PJI) can be challenging. We hypothesized that obtaining preoperative tissue samples for culture in hip arthroplasty will increase the likelihood of diagnosing an infection before revision surgery. The aim of this cohort study was to determine the diagnostic accuracy of 2 tissue acquiring biopsy strategies to diagnose a PJI.

Methods: Patients with a painful hip arthroplasty, in which a chronic PJI was suspected, were included. Tissue samples were obtained either by ultrasound guidance with a 16-Gauge needle (2012-2013) or in the operating room with a thick-bore needle (2013-2016). Revision surgery tissue biopsies were used as the gold standard. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were calculated.

Results: A total of 16 patients in the ultrasound cohort and 29 patients in the surgical cohort were included. Thirty-one percent (n = 14) were finally diagnosed with a PJI. The addition of thick bore needle tissue biopsies resulted in 9% more diagnosed PJIs compared with synovial fluid alone. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio was 33%, 85%, 33%, 85%, 2.2, and 0.8, respectively, for the ultrasound-guided biopsy cohort and 82%, 100%, 100%, 90%, 0, and 0, respectively, for the surgical biopsy cohort.

Conclusion: Obtaining multiple good quality tissue biopsies in a sterile environment will contribute to the diagnosis of a chronic PJI of the hip, with a higher diagnostic accuracy compared with ultrasound-guided thin needle biopsies and compared with synovial fluid culture alone.

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To diagnose a chronic prosthetic joint infection (PJI) can be a clinical challenge [1]. In contrast with an acute PJI, patients with a chronic infection may only have mild pain or discomfort at the site of the prosthesis, which can be present for months or even years after the primary arthroplasty, whereas evident signs of infection during additional work-up may be absent [2]. To illustrate, patients with a presumed aseptic loosening of the prosthesis are eventually diagnosed with a PJI during revision surgery in 10%-20% of cases by the presence of positive intraoperative cultures [3–5]. Although inflammatory parameters, (synovial) biomarkers, and advanced nuclear imaging greatly increase the likelihood of diagnosing a PJI, it is important to know the causative microorganism and its susceptibility pattern preoperatively to tailor antibiotic therapy as soon as possible [6–11]. Empirical treatment leads to the unnecessary use of broad spectrum antibiotics with, as a consequence, a higher chance of adverse events, longer hospital admissions, inadequate therapy, and the induction of bacterial resistance in a subset of patients. Moreover, when the causative microorganism is considered as difficult to treat, a 2-stage revision strategy might be preferred [1,12–14].

Synovial fluid culture has a high specificity (95%), but a moderate sensitivity (72%) for detecting the causative microorganism preoperatively [10,15]. In addition, synovial fluid cannot be obtained in some patients, especially in those patients who are suspected for a chronic infection of a total hip arthroplasty in which a “dry tap” occurs (23% of cases) [16]. Therefore, it is of utmost importance that the preoperative diagnostic work-up should be

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improved in cases with negative synovial fluid cultures and in patients with a dry tap, but with a remaining suspicion of a PJI. This might be accomplished by obtaining tissue biopsies for culture preoperatively [9,17,18].

We hypothesized that acquiring preoperative tissue samples for culture will increase the likelihood of diagnosing a PJI. Tissue acquiring biopsies are included in our PJI diagnostic protocol since 2012. At first, this was performed by ultrasound-guided thin Tru-Cut needle biopsy (16G), but after 2013 by oncology style Jamshidi surgical biopsies (8G) by an orthopedic surgeon in the operating room. The aim of our study was to determine the diagnostic accuracy of both tissue acquiring biopsy strategies to diagnose a PJI and to determine the added value of tissue biopsies over synovial fluid cultures alone in patients with a painful hip arthroplasty in which a chronic PJI was suspected.

Materials and Methods

In this consecutive cohort study (2012-2016), we retrospectively analyzed the diagnostic accuracy of tissue cultures acquired by ultrasound-guided thin needle biopsies (2012-2013) and by thick bore needle (Jamshidi, 8 Gauge) biopsies obtained in the operation theatre (2013-2016). Intraoperative tissue cultures obtained during revision surgery were used as gold standard. Patients with a clinical suspicion of a chronic hip PJI were included. A chronic PJI was suspected based on pain at the site of the implant for more than 3 weeks, with or without: increased inflammatory parameters in serum, signs of loosening on plain radiographic imaging, and/or signs suggestive of infection using advanced nuclear imaging [12,19]. Eligible for inclusion for this study were patients who received both diagnostic biopsies and a subsequent revision surgery to apply the intraoperative cultures as a gold standard.

Ultrasound-Guided Thin Needle Biopsies (Radiology Department)

The procedure was carried out at the radiology department in the ultrasound room. After prepping the skin with chlorhexidine-alcohol 0.5%/70% and after the placement of sterile surgical drapes, aspiration of synovial fluid was performed by ultrasound guidance. In addition, several biopsies of synovial tissue were taken with a 16-Gauge Tru-Cut biopsy needle [20].

Surgical Thick Bore Needle Biopsies (Operating Room)

In an outpatient setting, tissue biopsies were obtained in the operation room by one of the orthopedic surgeons or orthopedic residents. Patients received spinal or general anesthesia and the procedure was performed in supine position. Skin sterilization was achieved with chlorhexidine-alcohol 0.5%/70% and surgical drapes were placed. A 5 mm incision was made anterolaterally relative to the hip joint and with x-ray guidance, a thick bore 8G Jamshidi needle was used for obtaining synovial fluid and preferably at least 4 synovial tissue biopsies from different locations around the prosthetic components of the hip arthroplasty. In case of a specific hotspot on nuclear imaging, additional periprosthetic bone biopsies at these sites were obtained. No antibiotic prophylaxis was administered before, during, or after the procedure.

Tissue Culture Sampling During Revision Surgery (Gold Standard)

The revision surgery of the hip arthroplasty is performed in lateral decubital position. Skin sterilization was achieved with 5% povidone iodine−69% ethanol or, in case of an iodine allergy, chlorhexidine-alcohol 0.5%/70% and surgical drapes were placed as protocoled. The revision is performed by a posterolateral approach of the hip. Antibiotic prophylaxis is withheld until tissue biopsies are collected for culture. Aspiration of synovial fluid and tissue biopsies are collected from the fascia lata, articular capsule, soft tissue surrounding the acetabulum, and tissue from the femur. Removed prosthetic components are also sent for sonication. Handling of Cultures

During the puncture protocol as well as during the revision surgery, antibiotic prophylaxis was withheld until tissue samples were obtained. At least one aspiration of synovial fluid (if possible) and a minimum of 5 tissue biopsies (synovial/fibrous or bone) from different locations around the joint/prosthetic components were collected [21]. Tissue samples were placed in a sterile container and sent for culture to the medical microbiology department. Each sample was cultured for 9–11 days on blood and chocolate agar under aerobic conditions with 5% CO₂ and on Brucella blood agar under anaerobic conditions. In addition, all samples were cultured in fastidious broth. All broths were subcultured on blood and Brucella blood agar after 7 days of incubation. Subcultures were incubated for 2 days. Cultures were interpreted by the medical microbiologist and a PJI was diagnosed if a pathogen with the same antibiogram was isolated from at least two separate tissue or fluid samples, according to the Musculoskeletal Infection Society criteria [22]. Since 2016, extracted prosthetic components were also sent for sonication.

Statistical Analysis

Intraoperative tissue biopsies obtained during revision surgery were used as the gold standard. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and the diagnostic odds ratio for the preoperative acquired tissue biopsies were calculated. The likelihood ratios and the diagnostic odds ratio are diagnostic tests which are independent of prevalence [23,24].

Results

A total of 45 patients with a symptomatic hip arthroplasty were included. No patients were excluded as all eligible patients underwent a revision surgery. The ultrasound cohort consisted of 16 patients and the surgical cohort of 29 patients. Baseline characteristics are outlined in Table 1. Of the 45 included patients, a total

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographics.</th>
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<tbody>
<tr>
<td><strong>Baseline Data</strong></td>
<td><strong>Ultrasound Biopsy Cohort (n = 16)</strong></td>
</tr>
<tr>
<td>Female, %</td>
<td>75</td>
</tr>
<tr>
<td>Median age, y (range)</td>
<td>68.6 (37.8-81.4)</td>
</tr>
<tr>
<td>Median CRP, mg/L (range)</td>
<td>4 (2-13)</td>
</tr>
<tr>
<td>Median number of cultures acquired during biopsy protocol (range)</td>
<td>2 (1-2)</td>
</tr>
<tr>
<td>Median number of cultures acquired during revision (range)</td>
<td>5 (2-7)</td>
</tr>
<tr>
<td>Number of PJI diagnosed during revision surgery</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Median CRP in PJI patient, mg/L (range)</td>
<td>3 (2-6)</td>
</tr>
<tr>
<td>Median CRP in non-PJI patient, mg/L (range)</td>
<td>5 (2-13)</td>
</tr>
</tbody>
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CRP, C-reactive protein; PJI, prosthetic joint infection.
of 14 patients were diagnosed with a PJI (31%), including 3 of 16 in the ultrasound cohort (20%) and 11 of 29 in the surgical cohort (38%). The median serum C-reactive protein of the ultrasound cohort (20%) and 11 of 29 in the surgical cohort of 14 patients were diagnosed with a PJI (31%), including 3 of 16 in the ultrasound-guided biopsy cohort and 82%, 100%, 100%, 90%, and 0.2, respectively, for the ultrasound-guided biopsy cohort and 82%, 100%, 100%, 90%, infinite, and 0.2, respectively, for the surgical biopsy cohort. The addition of thick bore needle tissue biopsies resulted in 9% more diagnosis of a PJI with less false-negatives. The thin needle used in the ultrasound-guided biopsies (8G) showed a clear superiority above none in the surgical cohort (192 biopsies). Our results regarding the diagnostic accuracy of the preoperative biopsies for diagnosing a chronic PJI are in agreement with literature in which the sensitivity ranges between 80% and 90% and the specificity ranges between 90% and 100% [9,18,25–33].

To increase the homogeneity of our study population, we solely analyzed patients with a hip arthroplasty, but the same puncture protocol was used in our institution for knee (15 cases) and elbow (5 cases) arthroplasties in which the same diagnostic accuracy was demonstrated (data not shown).

One of the limitations of this study is the small number of inclusions in the ultrasound-guided biopsy cohort which makes direct comparison with the surgical cohort difficult. The low number of inclusions in the ultrasound cohort is explained by the fact that we changed the protocol in 2013, as we noticed important discrepancies between the ultrasound-guided cultures and the revision cultures. The small number of culture samples submitted by the radiologist resulted in a low internal validity, and introduced problems in the interpretation whether to interpret a positive culture as relevant in case of low-virulent microorganisms. The quality of the ultrasound-guided biopsies was poor because of their small size. In addition, the obtained tissue was not always representative as muscle instead of periprosthetic tissue was sometimes observed at histologic analysis (data not shown). Although the surgical biopsy technique is more invasive, requiring regional or general anesthesia, an operation room and a day care hospitalization, obtaining thick bore needle biopsies improves the quality and quantity of samples for both culture and histology. A limitation of our study is that we excluded patients with a painful arthroplasty joint in which biopsies were acquired but no subsequent revision surgery was performed. Although this exclusion was a necessity to have a gold standard (the intraoperative tissue cultures during revision), this could have overestimated the sensitivity of the preoperative biopsies.

A strong point is that our data is a result of a standardized diagnostic protocol which was applied by all orthopedic surgeons and residents making our results generally applicable. The sensitivity for finding a PJI preoperatively increased with 9%, allowing adequate tailoring of the surgical approach and antibiotic therapy.

Obtaining surgical biopsies has some disadvantages. Incorporating first, surgical biopsies do expose the patient to an extra invasive procedure including anesthesia. Second, although introducing a secondary infection by performing an arthrocentesis is very rare (0.02%), data are lacking about the risk of a more invasive procedure [34]. As we obtained the biopsies in a sterile environment (the operating room), we believe that the risk for introducing a secondary infection is very low. Third, it is a costly diagnostic procedure because of the need for the operation room and requirement of anesthesia, but probably cost-effective considering the advantage to choose the optimal surgical and antibiotic therapy.
Synovial biomarker such as alpha defensin, leucocyte esterase, interleukin 6, and calprotectin can be used to aid in the diagnosis of a PJI. Some of these biomarkers have a very high diagnostic accuracy and as a simple aspiration of joint fluid suffices, it is an easy way to exclude a PJI with a sufficient probability [35,36]. However, if a PJI is suspected, you still need a positive culture from the synovial fluid aspiration. Direct inoculation in blood culture flasks increases the sensitivity of joint fluid cultures [21]. If a PJI is suspected based on clinical assessment and positive biomarkers, but the culture of synovial fluid remains negative, biomarkers must be acquired to be informed about the microorganism and to be able to tailor treatment. We believe that this is a very sensitive and cost-effective strategy for the diagnosis of difficult to culture, low-grade, chronic PJI.

In conclusion, obtaining multiple good quality tissue biopsies in a sterile environment will contribute to the diagnosis of a PJI, with a higher diagnostic accuracy compared with joint aspiration alone and ultrasound-guided thin needle biopsies. In patients with a clinical suspicion of a chronic PJI, we recommend to obtain tissue biopsies before surgery in patients with culture-negative synovial fluid to tailor antibiotic treatment.

References