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QUESTION 4: In patients with multiple arthroplasties in place who have developed a periprosthetic infection (PJI) of one joint, should other joints be investigated for PJIs also?

RECOMMENDATION: We recommend that when a patient develops a PJI in one joint, the other total joint arthroplasties (TJAs) should be examined clinically and if suspicion for PJI remains, or the patient is immunocompromised, then other joints should be aspirated.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 92%, Disagree: 6%, Abstain: 2% (Super Majority, Strong Consensus)

RATIONALE

Up to 45% of patients undergoing primary TJA due to idiopathic osteoarthritis require at least one additional, distant, TJA [1]. Due to increasing numbers of TJAs performed every year and the continuous aging population, patients with multiple arthroplasties are expected to increase. Furthermore, mortality rates after revision for PJIs are estimated to be significantly higher than mortality rates after aseptic revisions [2]. This highlights the importance in determining the infection status of other joints in patients with a PJI.

A frequent concern has always been the presence of distant joint PJIs secondary to possible hematogenous seeding [3–14]. Murray et al. were the first to define metachronous, different joint PJIs [12]. They estimated that the risk of failure of a second, prosthetic joint, already in place, when an initial PJI develops, could be as high as 18%. A limited number of studies have been published evaluating the risk of PJIs in patients with multiple arthroplasties [13–17]. Luessenhop et al. presented a similar incidence of 19% of other joint infections among 145 patients who had more than one joint in place at initial PJI [13]. They also identified rheumatoid arthritis as a risk factor among these patients. Furthermore, in a cohort of 55 patients, Jafari et al. showed a 20% incidence of distant subsequent infection at a mean of two years [14]. They also evaluated that the type of organism of the subsequent infection was found to be the same in 36% of the patients. Abblitt et al., in a more recent study, evaluated 76 patients with multiple joints replaced and estimated the rate of subsequent infection to be lower, at 8.3% [15]. This study also emphasized the role of bacteremia during the first infection in developing a subsequent infection. Haverstock et al. described a 6.3% risk of a subsequent PJI from a total of 206 patients [16]. They identified the same bacteria of the subsequent PJI in only 2.9%. Zeller et al. derived 16 patients with concomitant PJIs, from a cohort of 1,185 with prosthetic hip or knee infections, corresponding to 1.4% of their total PJI population [17].

Studies have been consistent in demonstrating that the risk of developing a PJI in a second prosthetic joint is higher than the base line PJI [12–17]. The estimated risk of second joint PJI ranges from 1.4 to as high as 20%. Rheumatoid arthritis and bacteremia have been identified as possible risk factors for an increased risk of multiple joint infections [13,15]. These published data acknowledge that the other prosthetic joints are at increased risk and raise suspicions whether an ongoing sub-acute infection is present at the time of the initial PJI. However, no study in the literature has evaluated whether at the time of the initial PJI, other arthroplasties should be also investigated.

Nevertheless, investigation of other prosthetic joints should be performed depending on the symptoms of that joint at the time of the other joint PJI. The initial approach should include clinical evaluation. If symptoms are present, initial radiographic evaluation should be performed and in the setting of suspected infection, synovial fluid aspiration should be attempted. Clinical investigation must be undertaken always to identify signs that can raise concern for underlying infection. If aspiration is performed, synovial white blood cell (WBC) count and polymorphonuclear (PMN) % should be requested as they have shown to be highly accurate test modalities [18]. On the contrary, cost-effectiveness of aspirating other joints has also not been investigated; therefore, recommendation in favor or against cannot be made with available data. However, we recommend clinical evaluation of other joints to minimize the risk of failure in the treatment of PJIs.

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QUESTION 5: Are point-of-care (POC) rapid tests for diagnosing periprosthetic joint infections (PJIs) validated and useful?

RECOMMENDATION: Yes, there are several useful POC tests which can be added to the diagnostic workup of PJIs. A number of studies support the usefulness and reliability of the leukocyte esterase (LE) test strip and the alpha-defensin lateral flow test kit. Diagnostic criteria for PJIs should be updated and consider inclusion of these tests.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 73%, Disagree: 21%, Abstain: 6% (Super Majority, Strong Consensus)

RATIONALE

A POC test is defined as a medical diagnostic tool which is used at the time of evaluation of a patient with an immediate result. These are rapid and simple medical tests that can be performed at the bedside. The idea behind a POC test is to provide real-time information upon which the treating physician can act.

After our systematic review, 11 original papers [1–11] and 4 review articles [12–15] assessing the diagnostic value of the LE test strip were included. The pooled data of 2,061 patients extracted from the original papers revealed a sensitivity of 85.7% (95% confidence interval (CI), 65.9 to 90.7%), a specificity of 94.4% (95% CI, 85.3 to 97.7%), a positive predictive value (PPV) of 84.3% (95% CI, 71.5 to 91.7%) and a negative predictive value (NPV) of 94.0% (95% CI, 85.8 to 97.1%).

The first prospective study investigating the utility of the LE strip test in diagnosing PJIs was conducted by Parvizi et al. A total of 108 patients who had painful total knee arthroplasties (TKAs) were investigated and the LE test (with a positive result being ++) had a sensitivity of 80.6% (95% CI, 61.9 to 91.9%), specificity of 100% (95% CI, 94.5 to 100.0%), and PPV of 100% (95% CI, 83.4 to 100.0%). The authors concluded that the LE strip test could be used effectively, by itself or in conjunction with other tests, either as a rapid screening mechanism or for confirmation of a suspected PJI [6].

In a systematic review of Wyatt et al. involving nearly 2,000 patients from five studies, the pooled diagnostic sensitivity and specificity of LE for PJI was 81% (95% CI, 49 to 95%) and 97% (95% CI, 82 to 99%), respectively [15]. Another meta-analysis of eight qualified studies with a total of 1,011 participants showed a higher pooled sensitivity of 90% (95% CI, 76 to 96%) and a similar specificity of 97% (95% CI, 95 to 98%) [14].

The limitation of the LE test is blood contamination interfering with readability of the test result. A recent study confirmed the reliability of the LE strip test by reporting an excellent sensitivity (92.0%) and specificity (93.1%). Furthermore, the latter study confirmed that synovial fluid centrifugation is an effective means of overcoming interference from erythrocytes [5].

After our systematic review, six original papers [16–21] and one review article [22] assessing the diagnostic value of the alpha-defensin lateral-flow test were included. The pooled data of 486 patients showed a sensitivity of 78.5% (95% CI, 64.7 to 94.5%), a specificity of 93.3% (95% CI, 87.0 to 99.6%), a PPV of 87.2% (95% CI, 74.6 to 98.1%) and a NPV of 90.2% (95% CI, 83.7 to 98.2%).

Deirmengian et al. introduced alpha-defensin as a robust synovial biomarker; however, the first studies were published about the laboratory-based enzyme-linked immunosorbent assay (ELISA) test (immuno-assay) [2]. Recent studies showed validated good results of the lateral-flow version of the alpha defensin test being a POC test [16–21]. A level II diagnostic study based on the results of 121 patients revealed a sensitivity and specificity of 97.1 and 96.6%, respectively [17]. The largest series was published by Gehrke et al. as a level I diagnostic study with 195 joints of 191 patients. The overall sensitivity of the alpha-defensin PJI test was 92.1% (95% CI, 83.6 to 97.1%), the specificity was 100% (95% CI, 97.0 to 100%), the PPV was 100% (95% CI, 94.9 to 100%), and the NPV was 95.2% (95% CI, 89.9 to 98.2%). The overall accuracy was 96.9% (95% CI, 93.4 to 98.9%) [18].

In the meta-analysis performed by Suen et al., the pooled sensitivity and specificity of the alpha-defensin lateral flow test was somewhat less appealing, being 77.4% (95% CI, 63.7 to 87.0%) and 91.3% (95% CI, 82.8 to 95.8%), respectively [22]. There is clear evidence that the lateral-flow test has a lower accuracy than the lab-based ELISA immuno-assay [18,22]. The test results may be influenced by metallosis [19] or crystal arthropathy, such as gout [23]. In addition, the