in each step. Ultimately, the algorithm shares many similarities to the previous algorithm as serological testing should be performed first, followed by more invasive tests. This stepwise approach of serological markers prior to joint aspiration has been demonstrated to be the most cost-efficient method of diagnosing PJIs using a multicriteria decision analysis in prior studies [11].

The first step in evaluating for a PJI should include serum testing for C-reactive protein, D-dimer and erythrocyte sedimentation rate. If at least one is elevated, or if there is a high clinical suspicion, clinicians should proceed with synovial fluid testing including a synovial fluid white blood-cell count with differential and leukocyte esterase testing. Intraoperative findings including purulence, histology, next generation sequencing (NGS) or a single positive culture can aid in cases where the diagnosis has not been conclusively ruled in or out prior to revision surgery, or when the aspiration does not yield fluid for analysis (a dry tap). The proposed algorithm was formally validated on a separate cohort of patients and demonstrated a high overall sensitivity (96.9%, 95% confidence interval (CI): 93.8-98.8) and specificity (99.5%, 95% CI: 97.2-100).

In the patient with a painful total joint arthroplasty, it is important to always consider infection. Initially, the first step considers patient risk factors, clinical findings and serum markers; the latter two of which have high sensitivity, but not necessarily high specificity in order to minimize false-negatives. In the multicenter study, approximately 13% of PJIs could be diagnosed with the first step based on a positive sinus tract. It is important to consider clinical suspicion and patient risk factors, (i.e., pretest probability), to optimize sensitivity as serum testing alone is negative in approximately 2.5% of patients who have a PJI [12]. The next step in the investigation of PJIs requires synovial fluid testing which has greater sensitivity and specificity, but is more invasive. The majority of PJIs will be identified following joint aspiration and synovial fluid analysis (approximately 65%). If a diagnosis of PJI cannot be confirmed or excluded at this point, intraoperative findings should be used and approximately 17% of PJIs will be diagnosed after incorporating intraoperative findings including culture, histology, operative appearance and NGS.

It is important to note that it is possible that the diagnosis of PJI may not be made even after reaching the third stage or may be inconclusive after obtaining synovial tests. These patients are often encountered in clinical practice and represent a real diagnostic challenge. Future research and novel tests are certainly needed in this patient population to reduce the gray area in these borderline patients without overt infection. Furthermore, it is important to note that the proposed algorithm and the definition of PJI may be inaccurate and require a modification in the tests utilized for the following conditions: adverse local tissue reactions, crystalline deposition arthropathies, inflammatory arthroplasty flares and infections with slow growing organisms, such as *Cutibacterium acnes* (formerly *Propionibacterium acnes*). Nevertheless, we hope that the introduction of this evidence-based and validated algorithm may simplify a very challenging process and account for recent advancements in the diagnosis of PJIs.

REFERENCES

[1] Parvizi J, Della Valle CJ. AAOS Clinical practice guideline: diagnosis and treatment of periprosthetic joint infections of the hip and knee. J Am Acad Orthop Surg. 2010;18:771–772.

[2] Della Valle C, Parvizi J, Bauer TW, DiCesare PE, Evans RP, Segreti J, et al. American Academy of Orthopaedic Surgeons clinical practice guideline on: the diagnosis of periprosthetic joint infections of the hip and knee. J Bone Joint Surg Am. 2011;93:1355–1357. doi:10.2106/JBJS.9314ebo.

[3] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Arthroplasty. 2014;29:77–83. doi:10.1016/j.arth.2013.09.040.

[4] Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Diagnosing periprosthetic joint infection: has the era of the biomarker arrived? Clin Orthop Relat Res. 2014;472:3254–3262. doi:10.1007/s11999-014-3543-8.

[5] Tarabichi M, Shohat N, Goswami K, Alvand A, Silibovsky R, Belden K, et al. Diagnosis of periprosthetic joint infection: the potential of next-generation sequencing. J Bone Joint Surg Am. 2018;100:147–154. doi:10.2106/JBJS.17.00434.

[6] Saleh A, George J, Faour M, Klika AK, Higuera CA. Serum biomarkers in periprosthetic joint infections. Bone Joint Res. 2018;7:85–93. doi:10.1302/2046-3758.71.BJR-2017-0323.

[7] Shahi A, Kheir MM, Tarabichi M, Hosseinzadeh HRS, Tan TL, Parvizi J. Serum D-dimer test is promising for the diagnosis of periprosthetic joint infection and timing of reimplantation. J Bone Joint Surg Am. 2017;99:1419–1427. doi:10.2106/JBJS.16.01395.

[8] Ahmad SS, Hirschmann MT, Becker R, Shaker A, Ateschrang A, Keel MJB, et al. A meta-analysis of synovial biomarkers in periprosthetic joint infection: Synovasure™ is less effective than the ELISA-based alpha-defensin test. Knee Surg Sports Traumatol Arthrosc. 2018;26:3039-3047. doi: 10.1007/s00167-018-4904-8.

[9] Wyatt MC, Beswick AD, Kunutsor SK, Wilson MJ, Whitehouse MR, Blom AW. The alpha-defensin immunoassay and leukocyte esterase colorimetric strip test for the diagnosis of periprosthetic infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2016;98:992–1000. doi:10.2106/JBJS.15.01142.

[10] Lee YS, Koo KH, Kim HJ, Tian S, Kim TY, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.

[11] Diaz-Ledezma C, Lichstein PM, Dolan JG, Parvizi J. Diagnosis of periprosthetic joint infection in Medicare patients: multicriteria decision analysis. Clin Orthop Relat Res. 2014;472:3275–3284. doi:10.1007/s11999-014-3492-2.

[12] Akobeng AK. Understanding diagnostic tests 2: likelihood ratios, pre- and post-test probabilities and their use in clinical practice. Acta Paediatr. 2007;96:487–491. doi:10.1111/j.1651-2227.2006.00179.x.

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QUESTION 2: Are there any contraindications to knee or hip aspiration prior to revision surgery?

RECOMMENDATION: There are no clearly identified contraindications to aspiration of the knee or hip joint performed as part of the patient workup for infection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 90%, Disagree: 8%, Abstain: 2% (Super Majority, Strong Consensus)

RATIONALE

Aspiration of a joint is one of the most important aspects of the workup of a patient suspected of having an infected joint. There are numerous studies that have demonstrated the utility of joint aspiration in aiding diagnosis of periprosthetic joint infections (PJIs). In fact, joint aspiration is one of the initial steps in the workup of a patient for diagnosis of PJI, which is reflected in the algorithm

that is proposed by the International Consensus Meeting (ICM) and presented elsewhere in this document.

The question here is not, however, regarding the utility of joint aspiration in the diagnosis of PJIs, but is regarding possible contraindications for joint aspiration. To our knowledge, there is no publication that specifically addresses this question. In clinical practice, there are a few situations that may compel an orthopaedic surgeon or other physicians to avoid aspiration of the joint. One situation is the presence of cellulitis around a joint that is being investigated, with the concern here being that placing a needle through a potentially infected tissue might transfer bacteria into the deeper space of the joint and result in infection. There are no studies that specifically address issues of cellulitis or skin problems overlying the site of aspiration.

The other situation when physicians may refrain from aspiration of a joint is when the patient is on an anticoagulant. There are several studies that discuss the issue of joint injection or aspiration for patients on concomitant anticoagulation medications. Most of the studies address injections and not aspirations, or have far fewer patients undergoing aspiration than injection. Of the studies that are available, there are several low to moderate quality investigations that discuss patients on anticoagulation during an injection or aspiration. None of these studies have found a statistically significant increase in complications including bleeding or infection related to the procedure.

Yui et al. performed a retrospective review of patients on direct oral anticoagulants (DOACs) undergoing arthrocentesis or joint injection [1]. There were 1,050 procedures reviewed with no major bleeding complications reported. Ahmed et al. conducted a retrospective review of clinical records of patients who were on therapeutic anticoagulation, comparing arthrocentesis or joint injection in patients who had an international normalized ratio (INR) of >2.0 (456 procedures) to those with INR <2.0 (184 procedures) [2]. The authors found only one major bleeding complication and one late infection in the group with an INR > 2.0 and no statistically significant differences between the two groups. It is important to note that many of the patients in both of these studies were also on antiplatelet agents, but subgroup analysis was not performed. Other small, low quality studies have shown no significant risk of complications [3][4]. A recent review of literature of bleeding risks associated with musculoskeletal procedures recommends that anticoagulation agents such as aspirin, clopidogrel, warfarin and low-molecular-weight heparin (LMWH) should not be discontinued in patients undergoing arthrocentesis and/or joint injections [5]. The conclusions of the latter study were based on the review of the available literature. Although high level studies are lacking, there is some support from retrospective studies for performing joint aspiration in patients who are on anticoagulation.

There is no high-level publication regarding the issue of aspirating a joint through skin affected by cellulitis or other skin lesions, such as psoriasis. The available studies are all expert opinions [6]. In the absence of concrete evidence, we feel that joint aspiration performed as part of workup for PJI is a critical diagnostic step and should be performed even in the presence of cellulitis or other skin lesions. Whenever possible, however, the aspiration should be performed through an area that is least affected. Consideration should also be given to postponing the aspiration in patients with stable and chronic issues until any skin lesions have resolved. The decision to proceed with aspiration in patients with skin lesions around the affected joint needs to be individualized and weighed against the theoretical risk of seeding the joint with bacteria from the overlying affected skin.

Another situation that may create issues regarding aspiration of a joint is in patients with bacteremia. It is hypothesized that traumatic arthrocentesis can theoretically introduce infected blood into the sterile joint. There are no human studies related to this subject matter and no studies have specifically evaluated the risk of PJIs in this situation. Olney et al. investigated the risk of performing a joint aspiration in the setting of bacteremia using a rabbit model and found that 30% of animals developed septic arthritis if blood drawn from an animal with bacteremia was injected into the joint [7]. Thus, one can extrapolate that performing a traumatic arthrocentesis in patients with positive blood cultures may potentially result in seeding of the aspirated joint and subsequent infection. This theoretical risk should also be individualized and weighed in the context of benefits versus risks of joint aspiration.

REFERENCES

[1] Yui JC, Preskill C, Greenlund LS. Arthrocentesis and joint injection in patients receiving direct oral anticoagulants. Mayo Clin Proc. 2017;92:1223–6. doi:10.1016/j.mayocp.2017.04.007.

[2] Ahmed I, Gertner E. Safety of arthrocentesis and joint injection in patients receiving anticoagulation at therapeutic levels. Am J Med. 2012;125:265–269. doi:10.1016/j.amjmed.2011.08.022.

[3] Thumboo J, O'Duffy JD. A prospective study of the safety of joint and soft tissue aspirations and injections in patients taking warfarin sodium. Arthritis Rheum. 1998;41:736–739. doi:10.1002/1529-0131(199804)41:4<736::AID-ART23>3.0.CO;2-P.

[4] Conway R, O'Shea FD, Cunnane G, Doran MF. Safety of joint and soft tissue injections in patients on warfarin anticoagulation. Clin Rheumatol. 2013;32:1811–1814. doi:10.1007/s10067-013-2350-z.

[5] Foremny GB, Pretell-Mazzini J, Jose J, Subhawong TK. Risk of bleeding associated with interventional musculoskeletal radiology procedures. A comprehensive review of the literature. Skeletal Radiol. 2015;44:619–627. doi:10.1007/s00256-014-2065-5.

[6] Dooley DP. Aspiration of the possibly septic joint through potential cellulitis: Just do it! J Emerg Med. 2002;23:210. doi:10.1016/S0736-4679(02)00496-1.

[7] Olney BW, Papasian CJ, Jacobs RR. Risk of iatrogenic septic arthritis in the presence of bacteremia: A rabbit study. J Pediatr Orthop. 1987;7:524–526. doi:10.1097/01241398-198709000-00004.

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QUESTION 3: In the setting of a dry tap, should lavage with a fluid be performed?

RECOMMENDATION: We recommend against injection of normal saline or other fluids into a joint that did not yield any synovial fluid (dry tap) and is being investigated for a periprosthetic joint infection (PJI); except in certain circumstances (e.g., a dedicated radiologist performing aspirate in a sterile fashion).

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 83%, Disagree: 14%, Abstain: 3% (Super Majority, Strong Consensus)