

QUESTION 2: What intraoperative findings during surgical management of orthopaedic infections need to be communicated with the infectious disease (ID) specialist?

RECOMMENDATION: Intraoperative findings that contribute to the diagnosis of periprosthetic joint infection (PJI) must be communicated to the ID specialist. The presence of a sinus tract (major diagnostic criteria) or any other valuable objective data such as cell count, neutrophil differential, frozen section, as well as the result of the point of care diagnostic tests, such as leukocyte esterase and lateral flow alpha-defensin need to be communicated to the ID specialist. The extent of infection, in terms of involvement of soft tissues and bone, any hardware retained and the antibiotic type and dose used in the cement spacer are also useful information that should be detailed in the operative report for communication with the ID specialist.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 90%, Disagree: 6%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

For the purposes of this review, information or data that could be obtained during the course of the surgery and that could impact or influence the surgeon's or infectious disease specialist's decision-making, were categorized into two groups: surgeon findings or observations and intraoperative tests. The recommendations below presume that the surgeon is already documenting/communicating the precise surgery performed (e.g., debridement with retention of prosthesis vs. resection arthroplasty vs. first-stage of two-stage revision) and any plans for future surgery.

The area with the least evidence to support recommendations was that of surgeon observations. Intraoperative findings observed by the surgeon that could impact the decision-making of either the surgeon or infectious disease specialist would seem to be reasonable information to relay to the ID specialist. However, the objectivity and standardization of these findings are highly variable. A prior study compared the clinical acumen of the orthopaedic surgeon to the addition of further advanced testing in diagnosing PJI and found that the addition of intraoperative visual inspection and histopathology improved the accuracy of the surgeon's preoperative diagnosis, though there was no description of discrete or objective definitions of the intraoperative visual inspection [1].

The presence of a sinus tract, one of the major diagnostic criteria of PJI, may be confirmed during the course of a surgery and should be relayed to the ID specialist [2]. The presence of purulence is one visual finding that had long been held as an important intraoperative finding that suggested infection [3] and was supported as a minor criteria in the definition of infection by the workgroup of the Musculoskeletal Infection Society (MSIS) [4]. Due to concerns about the subjectivity of the finding of purulence and the confusing picture that exists in the setting of other causes of cloudy synovial fluid, including metallosis and corrosion, purulence was removed from the minor diagnostic criteria by the International Consensus Meeting (ICM), when they revised the MSIS criteria. Alijanipour et al. [5] evaluated in their study whether purulence was a reliable marker of infection and found a sensitivity, specificity, positive and negative predictive values of 0.82, 0.32, 0.91 and 0.17, respectively. They noted that purulence was not correlated with higher culture positivity, but associated with higher synovial white blood cell (WBC) counts.

Recently, a publication by Parvizi et al. [6] entitled, "The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence Based and Validated Criteria," established a diagnostic algorithm, emphasizing the role of intraoperative findings that are determinant for diagnosis of PJI. The recent criteria do include purulence as a minor criterion. The other tests have also been assessed using the preprobability testing and assigned a diagnostic score.

As the diagnosis of PJI is made usually by relying on a combination of tests, it is critical that the intraoperative findings related to its diagnosis are communicated with the ID specialist. For example, the presence of a sinus tract (major diagnostic criteria) should be confirmed intraoperatively and communicated to the ID specialist.

Other intraoperative findings that may also provide insight into the condition of the joint and influence treatment includes the soft tissue quality or condition, bone quality or condition, implant stability and the amount or type of hardware that was removed or retained. The ID specialists may alter the course and duration of the antibiotic treatment based on these findings. It is critical that the surgeon informs the ID specialist about any hardware that may have been retained. The latter, in particular, influences the course of treatment of the patient [7–10].

The second category of data that is obtained during the course of the procedure and should be communicated to the ID specialist are the results of intraoperative tests. If an intraoperative aspiration of the joint is performed and/or frozen section of the intraoperative samples are analyzed, the result of such findings should also be communicated to the ID specialist. These studies may impact the decision-making and help confirm the diagnosis. However, the results of these studies are not immediately available in the medical record or may not be recorded anywhere else, other than the surgeon's report. Intraoperative frozen histopathology represents one such study. Typical workflow entails a sample being sent to the pathology lab during the course of the surgery and often the result is telephoned into the surgical theater, with a formal written report to follow, sometimes days later. Given the potential importance of those findings on the decision-making and impact it may have on treatment [11–14], the results from this study should be communicated to the ID consultant. In addition to communicating the histology results, it is important to document the anatomic area from which the specimen was taken. Similarly, tissue samples sent for culture should be clearly labeled so that the ID specialist can understand which pathogens were found (e.g., superficial or deep, bone or synovium).

Other intraoperative tests may be valuable in the diagnosis and treatment decision-making for periprosthetic infections and the results should also be available to the ID consultant. Buttaro et al. [15] reported that synovial C-reactive protein (SCRIP) had comparable diagnostic value compared to frozen sections. This was confirmed by Saleh et al. [16] who reported a high diagnostic value with SCRIP, but also demonstrated diagnostic value testing for leukocyte esterase (LE), interleukin-6 (IL-6), interleukin-1 β , α defensin, and interleukin-17 biomarkers. Given the comparable findings in the literature combined with both the relatively inexpensive and immediate point of care (POC) results, Saleh et al. [16] recommend the use of LE testing as a first-line assessment when the diagnosis of PJI is questionable. Another POC test includes the lateral flow IL-6 device, which has shown promising results in the PJI population. Kasperek et al. [17] reported on a POC lateral flow test for α defensin and suggest that although it lacks the accuracy of the lab-based α defensin, it is comparable to evaluating frozen sections. However, they note that it has limited use in cases involving metallosis and further suggest that it may not be used in isolation to rule out PJI [17]. These findings were further supported by a recent review where the authors recommend that care must be taken when interpreting the results of the lateral flow α defensin test for the diagnosis of PJI intraoperatively [18]. As

new POC tests are developed, or current ones are improved upon, the surgeon's intraoperative decision-making combined with these POC biomarker assays may prove to enhance the care that adult reconstruction patients are given, especially in the setting of revision total joint arthroplasty.

REFERENCES

- [1] Petti CA, Stoddard GJ, Sande MA, Samore MH, Simmon KE, Hofmann A. The suspected infected prosthetic joint: clinical acumen and added value of laboratory investigations. *PLoS One*. 2015;10:e0131609. doi:10.1371/journal.pone.0131609.
- [2] Osmon DR, Barbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2013;56:e1–e25. doi:10.1093/cid/cis803.
- [3] Schinsky MF, Della Valle CJ, Sporer SM, Paprosky WG. Perioperative testing for joint infection in patients undergoing revision total hip arthroplasty. *J Bone Joint Surg Am*. 2008;90:1869–1875. doi:10.2106/JBJS.G.01255.
- [4] Parvizi J, Zmstowski B, Barbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res*. 2011;469:2992–2994. doi:10.1007/s11999-011-2102-9.
- [5] Aljaniipour P, Adeli B, Hansen EN, Chen AF, Parvizi J. Intraoperative purulence is not reliable for diagnosing periprosthetic joint infection. *J Arthroplasty*. 2015;30:1403–1406. doi:10.1016/j.arth.2015.03.005.
- [6] Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. *J Arthroplasty*. 2018;33:1309–1314.e2. doi:10.1016/j.arth.2018.02.078.
- [7] Tremblay S, Lau TT, Ensom MH. Addition of rifampin to vancomycin for methicillin-resistant *Staphylococcus aureus* infections: what is the evidence? *Ann Pharmacother*. 2013;47:1045–1054. doi:10.1345/aph.1R726.
- [8] Marschall J, Lane MA, Beekmann SE, Polgreen PM, Babcock HM. Current management of prosthetic joint infections in adults: results of an Emerging Infections Network survey. *Int J Antimicrob Agents*. 2013;41:272–277. doi:10.1016/j.ijantimicag.2012.10.023.
- [9] Zimmerli W, Sendi P. Orthopaedic biofilm infections. *APMIS Acta Pathol Microbiol Immunol Scand*. 2017;125:353–364. doi:10.1111/apm.12687.
- [10] Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. *Foreign-Body Infection (FBI) Study Group. JAMA*. 1998;279:1537–1541.
- [11] Morawietz L, Classen RA, Schröder JH, Dynybil C, Perka C, Skwara A, et al. Proposal for a histopathological consensus classification of the periprosthetic interface membrane. *J Clin Pathol*. 2006;59:591–597. doi:10.1136/jcp.2005.027458.
- [12] Tsaras G, Maduka-Ezeh A, Inwards CY, Mabry T, Erwin PJ, Murad MH, et al. Utility of intraoperative frozen section histopathology in the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. *J Bone Joint Surg Am*. 2012;94:1700–1711. doi:10.2106/JBJS.J.00756.
- [13] Feldman DS, Lonner JH, Desai P, Zuckerman JD. The role of intraoperative frozen sections in revision total joint arthroplasty. *J Bone Joint Surg Am*. 1995;77:1807–1813.
- [14] Lonner JH, Desai P, Dicesare PE, Steiner G, Zuckerman JD. The reliability of analysis of intraoperative frozen sections for identifying active infection during revision hip or knee arthroplasty. *J Bone Joint Surg Am*. 1996;78:1553–1558.
- [15] Buttaro MA, Martorell G, Quinteros M, Comba F, Zanotti G, Piccaluga F. Intraoperative synovial C-reactive protein is as useful as frozen section to detect periprosthetic hip infection. *Clin Orthop Relat Res*. 2015;473:3876–3881. doi:10.1007/s11999-015-4340-8.
- [16] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. *J Am Acad Orthop Surg*. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.
- [17] Kasperek MF, Kasperek M, Boettner F, Faschingbauer M, Hahne J, Dominkus M. Intraoperative diagnosis of periprosthetic joint infection using a novel alpha-defensin lateral flow assay. *J Arthroplasty*. 2016;31:2871–2874. doi:10.1016/j.arth.2016.05.033.
- [18] Suen K, Keeka M, Ailabouni R, Tran P. Synovasure “quick test” is not as accurate as the laboratory-based alpha-defensin immunoassay: a systematic review and meta-analysis. *Bone Joint J*. 2018;100-B:66–72. doi:10.1302/0301-620X.100B1.BJJ-2017-0630.R1.

