Authors: Guido Marra, Matthew Ramsey

QUESTION 3: What is the role of intraoperative histology examination in the evaluation of an elbow arthroplasty for periprosthetic joint infection (PJI)?

RECOMMENDATION: Intraoperative histology for the evaluation of elbow PJI in isolation is not sufficient for the diagnosis of infection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 92%, Disagree: 4%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

There are a number of studies related to the use of histologic examination for the diagnosis of PJI in hip and knee arthroplasty [1–4]. The available literature suggests that although histology cannot be used as a standalone test for the diagnosis of PJI, it does provide valuable information in the work-up of patients with suspected PJI (in fact, the MusculoSkeletal Infection Society (MSIS) workgroup included histological examination as a criterion for its diagnosis) [5,6]. The controversy that exists is what constitutes a positive histology [4]. Currently, based on the MSIS criteria, the presence of more than five neutrophils in more than five high-power fields is indicative of positive histology. The latter is based on examination of periarticular tissues for the diagnosis of infection and the role of histology during reimplantation to assess the presence of persistence infection is less well studied.

The role of histology in the workup of patients with painful total elbow arthroplasty (TEA) is less well known. Our extensive search of the literature revealed only one study that specifically examines the subject of histology in the diagnosis of infected TEA [7]. This study was a retrospective analysis of 208 patients undergoing revision TEA. The sensitivity of histology in the diagnosis of PJI was 51.3%, with a specificity of 93.1%. The positive predictive value of histological examination was 60.6% with a negative predictive value of 90.2%.

Among the cohort, 65 (31%) did not have either histology or cultures taken at the time of revision, which raises the question of selection bias. The sampling sites of the histologic specimens were not standardized and were performed at the discretion of surgeon, averaging less than two samples per patient. Finally, the gold standard to define infection was the presence of a single positive intraoperative culture. Within these limitations, the data suggests that when intraoperative histology demonstrates acute inflammation (according to the criteria of Mirra et al. [8]) the probability of infection is high, but the absence of the acute inflammation does not rule out infection.

Based on the literature (mostly from hip and knee arthroplasty) and our understanding of the challenges that exist in the work-up of patients with painful TEA, we recommend that histological examination of tissues from around the elbow be part of the workup of patients undergoing revision TEA.

REFERENCES

[1] Fehring TK, McAlister JA. Frozen histologic section as a guide to sepsis in revision joint arthroplasty. Clin Orthop Relat Res. 1994:229–237.
[2] Della Valle CJ, Bogner E, Desai P, Lonner JH, Adler E, Zuckerman JD, et al. Analysis of frozen sections of intraoperative specimens obtained at the time of reoperation after hip or knee resection arthroplasty for the treatment of infection. J Bone Joint Surg Am. 1999;81:684–689.
[3] Francés Borrego A, Martínez FM, Cebrian Parra JL, Grañeda DS, Crespo RG, López-Durán Stern L. Diagnosis of infection in hip and knee revision surgery: intraoperative frozen section analysis. Int Orthop. 2007;31:33–37. doi:10.1007/s00264-005-0069-4.
[4] 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.
[5] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98-S107. doi:10.1002/jor.22553.
[6] Parvizi J, Zmistowski B, Berbari 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.
[7] Ahmadi S, Lawrence TM, Morrey BF, Sanchez-Sotelo J. The value of intraoperative histology in predicting infection in patients undergoing revision elbow arthroplasty. J Bone Joint Surg Am. 2013;95:1976–1979. doi:10.2106/JBJS.L.00409.
[8] Mirra JM, Amstutz HC, Matos M, Gold R. The pathology of the joint tissues and its clinical relevance in prosthesis failure. Clin Orthop Relat Res. 1976:221–240.

Authors: Michael McKee, Graham King

QUESTION 4: Is there a role for sonication of retrieved implants from an elbow in the diagnosis of a possible periprosthetic joint infection (PJI)?

RECOMMENDATION: At present, there is no evidence to support the routine use of sonication of removed elbow implants to improve the diagnostic accuracy or yield of cultures in the diagnosis of elbow PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Sonication involves the application of high-frequency ultrasound (approximately 40 kHz) to a retrieved implant in an ultrasound "bath" of appropriate fluid medium. The liquid medium from the bath is then collected and centrifuged, and these aliquots are

cultured with conventional techniques. The concept is that organisms ensconced in a biofilm on the implant are loosened or released by this process, and are more readily cultured.

There was some promising initial evidence from retrospective reviews that the sonication process increased the number of positive cultures, especially in patients who had been receiving antibiotics, or those who had previously negative cultures despite clinical and serological evidence of infection. However, these studies focused on lower extremity arthroplasty. A paper by Holinka et al. noted improved diagnostic accuracy with sonication ($p = 0.008$) compared to conventional cultures, but none of the 60 patients studied had an elbow prosthesis [1]. Similarly, a study by Achermann et al. reported on only one elbow implant in 37 cases, which significantly limits the applicability of this information to the upper extremity [2].

There is only one study in the literature that is specific to the elbow. A review of 27 presumptively uninfected and 9 infected patients with a prosthetic elbow noted that while sonification of removed elbow arthroplasty implants had a sensitivity of 89% and a specificity of 100%, this did not differ significantly from the results of standard microbiological culture techniques at their institution (sensitivity 55%, specificity 93%, $p = 0.18$ and $p = 0.16$, respectively). While this may represent a "beta-error" in which a true improvement in the yield of sonication is obscured by insufficient numbers to prove statistically significance, in the eight years since this paper was published, we were unable to find a more definitive or compelling study [3,4].

A larger study of 53 shoulder arthroplasty patients examining the results of sonication of retrieved upper extremity implants has recently been published by Grosso et al. [5]. They found that the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of the cultures were not improved by sonication (US) when compared to standard (S) techniques: Sensitivity 96% (S) versus 96% (US), specificity 75% (S) versus 64% (US), PPV 77% (S) versus 71% (US), NPV 95% (S) versus 95% (US) and accuracy 85% (S) versus 79% (US). None of these differences were statistically significantly different. Additionally, it is well-recognized that the microbiological flora of the shoulder, and the subsequent infections that result from it, are distinctly different than that of the elbow. Therefore, it is not advisable to directly compare (or extrapolate the findings of) one joint to the other.

To conclude, at the present time there is insufficient evidence to either support or refute the utility of routine sonication of prosthetic elbow implants removed at the time of surgery in order to increase the yield or accuracy of cultures. Until a sufficiently-powered, prospective study has been performed demonstrating the efficacy of sonication to diagnose infection for revision elbow arthroplasty, we cannot support the routine use of this technology.

REFERENCES

[1] Holinka J, Bauer L, Hirschl AM, Graninger W, Windhager R, Presterl E. Sonication cultures of explanted components as an add-on test to routinely conducted microbiological diagnostics improve pathogen detection. J Orthop Res. 2011;29:617–622. doi:10.1002/jor.21286.

[2] Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol. 2010;48:1208–1214. doi:10.1128/JCM.00006-10.

[3] Somerson JS, Morrey ME, Sanchez-Sotelo J, Morrey BF. Diagnosis and management of periprosthetic elbow infection. J Bone Joint Surg Am. 2015;97:1962–1971. doi:10.2106/JBJS.O.00170.

[4] Vergidis P, Greenwood-Quaintance KE, Sanchez-Sotelo J, Morrey BF, Steinmann SP, Karau MJ, et al. Implant sonication for the diagnosis of prosthetic elbow infection. J Shoulder Elbow Surg. 2011;20:1275–1281. doi:10.1016/j.jse.2011.06.016.

[5] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

Authors: Mark Morrey, Shawn O'Driscoll

QUESTION 5: Do molecular markers have a role in the diagnosis of elbow periprosthetic joint infection (PJI)?

RECOMMENDATION: Despite the presence of data related to the use of molecular markers for the diagnosis of infection in hip and knee arthroplasty, the role of molecular markers in the diagnosis of total elbow arthroplasty (TEA) infection remains unknown.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

An extensive literature search was performed to identify publications related to the use of molecular techniques for the diagnosis of PJI in TEA. Our detailed search revealed numerous articles in total hip and knee arthroplasty. From our search, 180 articles were ultimately reviewed. A complete search of the abstracts, references and selectively full text from systematic reviews specific to TEA revealed there were only three studies with a total of only three elbows examining the use of molecular techniques to diagnose periprosthetic infection in TEA.

The alpha-defensin immunoassay and leukocyte esterase (LE) tests were recently reviewed in a systematic review and meta-analysis by Wyatt et al. [1]. In this review, six studies examined alpha defensin; however, no TEAs were included. Five of the included studies utilized LE for the diagnosis of PJI and only one of these included a single TEA out of 52 prostheses examined [2]. In their study, Colvin at al. found a sensitivity, specificity, positive predictive value and negative predictive value of 100, 97, 95 and 100% respectively [2].

In another systematic review, Suen et al. [3] compared the "quick test" version of alpha-defensin to the laboratory-based test, which further led to a study by Sigmund et al. [4] which included hip, knee, shoulder and elbow revisions done for pain or instability in 49 patients. These authors found a sensitivity and specificity of 69% and 94%, respectively, with a positive and negative likelihood ratio of 12.46 and 0.33, respectively. Again, unfortunately this study only included a single patient with an elbow arthroplasty PJI. The larger systematic review found a pooled