lavage in order to improve the yield of aspiration. Newman et al. reported that saline lavage predictably affected the results of synovial cell counts and their diagnostic utility but has a less substantial effect on culture results [11].

In the absence of concrete evidence, with reliance on the available data from the hip and knee literature and taking into account the simplicity of aspirating an ankle joint, we recommend that aspiration of the ankle with an antibiotic spacer be strongly considered prior to reimplantation. The analysis of the aspirate fluid, if obtained, will provide valuable data that can influence the intended procedure and the ultimate success and failure of reconstruction.

REFERENCES

[1] Alrashidi Y, Galhoum AE, Wiewiorski M, Herrera-Pérez M, Hsu RY, Barg A, et al. How to diagnose and treat infection in total ankle arthroplasty. Foot Ankle Clin. 2017;22:405–423. doi:10.1016/j.fcl.2017.01.009.

[2] Myerson MS, Shariff R, Zonno AJ. The management of infection following total ankle replacement: demographics and treatment. Foot Ankle Int. 2014;35:855–862. doi:10.1177/1071100714543643.

[3] Patton D, Kiewiet N, Brage M. Infected total ankle arthroplasty: risk factors and treatment options. Foot Ankle Int. 2015;36:626–634. doi:10.1177/1071100714568869.

[4] Ghanem E, Azzam K, Seeley M, Joshi A, Parvizi J. Staged revision for knee arthroplasty infection: what is the role of serologic tests before reimplantation? Clin Orthop Relat Res. 2009;467:1699–1705. doi:10.1007/s11999-009-0742-9.

[5] Lonner JH, Siliski JM, Della Valle C, DiCesare P, Lotke PA. Role of knee aspiration after resection of the infected total knee arthroplasty. Am J Orthop. 2001;30:305–309.

[6] Meermans G, Haddad FS. Is there a role for tissue biopsy in the diagnosis of periprosthetic infection? Clin Orthop Relat Res. 2010;468:1410–1417. doi:10.1007/s11999-010-1245-4.

[7] Mont MA, Waldman BJ, Hungerford DS. Evaluation of preoperative cultures before second-stage reimplantation of a total knee prosthesis complicated by infection. A comparison-group study. J Bone Joint Surg Am. 2000;82-A:1552–1557.

[8] Van den Bekerom MPJ, Stuyck J. The value of pre-operative aspiration in the diagnosis of an infected prosthetic knee: a retrospective study and review of literature. Acta Orthop Belg. 2006;72:441–447.

[9] Hoell S, Borgers L, Gosheger G, Dieckmann R, Schulz D, Gerss J, et al. Interleukin-6 in two-stage revision arthroplasty: what is the threshold value to exclude persistent infection before re-implanatation? Bone Joint J. 2015;97-B:71–75. doi:10.1302/0301-620X.97B1.33802.

[10] Hoell S, Moeller A, Gosheger G, Hardes J, Dieckmann R, Schulz D. Two-stage revision arthroplasty for periprosthetic joint infections: what is the value of cultures and white cell count in synovial fluid and CRP in serum before second stage reimplantation? Arch Orthop Trauma Surg. 2016;136:447–452. doi:10.1007/s00402-015-2404-6.

[11] Newman JM, George J, Klika AK, Hatem SF, Barsoum WK, Trevor North W, et al. What is the diagnostic accuracy of aspirations performed on hips with antibiotic cement spacers? Clin Orthop Relat Res. 2017;475:204–211. doi:10.1007/s11999-016-5093-8.

[12] Shukla SK, Ward JP, Jacofsky MC, Sporer SM, Paprosky WG, Della Valle CJ. Perioperative testing for persistent sepsis following resection arthroplasty of the hip for periprosthetic infection. J Arthroplasty. 2010;25:87–91. doi:10.1016/j.arth.2010.05.006.

Authors: Khaled Emara, John M. Embil

QUESTION 7: Is there a role for measuring synovial biomarkers for diagnosis of infected total ankle arthroplasty (TAA)?

RECOMMENDATION: Based on the hip and knee arthroplasty literature, measuring synovial biomarkers may play a role in the diagnosis of infected TAA. The diagnosis of periprosthetic joint infection (PJI) in the setting of a TAA can be confirmed with cultures, provided that a plausible pathogen is recovered in the context of a compatible clinical picture. In the absence of a positive culture, synovial biomarker analysis may help in establishing the diagnosis.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 92%, Disagree: 8%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

TAA has emerged as a successful procedure, improving both pain and function in patients with end-stage arthritis of the ankle, with reported rates of infection ranging from 0 to 4.6% [1]. A specific approach does not yet exist for the diagnosis of PJI in TAA. However, the traditional approach for the diagnosis of PJI in other joints involves joint aspiration and sampling of the synovial fluid for analysis involving synovial white blood cell (WBC) count and differential fluid culture, as well as serum WBC count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels [2,3].

Elevation of several synovial biomarkers has been identified as indicators of potential PJI, including WBC count, percentage of polymorphonuclear cells (PMN%), α-defensin, leukocyte esterase (LE), interleukin IL-1a, IL-1, IL-6, IL-8, IL-10, IL-17, granulocyte colony-stimulating factor (G-CSF), vascular endothelial growth factor (VEGF), CRP, neutrophil elastase 2 (ELA-2), lactoferrin, neutrophil gelatinase-associated lipocalin (NGAL), resistin, thrombospondin and bactericidal/permeability-increasing protein (BPI) [4–6].

Among the previously-mentioned synovial biomarkers, α-defensin is regarded as the most accurate single test for the diagnosis of PJI, with a sensitivity of 97% and a specificity of 96% [5]. Therefore, the accuracy of α-defensin is closest to the 2013 International Consensus Meeting (ICM) criteria for the diagnosis of PJI [6]. Alpha-defensin also appears to provide the most consistent results, regardless of the causative microorganism or its virulence. Its accuracy even remains unaffected in the setting of antibiotic administration to the patient prior to obtaining the synovial fluid sample [4,5,7]. IL-8 has been shown to follow α-defensin in terms of performance, while the accuracy of synovial fluid culture has been shown to have a sensitivity of 62% and specificity of 94% [5]. Synovial fluid leukocyte count (sensitivity of 89% and specificity of 86%) and PMN percentage (sensitivity of 89% and specificity of 86%) both demonstrate accuracy in diagnosing PJI [5,6]. However, they are already part of the six minor criteria for the diagnosis of PJI according to the ICM 2013 definition of PJI [6]. There is great controversy regarding the cutoff point used for the synovial leukocyte count and PMN percentage, which prevents their use as stand-alone diagnostic tests [4,5,8–12].

LE, with a sensitivity of 77% and specificity of 95%, has the advantage of being inexpensive [5,13–16]. However, there is a level of subjectivity present with the interpretation of LE results, in addition to the possibility of the presence of blood in the fluid affecting the results.

The combination of two or more markers to detect PJI has been studied. It has been shown that the combination of synovial fluid α-defensin and CRP provided a sensitivity of 97% and a specificity of 100% in diagnosing PJI [17]. The combined use of synovial CRP and adenosine deaminase (ADA) improves the positive predictive value [18]. A synovial fluid CRP should be included in the synovial fluid analysis and correlated with other lab markers [17].

REFERENCES

[1] Gougoulias N, Khanna A, Maffulli N. How successful are current ankle replacements?: a systematic review of the literature. Clin Orthop Relat Res. 2010;468:199–208. doi:10.1007/s11999-009-0987-3.

[2] Alrashidi Y, Galhoum AE, Wiewiorski M, Herrera-Pérez M, Hsu RY, Barg A, et al. How to diagnose and treat infection in total ankle arthroplasty. Foot Ankle Clin. 2017;22:405–423. doi:10.1016/j.fcl.2017.01.009.

[3] Vulcano E, Myerson MS. The painful total ankle arthroplasty: a diagnostic and treatment algorithm. Bone Joint J. 2017;99-B:5–11. doi:10.1302/0301-620X.99B1.37536.

[4] Deirmengian C, Kardos K, Kilmartin P, Gulati S, Citrano P, Booth RE. The Alpha-defensin test for periprosthetic joint infection responds to a wide spectrum of organisms. Clin Orthop Relat Res. 2015;473:2229–2235. doi:10.1007/s11999-015-4152-x.

[5] 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.

[6] Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty. 2014;29:1331. doi:10.1016/j.arth.2014.03.009.

[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. 2017;99:1419–1427. doi:10.2106/JBJS.16.01395.

[8] Cipriano CA, Brown NM, Michael AM, Moric M, Sporer SM, Della Valle CJ. Serum and synovial fluid analysis for diagnosing chronic periprosthetic infection in patients with inflammatory arthritis. J Bone Joint Surg Am. 2012;94:594–600. doi:10.2106/JBJS.J.01318.

[9] Bedair H, Ting N, Jacovides C, Saxena A, Moric M, Parvizi J, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. Clin Orthop Relat Res. 2011;469:34–40. doi:10.1007/s11999-010-1433-2.

[10] Ghanem E, Azzam K, Seeley M, Joshi A, Parvizi J. Staged revision for knee arthroplasty infection: what is the role of serologic tests before reimplantation? Clin Orthop Relat Res. 2009;467:1699–1705. doi:10.1007/s11999-009-0742-9.

[11] Trampuz A, Hanssen AD, Osmon DR, Mandrekar J, Steckelberg JM, Patel R. Synovial fluid leukocyte count and differential for the diagnosis of prosthetic knee infection. Am J Med. 2004;117:556–562. doi:10.1016/j.amjmed.2004.06.022.

[12] Dinneen A, Guyot A, Clements J, Bradley N. Synovial fluid white cell and differential count in the diagnosis or exclusion of prosthetic joint infection. Bone Joint J. 2013;95-B:554–557. doi:10.1302/0301-620X.95B4.30388.

[13] Guenther D, Kokenge T, Jacobs O, Omar M, Krettek C, Gehrke T, et al. Excluding infections in arthroplasty using leucocyte esterase test. Int Orthop. 2014;38:2385–2390. doi:10.1007/s00264-014-2449-0.

[14] Wetters NG, Berend KR, Lombardi AV, Morris MJ, Tucker TL, Della Valle CJ. Leukocyte esterase reagent strips for the rapid diagnosis of periprosthetic joint infection. J Arthroplasty. 2012;27:8–11. doi:10.1016/j.arth.2012.03.037.

[15] Tischler EH, Cavanaugh PK, Parvizi J. Leukocyte esterase strip test: matched for musculoskeletal infection society criteria. J Bone Joint Surg Am. 2014;96:1917–1920. doi:10.2106/JBJS.M.01591.

[16] 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.

[17] Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Combined measurement of synovial fluid α-defensin and C-reactive protein levels: highly accurate for diagnosing periprosthetic joint infection. J Bone Joint Surg. 2014;96:1439. doi:10.2106/JBJS.M.01316.

[18] Sousa R, Serrano P, Gomes Dias J, Oliveira JC, Oliveira A. Improving the accuracy of synovial fluid analysis in the diagnosis of prosthetic joint infection with simple and inexpensive biomarkers: C-reactive protein and adenosine deaminase. Bone Joint J. 2017;99-B:351–357. doi:10.1302/0301-620X.99B3.BJJ-2016-0684.R1.

Authors: Khaled Emara, Amiethab Aiyer, Ryan Rogero

QUESTION 8: What is the role of molecular techniques for detection of pathogen deoxyribonucleic acid (DNA) (polymerase chain reaction (PCR) or next-generation sequencing) in patients with infected total ankle arthroplasty (TAA)?

RECOMMENDATION: Molecular techniques, particularly next-generation sequencing and the Ibis T5000 technology, have the potential to be used as an important adjunct in the diagnosis of bacterial infection following TAA, although sufficient clinical evidence is lacking.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

The culture of multiple periprosthetic tissue samples is currently considered the gold standard for microbiological diagnosis of periprosthetic joint infections (PJIs) [1]. However, biofilm-associated infections are not easily detected by culture-based methods and are often resistant to conventional antimicrobial therapy. Therefore, it seems imperative to promptly investigate and subsequently integrate molecular diagnostic techniques into the clinical practice for the management of PJI [2].

The most common molecular techniques that have been used to diagnose PJI are both based on PCR: specific PCR and broad-range PCR [3]. Specific PCR targets a single bacterial species (e.g., *Staphylococcus aureus*) or a group of closely-related species (e.g., all staphylococcal species). These are typically considered real-time PCR assays. Specific PCRs can be used in the diagnosis of any targeted pathogen with extreme sensitivity, potentially detecting even a single copy of the target DNA. This approach provides accurate results within hours and has the advantage of singling out any organisms deemed as significant, thereby making contamination easier to control for, as well as making quantification possible [3].

Broad-range PCR, in contrast to specific PCR assays, provides the opportunity to detect DNA from any pathogen rather than a specific preset of expected pathogens. Almost all broad-range PCR techniques utilized in diagnostic microbiology laboratories are based on the gene coding for the small subunit of the bacterial ribosome (16S rDNA). The main limitations of broad-range PCR relate to inherent problems with contamination and sensitivity. Contamination arises from bacterial DNA present in PCR reagents or inadvertently introduced during the collection and handling of the sample, particularly if additional fluids are added to the culture sample during transport or laboratory processing [4]. Unfortunately, these "contaminant" bacteria detected with broad-range PCR are closely related to the microorganisms that cause low-grade