TABLE 3. Criteria for infection categories

Category	Criteria
No infection	All negative cultures (tissue or aspirate) and no preoperative or intraoperative* findings of infection
Possible infection	Negative preoperative or intraoperative* finding *and* 1 positive intraoperative culture
Probably infection	>1 positive intraoperative culture *and* negative preoperative or intraoperative* findings *or* At least 1 positive preoperative or intraoperative finding *and* 1 positive culture
Definite infection	At least 1 positive preoperative or intraoperative* finding of infection *and* >1 positive intraoperative culture *or* 1 positive preoperative (aspirate) culture *and* 1 positive intraoperative culture

Note: Positive preoperative aspirate has its own category because it is more definitive than these findings.

*Preoperative or intraoperative findings of infection: preoperative clinical signs (swelling, sinus tract, redness, drainage); positive ESR or CRP; positive frozen section; intraoperative gross findings (e.g., pus, drainage, necrosis).

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value and accuracy of 0.14, 0.95, 0.67, 0.61 and 0.62, respectively, using a cut-off level of 10 pg/mL.

Subsequently, Grosso et al. [8] prospectively examined serum IL-6 levels in 69 cases of revision shoulder arthroplasty; 24 cases categorized as infected and 45 as not infected based on perioperative criteria (Table 3). The most commonly cultured bacteria was *C. acnes* (83% of cases) with CNSS the second most frequently cultured bacteria (16% of cases). Only 6 cases in the study had an elevated serum IL-6 level, 3 in the infected group and 3 in the not infected group. Serum IL-6 was found to have a sensitivity and specificity of 12% and 93%, respectively, using a cut-off level of 5 pg/mL.

REFERENCES

[1] 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.

[2] 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.

[3] Frangiamore SJ, Saleh A, Kovac MF, Grosso MJ, Zhang X, Bauer TW, et al. Synovial fluid interleukin-6 as a predictor of periprosthetic shoulder infection. J Bone Joint Surg Am. 2015;97:63–70. doi:10.2106/JBJS.N.00104.

[4] Frangiamore SJ, Saleh A, Grosso MJ, Farias Kovac M, Zhang X, Daly TM, et al. Neer Award 2015: analysis of cytokine profiles in the diagnosis of periprosthetic joint infections of the shoulder. J Shoulder Elbow Surg. 2017;26:186–196. doi:10.1016/j.jse.2016.07.017.

[5] Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2010;92:2102–2109. doi:10.2106/JBJS.I.01199.

[6] Xie K, Dai K, Qu X, Yan M. Serum and synovial fluid Interleukin-6 for the diagnosis of periprosthetic joint infection. Sci Rep. 2017;7(1):1496. doi:10.1038/s41598-017-01713-4.

[7] Villacis D, Merriman JA, Yalamanchili R, Omid R, Itamura J, Rick Hatch GF. Serum interleukin-6 as a marker of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:41–45. doi:10.2106/JBJS.L.01634.

[8] Grosso MJ, Frangiamore SJ, Saleh A, Kovac MF, Hayashi R, Ricchetti ET, et al. Poor utility of serum interleukin-6 levels to predict indolent periprosthetic shoulder infections. J Shoulder Elbow Surg. 2014;23:1277–1281. doi:10.1016/j.jse.2013.12.023.

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QUESTION 3: Is there a role for synovial fluid white blood cell (WBC) count and differential in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There may be a role, but synovial fluid cell count and differential currently lacks diagnostic thresholds from shoulder-specific literature.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

WBC count and polymorphonuclear leukocyte (PMN) percentage in synovial fluid continue to be used as parameters in the diagnosis of PJI [1–10]. As an indirect marker, synovial fluid WBC count and differential has been used as a reliable tool for diagnosing PJI of the lower

extremity [3,8,11]. However, shoulder-specific data is limited. The shoulder presents a unique challenge in diagnosis due to frequent culture growth of low-virulent organisms [12–14].

To evaluate the existing literature for use of synovial WBC and differential in the diagnosis of shoulder PJI, a PubMed search was undertaken with the query: "(periprosthetic OR PJI) AND shoulder AND (white OR WBC) AND (synovial OR aspirate)." This search provided three articles for review of which one was pertinent [15].

In a multicenter analysis of *C. acnes* PJI cases (as defined by original Musculoskeletal Infection Society (MSIS) criteria [16]), Nodzo et al. described the characteristics of the host inflammatory response in 18 knees, 12 hips and 35 shoulders [15]. They identified a significantly lower mean value for synovial WBC count for the shoulder (750 cells/ mm^3) compared to the knee (19,950 cells/ mm^3). This was, however, similar to the average reported for the infected hips (500 cells/ mm^3). Interestingly, the neutrophil percentage was similar between shoulders (90%) and knees (92.5%), while significantly lower for hips (61.0%). Unfortunately, while providing some insight into the inflammatory response to a low-virulent pathogen, this limited dataset was unable to calculate a diagnostic threshold or calculate sensitivity and specificity of synovial WBC for diagnosing PJI. As this analysis demonstrates a response commiserate with low-virulent infections of the hip, the diagnostic values reported for hip PJI (3,000 cells / mm^3 and 80% PMN) [3] may be the best current alternative.

WBC count and PMN percentage can remain high up to three months after arthroplasty. This limits the test utility in the first six postoperative weeks as a modified threshold has not been identified for the shoulder [17,18].

Compounding the uncertainty about the WBC count and PMN percentages as metrics that indicate shoulder PJI is the fact that shoulder synovial fluid aspirations frequently yield little to no fluid, a high percentage of "dry taps" [19,20].

REFERENCES

[1] Ahmad SS, Shaker A, Saffarini M, Chen AF, Hirschmann MT, Kohl S. Accuracy of diagnostic tests for prosthetic joint infection: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2016;24:3064–3074. doi:10.1007/s00167-016-4230-y.

[2] Ghanem E, Parvizi J, Burnett RSJ, Sharkey PF, Keshavarzi N, Aggarwal A, et al. Cell count and differential of aspirated fluid in the diagnosis of infection at the site of total knee arthroplasty. J Bone Joint Surg Am. 2008;90:1637–1643. doi:10.2106/JBJS.G.00470.

[3] Higuera CA, Zmistowski B, Malcom T, Barsoum WK, Sporer SM, Mommsen P, et al. Synovial fluid cell count for diagnosis of chronic periprosthetic hip infection. J Bone Joint Surg Am. 2017;99:753–759. doi:10.2106/JBJS.16.00123.

[4] Jacovides CL, Parvizi J, Adeli B, Jung KA. Molecular markers for diagnosis of periprosthetic joint infection. J Arthroplasty. 2011;26:99–103.e1. doi:10.1016/j.arth.2011.03.025.

[5] Parvizi J, Alijanipour P, Berbari E, Hickok N, Phillips KS, M Shapiro I, et al. Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg. 2015;23 Suppl:S32–S43. doi:10.5435/JAAOS-D-14-00455.

[6] Collins I, Wilson-MacDonald J, Chami G, Burgoyne W, Vineyakam P, Berendt T, et al. The diagnosis and management of infection following instrumented spinal fusion. Eur Spine J. 2008;17:445–450. doi:10.1007/s00586-007-0559-8.

[7] Lee YS, Koo K-H, Kim HJ, Tian S, Kim T-Y, 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.

[8] Mason JB, Fehring TK, Odum SM, Griffin WL, Nussman DS. The value of white blood cell counts before revision total knee arthroplasty. J Arthroplasty. 2003;18:1038–1043.

[9] 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.

[10] Kevin Ko J-W, Namdari S. The diagnosis and management of periprosthetic joint infections of the shoulder. Oper Tech Orthop. 2016;26. doi:10.1053/j.oto.2015.12.001.

[11] Ricchetti E, Frangiamore S, Grosso M, Alolabi B, Saleh A, W. Bauer T, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1:e3. doi:10.2106/JBJS.

[12] Matsen FA, Russ SM, Bertelsen A, Butler-Wu S, Pottinger PS. Propionibacterium can be isolated from deep cultures obtained at primary arthroplasty despite intravenous antimicrobial prophylaxis. J Shoulder Elbow Surg. 2015;24:844–847. doi:10.1016/j.jse.2014.10.016.

[13] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[14] 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.

[15] Nodzo SR, Boyle KK, Bhimani S, Duquin TR, Miller AO, Westrich GH. Propionibacterium acnes host inflammatory response during periprosthetic infection is joint specific. HSS J. 2017;13:159–164. doi:10.1007/s11420-016-9528-2.

[16] 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.

[17] Christensen CP, Bedair H, Della Valle CJ, Parvizi J, Schurko B, Jacobs CA. The natural progression of synovial fluid white blood-cell counts and the percentage of polymorphonuclear cells after primary total knee arthroplasty: a multicenter study. J Bone Joint Surg Am. 2013;95:2081–2087. doi:10.2106/JBJS.L.01646.

[18] 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. 2010. doi:10.1007/s11999-010-1433-2.

[19] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[20] Millett PJ, Yen Y-M, Price CS, Horan MP, van der Meijden OA, Elser F. Propionibacterium acnes infection as an occult cause of postoperative shoulder pain: a case series. Clin Orthop Relat Res. 2011;469:2824–2830. doi:10.1007/s11999-011-1767-4.

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QUESTION 4: Is there a role for synovial cytokines in the diagnosis of shoulder periprosthetic (PJI)?

RECOMMENDATION: While not yet widely available, evaluation of cytokine levels in synovial fluid shows promise in clarifying the probability of shoulder PJI. See Questions 2 and 5 (Section 1.2. Prevention: Intraoperative) for discussion of specific cytokine evaluations.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Although the majority of previous literature on the use of cytokines for PJI diagnosis was focused on hip and knee arthroplasty [1–4], there are a number of recent publications regarding shoulder PJI [5–13]. It is established that shoulder PJI is often caused by less viru-