Outcomes

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QUESTION 1: What is the definition of success of surgical treatment of a patient with a periprosthetic joint infection (PJI)? What clinical, operative, microbiological and functional metrics should be considered?

RECOMMENDATION: The treatment of PJIs typically does not have a dichotomous outcome. More commonly, the result is a gradient of success or failure. As such, the outcome-reporting tool has been organized into four tiers with each tier encompassing different levels of perceived success or failure. The outcomes reporting for the treatment of PJIs are the following (definitions regarding items within each tier are explained in the rationale section):

Tier 1. Infection control with no continued antibiotic therapy

Tier 2. Infection control with patient on suppressive antibiotic therapy

Tier 3. Need for reoperation and/or revision and/or spacer retention (assigned to subgroups of A, B, C, D, E, and F based on the type of reoperation)

- A. Aseptic revision > 1 year from initiation of PJI treatment
- B. Septic revision (including debridement, antibiotic and implant retention (DAIR)) > 1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty and fusion)
- C. Aseptic revision ≤ 1 year from initiation of PJI treatment
- D. Septic revision (including DAIR) ≤ 1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty, and fusion)
- E. Amputation, resection arthroplasty, or fusion
- F. Retained spacer

Tier 4. Death (assigned to subgroups A or B)

- A. Death ≤ to 1 year from initiation of PJI treatment
- B. Death > 1 year from initiation of PJI treatment

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 82%, Disagree: 14%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

The MusculoSkeletal Infection Society (MSIS) definition for PJIs provided standardization to the patient populations in PJI research [1]. As evidenced by the numerous definitions of success and failure in the literature, the same standardization has not been provided for defining the outcomes for the treatment of PJIs [2–11]. Therefore, a multi-national, multi-institutional and multi-disciplinary workgroup was organized by the MSIS to review the available evidence and propose a gold standard definition in the outcome reporting for the treatment of PJIs to improve the transparency in outcome studies and guide the definition of success for the treatment of PJIs.

Definitions and Considerations

Starting Point of Treatment Assessment

The starting point for the assessment of a treatment can influence the size of the population and alter the reported treatment success. A prior Delphi method definition of success after treatment of PJIs proposed the starting point for assessment does not begin until reimplantation surgery during a two-stage exchange [8]. However, literature on the outcomes of spacers in the treatment of PJI demonstrated that 17% of the patients underwent amputation, resection arthroplasty, arthrodesis or remained with a retained spacer instead of undergoing reimplantation [12]. The starting point for assessing the treatment of PJIs will begin at the time of the initial operation for PJIs, which will be irrigation and debridement, the first stage of a two-stage exchange or following a one-stage exchange.

Infection Control

Because bacterial organisms can undergo internalization by osteoblasts, "infection eradication" may not always be feasible and "infection control" better represents the process of treating PJIs [13]. Since the MSIS criteria for diagnosis of PJIs is simple and well established, the workgroup has defined infection control as a patient not meeting the MSIS criteria for PJIs and not having undergone or in need of further surgery (excluding the planned reimplantation of

a two-stage exchange, a procedure for a complication related to the antibiotic spacer or a planned operation to address soft-tissue issues between two-stages) [14].

Antibiotics

Given the promising results of a recent preliminary study on extended oral antibiotics after the reimplantation of a two-stage exchange, the use of antibiotics beyond the historical treatment period will become extended as more clinicians adopt this approach [15]. The workgroup has defined "off antibiotic therapy" as cessation of antibiotics within 1 year after the initial surgery. Patients are still allowed to be on antibiotics of 10 days or less for a documented infection other than PJI or antibiotics for a pre-procedure prophylaxis (i.e., dental prophylaxis or preoperative antibiotics for another operation).

Reoperation

The reasons for reoperation (excluding the planned reimplantation of a two-stage exchange, a procedure for a complication related to the antibiotic spacer or a planned operation to address soft-tissue issues between two-stages) should be reported as aseptic revisions, septic revisions or amputations, resection arthroplasties or fusions. Any patient undergoing a revision surgery who does not meet the MSIS criteria for PJIs at the time of revision is considered an aseptic revision. Aseptic revision was divided into subgroups with patients revised ≤ year or > one year from the initial surgery in the treatment for PJI. Due to advancements in DNA sequencing demonstrating higher rates of polymicrobial PJI than standard laboratory cultures, assignment of septic revision will apply to any patient revised for infection regardless of the organism [16]. Similar to aseptic revision, subgroups have been assigned based on the duration from surgery. Given some patients continue to live with the spacer, subgroup has been established for patients with a retained spacer.

Minimum Duration of Follow-up

The minimum reporting of any outcome should be 1-year follow-up. When any study reports a minimum follow-up of 1, 5 or 10 years, it will be defined as having short-term, mid-term, or long-term results, respectively.

Death

In the reporting of outcomes in Tier 4, "death" is defined as all-cause mortality with a differentiation between mortality ≤1 year or > 1 year from the initial operation for the treatment of PJIs. As more literature demonstrates the increased risk of mortality for patients undergoing treatment for PJIs, we are gaining a greater appreciation for the effects of PJIs on the host [17–19]. Despite the increased risk of mortality among PJI patients, we still lack the ability to directly or indirectly assign the cause of mortality due to PJIs. Therefore, the workgroup has used all-cause mortality in defining Tier 4.

Appropriate Use of the Outcome Reporting Tool

The system of tiers in the outcome reporting tool is meant to allow for a comprehensive accounting of patients in the treatment of PJIs. Therefore, each patient can only be assigned to a single tier whereby the percentage of patients among all the tiers will amount to a total of 100%. The workgroup suggests all publications reporting on the outcomes of PJI treatment include a table presenting the number of patients assigned to each tier and subgroup with certain tiers. The workgroup has recommended grouping the outcome tiers into three categories as the following: success, failure of secondary causes and failure of PJIs. Patients assigned to Tiers 1 and 2 are considered a successful outcome by representing infection control with no further reoperations. Since not all patients will experience a successful outcome or failure not due to PJIs, Tiers 3B, 3D and 4B are a failure of secondary causes not associated with PJI. Lastly, Tiers 3A, 3C, 3E, 3F and 4A are considered a failure that is directly or indirectly related to PJIs.

REFERENCES

[1] 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.

[2] Mahmud T, Lyons MC, Naudie DD, Macdonald SJ, McCalden RW. Assessing the gold standard: a review of 253 two-stage revisions for infected TKA. Clin Orthop Relat Res. 2012;470:2730–2736. doi:10.1007/s11999-012-2358-8.

[3] Parvizi J, Saleh KJ, Ragland PS, Pour AE, Mont MA. Efficacy of antibiotic-impregnated cement in total hip replacement. Acta Orthop. 2008;79:335–341. doi:10.1080/17453670710015229.

[4] Bradbury T, Fehring TK, Taunton M, Hanssen A, Azzam K, Parvizi J, et al. The fate of acute methicillin-resistant Staphylococcus aureus periprosthetic knee infections treated by open debridement and retention of components. J Arthroplasty. 2009;24:101–104. doi:10.1016/j.arth.2009.04.028.

[5] Azzam KA, Seeley M, Ghanem E, Austin MS, Purtill JJ, Parvizi J. Irrigation and debridement in the management of prosthetic joint infection: traditional indications revisited. J Arthroplasty. 2010;25:1022–1027. doi:10.1016/j.arth.2010.01.104.

[6] Senneville E, Joulie D, Legout L, Valette M, Dezèque H, Beltrand E, et al. Outcome and predictors of treatment failure in total hip/knee prosthetic joint infections due to Staphylococcus aureus. Clin Infect Dis. 2011;53:334–340. doi:10.1093/cid/cir402.

[7] Jämsen E, Stogiannidis I, Malmivaara A, Pajamäki J, Puolakka T, Konttinen YT. Outcome of prosthesis exchange for infected knee arthroplasty: the effect of treatment approach. Acta Orthop. 2009;80:67–77. doi:10.1080/17453670902805064.

[8] Diaz-Ledezma C, Higuera CA, Parvizi J. Success after treatment of periprosthetic joint infection: a Delphi-based international multidisciplinary consensus. Clin Orthop Relat Res. 2013;471:2374–2382. doi:10.1007/s11999-013-2866-1.

[9] Waagsbø B, Sundøy A, Martinsen TML, Nymo LS. Treatment results with debridement and retention of infected hip prostheses. Scand J Infect Dis. 2009;41:563–568. doi:10.1080/00365540902984719.

[10] Volin SJ, Hinrichs SH, Garvin KL. Two-stage reimplantation of total joint infections: a comparison of resistant and non-resistant organisms. Clin Orthop Relat Res. 2004:94–100.

[11] Estes CS, Beauchamp CP, Clarke HD, Spangehl MJ. A two-stage retention débridement protocol for acute periprosthetic joint infections. Clin Orthop Relat Res. 2010;468:2029–2038. doi:10.1007/s11999-010-1293-9.

[12] Gomez MM, Tan TL, Manrique J, Deirmengian GK, Parvizi J. The fate of spacers in the treatment of periprosthetic joint infection. J Bone Joint Surg Am. 2015;97:1495–1502. doi:10.2106/JBJS.N.00958.

[13] Josse J, Velard F, Gangloff SC. Staphylococcus aureus vs. osteoblast: relationship and consequences in osteomyelitis. Front Cell Infect Microbiol. 2015;5:85. doi:10.3389/fcimb.2015.00085.

[14] Springer BD. The diagnosis of periprosthetic joint infection. J Arthroplasty. 2015;30:908–911. doi:10.1016/j.arth.2015.03.042.

[15] Frank JM, Kayupov E, Moric M, Segreti J, Hansen E, Hartman C, et al. The Mark Coventry, MD, Award: oral antibiotics reduce reinfection after two-stage exchange: a multicenter, randomized controlled trial. Clin Orthop Relat Res. 2017;475:56–61. doi:10.1007/s11999-016-4890-4.

[16] 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.

[17] Boddapati V, Fu MC, Mayman DJ, Su EP, Sculco PK, McLawhorn AS. Revision total knee arthroplasty for periprosthetic joint infection is associated with increased postoperative morbidity and mortality relative to noninfectious revisions. J Arthroplasty. 2018;33:521–526. doi:10.1016/j.arth.2017.09.021.

[18] Yao JJ, Maradit Kremers H, Abdel MP, Larson DR, Ransom JE, Berry DJ, et al. Long-term mortality after revision THA. Clin Orthop Relat Res. 2018;476:420–426. doi:10.1007/s11999.0000000000000030.

[19] Zmistowski B, Karam JA, Durinka JB, Casper DS, Parvizi J. Periprosthetic joint infection increases the risk of one-year mortality. J Bone Joint Surg Am. 2013;95:2177–2184. doi:10.2106/JBJS.L.00789.