Authors: Kent Ellington, Thomas B. Bemenderfer

QUESTION 7: What are the indications for one-stage versus two-stage exchange arthroplasty in management of the infected total ankle arthroplasty (TAA)?

RECOMMENDATION: Two-stage exchange arthroplasty is recommended in the majority of cases following infected TAA. One-stage arthroplasty is only indicated in a limited patient population with acute infection, preoperatively identified low-virulence organisms and low-risk patient factors.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

The management of the infected arthroplasty remains a challenging and controversial topic in relation to any joint [1–5]. Reported rates of infection following TAA requiring re-operation (surgical irrigation and debridement (I&D), component removal and exchange, or revision) range from 0 to 8.6% [6–11]. Special consideration must be taken into account in the management of the infected total ankle given the tenuous soft tissue coverage, frequent history of multiple preceding operations, and, relative to hip and knee arthroplasty, a more recent arthroplasty design and more limited experience [12]. Currently, two-stage revision exchange arthroplasty surgery is the most popular surgical option for the management of periprosthetic joint infection (PJI) in North America and worldwide. However, it may result in significant bone loss, patient morbidity and prolonged disability, leading to a more challenging reconstruction and ultimately prolonged recovery, poorer patient-reported clinical functional outcomes, higher rates and risk of subsequent infection and potential failure of salvage operations leading to amputation.

Surgical treatment goals of the infected TAA are to eradicate the infection, obtain mechanical stability and soft-tissue coverage, alleviate pain and maximize clinical function. Historic treatment strategies have included antibiotics with hardware retention, aggressive debridement with or without polyethylene exchange and removal of hardware and exchange or arthrodesis in one or two stages with an antibiotic-impregnated cement spacer.

Extreme care should be taken when considering appropriate management of the infected TAA. Kessler et al. published the largest study to date evaluating 34 patients following revision TAA for infection [10]. An infection-free outcome with satisfactory function of the ankle was obtained in only 23 patients (67.6%). One-stage revisions with retention of one or both components resulted in 33.3% (7/21) failure with persistent infection, whereas two-stage revision with explantation of all components results in 10% (1/10) failure. Myerson et al. retrospectively evaluated 19 revision cases, and only 3 of the 19 patients underwent successful revision with replacement (15.7%), 6 with arthrodesis (31.6%), 7 with a permanent antibiotic spacer (36.8%) and 3 patients required a transtibial amputation (15.7%) [11]. Although prosthesis salvage was attempted in three early postoperative and one acute hematogenous cases, all revision cases ultimately required subsequent removal of the prosthesis. Whereas Myerson et al. reported that no patient was successfully treated with retention of the hardware, Patton reported conflicting results with four of four patients (100%) successfully treated with retention of hardware and irrigation and debridement (two with and two without exchange of polyethylene liner) for heterogeneous presentations (one acute presentations with cellulitis, one acute presentation with dehiscence, one late chronic, and one remote hematogenous) [12]. However, the majority of the patients in this study were treated with two-stage revision arthroplasty or amputation with retention of arthroplasty only achieved in 19 (65%) cases of infection (n = 29). Given the currently available literature, there are conflicting data for the utility of surgical I&D with retention of hardware. Future studies are necessary to evaluate the feasibility of surgical I&D of PJI in TAA.

To date, there is no level I evidence that provides indications or contraindications for a one-stage exchange arthroplasty in TAA. Furthermore, there are no randomized controlled trials that provide absolute indications or contraindications for two-stage exchange arthroplasty in hip and knee arthroplasty [13–16]. Care must be taken to determine the need for implant removal given that the reported success of treating the infected TAA with retention of one or both implants ranges from 0 to 100% [7,11,12]. Given the variability in the reported rates of success in eradicating infection, morbidity and mortality among observed patient populations and variable time periods prior to reimplantation, direct comparisons with one-stage exchange arthroplasty are difficult due to a patient selection bias in the current literature [15–18]. Although no literature is available with respect to TAA, a recent systematic review of the knee arthroplasty literature by Romano et al. demonstrated that a two-stage exchange provides, on average, a better outcome with respect to the control of infection in the knee [19]. The same group recently presented similar but less notable findings for the hip [20]. It is not clear how these findings would translate to the ankle, and future studies are necessary to better understand the potential for infection control and functional outcome with one- versus two-stage revision arthroplasty.

There are, however, circumstances that necessitate the removal of implants. Systemic infection necessitates timely administration of appropriate antibiotics and prompts removal of implants with thorough debridement of the soft tissues and bone in order to address the potential life-threatening sequelae of PJI. The immunocompromised patient or the presence of medical comorbidities, including metastatic disease, advanced cardiac disease and renal and/or liver dysfunction, have been shown to impact the rate of success for infection eradication and certainly influence morbidity and mortality [7,10]. It is unknown if the presence of these comorbidities constitutes a contraindication for one-stage exchange arthroplasty in TAA [14–16,18,21,22].

Since 1999, when Costerton first attributed the persistence of certain chronic infections to the presence of biofilm, the majority of implant-related infections in orthopaedics are believed to be secondary to biofilm-related infections [23]. These infections are associated with glycocalyx polysaccharide biofilms that pose unique challenges including frequently being recalcitrant to antibiotic treatment and may be culture-negative with ineffective clearance from the host [24,25]. Failure to identify the offending organism and/or culture-negative PJI is a relative contraindication to one-stage exchange arthroplasty [13,16,26,27]. Given the risk of biofilm-related

TABLE 1. Indications for one- versus two-stage exchange for infected TAA

Treatment Type	Indications
One-stage Exchange Arthroplasty	No sinus tract or exposed hardware Healthy patient and soft tissue No prolonged antibiotic use No significant bone loss requiring bone graft Low-virulence Organism with good antibiotic sensitivity
Two-stage Exchange Arthroplasty	**Sepsis.** Patients with systemic manifestations of infection **No Cultured Organism.** High suspicion for infection but no organism has been identified **Antibiotic-resistant Organism.** Preoperative cultures identifying difficult to treat and antibiotic-resistant organisms **High-risk Patient Factors.** a. Presence of a sinus tract or exposed hardware b. Immunocompromised c. Inadequate and non-viable soft tissue coverage d. Need to utilize higher order reconstructive techniques (bone graft, augmentation, soft-tissue flaps)

TAA, total ankle arthroplasty

infections, several authors advocate that reimplantation of a prosthesis should be delayed until adequate resuscitation and eradication of the offending organism have been confirmed [13–16,21,26–31].

The presence of compromised soft tissues (e.g., sinus tract, exposed hardware, etc.) that may limit adequate implant coverage is another indication for two-stage exchange arthroplasty. Sinus tracts frequently present with indurated, poorly elastic surrounding tissue near and around the ankle that limits the potential for adequate primary closure. In addition, the presence of a sinus tract may contaminate preoperative cultures and preclude the prerequisite for the identification of the offending organism [4,13,16,26,27]. Tissue expanders, musculocutaneous flaps and possible repeat debridements may all be indicated, necessitating further time between initial resection and reimplantation [14–16,22]. If soft tissue coverage cannot be obtained at index revision of a one-stage exchange arthroplasty, a two-stage surgery should be considered [13–15].

If the decision is made to pursue two-stage arthroplasty, there is no definitive evidence in the literature concerning the optimal timing between the two stages. However, there should be ample time to allow administration of a complete full course of antibiotics, eradication of the offending organism supported by a decrease in inflammatory markers (C-reactive protein [CRP]/erythrocyte sedimentation rate [ESR]), and adequate soft tissue preparation. Although no literature exists demonstrating the optimal timing of replantation in TAA, there is evidence that replantation prior to completing a complete six-week course of antibiotics may result in increased positive cultures at the time of surgery in the hip and knee [14,16]. In the United States, the most common practice is to complete a course of six weeks of intravenous or oral antibiotics followed by a cessation of antibiotics for two to eight weeks prior to reimplantation [16,32,33]. In addition, in the adult hip arthroplasty literature, there is evidence that delaying replantation beyond six months impairs functional improvement compared to patients who underwent two-stage exchange within six months of resection and reimplantation [34]. Although we recommend trending the ESR and CRP, the need for serologic evaluation prior to reimplantation is unclear. Although ESR and CRP alone are poorly diagnostic of persistent PJI with no optimal cutoff values, changes in inflammatory marker values from the time of resection may demonstrate improved pathogen control and decreased overall biologic burden [15,35–37]. There is currently no literature with respect to TAA to guide decision-making on the optimal timing between exchanges, nor serologic cutoff values.

All patients, regardless of nonoperative or operative management, should be critically evaluated clinically and every effort to minimize the risk of wound breakdown should be pursued, including optimization of diabetes, reduction of inflammatory conditions, the absence of tobacco use and optimal nutrition. Soft tissue defects may require flap coverage. We recommend revision to ankle arthroplasty after clearance of infection.

REFERENCES

[1] Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, et al. Risk factors for prosthetic joint infection: case-control study. Clin Infect Dis. 1998;27:1247–1254.

[2] Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop Relat Res. 2001:15–23.

[3] Giulieri SG, Graber P, Ochsner PE, Zimmerli W. Management of infection associated with total hip arthroplasty according to a treatment algorithm. Infection. 2004;32:222–228. doi:10.1007/s15010-004-4020-1.

[4] Del Pozo JL, Patel R. Clinical practice. Infection associated with prosthetic joints. N Engl J Med. 2009;361:787–794. doi:10.1056/NEJMcp0905029.

[5] Jämsen E, Huhtala H, Puolakka T, Moilanen T. Risk factors for infection after knee arthroplasty. A register-based analysis of 43,149 cases. J Bone Joint Surg Am. 2009;91:38–47. doi:10.2106/JBJS.G.01686.

[6] 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.

[7] Kessler B, Sendi P, Graber P, Knupp M, Zwicky L, Hintermann B, et al. Risk factors for periprosthetic ankle joint infection: a case-control study. J Bone Joint Surg Am. 2012;94:1871–1876. doi:10.2106/JBJS.K.00593.

[8] Adams SB, Demetracopoulos CA, Queen RM, Easley ME, DeOrio JK, Nunley JA. Early to mid-term results of fixed-bearing total ankle arthroplasty with a modular intramedullary tibial component. J Bone Joint Surg Am. 2014;96:1983–1989. doi:10.2106/JBJS.M.01386.

[9] Daniels TR, Younger ASE, Penner M, Wing K, Dryden PJ, Wong H, et al. Intermediate-term results of total ankle replacement and ankle arthrodesis: a COFAS multicenter study. J Bone Joint Surg Am. 2014;96:135–142. doi:10.2106/JBJS.L.01597.

[10] Kessler B, Knupp M, Graber P, Zwicky L, Hintermann B, Zimmerli W, et al. The treatment and outcome of peri-prosthetic infection of the ankle: a single cohort-centre experience of 34 cases. Bone Joint J. 2014;96-B:772–777. doi:10.1302/0301-620X.96B6.33298.

[11] 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.

[12] 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.
[13] Jackson WO, Schmalzried TP. Limited role of direct exchange arthroplasty in the treatment of infected total hip replacements. Clin Orthop Relat Res. 2000:101–105.
[14] Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351:1645–1654. doi:10.1056/NEJMra040181.
[15] Parvizi J, Adeli B, Zmistowski B, Restrepo C, Greenwald AS. Management of periprosthetic joint infection: the current knowledge: AAOS exhibit selection. J Bone Joint Surg Am. 2012;94:e104. doi:10.2106/JBJS.K.01417.
[16] Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Executive summary: diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56:1–10. doi:10.1093/cid/cis966.
[17] Senthi S, Munro JT, Pitto RP. Infection in total hip replacement: meta-analysis. Int Orthop. 2011;35:253–260. doi:10.1007/s00264-010-1144-z.
[18] Berend KR, Lombardi AV, Morris MJ, Bergeson AG, Adams JB, Sneller MA. Two-stage treatment of hip periprosthetic joint infection is associated with a high rate of infection control but high mortality. Clin Orthop Relat Res. 2013;471:510–518. doi:10.1007/s11999-012-2595-x.
[19] Romanò CL, Gala L, Logoluso N, Romanò D, Drago L. Two-stage revision of septic knee prosthesis with articulating knee spacers yields better infection eradication rate than one-stage or two-stage revision with static spacers. Knee Surg Sports Traumatol Arthrosc. 2012;20:2445–2453. doi:10.1007/s00167-012-1885-x.
[20] Romanò CL, Romanò D, Albisetti A, Meani E. Preformed antibiotic-loaded cement spacers for two-stage revision of infected total hip arthroplasty. Long-term results. Hip Int. 2012;22 Suppl 8:S46–S53. doi:10.5301/HIP.2012.9570.
[21] Engesæter LB, Dale H, Schrama JC, Hallan G, Lie SA. Surgical procedures in the treatment of 784 infected THAs reported to the Norwegian Arthroplasty Register. Acta Orthop. 2011;82:530–537. doi:10.3109/17453674.2011.623572.
[22] Wongworawat MD. Clinical faceoff: one- versus two-stage exchange arthroplasty for prosthetic joint infections. Clin Orthop Relat Res. 2013;471:1750–1753. doi:10.1007/s11999-013-2882-1.
[23] Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999;284:1318–1322.
[24] Zoubos AB, Galanakos SP, Soucacos PN. Orthopedics and biofilm–what do we know? A review. Med Sci Monit. 2012;18:RA89–RA96.
[25] Mauffrey C, Herbert B, Young H, Wilson ML, Hake M, Stahel PF. The role of biofilm on orthopaedic implants: the "Holy Grail" of post-traumatic infection management? Eur J Trauma Emerg Surg. 2016;42:411–416. doi:10.1007/s00068-016-0694-1.
[26] Buechel FF, Femino FP, D'Alessio J. Primary exchange revision arthroplasty for infected total knee replacement: a long-term study. Am J Orthop. 2004;33:190–198; discussion 198.
[27] Winkler H, Stoiber A, Kaudela K, Winter F, Menschik F. One stage uncemented revision of infected total hip replacement using cancellous allograft bone impregnated with antibiotics. J Bone Joint Surg Br. 2008;90:1580–1584. doi:10.1302/0301-620X.90B12.20742.
[28] Göksan SB, Freeman MA. One-stage reimplantation for infected total knee arthroplasty. J Bone Joint Surg Br. 1992;74:78–82.
[29] Callaghan JJ, Katz RP, Johnston RC. One-stage revision surgery of the infected hip. A minimum 10-year followup study. Clin Orthop Relat Res. 1999:139–143.
[30] Cordero-Ampuero J, Esteban J, García-Cimbrelo E, Munuera L, Escobar R. Low relapse with oral antibiotics and two-stage exchange for late arthroplasty infections in 40 patients after 2-9 years. Acta Orthop. 2007;78:511–519. doi:10.1080/17453670710014167.
[31] Kurd MF, Ghanem E, Steinbrecher J, Parvizi J. Two-stage exchange knee arthroplasty: does resistance of the infecting organism influence the outcome? Clin Orthop Relat Res. 2010;468:2060–2066. doi:10.1007/s11999-010-1296-6.
[32] Brandt CM, Duffy MC, Berbari EF, Hanssen AD, Steckelberg JM, Osmon DR. Staphylococcus aureus prosthetic joint infection treated with prosthesis removal and delayed reimplantation arthroplasty. Mayo Clin Proc. 1999;74:553–558. doi:10.4065/74.6.553.
[33] Segawa H, Tsukayama DT, Kyle RF, Becker DA, Gustilo RB. Infection after total knee arthroplasty. A retrospective study of the treatment of eighty-one infections. J Bone Joint Surg Am. 1999;81:1434–1445.
[34] Joseph J, Raman R, Macdonald DA. Time interval between first and second stage revision hip arthroplasty for infection, the effect on outcome. J Bone Joint Surg Br. 2003;58.
[35] 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.
[36] 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.
[37] Kusuma SK, Ward J, Jacofsky M, Sporer SM, Della Valle CJ. What is the role of serological testing between stages of two-stage reconstruction of the infected prosthetic knee? Clin Orthop Relat Res. 2011;469:1002–1008. doi:10.1007/s11999-010-1619-7.

Authors: Eric Senneville, Gaston Slullitel, Valeria Lopez

QUESTION 8: What metrics can be used to determine the optimal timing of reimplantation in patients who have undergone resection arthroplasty as part of a two-stage exchange for infected total ankle arthroplasty (TAA)?

RECOMMENDATION: There is no conclusive data regarding what metrics can be used in order to determine the optimal timing of reimplantation for an infected TAA. We recommend that reimplantation is performed when there are clinical signs of resolution of infection (well-healed wound, lack of erythema, etc.), and the serological markers have substantially declined (> 40%) from baseline (measured at the time of diagnosis of infection).

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Infected TAA is a serious complication that is thought to occur in as many as 5% of patients [1,2]. Management of infected TAA often requires surgical intervention that includes removal of the prosthesis, local and systemic antibiotic treatment, and subsequent reimplantation in a select group of patients. One of the most challenging questions pertains to optimal timing of reimplantation. There is little in the literature regarding the optimal treatment of an infected TAA. Most of the available literature has limitations including low numbers of patients, short duration of follow-up and so on [1–5].

There are a number of publications related to patients with infected TAA who underwent two-stage exchange arthroplasty. Patton et al. reported on 29 of 966 (3.2%) cases of infected TAA [3]. Among the infected TAA, 13 patients underwent two-stage exchange arthroplasty and antibiotic spacer placement. While infection type and operative cultures were listed, no specific recommendations on timing of reimplantation were made. Similarly, Lee et al. omitted data regarding timing of reimplantation but reported one case of deep infection, out of 50 TAAs (2%) that required implant removal, antibiotic-impregnated spacer placement, and later revision TAA [4].

Thoroughly outlining the timeline, Young et al. detailed a case report of a two-stage TAA revision [5]. Irrigation and debridement (cefazolin 1 gm diluted in 1L 0.9% saline) and antibiotic cement