Treatment

3.1. TREATMENT: TOTAL ANKLE ARTHROPLASTY-SPECIFIC

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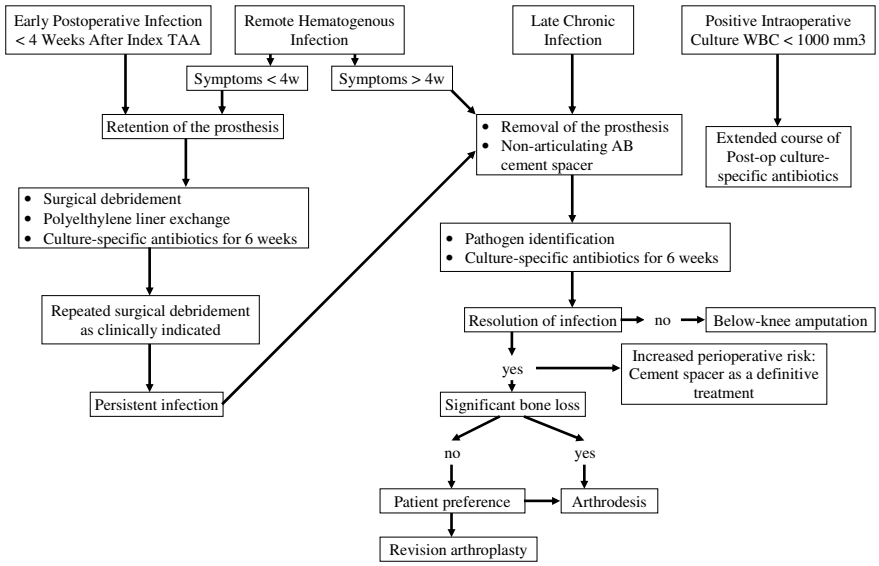
QUESTION 1: What is the treatment "algorithm" for an infected total ankle arthroplasty (TAA)?

RECOMMENDATION: The treatment of an infected TAA is largely dictated by the acuity of the infection. The following treatment algorithm modified for TAA is recommended [1].



LEVEL OF EVIDENCE: Limited

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

RATIONALE

The reported rate of infection after TAA is between 0 to 5% [2–4]. The management options are based on the time of presentation after index TAA and the duration of infection symptoms. It is a common practice to attempt to retain the ankle prosthesis when the infection is acute, particularly when it occurs during the early postoperative period. There are a number of treatment options available for infected TAA that includes surgical debridement, retention of the prosthesis and administration of intravenous antimicrobial therapy (DAIR), one or two-stage exchange arthroplasty, arthrodesis or amputation.

TAA infection literature cautions that great attention should be paid to delayed wound healing and its association with infection [5–10]. van der Heide et al. reported on the outcome of 58 TAAs in 51 patients with underlying rheumatoid arthritis (RA) or juvenile inflammatory arthritis (JIA) who had Buechel-Pappas or STAR implants [5]. Among this cohort, three patients (5%) developed early surgical site infection (SSI) and one of three (33%) patients treated with the van der Heide SSI protocol went on to develop a deep infection. The SSI protocol involved exploration of the surgical site, debridement of the wound and administration of systemic and local antibiotics. The ankle that developed deep infection underwent resection of the implant and subsequent fusion at six months. Further, Patton et al. reported on 29 cases of infected TAA and noted that 9 of the 29 (31%) infected TAAs were cases of delayed surgical wound healing that went on to deep infection [6].

Irrigation and debridement (I&D) can be a key first-step treatment of early TAA infections (early being defined as less than four weeks from the index TAA or remote hematogenous infection with symptoms less than four weeks) [7,11,12]. In a level III prognostic study, Kessler et al. defined infection parameters and proposed a treatment algorithm [7]. They selected 26 patients with PJI of TAA and matched patients with two control groups with 52 patients in each group. From this prognostic study, Kessler et al. proposed a diagnostic criteria for TAA infection which was based on presence of clinical

signs of pain, effusion, erythema and induration as well as one of the following criteria: (1) same microorganism growth in two or more cultures of synovial fluid and/or periprosthetic tissue, (2) visible pus surrounding the joint, (3) acute inflammation upon histopathological examination (greater than or equal to 10 neutrophils/high-power field) or (4) the potential to probe the base of a wound at the implant. They defined exogenous cases as locally acquired through the wound and hematogenous cases had an uneventful postoperative course for a minimum of *three months* after the initial TAA and/or there was a distant infection source. Four of 26 (15%) TAA infections were hematogenous in origin, and 22 of 26 (85%) TAA infections were exogenous. Meanwhile, *Staphylococcus aureus* and then coagulase-negative staphylococci were the most common pathogens. When compared to the control, risk factors for developing deep infection included persistent wound dehiscence (odds ratio (OR) = 15.38, 95% confidence interval (CI) = 2.91 to 81.34, p = 0.01, in comparison with both control groups) and secondary wound drainage (OR = 7.00, 95% CI = 1.45 to 33.70 in comparison with the age/sex-matched group and OR = 5.31, 95% CI = 1.01 to 26.78 in comparison with the time-matched group, p £ 0.04).

The TAA literature reports upon the success of irrigation and debridement (I&D) in early postoperative cases. Mann et al. reported on 84 ankles in 80 patients with a mean follow-up of 9.1 years with a 3 in 84 (3.5%) incidence of deep infection [10]. All deep infections were exogenous and occurred immediately postoperatively as a result of incomplete wound healing. Mann et al. treated all deep infections with open debridement and six weeks of intravenous antibiotics. One of the deep infections required a local skin graft and another required a free vascularized tissue flap for closure. No metallic prostheses were removed and there was no evidence of recurrent infection with an average follow-up of 9.3 years [10]. These results demonstrate the success of early debridement. Further demonstrating the success of I&D amongst exogenous cases, Nodzo et al. reported on 75 ankles with Salto Talaris prostheses. One of the 75 (1.3%) went on to develop deep infection within the first three weeks following TAA [11]. The patient was treated with I&D and intravenous antibiotics and the patient retained all components. Similarly, Borenstein et al. reported one ankle out of 65 consecutive TAAs (1.5%) that experienced deep infection [12]. The patient was treated with I&D and six weeks of intravenous antibiotics. Additionally, Patton et al. demonstrated the merits of I&D in detailing 29 cases of infected TAA [6]. If an I&D and revision arthroplasty were performed, 23 of 29 (79%) limbs were salvaged. Meanwhile, if revision TAA alone was performed, 19 of 29 (65%) TAA retention was reported.

In addition to I&D, the literature details the effectiveness of polyethylene liner exchange in cases of early postoperative infection and remote hematogenous infection when symptoms extend for less than four weeks [14–17]. Claridge et al. responded to the 2 of 28 (7%) cases of deep infection with polyethylene exchange only [13]. Similarly, Stoodley et al. detailed polyethylene liner exchange as an important early treatment step [16].

Reports on revision TAA after deep infection are variable [15,16,18–21]. In a case report describing TAA infection after a routine dental procedure, Young et al. described the work-up, blood cultures positive for *Streptococcus mitis* and a 6-week course of antibiotics with penicillin G and 18 million units intravenously daily for one additional week [17]. The patient remained non-weightbearing in a CAM boot until revision TAA surgery at three-months post-infection. Good outcomes with the patient walking pain-free at 16-month follow-ups were recorded. While Sproule et al. also opted for a revision TAA to treat the 1 of 88 (1%) for deep infection, they opted for a two-stage revision and recounted successful results [18]. Further reports of metal component revision after deep infection TAA demonstrated good results [15,19].

In a retrospective case series on 613 TAA, the 19 cases of deep infection were treated by established algorithms depending on if they were exogenous or late chronic infection [14]. For exogenous infection, Myerson et al. attempted prosthesis retention for 4 of 19 (21%) implants. Three (16%) had early post-op infections at three, five and seven weeks following initial implantation. All had I&D plus polyethylene liner exchange and later antibiotic therapy. One (5%) had an acute hematogenous infection. In this strategy, all four patients had recurrent infection and went on to require removal of the implant and staged treatment. Meanwhile, 15 of 19 (79%) deep infections in this series were late chronic infections. Of the deep infections, seven revision TAA were attempted but only three (16%) were successful. Of the four that failed revision TAA, three had recurrent infection and one aseptic loosening. Otherwise, for successful revision surgery, six patients were converted to arthrodesis; seven patients had a permanent antibiotic spacer, and three patients underwent transtibial amputation. The mean time to revision TAA or arthrodesis following initial infection treatment was 7.8 months (range, 2.5 to 13 months).

Revision TAA after late chronic infection has no consensus, and others advocate for conversion to arthrodesis in the case of infected TAA [8,15,22–25]. As reported by Myerson et al., six patients converted to arthrodesis all had successful revision, but only three of seven (43%) TAA revisions were successful [14]. Additionally, McCoy et al. reported on three failed TAAs due to infection [22]. These patients were revised using circular external fixator-assisted ankle arthrodesis and distraction osteogenesis for limb length equalization. All patients reported solid pain-free fusion and good subtalar joint alignment. Further evidence of good results, Mulhern et al. recounted the successful conversion to tibiotalocalcaneal arthrodesis with custom titanium alloy truss and retrograde intramedullary nail after revision TAA polyethylene became infected with *Staphylococcus aureus* [23]. Devries et al. added evidence to support arthrodesis instead of revision TAA after infection [24]. In their case series of five revision TAAs, Devries et al. initially converted the one deep infection directly to a revision TAA. While the deep infection was cleared at the time of replacement, the revision TAA went on to develop an infection. After failing two courses of long-term IV antibiotics, an antibiotic spacer was implanted and later converted to a tibiotalocalcaneal arthrodesis.

However, if deciding to proceed with a revision TAA after deep infection, there is evidence to support that single hydroxyapatite component coating should not be used in the revision [25]. When examining 117 consecutive ankles in which TAA failed after mean 4.3 years, Hinterman et al. found that 9 of 117 (8%) TAAs failed due to infection [26]. Avoiding single hydroxyapatite component coating, the group reported that the custom long-stemmed talar implant had good results amongst revisions with a 100 in 117 (85%) success rate, and one revision TAA attributed to deep infection.

While wound closure for deep infection is a coordinated effort with plastic surgery, plastics' perspective on wound closure for infected TAA is valuable when discussing a TAA infection algorithm. Goldstein et al. reported on two infected TAA treated for random local flap for wound coverage of the ankle [9]. Patients presented at a wound healing center for random local flap for wound coverage of the ankle. "Patient 3" required two flaps for infected TAA with lateral ankle wound: one peroneus longus muscle flap with hardware as exposed structure and one fasciocutaneous transposition flap with fibula as the exposed structure. "Patient 3" required 4 total operations and had a 55-day follow-up with no resultant complications. Meanwhile, "Patient 9" required two flaps for infected TAA with lateral ankle wound: one lateral calcaneal artery fasciocutaneous flap with hardware as the exposed structure and one fasciocutaneous transposition flap with hardware as the exposed structure. "Patient

9" required 2 total operations and had a 75-day follow-up with no resultant complications.

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QUESTION 2: What is the optimal (type, dose and route of administration) antibiotic treatment for patients with infected total ankle arthroplasty (TAA)?

RECOMMENDATION: Though literature specific to TAA is lacking, based on recommendations for the management of hip and knee arthroplasties, the choice of antibiotic should be made based on the identification and sensitivities of the infecting organism(s). Dosing, frequency and route of administration of antibiotics may be determined in consultation with an infectious disease specialist and by taking into account the patient's weight and comorbidities, such as renal impairment and the antibiogram.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

There is a paucity of literature regarding the treatment and outcomes of periprosthetic joint infection (PJI) in TAA. The two largest studies on post-TAA infection from the United States report the use of six weeks of intravenous (IV) antibiotic therapy following surgical treatment of the infection [1,2]. In a study from Europe, Kessler et al. reported the use of one to two weeks of IV antibiotics followed by three months of oral antibiotics following surgical treatment for infection [3]. In all of these studies, the choice of antibiotic(s) was made based on the identified infecting organism(s) and its antibiotic sensitivity and with the assistance of an infectious disease specialist. In general, the most common pathogens responsible for PJI are *Staphylococcus aureus* (methicillin-susceptible or -resistant), coagulase-negative Staphylococci and other constituents of the skin's bacterial flora [4,5].

The timing of PJI following TAA is also important in determining infection management. If the infection developed within 6-12 weeks of implantation, this is considered an acute infection and debridement with retention of the implants (DAIR) and antimicrobial treatment are the most desirable approach. Conversely, for a device that has been present for more than three months, a chronic infection is presumed to be present, and a one- or two-stage exchange with antimicrobial treatment is the desired course of action [5–7].