

## 2.1. DIAGNOSIS: TOTAL ANKLE ARTHROPLASTY-SPECIFIC

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### QUESTION 1: What is the definition of acute and chronic periprosthetic joint infection (PJI) of total ankle arthroplasty (TAA)?

**RECOMMENDATION:** There is a paucity of data for defining acute or chronic PJI following TAA in the literature. Any discussion of PJI after ankle replacement is entirely reliant on the literature surrounding knee and hip arthroplasty.

**LEVEL OF EVIDENCE:** Consensus

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

#### RATIONALE:

PJI after TAA is an unfortunate and serious complication that bears significant consequences to the patient and impediments to the natural history of ankle replacement, often prompting revision arthroplasty, conversion to arthrodesis or potentially below-the-knee amputation. While the practice of TAA has gained popularity in recent years [1], there is a paucity of data describing wound complications and acute or chronic PJI of TAA. The review of the current literature fails to identify a specific set of accepted criteria for defining an acute or chronic PJI of TAA.

Diagnostic criteria of acute or chronic PJI (non-specific to TAA) is guided by the definition developed by the Musculoskeletal Infection Society, which was later modified in 2013 by the International Consensus Group on Periprosthetic Joint Infection (Table 1) [2]. Diagnosis of PJI requires the presence of one major criterion or presence of at least three of five minor criteria. Acute infections were defined by presentation within 90 days of index surgery and chronic infections after 90 days. Acute and chronic infections each have a different set of threshold levels for the minor criteria (Table 1) [2].

The current literature regarding ankle replacement is significantly limited in data available on PJI. Of the studies that reference diagnosis of PJI in TAA, only one study by Alrashidi et al. offers any explicit reference to a diagnostic algorithm used to classify patients with periprosthetic ankle infections [1]. While not explicitly delineated, the authors appear to invoke laboratory threshold measurements described by the International Consensus Group on Periprosthetic Joint Infection in their proposed diagnostic diagram. Our systematic review failed to identify any clinical study or publication that had implemented or referenced the diagnostic algorithm submitted by Alrashidi et al.

While Alrashidi et al. have presented the most comprehensive and systematic pathway to date specific to diagnosing a PJI in TAA [1], the criterion utilized in this pathway are derived from previously described literature specific to knee and hip arthroplasty [2,3]. TAA data is significantly more limited and thus difficult to establish statistically significant infectious indicators specific to the ankle joint. Alrashidi et al. present clinically useful data in their diagnostic algorithm including the presence of a sinus tract, cell count, and differential from synovial aspiration, culture from syno-

vial aspiration, nuclear imaging studies and histological frozen sections. However, no sensitivities or specificities of the results have been described in determining PJI specific to TAA. Ferrao et al. also described similar work-up in diagnosing PJI in TAA including clinical history, physical examination, radiographic evaluation and laboratory values [4]. Pertinent history, such as sudden onset of pain, swelling, drainage, fever and associated clinical findings, such as tenderness, increased local temperature and effusion, were components concerning for PJI as described by the authors. This study presented a similar diagnostic pathway, including inflammatory markers and joint aspiration, and also made reference to the hip and knee arthroplasty literature in setting criteria and thresholds [5-7]. The trend of referencing hip and knee arthroplasty data in the work-up of PJI in TAA in our systematic review was common in the literature [8-14].

Patton et al. define PJI by positive preoperative or intraoperative cultures or the presence of chronic draining sinus tract, but do not provide reference for this definition [15]. Meyerson et al. similarly defined PJI by draining sinus tract, positive preoperative aspiration (purulent aspirate, positive Gram stain and/or elevated leukocyte count > 1,000 per mm<sup>3</sup>) or positive intraoperative culture [16]. The authors subdivided infections into acute and chronic, but did not specify criteria for differentiating between the two. Kessler et al. defined PJI as clinical signs of infection plus at least one of the following: (1) same bacteria grown on two separate preoperative or intraoperative cultures, (2) visible pus surrounding the joint, (3) acute inflammation on histopathological examination (> 10 neutrophils/HPF) or the ability to probe the base of the wound to the implant) [10,11].

Other mentions of PJI in TAA in our literature search did not specifically describe the criteria used to reach that diagnosis [9,17-19]. Case reports of PJI in TAA were also described without defining parameters for diagnosis of acute or chronic infection [20,21]. Further review did demonstrate several manuscripts, which identified risk factors for PJI, including proximity to dental procedures or medical comorbidities but failed to provide a definition for diagnosis of acute or chronic PJI [22,23]. Our systematic review yielded definitions of acute and chronic PJI defined in total hip and knee literature, case

**TABLE 1. Diagnostic criteria of periprosthetic joint infection according to the International Consensus Group on Periprosthetic Joint Infection**

Major Criteria		
<ul style="list-style-type: none"> <li>• Identification of 2 positive periprosthetic cultures with phenotypically identical microorganisms OR</li> <li>• Presence of a sinus tract communicating with the joint</li> </ul>		
Minor Criteria		
<ul style="list-style-type: none"> <li>• Elevated serum CRP AND elevated ESR</li> <li>• Elevated synovial fluid WBC count OR ++ change on leukocyte esterase test strip</li> <li>• Elevated synovial fluid PMN%</li> <li>• Positive histologic analysis of periprosthetic tissue</li> <li>• A single positive culture</li> </ul>		
Threshold Levels for minor criteria for PJI		
Criterion	Acute PJI	Chronic PJI
ESR (mm/h)	Not helpful with no defined threshold	30
CRP (mg/L)	100	10
Synovial WBC count (cells/ $\mu$ l)	10,000	3000
Synovial PMN %	90	80
Leukocyte esterase	+ OR ++	+ OR ++
Histologic analysis of tissue	> 5 neutrophils per HPF (x 400) in 5 HPF	

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMN%, polymorphonuclear neutrophil percentage; WBC, white blood cell count; HPF, high-powered field; PJI, periprosthetic joint infection, mm/h, millimeters per hour;  $\mu$ l, microliters. (Adapted with permission [2].)

reports, as well as suspected risk factors, signs, symptoms and history related to PJI.

In summary, there remains no definitive criterion in the literature for defining acute or chronic PJI after ankle arthroplasty. In the absence of specific diagnostic criteria for PJI of TAA, we may need to rely on the literature related to total hip arthroplasty and total knee arthroplasty to investigate this area further. A recent study published offers an evidence-based and validated definition for PJI of the hip and knee [24]. The criteria based on pretest probability offer each diagnostic criteria a score that is commensurate with the performance of the test in the pre-test probability and diagnostic odds ratio [24].

## 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] Parvizi J, Gehrke T. Definition of periprosthetic joint infection. *J Arthroplasty.* 2014;29:1331. doi:10.1016/j.arth.2014.03.009.
- [3] Parvizi J, Fassihi SC, Enayatollahi MA. Diagnosis of periprosthetic joint infection following hip and knee arthroplasty. *Orthop Clin North Am.* 2016;47:505–515. doi:10.1016/j.oocl.2016.03.001.
- [4] Ferrao P, Myerson MS, Schuberth JM, McCourt MJ. Cement spacer as definitive management for postoperative ankle infection. *Foot Ankle Int.* 2012;33:173–178. doi:10.3113/FAI.2012.0173.
- [5] Lonner JH, Desai P, Dicesare PE, Steiner G, Zuckerman JD. The reliability of analysis of intraoperative frozen sections for identifying active infection during revision hip or knee arthroplasty. *J Bone Joint Surg Am.* 1996;78:1553–1558.
- [6] Spanghel MJ, Masri BA, O'Connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. *J Bone Joint Surg Am.* 1999;81:672–683.
- [7] Windsor RE, Insall JN, Urs WK, Miller DV, Brause BD. Two-stage reimplantation for the salvage of total knee arthroplasty complicated by infection. Further follow-up and refinement of indications. *J Bone Joint Surg Am.* 1990;72:272–278.
- [8] Bibbo C. Controversies in total ankle replacement. *Clin Podiatr Med Surg.* 2013;30:21–34. doi:10.1016/j.cpm.2012.08.003.
- [9] Doets HC, Brand R, Nelissen RGH. Total ankle arthroplasty in inflammatory joint disease with use of two mobile-bearing designs. *J Bone Joint Surg Am.* 2006;88:1272–1284. doi:10.2106/JBJS.E.00414.
- [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] 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.
- [12] Mulcahy H, Chew FS. Current concepts in total ankle replacement for radiologists: complications. *AJR Am J Roentgenol.* 2015;205:1244–1250. doi:10.2214/AJR.14.14171.
- [13] Rippstein PF, Huber M, Naal FD. Management of specific complications related to total ankle arthroplasty. *Foot Ankle Clin.* 2012;17:707–717. doi:10.1016/j.fcl.2012.08.010.
- [14] Usulli FG, Indino C, Maccario C, Manzi L, Liuni FM, Vulcano E. Infections in primary total ankle replacement: anterior approach versus lateral transfibular approach. *Foot Ankle Surg.* 2017. doi:10.1016/j.fas.2017.07.643.
- [15] Patton D, Kiewiet N, Brage M. Infected total ankle arthroplasty: risk factors and treatment options. *Foot Ankle Int.* 2015;36:626–634. doi:10.1177/107100714568869.
- [16] 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:10.1177/107100714543643.
- [17] Althoff A, Cancienne JM, Cooper MT, Werner BC. Patient-related risk factors for periprosthetic ankle joint infection: an analysis of 6977 total ankle arthroplasties. *J Foot Ankle Surg.* 2018;57:269–272. doi:10.1053/j.jfas.2017.09.006.
- [18] Raikin SM, Kane J, Ciminiello ME. Risk factors for incision-healing complications following total ankle arthroplasty. *J Bone Joint Surg Am.* 2010;92:2150–2155. doi:10.2106/JBJS.I.00870.
- [19] *Infected Total Joint Arthroplasty.* Trebse, Richard (Editor). London: Springer-Verlag; 2012.
- [20] Criswell BJ, Douglas K, Naik R, Thomson AB. High revision and reoperation rates using the Agility™ Total Ankle System. *Clin Orthop Relat Res.* 2012;470:1980–1986. doi:10.1007/s11999-012-2242-6.

- [21] Doets HC, Zürcher AW. Salvage arthrodesis for failed total ankle arthroplasty. *Acta Orthop*. 2010;81:142–147. doi:10.3109/17453671003628764.
- [22] Gross CE, Green CL, DeOrto JK, Easley M, Adams S, Nunley JA. Impact of diabetes on outcome of total ankle replacement. *Foot Ankle Int*. 2015;36:1144–1149. doi:10.1177/1071100715585575.
- [23] Young JL, May MM, Haddad SL. Infected total ankle arthroplasty following routine dental procedure. *Foot Ankle Int*. 2009;30:252–257. doi:10.3113/FAI.2009.0252.
- [24] Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. *J Arthroplasty*. 2018;33:1309–1314.e2. doi:10.1016/j.arth.2018.02.078.

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## QUESTION 2: What is the diagnostic “algorithm” for infected total ankle arthroplasty (TAA)?

**RECOMMENDATION:** Patients who present with clinical symptoms and signs of periprosthetic ankle infection (pain, erythema, warmth, sinus tract, abscess around the wound) and sinus tracts communicating with the ankle/subtalar joint are likely to have TAA infection.

In the absence of a sinus tract, elevated inflammatory markers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)) should prompt ankle joint aspiration for cell count, differential and culture. The joint aspiration is to be repeated.

If the same organism is identified in at least two cultures of synovial fluid, the patient is diagnosed to have an infection. If the repeat aspiration is negative, further investigation is warranted.

In patients not requiring surgical intervention for other reasons, nuclear imaging should be considered for diagnosis. If an operation is indicated, histologic examination (> 5 neutrophils/high-power field) or synovial fluid analysis is conducted to confirm infection.

**LEVEL OF EVIDENCE:** Limited

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

### RATIONALE

Diagnosis of infected TAA is mainly guided by the periprosthetic joint infection (PJI) diagnostic criteria developed from the MusculoSkeletal Infection Society (MSIS) and the International Consensus Meeting [1–3]. Although the current PJI diagnostic criteria were developed based on hip and knee patients, the majority of the infected TAA clinical studies have employed the same or a variation of the MSIS criteria [3–9]. The major diagnostic criteria include (1) presence of a sinus tract which communicates with the joint or (2) two positive cultures isolating the same pathogen from the periprosthetic tissue or synovial fluid samples [1–3]. Minor criteria include elevation of inflammatory markers (CRP, ESR), elevated synovial fluid white blood cell (WBC) count or change on leukocyte esterase test strip, elevated synovial fluid polymorphonuclear cells, positive histologic analysis of periprosthetic tissue and single positive culture [1–3]. The above diagnostic algorithm was also recommended by the same authors [1–3].

Systematic literature reviews and meta-analyses have shown a 0 to 4.6% occurrence of deep infection after TAA [10,11]. Myerson et al. reported a 3.1% infection rate after TAA [6]. Their criteria for diagnosis was based on clinical findings of swelling, inflammation, drainage or persistent wound problem which prompted the protocol of joint aspiration for culture and microscopy. Synovial fluid analysis and lab analysis of inflammatory markers (CRP, ESR, WBC count) were tested to confirm infection. Patton et al. utilized similar criteria and reported a 3.2% rate of ankle PJI [7]. Uselli et al. employed the same diagnostic criteria suggested by the MSIS and reported a 3.7% deep infection rate in the anterior approach group compared to a 1.4% deep infection rate in lateral approach group [9].

However, some authors have raised the possibility that the current MSIS guideline for diagnosis and treatment of hip and knee PJI may be different from the ankle joint, given the relatively thinner soft tissue envelope and limited number of patients who underwent

successful joint-preserving revision ankle arthroplasty [3,5]. Moreover, no clinical study has validated utilization of the current hip and knee PJI diagnostic criteria for ankle PJI. Therefore, a high-quality clinical investigation is needed to validate the current criteria and algorithm for diagnosis and treatment of the ankle PJI.

### REFERENCES

- 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.
- Springer BD. The diagnosis of periprosthetic joint infection. *J Arthroplasty*. 2015;30:908–911. doi:10.1016/j.arth.2015.03.042.
- 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.
- 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.
- 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.
- 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.
- 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.
- Althoff A, Cancienne JM, Cooper MT, Werner BC. Patient-related risk factors for periprosthetic ankle joint infection: an analysis of 6977 total ankle arthroplasties. *J Foot Ankle Surg*. 2018;57:269–272. doi:10.1053/j.jfas.2017.09.006.
- Uselli FG, Indino C, Maccario C, Manzi L, Liuni FM, Vulcano E. Infections in primary total ankle replacement: anterior approach versus lateral transfibular approach. *Foot Ankle Surg*. 2017. doi:10.1016/j.fas.2017.07.643.
- 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.
- Zaidi R, Cro S, Gurusamy K, Siva N, Macgregor A, Henricson A, et al. The outcome of total ankle replacement: a systematic review and meta-analysis. *Bone Joint J*. 2013;95-B:1500–1507. doi:10.1302/0301-620X.95B11.31633.