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Revision After Total Transmetatarsal Amputation

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ABSTRACT

Total transmetatarsal amputation (TMA) can be an option for foot salvage in gangrene, sepsis, or infected necrosis. However, the literature concerning predictive outcome factors and bacterial sampling is scarce. To identify potential associations between revision surgery and underlying bacteria or other preoperative selection criteria, we reviewed all patients with TMA who were treated at our institution. We compared the patients with remissions with surgical revisions. Among 96 adult patients with TMA (105 amputations), 42 required a revision surgery (40%), 18 had a further minor proximal surgical reamputation (17%) and 18 had a major proximal surgical reamputation (14%). In group comparisons, a previous infection with *Staphylococcus aureus* was protective with a lower revision risk (4/26 with revision surgery vs 22/26 without revisions; $p = .03$). This was the opposite for postoperative persistent soft tissue or bone infections ($p < .01$) and delayed wound healing ($p < .01$), which were positively associated with a revision risk. The American Society of Anesthesiologists Score, sex, age, body mass index, diabetes, polyneuropathy, chronic renal failure, dialysis, peripheral arterial disease, smoking status, and antibiotic regimen did not influence this revision risk. These results must be interpreted cautiously because no multiple variable calculations could be conducted as a result of the paucity of cases and confounding could not be evaluated sufficiently. TMA is an option to prevent major amputations, but it may be associated with a subsequent revision risk of 40% in adult patients. In our cohort study, persistent postamputation infection and delayed wound healing were associated with revision. However, no preoperative selection criteria were found that lead to revision surgery except for an infection with *Staphylococcus aureus,* which protected against revision surgery.

Foot and ankle surgeons often perform total transmetatarsal amputation (TMA) for chronic destructive infection and/or irreversible painful ischemia and necrosis. The primary goal is to maintain limb function by preserving the ankle joint and limb length (1). However, the literature suggests high failure risks leading to more proximal amputations (2,3) and wound breakdowns with rates ranging from 30% to 60% (3,4). To save time, patient suffering, and resources, TMA should probably be avoided in selected patients, but these patients are difficult to identify preoperatively, especially if they present with an infection without severe necrosis. In this cohort study, we evaluate the revision risk after TMA and associated clinical variables including bacterial sampling and antibiotic treatment.

Patients and Methods

Balgrist University Hospital is a tertiary referral orthopaedic center for podiatric care, technical off-loading, and diabetic foot surgery (5). We performed a case-control analysis among all adult hospitalized patients with TMA who underwent surgery between April 1, 1996, and January 31, 2018 (BASEC number 2016-000387), and we have added an extensive literature review. We searched PubMed for articles containing the 2 MeSH terms "transmetatarsal amputation" and "infection" together in English and German languages and reporting of bacterial sampling or antibiotic treatment.

We defined *infection* as the presence of pus with microbiological and intraoperative clinical signs of infection or with clinical, microbiological, and radiological signs of osteomyelitis. Exclusion criteria were partial TMA, TMA performed elsewhere, pediatric and adolescent patients, and missed follow-up. We reviewed all medical charts on the following variables: surgery; age; sex; body mass index (BMI); smoking; American Society of Anesthesiologists (ASA) Score (6); indication for surgery; presence of preoperative gangrene, ulcer, and/or infection; history of ipsilateral or contralateral amputation; diabetes mellitus (DM); polyneuropathy (PNP); chronic renal failure; dialysis; peripheral arterial disease; bacterial sampling; antibiotic therapy; postsurgical wound complications; and

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Table 1
Frequency of comorbidities (N = 105 cases in 96 patients)

Comorbidity	Not present, no. of cases (%)	Present, no. of cases (%)
DM	17 (16)	88 (84)
PNP	33 (31)	72 (69)
Peripheral arterial disease	26 (25)	79 (75)
Chronic renal failure	42 (40)	63 (60)
Dialysis	89 (85)	16 (15)
ASA Score		
2		10 (10)
3		65 (62)
4		15 (14)
Smoking habits		
Smoker		21 (20)
Nonsmoker		32 (31)
Former smoker		39 (37)

Abbreviations: ASA = American Society of Anesthesiologists; DM, diabetes mellitus; PNP, polyneuropathy.

revision surgery. Because of missing data, we could not review the length of any specific antibiotic therapy, the presence of a presurgical or postsurgical revascularization, and the type of postsurgical off-loading (eg, cast, orthosis, orthopaedic shoe wear). All patients received surgery, so we lacked the possibility of comparison with patients who received conservative therapy.

Statistical Analysis

Our primary objective was the occurrence of unplanned revision surgery at the same TMA localization. Secondary endpoints were associations of clinical variables with revision. We compared variables by using *t* tests and Fisher exact tests with a Bonferroni post-hoc correction because of the explorative analysis. Because of the paucity of cases, we renounced multivariate analyses. SPSS Version 23 (IBM Corp, Armonk, NY) was used for analysis. Statistical significance was defined at the 5% ($p \leq .05$) level.

Results

We assessed 105 TMAs matching our study criteria (96 different patients; 83 [79.05%] feet in males; 22 [20.95%] feet in females; mean age 67 [range 43 to 91] years; and mean BMI 27.7 [range 17.3 to 45.6] kg/m^2). The frequency of the evaluated comorbidities is shown in Table 1. Nine (9.4%) patients had bilateral TMAs. Overall, 68% of the patients had a prior ipsilateral toe amputation or metatarsophalangeal joint resection, and 42% had had a prior contralateral amputation. Fig. 1 displays the main indications for TMA. Bacteria were detected in 90% of patients (Fig. 2), and Fig. 3 details the antibiotic therapy. Forty-seven infections were polymicrobial.

All our patients had postsurgical professional wound care and were advised to perform adequate off-loading, meaning that patients were not allowed to walk on their cast.

Outcomes

The revision rate was 40% (42/105 patients): 9 (9%) patients required a soft tissue revision, 18 (17%) patients required a minor amputation, and 15 (14%) patients required a major amputation. Overall, 26 patients had 1 revision operation, 13 patients needed 2 operations, and 3 patients needed >2 operations. The mean time until the first revision was 2.9 months (minimum 5 days, maximum 11.1 months). The most common reasons for revision surgery were delayed wound healing, new soft tissue infection, new or persistent osteomyelitis, gangrene, or ulceration (Fig. 4). During the follow-up, 26 (25%) patients died after a mean delay of 33.6 months after the index TMA.

The presence of postoperative infection ($p < .01$) and delayed wound healing ($p < .01$) were significantly associated with revision surgery, whereas infections with *Staphylococcus aureus* protected against revision ($p = .03$). All other pathogens showed no difference. There was equally no association between antibiotic regimens, age, sex, BMI, ASA Score, DM, PNP, chronic renal failure, peripheral arterial disease, dialysis, smoking, prior amputations, and ulcers with overall revision risk.

Literature Review

Of 87 articles found in PubMed on December 4, 2018, we display all articles (n = 8) that included reporting on bacteria or antibiotic regimens including the present study (Table 2). All of the articles are retrospective reports that include TMA. The literature equally lacks comparisons between TMA and conservative therapy.

Discussion

According to our single-center cohort of adult patients with TMA, the procedure ultimately fails in 40%. Among many of the clinical variables, only postoperative infection and delayed wound healing were formally associated with further revision. Only 14% of patients required a further major amputation, which is a lower rate than previously reported in the literature for TMAs (up to 56%) (2,4,6–12) and

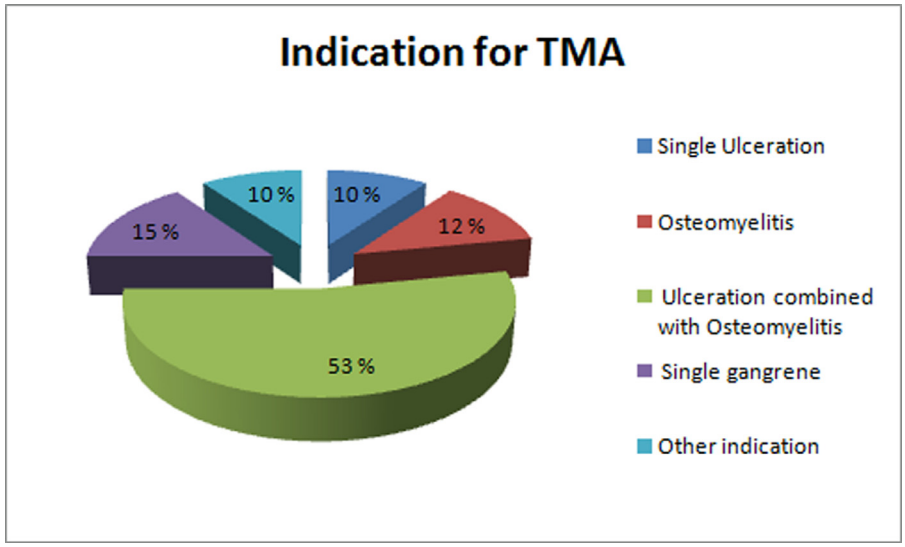

Fig. 1. Indications for transmetatarsal amputation.

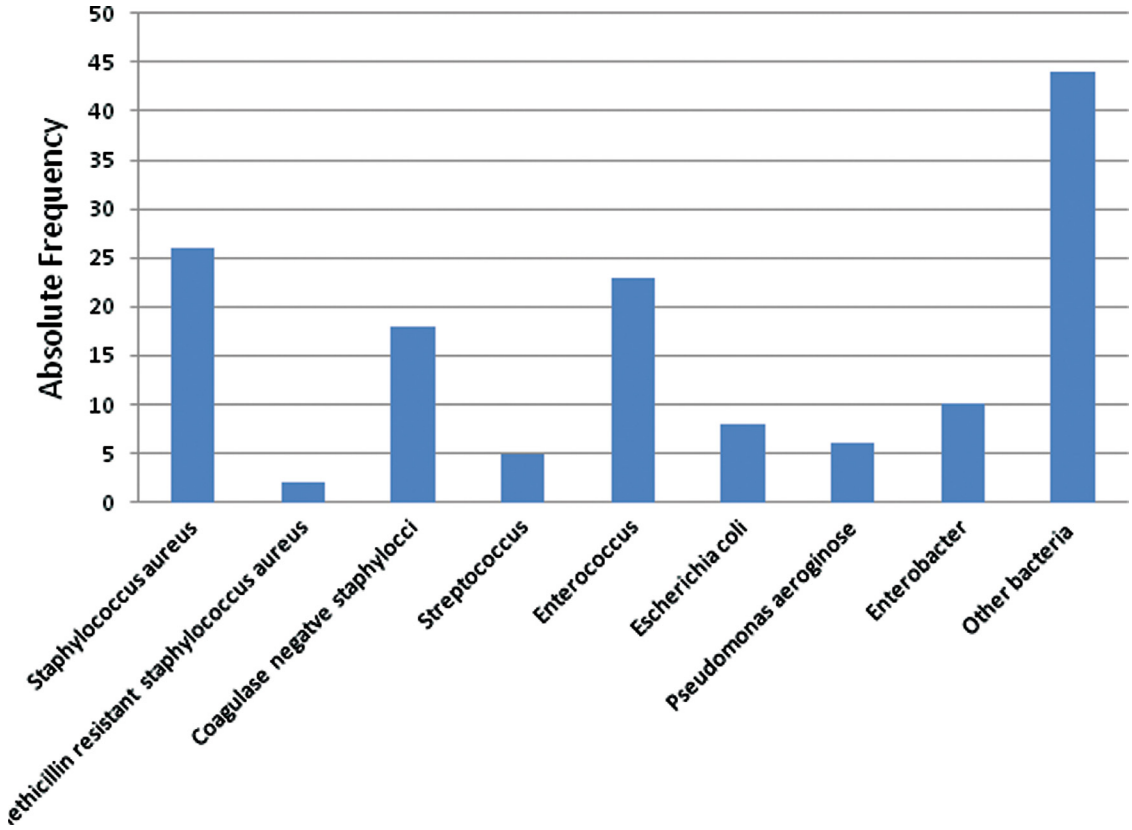

Fig. 2. Pathogens of infection.

Chopart amputations (27.7%) (13). However, an additional 17% of patients required minor amputations. Potentially, the explanation for this rather low major amputation rate is our conservative approach when determining the revision level. If angiology (eg, transcutaneous oximetry, angiography) makes wound healing probable, we try to preserve the foot whenever possible. Other hospitals tend to perform below-knee amputation sooner, potentially because below-knee amputation may seem inevitable in this patient cohort and because of

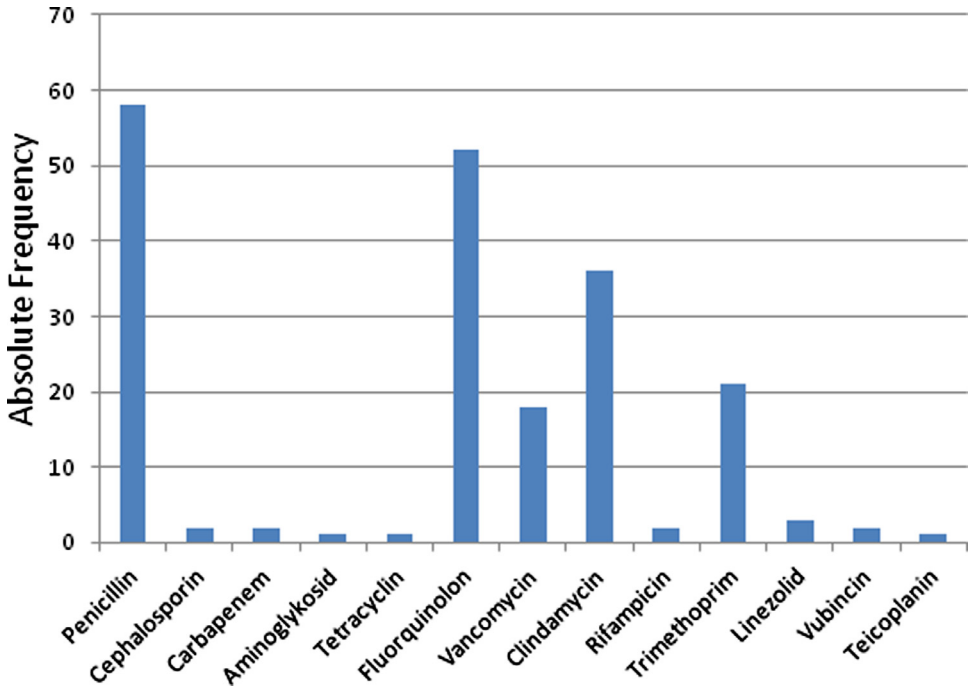

Fig. 3. Antibiotic therapy.

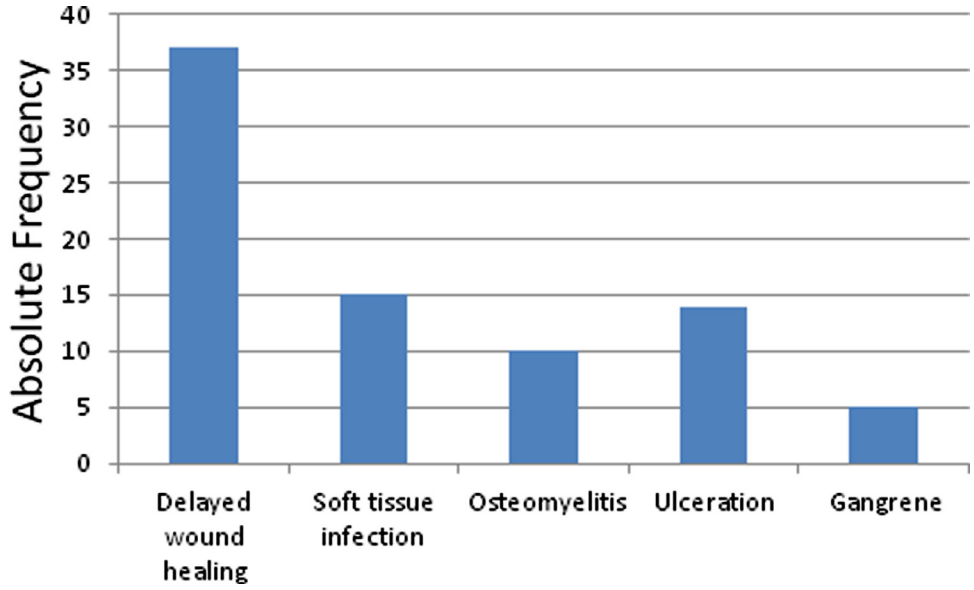

Fig. 4. Indication for revision surgery (multiple factors possible).

Table 2
Literature concerning transmetatarsal amputation in adult patients and pathogen and/or antibiotic reporting

Author, Year	No. of Cases	Indication	Main Pathogen	Duration of Antibiotics	Revisions	Remarks
Atway et al, 2012 (29)	27/3 TMA	Osteomyelitis	*Citrobacter loseri/KNS, Pseudomonas aeruginosa/ Proteus mirabilis/Enterococcus faecalis,* KNS diphtheroids	Linezolid, vancomycin/ ertapenem, sulfamethoxazole/ trimethoprim 1-6 weeks	2× delayed healing with wound dehiscence, 1× deceased	Residual osteomyelitis after resection leads to a poorer outcome
Baumfeld et al, 2018 (30)	139/28 TMA	Ischemia, osteomyelitis, infected ischemia	*Staphylococcus aureus, P aeruginosa, E faecalis*	Amoxicillin-clavulanate, ampicillin-sulbactam, ciprofloxacin/ clindamycin	—	Preoperative antibiotic use decreased healing time
Dunkel et al., 2012 (3)	289/16 TMA	Infection, ischemia	*S aureus, E faecalis, P aeruginosa, Enterobacter cloace*	Imipenem, vancomycin, amoxicillin/clavulanic acid for a mean of 5 days (0-90 days for all amputation levels)	18% wound dehiscence	The duration of antibiotic administration before and after surgery does not change the epidemiology of stump complications
Krause et al., 2009 (8)	65	Ulceration, Necrosis	Methicillin-resistant *S aureus, S aureus, P aeruginosa, Escherichia coli*	Average 2.3 weeks intravenously and 2.6 weeks orally; group 1 had local tobramycin vs group 2 without local antibiotics	27%/25% more proximal amputation; 8%/25% wound breakdown (group 1/group 2), 28% deceased	Local bioabsorbable calcium sulfate antibiotic beads may be useful in preventing wound breakdown
Mandolfino et al., 2016 (9)	218	Foot infection, gangrene	*S aureus, P aeruginosa, Enterobacter, Staphylococcus epidermidis, E coli, Proteus vulgaris, Proteus mirabilis, Streptococcus pyogenes, Serratia, Streptococcus viridians, Enterococcus, Klebsiella pneumonia*	—	34% re-amputation	TMA associated with revascularization can provide an effective limb salvage and functional results in diabetic patients with forefoot tissue loss and infection
Thomas et al., 2001 (15)	41	Gangrene, unhealed ulcerations, osteomyelitis	—	Intravenous flucloxacillin, metronidazole and cefuroxime in of cellulitis, extensive ulceration, or wet gangrene	37% more proximal amputation, 17% deceased, 46% healed stump	Nondiabetics healed better than diabetic patients
Younger et al., 2009 (4)	42	Infection, ischemia	Methicillin-resistant *S aureus,* coliforms	—	35% more proximal amputation	Presence of methicillin-resistant *S aureus* or gram-negative infections showed no difference regarding more proximal amputation
Present study, 2018	105	Infection, ischemia	*S aureus, Enterococcus*, coagulase-negative staphylococci, *Enterobacter, E coli, P aeruginosa, Streptococcus*, methicillin-resistant *S aureus*, other bacteria	Penicillin, fluroquinolone, clindamycin, trimethoprim, vancomycin, linezolid, rifampicin, cephalosporin, carbapenem, teicoplanin, aminoglycoside, tetracycline	40% revision surgery, 17% minor amputation, 14% major amputation	*S aureus* infection protected from revision surgery

a fear of potentially compromising the patient's best chance of rehabilitation (14). As in our study, the literature describes wound failures after TMA and lower extremity amputations with rates as high as 40% to 70% (1,6,10–12,15,16).

Higher healing rates might be achieved if preoperative selection criteria are adapted and risk factors ameliorated. However, in contrast to other studies, we lacked associations of failures with a high BMI (>30 kg/m^2), dialysis, active smoking, ASA Score, or non–insulin-dependent DM (1,6,10–12,15,17,18). Other investigators also could not find significant associations among healing, reamputation, and these variables in midfoot amputations (13,19). Our study population, however, is not exceptional; all demographic features are in line with the literature (Table 1).

To cite additional examples, Thomas et al (15) reported that nondiabetic patients healed significantly better than did diabetic patients. Younger et al (4) identified diabetic control as an important determinant of the outcome of TMA. The authors even state that it is prudent to delay surgery until daily glycemic control is acceptable. As a result of their study, the authors do not perform any elective, trauma, or emergency surgery on diabetic patients with a glycated hemoglobin of >8 unless the need for surgery is to save life or limb.

In addition, TMA stumps might be prone to new foot ulcers because of the high pressure below the resected bone. Indeed, we witnessed 30% of postoperative ulcers during the follow-up period. However, only a few of them required revision. Therefore, mechanical stump irritations, without additional infection, seemed to play a minor role in the need for revision surgeries.

Literature reporting on bacteria and/or antibiotic treatment in cases of TMA is scarce (Table 2). In this study, bacterial sampling showed mainly a polymicrobial flora (53%), similar to the study of Rahim et al (20). Although polymicrobial posttraumatic osteomyelitis was shown to result in a worse outcome, including a higher amputation rate (21), the present study results could not prove this.

Staphylococcus aureus was the most common pathogen, similar to reports of patients with osteomyelitis and diabetic foot infections (20–24). Other main pathogens were Enterobacteriae and coagulase-negative staphylococci, all of which can be isolated in diabetic foot infections (22,25).

A postoperative infection was highly associated with a revision surgery, unless the infection was with *S aureus*. The reason for this discrepancy is not clear. We believe that a possible explanation may be a more aggressive resection and favorable antibiotic response in cases of an *S aureus* infection (26). Another possible reason might be that these specific bacteria are widely prevalent and that any antibiotic treatment targets these specific bacteria before definitive identification (22,25).

Results from this study may find entry into a potential risk score, allowing prediction of which patient will heal at a specific amputation level (14).

The choice of the most appropriate antibiotic therapy in cases of a postoperative infection improves stump management and avoids TMA failures (27).

However, because of lack of data, we could not investigate the effects of antibiotic regimens in the prevention of revision surgeries. In patients with a diabetic foot osteomyelitis, the duration of antibiotic therapy ranged from 2 to 44 weeks (mean 10 ± 2 weeks) (23). Moreover, it was shown that the duration of antibiotic administration before and after amputation was not related to infection. An antibiotic course of 2 to 3 days or >5 days compared with 1-day postamputation prophylaxis did not prevent stump infection (3). Further search of the literature also could not reveal any specific antibiotic regimen in cases of TMAs that could reduce the revision rate (Table 2). Because many infections are polymicrobial and a majority of bacteria are resistant to the antibiotics commonly used, antibiotic treatment should usually consist of 2 antibiotics and include adequate coverage for the expected bacteria (20).

In addition to the fact that this study is retrospective, there are 2 major limitations. First, the size of our TMA population was small, with only 105 cases. However, our 22-year cohort is the largest in the scientific literature, reflecting the experience of a center known for these pathologies (5). Considering the large case-mix of TMA patients and the different approaches preferred by individual surgical teams, we believe that a multicenter data set would be equally difficult to interpret. Second, we cannot adjust for the large case-mix and therefore calculate a multivariate analyses. Furthermore, we did not compare additional parameters such as serum glycated hemoglobulin levels, degree of PNP, detailed nutrition status, duration of DM, anamnestic duration of infection, anticoagulation, statin use, type of bone grafts, specific blood flows, preoperative wound size, active psychiatric diseases, and overall compliance of different patient subgroups. Additionally, the 5-year mortality is very high among patients who need amputation (25% in this study) (28), which makes the acquirement of large homogeneous cohorts difficult. Further, the length of antibiotic therapy, antibiotic sensitivity of bacteria, and visible osteomyelitis on preoperative and postoperative magnetic resonance images including R0 or R1 amputations within the present osteomyelitis could not be evaluated and might potentially influence results; Atway et al (29) showed that patients with residual osteomyelitis after surgical bone resection have a worse outcome. Potentially, the greatest limitation is the fact that no multiple variable method could be calculated because of the paucity of cases, which limits the power of the conclusion. Therefore, results must be interpreted with caution as confounding factors might influence our results.

In conclusion, TMA is a surgical option to prevent major amputations, but TMA may be associated with a risk for revision in 40% in our study. In our cohort study, an occurrence of postoperative infection or wound healing was the only variable associated with further revisions. No preoperative selection criteria were found that lead to revision surgery except for an infection with *S aureus*, which protected against revision surgery. Before the surgeon engages in TMA, the patient should be informed about its performance and possible alternative solutions. Finally, every effort should be made to prevent stump breakdowns in this patient population.

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