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Functional and Patient-reported Outcomes following Transmetatarsal Amputation in High-risk Limb Salvage Patients

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Background: Transmetatarsal amputation (TMA) is performed in patients with nonhealing wounds of the forefoot. Compared with below-knee amputations, healing after TMA is less reliable, and often leads to subsequent higher-level amputation. The aim of this study was to evaluate the functional and patient-reported outcomes of TMA.

Methods: A retrospective review of patients who underwent TMA from 2013 to 2021 at our limb-salvage center was conducted. Primary outcomes included postoperative complications, secondary proximal lower extremity amputation, ambulatory status, and mortality. Univariate and multivariate analyses were performed to evaluate independent risk factors for higher-level amputation after TMA. Patient-reported outcome measures for functionality and pain were also obtained.

Results: A total of 146 patients were identified. TMA success was achieved in 105 patients (72%), and 41 patients (28%) required higher-level amputation (Lisfranc: 31.7%, Chopart: 22.0%, below-knee amputations: 43.9%). There was a higher incidence of postoperative infection in patients who subsequently required proximal amputation (39.0 versus 9.5%, $P < 0.001$). At mean follow-up duration of 23.2 months (range, 0.7–97.6 months), limb salvage was achieved in 128 patients (87.7%) and 83% of patients (n = 121) were ambulatory. Patient-reported outcomes for functionality corresponded to a mean maximal function of 58.9%. Pain survey revealed that TMA failure patients had a significantly higher pain rating compared with TMA success patients ($P = 0.016$).

Conclusions: TMA healing remains variable, and many patients will eventually require a secondary proximal amputation. Multi-institutional studies are warranted to identify perioperative risk factors for higher-level amputation and to further evaluate patient-reported outcomes. *(Plast Reconstr Surg Glob Open 2022;10:e4350; doi: 10.1097/GOX.0000000000004350; Published online 25 May 2022.)*

INTRODUCTION

Chronic foot ulcers affect up to 13% of the United States population, and the prevalence is rising as a result of an aging and increasingly comorbid population.[1–3] Transmetatarsal amputation (TMA) is a limb salvage procedure for nonhealing forefoot pathologies. Current indications for a TMA include, but are not limited to, forefoot ulceration, ischemia, failed ray amputations, trauma, tumors, frostbite, and congenital deformities.[4]

When successful, TMAs allow patients to maintain ambulation without a prosthesis, and at less energy expenditure than higher-level amputations.[4,5] However, TMAs have variable healing rates, reportedly ranging from 28% to 78%, and are not without risk of complications.[6–8] The large degree of variability in the reported rates of TMAs may be due to variations in how TMA success is defined. Some authors define “success” as closure of the wound, re-epithelialization of the wound, or when the stump is able to bear weight without a prosthesis.[8]

Patients whose TMA wounds do not heal will require further operations, and up to one-third of TMAs will result in major amputation.[9] Failed TMA can significantly burden patients and the healthcare system.[10] Determining the degree to which patient comorbidities and surgical

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factors increase risk of failed TMA and secondary major lower extremity (LE) amputation may guide surgeons to initially perform the surgery with the best possible functional outcome for patients. However, the literature contains conflicting reports on factors associated with TMA failure. Thus, the primary aim of this study was to review our institution's experience with TMA and to evaluate patient-reported outcomes in comorbid patients with chronic foot wounds.

METHODS

Following institutional review board approval, we performed a retrospective review of patients who underwent TMA from 2015 to 2021. TMA procedures were performed by authors of this study (J.N.A., J.S.S., C.E.A.). To identify independent predictors of secondary higher-level amputation after TMA, patients were stratified into successful TMA or higher-level amputation cohorts. For the purposes of this study, TMA failure was defined as the TMA sites that did not heal and required a more proximal amputation.

Perioperative Management

Preoperatively, patients were evaluated for medical comorbidities, and their LE wounds were serially debrided in the operating room. Their affected limb was evaluated by a vascular surgeon and they underwent LE endovascular angiography when indicated. The affected foot biomechanics were evaluated by podiatry and when indicated, correction was performed at the time of amputation. Between debridements, sterile negative-pressure wound therapy dressings were used to minimize wound contamination. Antibiotic administration was determined by foot wound culture sensitivities. Primary closure of the TMA wound was performed if there was adequate plantar and dorsal soft tissue for coverage without undue tension. Other closure methods consisted of local flaps (performed by authors C.E.A. and K.K.E.), or free tissue transfer (by K.K.E.). In cases of infection, open TMA with subsequent serial debridements was performed until the wound was considered ready for delayed primary closure. Additional procedures, including tendon Achilles lengthening or anterior tendon rebalancing, were performed to optimize functional results of TMA by preventing postoperative equinovarus deformity. Once healed, patients were fitted by pedorthotists or prosthetists for custom inserts with toe fillers to allow for ambulation in regular shoes.

Retrospective Review

Electronic medical records were reviewed to collect preoperative, intraoperative, and postoperative variables of interest. Preoperative data included patient demographics, comorbidities, wound conditions, and LE angiography findings. Intraoperative variables included TMA closure type and any additional procedures performed. Postoperative factors consisted of hospital length of stay, postoperative complications, TMA success, and long-term outcomes, such as higher-level amputation, limb salvage, ambulatory status at most recent follow-up, and mortality.

> **Takeaways**
>
> **Question**: What are the surgical and functional outcomes of transmetatarsal amputation (TMA)?
>
> **Findings:** A retrospective review of 106 patients who underwent TMA was performed. TMA success was achieved in 72%, whereas 28% required higher-level amputation. Postoperative infection was an independent predictor of higher-level amputation. Limb salvage and ambulatory rates were 87.7% and 83%, respectively. Surveyed patients reported an average maximal function of 58.9%. TMA failure patients had a significantly higher pain rating compared with TMA success patients.
>
> **Meaning:** TMA healing is variable, and many patients will eventually require a secondary proximal amputation.

Patient-reported Outcomes Measurements

Phone surveys were conducted to collect patient-reported outcome measures in 2021. The Lower Extremity Functional Scales (LEFS) survey was used to assess patient-reported functional outcomes in our study population. Pain data were captured using three PROM scales. The 11-point Numerical Rating Scale (NRS) provided the gold standard for direct assessment of pain, scored from 0 (no pain) to 10 (worst pain). Patients were asked to report their current pain levels, and best and worst pain levels in the past 24 hours. To supplement this survey, two Patient-Reported Outcomes Measurement Information System (PROMIS) assessments were utilized: (1) Pain Intensity Short Form 3a, which measures current pain, average pain, and worst pain over the past 7 days, with higher t-scores indicating greater pain intensity, and (2) Pain Interference Short Form 8a, which measures the extent that pain interferes with the ability to participate in social, cognitive, emotional, physical and recreational activities over the past 7 days, with higher t-scores indicating greater pain interference. All surveyed patients provided verbal informed consent.

Statistical Analyses

Univariate analyses were performed with Student *t*-test, Mann-Whitney U-test, chi-squared test, or Fisher exact test based on statistical parameters. Multivariate regression analysis of significant univariate findings was then performed to identify independent risk factors for secondary proximal amputation after TMA. Odds ratios with 95% confidence intervals were calculated for each risk factor. Data analysis was performed using STATA, version 17.0 (StataCorp, College Station, Tex.), with statistical significance set at P values less than 0.05.

RESULTS

A total of 146 patients were identified. The majority of patients were men (n = 102, 70%). Average age and body mass index for the study population was 61.7 years and 28.7 kg per m^2, respectively. TMA success was achieved in 105 patients (72%), and 41 patients (28%) eventually required higher-level amputation. There were no significant differences in comorbidities among TMA success and TMA failure patients. Similarly, preoperative nutrition labs and hemoglobin A1c levels were similar among the two cohorts. Osteomyelitis was significantly more prevalent in the TMA success group (61.0 versus 41.5%, *P* = 0.033). On preoperative angiography, LE vessel runoff and endovascular intervention were similar between the two groups. Table 1 summarizes patient demographics, comorbidities, and preoperative testing for the study cohorts.

Table 2 compares surgical factors between the two groups. There were no differences in closure types among TMA success versus amputation patients. The prevalence of positive cultures on day of TMA closure was similar between those with TMA success and those who required a higher-level amputation (68.6% versus 70.7%, *P* = 0.946). Additional procedures performed to treat or prevent equinovarus deformity were similar among the two groups, as well. Patients who required higher-level amputation had a significantly longer postoperative length of stay (22.5 versus 11.7 days, *P* = 0.002). There was no difference in route of antibiotics administered on discharge between the groups.

Median time to higher-level amputation was 1.8 months (interquartile range, 0.6–6.2 months). There was a higher incidence of postoperative infection in patients who required more proximal amputation (39.0 versus 9.5%, *P* < 0.001). Similarly, unplanned return to the operating room (82.9 versus 26.7%, *P* < 0.001) occurred significantly more commonly in the higher-level amputees. Wound dehiscence was found to occur at higher rates in the higher-level amputee group, as well (56.1 versus 40.0%, *P* = 0.079). Among the 41 patients who eventually underwent higher-level amputation, Lisfranc amputation was performed in 13 patients (31.7%), Chopart amputation was performed in 9 patients (22.0%), and below-knee amputation (BKA) was performed in 18 patients (43.9%). At a mean follow-up duration of 23.2 months (range, 0.7–97.6 months), limb salvage was achieved in 128 patients (87.7%). At most recent follow-up, 83% of patients (n = 121) were ambulatory. Forty-three patients (29.5%) had died. Table 3 summarizes the postoperative complications and long-term outcomes among TMA success and higher-level amputee groups. On multivariate regression analysis, postoperative infection (odds ratio: 4.39, *P* = 0.005) was an independent predictor of TMA failure and subsequent proximal amputation (Table 4).

Of the 103 surviving patients, 46 patients (44.7%) completed LEFS surveys at a mean time from surgery of 38.7 months (SD 30.3). The mean LEFS score was 47.1 (SD 14.7), which corresponded to a mean maximal function of 58.9% (SD 18.4). When stratifying by patients who required higher-level amputation (n = 9) versus those who did not (n = 37), higher-level amputees trended toward having lower patient-reported functionality scores (39.1 versus 49.1, *P* = 0.068) (Table 5).

Seventeen patients (16.5%) completed three pain surveys at an average time from surgery of 12.7 months (SD 13.9). Mean PROMIS pain interference *t*-score was 52.5 (SD 8.4) and pain intensity *t*-score was 50.4 (SD 10.7), with no significant difference in t-scores between higher-level amputee patients and those with TMA success. NRS pain scales found mean current pain of 1.8 (SD 2.2), best pain of 1.7 (SD 2.1) and worst pain of 2.8 (SD 2.5). Regarding NRS results, TMA failure patients had a significantly higher rating of current pain compared with TMA success patients (4.0 versus 1.1, *P* = 0.016) (Table 6).

DISCUSSION

To our knowledge, this is the first study to compare patient-reported outcomes among patients with TMA success versus those who required higher-level amputation. TMA was originally described in 1855 by Bernard for treatment of trenchfoot.[11] McKittrick et al then popularized TMA as a limb salvage procedure in 1949 for management of gangrene and diabetic forefoot infections.[12] The

Table 1. Patient Demographics and Comorbidities

Variable	Total (n = 146)	TMA Success (n = 105)	Higher-level Amputation (n = 41)	*P*
Men	102 (69.9%)	78 (74.3%)	24 (58.5%)	0.062
Age (y)	61.7 + 12.3	61.7 + 12.7	61.7 + 11.0	0.981
BMI (kg/m^2)	28.7 + 7.1	28.6 + 6.6	28.9 + 8.4	0.998
Comorbidities				
Diabetes mellitus	121 (82.9%)	87 (82.9%)	34 (82.9%)	0.992
Peripheral vascular disease	117 (80.1%)	80 (76.2%)	37 (90.2%)	0.066
Peripheral neuropathy	86 (58.9%)	65 (61.9%)	21 (51.2%)	0.238
Active tobacco use	20 (13.7%)	15 (14.3%)	5 (12.2%)	0.237
ESRD	44 (30.1%)	28 (26.7%)	16 (39.0%)	0.144
Charlson comorbidity index	5.7 + 2.0	5.6 + 2.0	5.9 + 2.1	0.484
Preoperative factors				
Pre-albumin (mg/dL)	15.2 + 6.8	15.5 + 6.9	14.5 + 6.7	0.516
Albumin (g/dL)	2.8 + 0.7	2.9 + 0.7	2.7 + 0.7	0.196
Hemoglobin A1c (%)	7.8 + 2.4	7.7 + 2.3	8.0 + 2.8	0.873
Acute osteomyelitis	81 (55.5%)	64 (61.0%)	17 (41.5%)	**0.033**
Positive cultures on day of TMA	101 (69.2%)	28 (26.7%)	10 (24.4%)	0.946
LE Angiography	42 (28.8%)	30 (28.6%)	12 (29.3%)	0.910
One-vessel runoff	42 (28.8%)	29 (27.6%)	13 (31.7%)	
Two-vessel runoff	42 (28.8%)	32 (30.5%)	10 (24.4%)	
Three-vessel runoff				
Endovascular intervention	80 (54.8%)	55 (52.4%)	24 (58.5%)	0.553

BMI, body mass index; ESRD, end-stage renal disease.
P-values in boldface signify statistical significance.

Table 2. Perioperative Factors

Variable	Total (n = 146)	TMA Success (n = 105)	Higher-level Amputation (n = 41)	*P*
Open TMA	41 (28.1%)	26 (24.8%)	15 (36.6%)	0.153
Closure types	67 (45.9%)	48 (45.7%)	19 (46.3%)	0.946
Primary closure	28 (19.2%)	22 (21.0%)	6 (14.6%)	0.486
Local flap	23 (15.8%)	19 (18.1%)	4 (9.8%)	0.312
Free tissue transfer	21 (14.4%)	15 (14.3%)	6 (14.6%)	1.000
Delayed primary closure				
Positive cultures on day of TMA closure	101 (69.2%)	72 (68.6%)	29 (70.7%)	0.946
Additional procedures	69 (47.3%)	51 (48.6%)	18 (43.9%)	0.612
TAL	4 (2.7%)	3 (2.9%)	1 (2.4%)	1.000
Gastrocnemius resection				
Postoperative LOS (d)	14.7 + 16.3	11.7 + 11.6	22.5 + 22.9	**0.002**
Antibiotics on discharge	20 (13.7%)	14 (13.3%)	6 (14.6%)	0.403
None	88 (60.3%)	66 (62.9%)	22 (53.7%)	
Oral	28 (19.2%)	20 (19.0%)	8 (19.5%)	
Parenteral	10 (6.9%)	5 (4.8%)	5 (12.2%)	
Oral and parenteral				

LOS, length of stay; TAL, tendon Achilles lengthening;
P-values in boldface signify statistical significance.

Table 3. Complications and Long-term Outcomes

Variable	Total (n = 146)	TMA success (n = 105)	Higher-level amputation (n = 41)	*P*
Postoperative infection	26 (17.8%)	10 (9.5%)	16 (39.0%)	**<0.001**
Wound dehiscence	65 (44.5%)	42 (40%)	23 (56.1%)	0.079
Unplanned return to operating room	62 (42.5%)	28 (26.7%)	34 (82.9%)	**<0.001**
Hematoma	6 (4.1%)	4 (3.8%)	2 (4.9%)	0.673
Re-ulceration at TMA site	55 (37.7%)	38 (36.2%)	17 (41.5%)	0.555
Higher-level amputation	41 (28.1%)	—	—	—
Lisfranc amputation	13			
Chopart amputation	9			
Below-knee amputation	18			
Median time to amputation (IQR; mo)	—	—	1.8 (0.6, 6.2)	—
Limb Salvage	128 (87.7%)	105 (100%)	23 (56.1%)	**<0.001**
Ambulatory	121 (82.9%)	90 (85.7%)	31 (75.6%)	0.145
Deceased	43 (29.5%)	29 (27.6%)	14 (34.1%)	0.437
Follow-up duration (mo)	23.2 + 21.5	22.8 + 22.1	24.2 + 20.1	0.496

IQR, interquartile range.
P-values in boldface signify statistical significance.

goal of a TMA is to provide a functional remaining foot that allows for reasonable weight-bearing and ambulation without a prosthesis. Yet, despite improvements in preoperative revascularization and medical optimization, TMA healing rates remain suboptimal and variable, with up to one-third of patients requiring proximal amputation.[9]

In this study, TMA success was achieved in 72% of patients, which parallels results of multiple other studies.[12–15] The literature contains conflicting reports on individual patient and surgical factors that negatively impact TMA healing. Sheahan et al found that a revascularization procedure performed subsequent to partial foot amputation was a predictor of subsequent limb loss and advocated early revascularization to optimize healing of the TMA site.[16] However, in this present study, preoperative revascularization was performed in similar proportions among those who experienced TMA success and those who required higher-level amputation. Poorly controlled hyperglycemia has also been associated with worse healing of TMA sites.[17] Yet, hemoglobin A1c levels were similar between our two cohorts.

On multivariate analysis, we found postoperative infection to confer over a fourfold increase in odds of eventual proximal amputation. However, we did not find positive postdebridement cultures on day of TMA closure to be significantly associated with TMA failure. Results have been mixed in regard to the current literature on the effect of positive cultures on TMA healing. A recent study by Harris et

Table 4. Predictors of Secondary Proximal Amputation after Transmetatarsal Amputation

Variable	Total Patients (n = 46)	TMA (n = 37)	Higher-level Amputation (n = 9)	*P*
Time from surgery to survey completion (mo)	38.7 (30.3)	—	—	—
LEFS				
Score	47.1 (14.7)	49.1 (14.0)	39.1 (15.7)	0.068
Percent maximal function	58.9 (18.4)	61.3 (17.5)	48.9 (19.6)	

CI, confidence interval; PVD, peripheral vascular disease.

Table 5. Lower Extremity Functional Scale Outcomes in Patients with Transmetatarsal Amputations

	Higher-level Amputation		
	Odds Ratio	**95% CI**	***P***
PVD	3.57	0.89–14.28	0.072
ESRD	1.48	0.62–3.57	0.379
Albumin < 2.7 g/dL	1.87	0.80–4.37	0.151
Postoperative infection	4.39	1.56–12.37	**0.005**
Dehiscence	1.90	0.81–4.45	0.137

Data are reported as mean (SD).
ESRD, end-stage renal disease.
P-values in boldface signify statistical significance.

al reported that a positive postdebridement pathology finding of osteomyelitis was significantly associated with healing status on univariate analysis, but this lost significance on multivariate regression analysis when age, gender, and body mass index were accounted for.[18] Atway et al found 81.8% of patients with a positive bone margin had poor outcomes, whereas 25% of patients with a negative bone margin had poor outcomes.[19] Future studies should investigate whether only patients with high Charlson comorbidity index scores need to be debrided until negative cultures before TMA closure. We were unable to investigate this in our study because the morbidity was uniformly high in our population, with an average Charlson comorbidity index above 5.

Major limb amputation has been associated with higher energy expenditure with ambulation and is frequently regarded as a premortal event.[20] The overall ambulation rate in this study was 83% and overall mortality rate was 29.5%, both of which did not significantly differ between patients who had TMA success and those who required higher-level amputation. These findings suggest that ambulatory status, rather than limb salvage, may be the critical influencer on mortality.[21,22]

Function and quality of life may be optimized through either limb salvage or amputation. With recent advancements in BKA techniques and innovative prosthetic designs, mortality rates in the amputee population may not be as high as previously reported.[23] Singh and Prasad published the first study to advise that wearing a prosthetic limb confers an independent survival benefit.[24] Wukich et al noted a five-year mortality rate of 30% in patients who were ambulatory after major LE amputation compared with 70% in those unable to walk.[22] The decision to perform primary BKA or TMA should be individualized to each patient depending on their comorbid status and functional goals. Active patients may not want to have the less predictable healing and revision surgery associated with a TMA and would rather undergo a BKA to return to their active lifestyle earlier with a custom-fitting prosthesis.

Patient-reported outcomes have become increasingly important as measures of treatment efficacy on patient symptoms and overall quality of life.[25] The literature on the impact of surgical interventions on patient-reported outcomes within the chronic LE wound population is scarce. In this study, we found the overall LEFS score to correspond to 59% of maximal function. When stratified by TMA versus proximal amputation, patients with TMA success had a 12% higher maximal function compared with higher-level amputees. Moreover, the PROMIS pain surveys revealed the pain interference and intensity scores to be relatively equal among the two cohorts. The NRS pain survey, however, revealed that higher-level amputees had greater acute levels of pain within 24 hours compared with TMA only patients, with a significantly higher level of current pain. However, these patients may not have received our current protocol of indwelling peripheral nerve blocks and prophylactic targeted muscle reinnervation at the time of their higher-level amputation. This may have impacted their overall subjective pain scores.[26] While our patient-reported outcomes are noteworthy, readers should not extrapolate our results into real-world practice until larger PROM studies are undertaken.

This study is limited by its retrospective nature, which relies on the quality of electronic medical records. We obtained mortality data solely from the electronic medical record; thus, the mortality rate may be underreported in this study. Furthermore, because of the tertiary referral nature of our practice, many patients come from long distances, and long-term follow-up of this population is often difficult to obtain. The heterogeneity among pre-TMA debridements, adjunctive procedures, and type of closures performed in our study population may have confounded our findings. In addition, the PROM surveys were not collected at the same time point for each patient, and the low response rates limit robust conclusions from being made. Nevertheless, this study contributes to the current foot and ankle literature and introduces

Table 6. Pain Survey Outcomes in Patients with Transmetatarsal Amputations

Variable	Total Patients (n = 17)	TMA (n = 13)	Higher-level Amputation (n = 4)	*P*
Time from surgery to survey completion (mo)	12.7 (13.9)	—	—	—
PROMIS				
Pain interference*	52.5 (8.4)	53.6 (8.9)	49.0 (6.2)	0.352
Pain intensity†	50.4 (10.7)	50.0 (11.9)	53.0 (6.4)	0.591
NRS‡				
Current pain	1.8 (2.2)	1.1 (1.9)	4.0 (1.6)	**0.016**
Best pain over 24 h	1.7 (2.1)	1.5 (2.1)	2.3 (2.1)	0.562
Worst pain over 24 h	2.8 (2.5)	2.5 (2.7)	3.8 (1.7)	0.382

Data are reported as mean (SD).
*PROMIS Pain Interference measures the extent that pain interferes with the ability to participate in social, cognitive, emotional, physical, and recreational activities over the past 7 days. T-scores range from 40.7 to 77, with higher scores indicating greater pain interference.
†PROMIS Pain Intensity measures current pain, average pain, and worst pain over the past 7 days. T-scores range from 36.3 to 81.8, with higher scores indicating greater pain intensity.
‡NRS rates pain on a scale of 0 (no pain) to 10 (worst pain).

patient-reported outcomes for patients with TMA versus higher-level amputees.

CONCLUSIONS

The variable healing rate and need for revision surgery following TMA should be discussed with patients to establish realistic postoperative expectations. Multi-institutional studies are warranted to identify perioperative risk factors for higher-level amputation and to further evaluate patient-reported outcomes.

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