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Three-Year Morbidity and Mortality Rates After Nontraumatic Transmetatarsal Amputation

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ABSTRACT

Patients requiring a nontraumatic transmetatarsal amputation (TMA) typically have multiple comorbidities that place them at high risk of postoperative complications and additional surgery. The present study identified the demographic, clinical, and surgical risk factors that predict complications after a nontraumatic TMA, including the incidence of 3-year mortality, proximal limb amputation, and lack of healing. The electronic medical records of patients who had undergone TMA within a Kaiser Permanente Northern California facility from March 2007 to January 2012 (n = 375) were reviewed. We used bivariate and multivariate analyses to examine the variations in the rates of TMA complications according to sex, age, race, and comorbid conditions, including nonpalpable pedal pulses, end-stage renal disease, coronary artery disease, hypertension, smoking status, and preoperative albumin <3.5 mg/dL. After a nontraumatic TMA, 136 (36.3%) patients had died within 3 years, 138 (36.8%) had required a more proximal limb amputation, and 83 (22.1%) had healed without complications. The patients with nonpalpable pedal pulses had 3 times the odds of requiring a proximal limb amputation (adjusted odds ratio [aOR] 3.07; 95% confidence interval [CI] 1.84 to 5.11), almost twice the odds of dying within 3 years (aOR 1.70; 95% CI 0.98 to 2.93), and >2 times the odds of not healing after the TMA (aOR 2.45; 95% CI 1.40 to 4.31). The patients with end-stage renal disease had 3 times the odds of dying within 3 years (aOR 3.10; 95% CI 1.69 to 5.70). The present findings can help us identify patients with an increased risk of postoperative complications after nontraumatic TMA, including patients with nonpalpable pedal pulses or end-stage renal disease, and suggest the vulnerability of this patient population.

The rates of lower extremity amputations and diabetic-related complications have been increasing, owing to the ~30 million Americans with type 2 diabetes mellitus (DM) and another 1.4 million with a new diagnosis of DM annually (1). From 2006 to 2010, the increase in nontraumatic lower extremity amputations performed on patients with DM in the United States was >10% (65,700 versus 73,000, respectively) (2).

Amputations are used to treat chronic ulceration of the diabetic or ischemic limb and severe infection and gangrene (3,4). Significant morbidity and mortality are associated with lower extremity amputations, including above-the-knee (AKA) and below-the-knee (BKA) amputations, both referred to as proximal limb amputations. A 2012 study from the American College of Surgeons National Surgical Quality Improvement Program found a 30-day postoperative mortality of 12.8% for AKA and 6.5% for BKA (5). Previous studies have shown that the 3-year mortality after AKA was 61%, and the 3-year mortality after BKA was 43% (6). Thorud et al (7) reported a 5-year mortality rate after BKA and AKA of 40% to 82% and 40% to 90%, respectively, in a systematic review. A recent meta-analysis examining long-term mortality after lower extremity amputation found an overall mortality rate of 71% and 62% at the 3- and 5-year follow-up points, respectively (8).

In an attempt at limb salvage, transmetatarsal amputations (TMAs) are performed as an alternative to proximal limb amputations (4,9). If successful, a TMA can maintain limb function and the ability to ambulate independently of a prosthesis. Although TMA is a lower risk surgery compared with a major lower limb amputation, such as an

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AKA or a BKA, the 30-day mortality after a TMA has been 1.9% to 5.6% (3,10,11). Also, TMAs have been associated with an increased incidence of postoperative complications. Some of the known risk factors for mortality include end-stage renal disease (ESRD) requiring hemodialysis, chronic obstructive pulmonary disease, hypertension, gangrene, stroke, and hypoalbuminemia (3,5,6). However, few previous studies have assessed the intermediate- and long-term mortality after TMA.

The primary aim of the present study was to determine the 3-year rate of mortality, proximal limb amputation, and failure to heal after a nontraumatic TMA. The secondary aim was to identify the demographic, clinical, and surgical risk factors predictive of these complications. We reviewed the incidence of complications after nontraumatic TMAs in a contemporary, racially diverse, community-based patient population.

Patients and Methods

The electronic medical records were reviewed for patients who had undergone TMA at a Kaiser Permanente Northern California facility from March 2007 to January 2012. Only patients with a minimum 3-year postoperative follow-up period or those who had died within 3 years of the index procedure were included in the present study. We found a total of 375 TMAs performed by 82 different surgeons.

Information was obtained from the preoperative history and physical examination records. The indications for surgery were infection, gangrene, ulceration of the forefoot, or a combination of these. The surgical technique (whether percutaneous Achilles tendon lengthening [TAL] was performed) and postoperative management (casting, suture removal, and weightbearing status) were determined by the operative surgeon.

The patient demographic and clinical data were collected by a review of the medical records. The demographic variables included age (in years), sex, and race (white versus nonwhite). The comorbidities included DM, coronary artery disease (CAD), hypertension, peripheral vascular disease (PVD), ESRD, and current smoking status. The diagnoses were identified using the International Classification of Diseases, 9th and 10th revision, codes. We also assessed albumin if results were available within 90 days before the procedure. The albumin was recorded as >3.5 or <3.5 mg/dL to indicate the patient's nutritional status (an albumin level <3.5 mg/dL suggests chronic malnutrition). The preoperative progress notes were reviewed to determine the patient's vascular status, which was recorded as palpable versus nonpalpable pedal pulses.

The primary outcome variables were 3-year mortality (i.e., dying within 3 years after the nontraumatic TMA), proximal amputation (defined as additional amputation of the leg within 3 years after the initial TMA procedure), and healing (defined as the absence of postoperative complications during the 3-year follow-up period). The complications considered indicative of nonhealing included: (1) revision of the amputation, defined as a return to the operating room for any reason; (2) postoperative infection, defined as any superficial or deep infection requiring oral antibiotics, admission to the hospital for intravenous antibiotics, and/or an unplanned return to the operating room; (3) chronic stump ulceration, defined as a nonhealing wound at the surgical site requiring >4 weeks of wound care; (4) calcaneal gait, defined as any increased pressure at the plantar heel resulting in a pressure sore; (5) stump deformity, defined as a nonplantigrade foot; and (6) stump infarction, defined as ischemia or necrosis of the incision site.

Comparisons involving categorical variables were performed using a χ^2 or Fisher's exact test. Normally distributed continuous variables were compared using Student's *t* test or analysis of variance. All analyses were performed using Statistical Analysis Systems, version 9.3 (SAS Institute, Cary, NC), and a 2-sided $p < .05$ was considered to indicate statistical significance. Multivariable logistic regression analyses were conducted to examine the adjusted associations between the patient demographic, clinical, and surgical characteristics and postoperative outcomes (death within 3 years, proximal amputation requirement, and failure to heal).

Results

Descriptive Characteristics

Of the 375 patients who underwent TMA from 2007 to 2012, the most common indication for TMA was ulceration with infection (30.3%), followed by gangrene of the foot (27.5%). The mean patient age at surgery was 66.4 ± 12.8 (range 26 to 96) years. Of the 375 patients, 266 (70.9%) were male, and 200 (53.3%) were white (Table 1). Regarding the clinical and surgical characteristics, of the 375 patients, 36 (9.8%) were current smokers, 326 (86.9%) had DM, 326 (86.9%) had hypertension, 225 (60.0%) had nonpalpable pulses, and 93 (24.8%) had ESRD and required hemodialysis (Table 1). Finally, only 126 (33.6%) patients underwent TAL concurrent with the TMA.

Mortality

Of the 375 patients, 136 (36.3%) died within 3 years of the TMA, with 8 (2.1%) dying within 30 days. The mean age of those who died was slightly older than that of the mean overall study population, and females were more likely to die within 3 years compared with males (45.0% versus 32.7%, $p = .025$; Table 1). We found no variations in mortality when stratified by race. A larger proportion of patients with CAD (43.2% versus 31.7%), ESRD (49.5% versus 31.9%), PVD (46.2% versus 21.3%), and a preoperative albumin <3.5 mg/dL (45.4% versus 31.8%) had died within 3 years compared with their disease-free counterparts ($p < .05$). The 3-year mortality for patients with nonpalpable pedal pulses was 46.2% compared with 21.3% for patients with palpable pulses ($p = .0001$). On multivariable logistic regression analysis, older age, current smoking, nonpalpable pulses, and ESRD conferred an increased odds of mortality within 3 years (Table 2). The c-stat for the model was 0.81, indicating good predictability.

Proximal Limb Amputation

The presence of nonpalpable pedal pulses was a significant risk factor for proximal limb amputation. Of the patients with nonpalpable pedal pulses, 103 (45.8%) required proximal limb amputations compared with 35 (23.3%) of those with palpable pedal pulses ($p = .0001$). Of the 138 patients who underwent a proximal limb amputation, 44 (31.9%) had ESRD and 94 (68.1%) did not ($p = .015$). On multivariable analysis, the presence of nonpalpable pulses was the only risk factor associated with an elevated odds of proximal limb amputation (adjusted odds ratio [aOR] 3.07; 95% confidence interval [CI] 1.84 to 5.11; Table 2).

Failure to Heal

Of the 375 patients, only 83 (22.1%) healed from their amputation without complications (Fig.). The common complications included chronic stump ulceration in 224 (59.7%), revision amputation in 127 (33.9%), postoperative infection in 115 (30.7%), and stump infarction in 117 (31.3%). Males were less likely to heal than were females (81.2% versus 69.7%; $p = .0151$). Of the patients with nonpalpable pedal pulses, 188 (83.6%) developed a complication and failure to heal the stump compared with 104 (69.3%) of the patients with palpable pedal pulses ($p = .0012$). The other predictors of a failure to heal without complications were no TAL (81.1% versus 71.4%; $p = .0327$) and hypertension (80.4% versus 61.2%; $p = .0026$; Table 1). On multivariable analysis, male sex, hypertension, nonpalpable pulses, and no TAL continued to be associated with increased odds of not healing (Table 2).

Discussion

The present study identified multiple risk factors associated with the development of complications after a nontraumatic TMA, a procedure performed for the treatment of limb-threatening infection, gangrene, and ulceration in patients with DM and PVD. Despite the high 3-year mortality and complication rate in the present study, this rate is lower than those reported after BKA or AKA (6) and provides evidence that nontraumatic TMA could be an effective procedure for limb salvage. However, Thorud et al (12), in a recent systematic review and meta-analysis, questioned the utility of performing an amputation at this level compared with other forefoot amputations. They found a reoperation rate of 26.9% (391 of 1453), with a rate of reamputation

Table 1
Descriptive characteristics of patients who underwent nontraumatic transmetatarsal amputation stratified by morbidity and mortality

Variable	All Patients (N = 375)	3-y Mortality (n = 136)	*p* Value	Proximal Amputation (n = 138)	*p* Value	Failure to Heal (n = 292)	*p* Value
Demographic characteristics							
Age (y)	66.4 ± 12.8	73.2 ± 11.3	NA	66.4 ± 12.8	NA	66.3 ± 12.5	NA
Sex			.025		.6184		.0151
Male	266 (70.9)	87 (32.7)		100 (37.6)		216 (81.2)	
Female	109 (29.1)	49 (45.0)		38 (34.9)		76 (69.7)	
Race			.0571		.2426		.4382
White	200 (53.3)	73 (36.5)		64 (32.0)		150 (75.0)	
Nonwhite	175 (46.7)	63 (36.0)		74 (42.2)		142 (81.1)	
Clinical characteristics							
Current smoker*			.0063		.4976		.9058
No	330 (90.1)	121 (36.7)		124 (37.6)		259 (78.5)	
Yes	36 (9.8)	13 (36.1)		10 (27.8)		27 (75.0)	
DM			.477		.743		.2443
No	49 (13.1)	20 (40.8)		17 (34.7)		35 (71.4)	
Yes	326 (86.9)	116 (35.6)		121 (37.1)		257 (78.8)	
CAD			.023		.579		.2260
No	227 (60.5)	72 (31.7)		81 (35.7)		172 (75.8)	
Yes	148 (39.5)	64 (43.2)		57 (38.5)		120 (81.1)	
Hypertension			.810		.335		.0026
No	49 (13.1)	17 (34.7)		15 (30.6)		30 (61.2)	
Yes	326 (86.9)	119 (36.5)		123 (37.7)		262 (80.4)	
Nonpalpable pulses			< .0001		< .0001		.0012
No	150 (40.0)	32 (21.3)		35 (23.3)		104 (69.3)	
Yes	225 (60.0)	104 (46.2)		103 (45.8)		188 (83.6)	
ESRD			.002		.015		.1867
No	282 (75.2)	90 (31.9)		94 (33.3)		215 (76.2)	
Yes	93 (24.8)	46 (49.5)		44 (47.3)		77 (82.8)	
Albumin† (≤3.5 mg/dL)			.0028		.6512		.3197
No	66 (17.6)	21 (31.8)		27 (40.9)		54 (81.8)	
Yes	172 (45.9)	78 (45.4)		64 (37.2)		137 (79.7)	
Surgical characteristic							
TAL			.0001		.5914		.0327
No	249 (66.4)	107 (43.0)		94 (37.8)		202 (81.1)	
Yes	126 (33.6)	29 (23.0)		44 (34.9)		90 (71.4)	

Data presented as mean ± standard deviation or n (%).
Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; ESRD, end-stage renal disease; NA, not applicable; TAL, Achilles tendon lengthening.
* Data missing for 9 patients.
† Data missing for 137 patients.

at any level of 29.7% (152 of 365) and major amputation rate of 33.2% (380 of 1146) after TMA (12).

More than one third of the patients in the present study had died within 3 years after their nontraumatic TMA. Death largely resulted from the multiple comorbidities of the patient population and not the procedure itself. In adjusted analyses, mortality within 3 years was predicted by nonpalpable pedal pulses, ESRD, CAD, and an albumin <3.5 mg/dL. This is what we would expect to find, because these associated comorbidities all suggest poor overall health and an inherent risk of mortality. Female sex was also predictive of mortality within 3 years. These risk factors are consistent with those previously reported (3,5,6). Brown et al (13) reported a 30% 5-year mortality rate

Table 2
Multivariable logistic regression analyses of association between demographic, clinical, and surgical characteristics and 3-year morbidity and mortality (N = 375)

Variable	3-y Mortality		Proximal Amputation		Failed to Heal	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Demographic characteristics						
Age (y)	1.08	1.06 to 1.11	0.99	0.97 to 1.01	0.98	0.96 to 1.00
Sex (reference: male)	1.53	0.88 to 2.68	0.87	0.87 to 0.53	0.49	0.28 to 0.86
Race (reference: nonwhite)	1.17	0.69 to 1.98	0.8	0.50 to 1.27	0.97	0.55 to 1.69
Clinical characteristics						
Current smoker (reference: nonsmoker)	3.47	1.42 to 8.47	0.75	0.33 to 1.70	0.95	0.40 to 2.27
DM (reference: no)	0.92	0.42 to 1.99	1.08	0.54 to 2.16	1.14	0.53 to 2.44
CAD (reference: no)	1.22	0.72 to 2.05	0.86	0.53 to 1.38	0.93	0.52 to 1.67
Hypertension (reference: no)	0.70	0.32 to 1.56	1.32	0.65 to 2.68	2.86	1.39 to 5.87
Palpable pulses (reference: yes)	1.70	0.98 to 2.93	3.07	1.84 to 5.11	2.45	1.40 to 4.31
ESRD (reference: no)	3.10	1.69 to 5.70	1.61	0.95 to 2.73	1.42	0.71 to 2.82
Albumin (reference: >3.5 mg/dL)	1.80	0.89 to 3.64	0.74	0.40 to 1.38	0.77	0.36 to 1.66
Surgical characteristics						
TAL (reference: yes)	1.72	0.98 to 3.02	1.13	0.69 to 1.84	1.79	1.04 to 3.10

Abbreviations: aOR, adjusted odds ratio; CAD, coronary artery disease; CI, confidence interval; DM, diabetes mellitus; ESRD, end-stage renal disease; TAL, Achilles tendon lengthening.

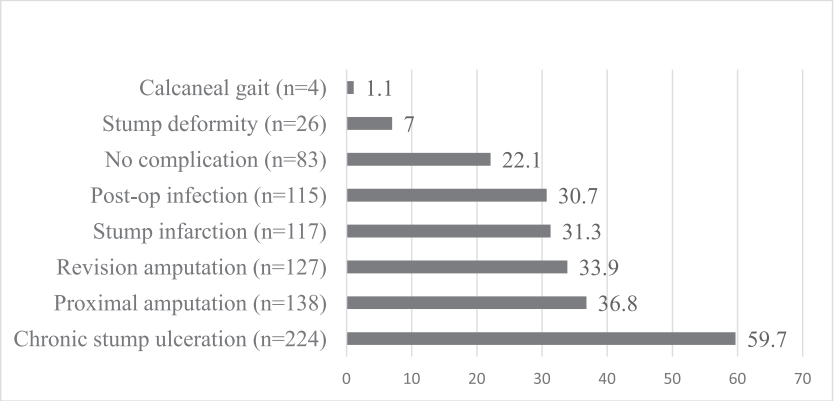

Fig. Incidence of postamputation complications.

after 21 TMAs. A systematic review by Thorud et al (7) reported an overall 5-year mortality rate ranging from 53% to 100% after any lower extremity amputation (major and minor combined) but did not specifically consider TMA (7). Parodoxically, the TMA was more likely to heal without complications in females (30.3% versus 18.8%; $p = .0151$), but females experienced increased mortality.

Regarding proximal limb amputation after the TMA, nonpalpable pedal pulses was the only predictive surgical factor in the adjusted analyses. Of the 375 patients, 138 (36.8%) subsequently required either a BKA or an AKA within 3 years, 103 (45.8%) of whom had nonpalpable pedal pulses. In a study assessing a series of 77 TMAs, 21 (27.3%) required a proximal limb amputation (11). Those investigators also concluded that vascular status was a significant factor associated with healing. Patients with a biphasic pedal waveform and an ankle pressure >100 mm Hg had a positive predictive value of 79%, and those with a toe pressure >50 mm Hg had a positive predictive value of 91% for determining healing of TMA or midfoot amputations (11). Blume et al (14) reported that 25 (27%) of 91 patients required a more proximal amputation 1 year after TMA and that renal failure was a predictor of major amputation after TMA. Using a random effects model, Thorud et al (12) estimated a reoperation rate of 24.43%, a reamputation rate of 28.37%, and a major amputation rate of 30.16% after TMA in a systematic review and meta-analysis. The findings from the present study are consistent with those from previous reports (3,5,11), which concluded that arterial occlusion is a risk factor for proximal limb amputation. However, revascularization is not always an option; thus, despite the risk of failure, TMA can be attempted before a BKA or an AKA, in accordance with the patient's goals.

Healing of the TMA without complications was associated with palpable pedal pulses, performance of TAL, normal blood pressure, and female sex. O'Brien et al (15) reported a 26.4% early failure rate after 1205 TMAs. They noted several pre- and intraoperative variables that were independently associated with early failure, including emergency operation, TMA, sepsis, septic shock, ESRD, systemic inflammatory response syndrome, body mass index ≥30 kg/m^2, and ongoing tobacco use (15). Beaulieu et al (16) examined the predictors for readmission and reamputation after 717 minor lower extremity amputations (defined as toe or TMA). Readmission was required for 100 (13.9%) patients, including 28 (3.9%) within 30 days, 28 (3.9%) within 30 to 60 days, and 44 (6.1%) >60 days after the index amputation. In addition, a multivariable analysis revealed elective readmission, peripheral arterial disease, and chronic renal insufficiency were all statistically significant for readmission. The reason for readmission was infection (49%), ischemia (29%), a nonhealing wound (19%), and indeterminate (4%) (16). Although our study did not specifically examine the readmission rates, we found that only 83 (22.1%) of the patients healed without complications and 138 (36.8%) subsequently required a proximal limb amputation.

In the present study, of the 292 patients who failed to heal, 90 (30.8%) had undergone TAL concurrent with the TMA compared with 202 (69.2%) who did not ($p = .0327$). The indication for performing TAL was determined by the individual surgeon and based on the patient's ambulatory status at the time of surgery and their expected functional capacity after the TMA. Despite performing a TAL at the time of TMA, the possibility still exists for recurrent plantar stump ulceration. Maluf et al (17) found that a TAL resulted in an initial decrease in forefoot peak pressure, forefoot pressure–time interval, and plantarflexion moment and power, with an increase in the ankle dorsiflexion range of motion during gait. However, the forefoot pressure and plantarflexion moment and power increased toward pretreatment values during the 8-month follow-up period. Their results suggest that a TAL causes a temporary reduction in forefoot pressures, primarily by decreasing the plantarflexion muscle power during the push-off phase of gait (17). In addition, Barry et al (18) performed an isolated TAL for chronic plantar forefoot ulceration after TMA in 33 patients and reported a healing rate of 91%. The primary potential complication of a TAL is a calcaneal gait or plantar heel ulceration. La Fontaine et al (19) noted 5 new heel ulcerations in 28 patients after an isolated TAL for treatment of new or recurrent ulceration after TMA. In the present study, we noted only 4 (1.1%) patients developed plantar heel ulceration after TAL. Therefore, we believe the benefits of performing a TAL in conjunction with TMA outweigh the potential risk in the ambulatory patient; however, every patient should be evaluated regarding the need for a TAL procedure.

Among the patients with ESRD requiring hemodialysis, 46 (49.5%) died within 3 years. Overall, patients requiring hemodialysis and aged ≥65 years have a life expectancy of 4 years (20). Eggers et al (20) studied nontraumatic lower extremity amputations in patients with ESRD and found that the rate of amputation among people with DM and ESRD was 10 times greater than among the general DM population. Two thirds of the patients with ESRD died within 2 years after amputation (21). This included all amputations of the lower extremity, ranging in severity from toe amputations to hip disarticulations. A high complication rate after a TMA should be expected in patients with ESRD because hemodialysis causes uremia, calciphylaxis, and protein loss, which impairs wound healing (21).

Our findings also support the findings from the original report by Pollard et al (3) on short-term mortality after TMA. The 30-day

mortality within our cohort was 2.1% compared with 1.9% in the study reported in 2006 (3). With these reproducible results, we can reliably inform patients that the probability of death within 30 days after a TMA is ~2%. This is in contrast to the early postoperative mortality after major lower limb amputation, which can range from 7% to 22% (22).

Given the nature of our study design, our study had inherent limitations. Although TMAs were performed by 82 different surgeons and the surgical technique and postoperative protocol were not standardized, our study focused on the preoperative variables that can predict poor outcomes after TMA. This minimized the statistical effect the surgical technique or postoperative protocol might have on the outcomes of interest. Another limitation was that we did not identify the specific cause of mortality. Especially in our patient population, confounding factors were present that contributed to mortality.

In conclusion, the present study contributes to the current foot and ankle data because our findings support what we have empirically found while treating the high-risk population of patients with DM, PVD, and ESRD. Ours was a descriptive study of the perioperative course of patients requiring TMAs, and our findings provide a better understanding of the associated mortality and morbidity. In our study, nonpalpable pedal pulses were a risk factor for 3-year mortality, proximal limb amputation, and failure of the TMA to heal. However, some patients will have arterial occlusive disease with limited options for revascularization. In an attempt at limb salvage, a TMA can still be performed, although the risk of postoperative complications is increased compared with that for patients without PVD. Future studies could attempt to identify whether this places an increased burden on the patient and healthcare resources compared with primary proximal limb amputation.

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