From the Western Vascular Society

Open revascularization approach is associated with healing and ambulation after transmetatarsal amputation in patients with chronic limb threatening ischemia

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ABSTRACT

Background: Transmetatarsal amputation (TMA) allows for maintenance of ambulatory function for patients with significant forefoot tissue loss. Effective revascularization is key to optimizing limb salvage for patients with chronic limb threatening ischemia (CLTI). We hypothesized that CLTI patients requiring TMA will have better healing and functional outcomes with open bypass than with endovascular revascularization.

Methods: Consecutive TMAs performed at three affiliated centers between 2008 and 2020 were retrospectively reviewed. The baseline characteristics, including WIfI (wound, ischemia, foot infection) stage, noninvasive vascular studies, healing, and ambulatory outcomes, were collected. Catheter-based angiographic images were evaluated using the GLASS (global limb anatomic staging system). The primary outcomes were TMA healing and community ambulation. The secondary outcomes were TMA that had healed at study end, any ambulatory function postoperatively, major amputation, and mortality. Descriptive statistics and univariate, multivariable, and Kaplan-Meier analyses were performed.

Results: A total of 346 TMAs had been performed in 318 patients, 209 of whom had had peripheral artery disease (PAD). The median follow-up was 2.5 years. Patients with PAD had had significantly lower rates of healing compared with those without PAD (64% vs 77%; $P = .007$). Revascularization was performed in 185 limbs, with 102 treated endovascularly and 83 with open surgery. The patients who had undergone endovascular surgery were significantly less likely to have had the TMA healed at any point (55% vs 76%; $P = .003$) and less likely to have remained healed at study end (49% vs 66%; $P = .02$). Patients with GLASS stage 3 anatomy were significantly more likely to have healed after open surgery (75% vs 45%; $P = .003$). Long-term ambulation data were available for 72% of the revascularized patients. Endovascular surgery was associated with a lower likelihood of community ambulation after TMA (34% vs 57%; $P = .002$). On multivariable analysis, open surgery was significantly associated with TMA healing (odds ratio, 2.8; $P = .007$) and ambulation (odds ratio, 2.9; $P = .001$).

Conclusions: For patients with CLTI and significant tissue loss requiring TMA, an initial open approach to revascularization was associated with improved healing and higher rates of ambulation compared with endovascular interventions. The metabolic requirement for healing of a TMA in patients with CLTI might be better met by open revascularization. (J Vasc Surg 2023;■:1-8.)

Keywords: Amputation; Chronic limb threatening ischemia; Peripheral arterial disease; Surgical

Achieving healing and preserving function for patients with advanced pedal tissue loss has remained a daunting challenge. For patients with extensive tissue loss involving multiple toes or the forefoot, transmetatarsal amputation (TMA) can maintain ambulatory function with a well-balanced foot and preservation of a sensate

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Author conflict of interest: M.S.C. is an Abbott Vascular Advisory Board member. C.G.-S., E.W., T.S., R.E.K., E.L., C.P., B.G., M.D., J.I., A.R., and W.G. have no conflicts to disclose.

Presented at the Thirty-seventh Annual Meeting of the Western Vascular Society, Victoria, BC, Canada, September 17-20, 2022.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2022.12.035

heel.[1-4] However, successful healing of the TMA can require many months, additional procedures will often be necessary,[5] and TMA failure can result in major amputation.[2,6,7] Recognizing the significant investment of time and effort that can be required to heal a TMA, some providers might forgo the attempt and proceed directly to recommending a major below-the-knee amputation (BKA) or above-the-knee amputation (AKA). In particular, increasing age and the presence of comorbidities, especially peripheral artery disease (PAD), will increase the risk of TMA failure.[6,8,9] The most common alternative to TMA, BKA, might have a higher healing rate; however, achieving independent ambulatory status after a major amputation has been inversely related to age and the number of accumulated comorbidities.[10-12] Older patients with multiple comorbidities, in particular, PAD, are those with the most to benefit in terms of survival and independent ambulation with a successful TMA and avoidance of major amputation.[12,13]

Optimizing perfusion in those with PAD is key to improving the chances of successful TMA healing and, thus, preserving ambulation.[14,15] Patients with PAD and tissue loss, by definition, have chronic limb threatening ischemia (CLTI),[16] and vascular surgeons have a myriad of tools available to achieve lower extremity revascularization. However, the extent of occlusive disease will often be advanced in those with CLTI. Understanding the value of the endovascular and open options for various scenarios is an ongoing process. Although endovascular techniques offer a less invasive option, the long-term outcomes have suggested that open procedures might have better durability and limb salvage rates.[17,18] It is especially important to compare the effectiveness of the revascularization approach for patients requiring a TMA because it represents a critical turning point between functional limb salvage and major amputation.

The primary goal of the present study was to evaluate the outcomes of TMA across a multi-institutional academic health system with a focus on patients with CLTI. We hypothesized that CLTI patients would have better healing and functional TMA outcomes with an open or a hybrid revascularization (open) approach compared with an endovascular approach.

ARTICLE HIGHLIGHTS

- **Type of Research:** A multicenter, retrospective cohort study
- **Key Findings:** Patients with chronic limb threatening ischemia requiring transmetatarsal amputation had a higher rate of healing after open revascularization procedures compared with endovascular procedures. Additionally, postoperative community-level ambulation was more frequently achieved after open revascularization.
- **Take Home Message:** Good healing and functional outcomes after transmetatarsal amputation for patients with chronic limb threatening ischemia might be more likely with open revascularization approaches.

METHODS

We performed a retrospective review of all consecutive patients who had undergone TMA at three centers (university/tertiary referral medical center, Veterans Affairs medical center, and county hospital) of a multi-institutional academic practice from 2008 through 2020. Data on demographics, limb characteristics, procedural details, healing, and ambulatory outcomes were collected from the electronic medical records. The patients were considered healed if the postoperative physical examination report had stated that the wound was healed after suture removal, which typically occurred 6 to 8 weeks after the TMA. Ambulatory status was defined as "community-level ambulation" if the patient could ambulate outside the home with or without an ambulatory device, "any degree of ambulation" if they were able to stand for transfer or take a limited number of steps, and "nonambulatory" if the patient was entirely wheelchair or bedbound. The primary outcomes were TMA healing at any point during the study and community-level ambulation status. The secondary outcomes were the TMA remaining healed at the end of follow up, any degree of ambulation, major amputation, and survival.

Patients were considered to have PAD if the ankle brachial index (ABI) was <0.9, the ankle arteries could not be compressed, the toe brachial index (TBI) was abnormal, or clinically significant stenosis had been found on duplex ultrasound or angiography before TMA. The preoperative limb status was classified according to the Society for Vascular Surgery lower extremity threatened limb classification system (WIfI [wound, ischemia, foot infection]).[16] For the purposes of the present study, patients were considered to have undergone revascularization if the procedure had been performed within 6 months before or 1 month after the TMA. Endovascular attempts during which the diseased segment could not be crossed were not considered revascularizations; at least one lesion had to have been treated to be included. If a patient had undergone multiple revascularization procedures in the 6 months before the TMA, the most recent intervention was considered the index procedure for our analysis. If a patient had undergone revascularization both before and after TMA, the procedure most immediately before the TMA was considered the index procedure. For patients who had undergone open TMA, followed by delayed primary closure or another closure procedure, the initial open TMA was considered the index TMA. Any patient with an angiogram demonstrating their native vascular anatomy within 6 months of the TMA was graded using the

Society for Vascular Surgery global limb anatomic staging system (GLASS) for CLTI.[19] The angiographic images were independently reviewed and assigned a GLASS stage by at least two study personnel. Discordant scores were reviewed, and a final score was assigned by consensus of the reviewers. The Vascular Quality Initiative CLTI mortality prediction model was used to stratify the patients into low-, medium-, and high-risk categories using the data from admission for the TMA.[20]

The three centers encompass a tertiary referral care academic medical center, a public safety net hospital, and a Veterans Affairs medical center staffed by vascular surgeons from a single division. Before 2012, limb preservation was directed primarily by vascular surgery, and TMAs were performed by a combination of vascular surgeons and podiatrists. However, after 2012, a multidisciplinary limb preservation service was established at all three centers, with the addition of podiatrists dedicated to limb preservation. The multidisciplinary team has protocolized the care of threatened limbs, including routine documentation of the WIfI stage after publication of the WIfI system in 2014. Patients included from before 2014 had the WIfI stage determined retrospectively by a review of the medical records. The institutional review board approved the present study.

Statistical analysis was performed using STATA/IC, version 15.0 (StataCorp, College Station, TX). Descriptive statistics were performed using paired *t* tests for continuous data and χ^2 tests for categorical variables. Logistic regression was used for univariate and multivariable modeling for risk factors for the primary outcomes. Kaplan-Meier analysis was used for survival functions. A competing risks model was developed using a nonparametric cumulative incidence function to determine the cumulative incidence of amputation, accounting for death as a competing event. A subgroup analysis was performed to examine the effect of graft type for patients with open bypass.

RESULTS

Demographics, comorbidities, and limb status at admission for TMA. A total of 346 TMAs had been performed for 318 unique patients during the study period. Of these, 225 TMAs had been performed for 209 patients (65.7%) with PAD (Supplementary Table I, online only). Almost 85% of the overall cohort had diabetes, either type 1 or 2, and 37% had chronic renal insufficiency, with 17% requiring hemodialysis at surgery. The patients with PAD were older (66 vs 55 years; $P < .001$) and had higher rates of coronary artery disease (44% vs 17%; $P < .001$) and end-stage renal disease requiring dialysis (22% vs 9%; $P = .006$; Supplementary Table I, online only). The patients with PAD had also had significantly lower rates of healing compared with those without PAD (64% vs 77%; $P = .007$). All further analyses described included only the cohort of patients with PAD.

Among the subgroup with PAD, full WIfI staging was available for 216 limbs (96%) before the intervention. An ABI was available for 205 limbs, of which 76 had had incompressible ankle vessels. The toe pressure was available for 149 limbs. The wounds in this cohort were advanced, with 208 limbs having a WIfI wound grade of ≥2, and 93% of patients having a WIfI stage of 3 or 4. GLASS staging was available for 201 limbs (89%), of which 49% had had the highest complexity anatomy, GLASS stage 3. The most common combination of WIfI and GLASS stage was WIfI stage 4 and GLASS stage 3 (40%; Fig 1).

Revascularization procedures. Revascularization was performed in 185 limbs, with 90% performed before the index TMA at a mean of 8 days between the vascular procedure and the TMA. The patients with PAD who had not undergone any revascularization had had a significantly higher mean ABI (0.85 vs 0.57; $P < .001$) and toe pressure (35.5 mm Hg vs 18 mm Hg; $P = .009$) at presentation for TMA, with a lower proportion of WIfI stage 3 or 4 (87% vs 97%) and less severe occlusive disease on angiography (fewer with GLASS stage 2 or 3, 60% vs 82%). Among those who had undergone revascularization, an initial endovascular approach was undertaken for 102 limbs and an open or hybrid approach for 83 limbs. The specific interventions performed are detailed in Supplementary Table II (online only). More than one half of the endovascular group had undergone multilevel interventions. Most patients had undergone intervention involving the infrapopliteal vessels. In addition, 67% of the endovascular group had included tibial interventions, and 70% of the open group had involved tibial or pedal targets. Among the open subgroup, 71% of infrainguinal bypasses were performed with an autogenous conduit, 56% of which were a single-segment greater saphenous vein. A cryopreserved venous allograft was used in 25% of bypasses and a prosthetic graft (polytetrafluoroethylene or Dacron) in 4%.

The patient demographics and baseline characteristics of the index limb revascularization group are summarized in Table I. The open group tended to have a more severe anatomic distribution of vascular disease with a higher prevalence of GLASS stage 3 (72% vs 41%; $P < .001$). Seventy patients had undergone repeat ABI or TBI testing after the index revascularization. After excluding 11 limbs with incompressible vessels, 50 limbs had had a postprocedural ABI available, with a mean increase of 0.3 (open, +0.34; vs endovascular, +0.25; $P = .54$) after revascularization. Seventeen limbs had the toe pressure available after revascularization, with a mean increase of 22 mm Hg (open, +42; vs endovascular, +18 mm Hg; $P = .23$).

Outcomes stratified by revascularization approach. The major outcomes stratified by the index revascularization approach are listed in Table II. The median follow-up

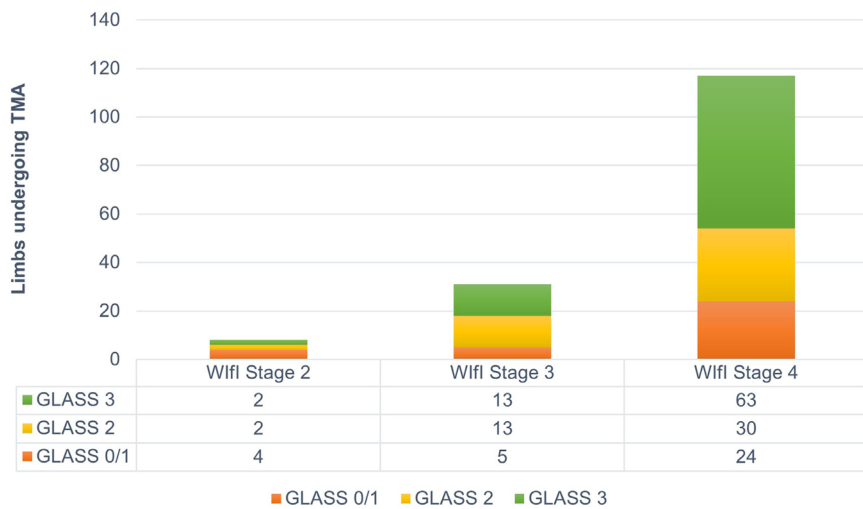

Fig 1. Distribution of global limb anatomic staging system (GLASS) stage stratified by Society for Vascular Surgery wound, ischemia, foot infection (WIfI) stage for limbs that had undergone revascularization and transmetatarsal amputation (TMA; n = 156).

Table I. Selected baseline characteristics stratified by revascularization approach (n = 173 patients; n = 185 limbs)

	Revascularization			
Variable	**All (n = 185)**	**Endovascular (n = 102)**	**Open or hybrid (n = 83)**	***P* value**
Age, years	66.7 ± 11.1	68.3 ± 11.3)	64.7 ± 10.6	.07
Female gender	39 (21.2)	22 (21.8)	17 (20.5)	.83
BMI, kg/m^2	27.4 ± 7.2	27.1 ± 7.8	27.9 ± 6.4	.46
CAD	83 (44.9)	41 (40.2)	42 (50.6)	.16
CHF	46 (24.9)	25 (24.5)	21 (25.3)	.9
ESRD, HD required	45 (24.3)	27 (26.5)	18 (21.7)	.45
Medium/high risk[a]	20 (17)	16 (21.1)	4 (9.5)	.11
Prior toe amputation on index foot	98 (62)	61 (64.9)	37 (57.8)	.37
GLASS stage 3	92 (54.4)	40 (41.2)	52 (72.2)	**<.001**
WIfI stage 3 or 4	138 (96.5)	79 (95.2)	59 (98.3)	.31

BMI, Body mass index; *CAD,* coronary artery disease; *CHF,* congestive heart failure; *ESRD,* end-stage renal disease; *GLASS,* global limb anatomic staging system; *HD,* hemodialysis; *WIfI,* wound, ischemia, foot infection.
Data presented as mean ± standard deviation or number (%).
Boldface *P* values represent statistical significance.
[a]Vascular Quality Initiative chronic limb threatening ischemia mortality predictor.

was 2.2 years (median, 798 days; interquartile range, 393-1544 days). No significant differences were found between the endovascular and open approaches in 30-day mortality (5.9% vs 2.4%; *P* = .12) or 30-day readmissions (28% vs 33%; *P* = .46). Also, no difference was found in the occurrence of any vascular reintervention during follow-up (26% vs 28%; *P* = .81).

At 3 years, no significant difference was found in the survival rate between the endovascular and open groups (70%; 95% confidence interval [CI], 59%-78%; vs 73%; 95% CI, 62%-82%; *P* = .1, log-rank; Fig 2). The VQI CLTI mortality prediction tool identified 20 patients who were at intermediate or high risk, with a trend toward endovascular use for this subset that did not reach statistical significance (Table I). The tool provided a reasonable prediction of 2-year survival for both the low-risk (predicted survival, 88%; vs observed survival, 85%) and the medium- to high-risk (predicted survival, 57%-66%; vs observed survival, 63%) groups.[20]

Healing outcomes. The primary outcome, TMA healed at any point, was significantly more likely for the patients who had undergone open revascularization (76% vs 55%; *P* = .003). Similarly, the open group were more likely to have remain healed at the end of the follow-up period (66% vs 49%; *P* = .02). When stratifying the patients by GLASS stage, the patients with more severe disease (GLASS stage 3) were significantly more likely to have healed after open revascularization than after an endovascular approach (Fig 3). On univariate analysis, active

Table II. Rates of healing and ambulation after transmetatarsal amputation (TMA) stratified by revascularization approach

	Revascularization			
Variable	All (n = 185)	Endovascular (n = 102)	Open or hybrid (n = 83)	*P* value
Healing outcomes				
TMA healed at any point[a]	119 (64.3)	56 (54.9)	63 (75.9)	**.003**
TMA healed at end of follow-up	105 (57.8)	50 (49)	55 (66.3)	**.02**
TMA healed with GLASS 3 anatomy	57 (62)	18 (45)	39 (75)	**.003**
TMA healed after infrapopliteal intervention	78 (63.9)	34 (52.3)	44 (77.2)	**.004**
TMA revision	45 (24.3)	24 (23.5)	21 (25.3)	.78
Midfoot amputation	12 (6.5)	8 (7.8)	4 (4.8)	.41
Major amputation	44 (23.8)	27 (26.5)	17 (20.5)	.34
BKA	35 (18.9)	25 (24.5)	10 (12.1)	**.03**
AKA	9 (4.9)	2 (2)	7 (8.4)	**.04**
Ambulation outcomes				
Community ambulation after TMA[a]	82 (44.32)	35 (34.31)	47 (56.63)	**.002**
Any ambulation after TMA	135 (72.97)	65 (63.73)	70 (84.34)	**.002**

AKA, Above the knee; *BKA*, below-the-knee; *GLASS*, global limb anatomic staging system; *WIfI*, wound, ischemia, foot infection.
Data presented as number (%).
Boldface *P* values represent statistical significance.
[a]Primary outcome.

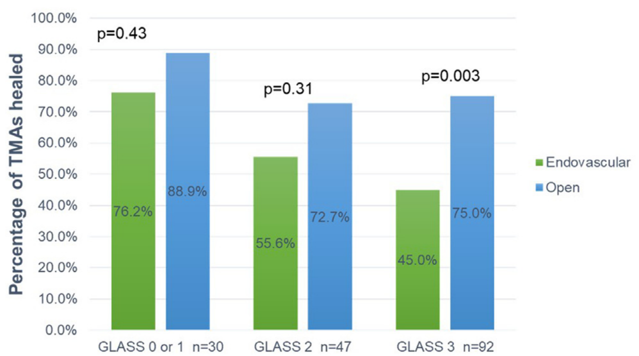

Fig 2. Transmetatarsal amputation (TMA) healing rate for patients with peripheral artery disease (PAD) who had undergone revascularization stratified by global limb anatomic staging system (GLASS) stage.

smoking, end-stage renal disease requiring dialysis, severe tibial disease (infrapopliteal GLASS stage 4), and revascularization approach were significant predictors of TMA healing. On multivariable logistic regression, only the choice of the index revascularization technique was significantly associated with TMA healing, with almost threefold better odds of healing for patients treated with open revascularization (odds ratio [OR], 2.8; 95% CI, 1.3-5.9; *P* = .007; Supplementary Table III, online only).

During follow-up, 24% of the revascularized patients had undergone TMA revision and 6.5% had undergone revision to a midfoot amputation on the index side, with similar rates between the two cohorts. A total of 66 limbs (35% of TMAs) had not healed during follow-up, with 21 patients remaining alive with an unhealed TMA at the end of follow-up. Overall, 44 of the revascularized patients (24%) had required a major amputation during the follow-up period at a median of 112 days after TMA, with no significant differences by type of revascularization. However, BKA was significantly more likely in the endovascular group (25% vs 12%; *P* = .03), and AKA was more likely in the open group (8% vs 2%; *P* = .04). We developed a competing risks model for major amputation, controlling for death as a competing risk (Fig 4), which demonstrated a nonsignificant trend toward a lower rate of major amputation for the open cohort (20% vs 29%; *P* = .16).

The GLASS stage was not significantly associated with major amputation but was strongly skewed by the revascularization approach selected, as outlined. The presence of severe tibial disease was similar in the open and endovascular groups (39.4% vs 44.3%; *P* = .53). The patients with the highest severity scores for below-the-knee disease (GLASS infrapopliteal score of 3 or 4 or pedal modifier score of 2) had required significantly more BKAs compared with those without severe distal disease (29.6% vs 16.5%; *P* = .04).

In a subgroup analysis of the open patients, those who had undergone infrainguinal bypass with cryopreserved venous allografts had had significantly lower rates of TMA healing than those with autogenous vein bypasses (61% vs 78%; *P* = .02). The rate of healing and major amputations in the endovascular group were similar for those with a cryopreserved vein vs an autogenous vein (55% vs 61%; *P* = .63; and 27% vs 39%; *P* = .28, respectively). Univariate and multivariable analysis by logistic regression did not find any significant association of the conduit choice on healing. However, our study was underpowered to directly address this question.

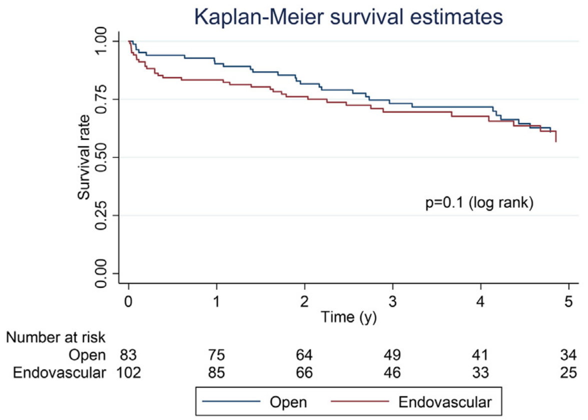

Fig 3. Kaplan-Meier estimates of survival after transmetatarsal amputation (TMA) for patients with peripheral artery disease (PAD) stratified by revascularization approach.

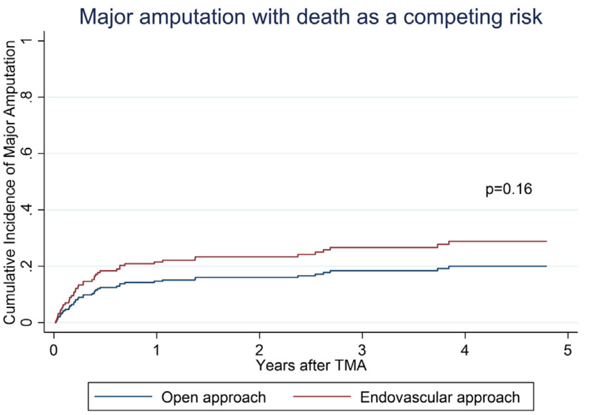

Fig 4. Competing risk model for major amputation after transmetatarsal amputation (TMA) for patients who had undergone revascularization with death as a competing risk.

Ambulation outcomes. The primary outcome for function, community-level ambulation, was more likely for the patients who had undergone open revascularization (57% vs 34%; *P* = .002). When including the patients who were only ambulatory to the extent of transferring, the rate was still significantly higher for the open cohort (84% vs 64%; *P* = .002; Table II). On univariate analysis, female gender, chronic obstructive pulmonary disease, stroke, and index choice of revascularization approach were significantly associated with community ambulation. Multivariable analysis by logistic regression identified chronic obstructive pulmonary disease as a significant negative predictor (OR, 0.17; 95% CI, 0.04-0.65; *P* = .01) and an open revascularization approach as a significant positive predictor (OR, 2.9; 95% CI, 1.5-5.7; *P* = .001) of community ambulation after TMA (Supplementary Table IV, online only).

DISCUSSION

In the present retrospective cohort study of consecutive patients who had undergone TMA for CLTI, an open revascularization approach was associated with significantly higher rates of TMA healing and community ambulation. To the best of our knowledge, the present study is the largest to investigate revascularization approaches for patients undergoing TMA and includes granular data about both the presenting limb severity and the arterial anatomy using the Society for Vascular Surgery WIfI staging system and GLASS, respectively. Our data have shown that patients with CLTI who require TMA will have a pattern of advanced limb pathology and multilevel arterial disease. The most common combination of limb severity and arterial anatomy score was WIfI stage 4 with GLASS stage 3. The small group of PAD patients who had not undergone revascularization had had less severe ischemia and a lower anatomic complexity of disease and had had outcomes comparable to those who had undergone revascularization, supporting the need for a systematic patient-centered approach for all patients requiring a TMA. Most of the patients who had undergone revascularization had received interventions that had involved tibial or pedal vessels, and severe infrapopliteal disease was associated with a higher progression to major amputation.

The healing benefit from open revascularization had primarily resulted from the use of an autologous conduit for infrainguinal bypass. The patients who had undergone bypass with a cryopreserved saphenous vein had had outcomes comparable to the outcomes of those who had undergone endovascular interventions. The decision regarding approach to perform was at the discretion of a vascular surgeon trained in both endovascular and open techniques. However, a tendency was found toward the use of open bypass for those with greater anatomic disease complexity. We were unable to control for a significant selection bias in our series between the two approaches, because the choice was determined by patient comorbidities, disease complexity, clinical presentation, bypass conduit availability, and patient preference. Additionally, although no differences were identified in need for any reintervention between the two cohorts, the follow-up for the open cohort was longer. Thus, additional reinterventions during follow-up for the endovascular group might not have been fully captured. Based on our experience with patients who have required TMA, if a question of clinical or hemodynamic effects exists after the initial revascularization procedure, we would advocate for early and aggressive reintervention, including conversion from an endovascular to an open approach if feasible for these patients. Our analysis showed that the amputation rates were not significantly different between the cohorts despite a significant difference in TMA healing. We believe this was due to an insufficient sample size (type II error) for this end point. It is also plausible that patients with non-healed TMAs had elected to continue with long-term wound care rather than undergo major amputation.

The open approach was also associated with a higher rate of postoperative ambulation compared with the endovascular approaches and was an independent predictor of community-level ambulation. This observation might have been biased by the selection of lower risk, higher functioning patients for the open procedures. No standardized measurement of preoperative ambulation status was used because many of the patients had had preceding toe amputations with variable restrictions on weight bearing. Thus, it would be difficult to know the effect of a potential selection bias on this outcome. However, it does suggest that for properly selected patients, functional recovery toward independent community-level ambulation might be frequently achieved with an open approach. Even in the setting of very advanced arterial disease, 72% of the patients who had undergone TMA in our study were able to maintain some degree of ambulatory function and almost 45% were able to maintain independent community-level ambulation. These functional results are similar to those reported in the development of the AMPREDICT-Mobility tool.[12] Our ultimate goal with limb salvage is to maintain function; however, success with TMA in the PAD population requires a significant investment in time and energy from both the patient and the team of providers. We would advocate that a multidisciplinary team should help to create protocols and standardize a unified "toe-and-flow" system to help meet those challenges.

We speculated that hemodynamic gain will be critically important for patients with advanced tissue loss and could be a differentiator between the open and endovascular approaches; however, we did not directly investigate this possibility using our data. An important limitation of the present study was the paucity of postrevascularization hemodynamic data available after the index revascularization. The high prevalence of diabetes in our cohort meant that many patients had had incompressible ankle vessels that precluded ABI use (76 patients had had incompressible ankle vessels found with initial ABI testing). After the TMA, the option of performing TBI testing. Postrevascularization surveillance was, thus, limited to duplex ultrasound for many patients with infrequent use of transcutaneous oximetry and skin perfusion pressures. Newer methods of hemodynamic assessment such as the pedal acceleration time and implantable oxygen sensors might eventually overcome the limitations of the ABI, TBI, transcutaneous oximetry, and skin perfusion pressure monitoring but have not yet been integrated into the surveillance practices at our centers.

The care of these patients was performed by an overlapping group of surgeons at three different institutions that serve very different patient populations: the San Francisco Veterans Affairs Medical Center, which provides care for veterans across a large catchment in Northern California; the University of California, San Francisco, Medical Center, which is a large academic tertiary referral center; and the Zuckerberg San Francisco General Hospital, which is a county trauma center and safety net hospital. This diverse setting is encouraging in terms of generalizability to a larger population. No direct information on the social determinants of health were collected in our database, because the information was entirely retrospective. However, such factors could have affected the individual outcomes.

CONCLUSIONS

The use of TMA represents a chance for sustained and functional limb salvage for patients with significant forefoot tissue loss from CLTI. Our data suggest that an open approach might be more effective as a revascularization strategy for patients undergoing TMA, especially for those with advanced occlusive disease patterns. Further studies are needed to clarify the hemodynamic requirements and optimal revascularization approaches for this high-risk CLTI population.

AUTHOR CONTRIBUTIONS

Conception and design: CG, EW, CP, BG, MD, AR, MC, WG
Analysis and interpretation: CG, EL, JI, MC, WG
Data collection: CG, EW, TS, RE, BG
Writing the article: CG, EW
Critical revision of the article: CG, TS, RE, EL, CP, BG, MD, JI, AR, MC, WG
Final approval of the article: CG, EW, TS, RE, EL, CP, BG, MD, JI, AR, MC, WG
Statistical analysis: CG, EL, WG
Obtained funding: Not applicable
Overall responsibility: WG
CG and EW contributed equally to this article and share co-first authorship.

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Submitted Oct 31, 2022; accepted Dec 22, 2022.

Additional material for this article may be found online at www.jvascsurg.org.

Supplementary Table I (online only). Patient characteristics stratified by peripheral artery disease (PAD)

Characteristic	Total cohort (n = 318)	With PAD (n = 209)	Without PAD (n = 109)	*P* value
Age at TMA, years	62.3 (23-94)	66.3 ± 10.9	54.9 ± 11.3	**<.001**
Female sex	61 (19)	42 (20.1)	19 (17.4)	.57
Non-White race	205 (64)	131 (62.7)	74 (67.9)	.36
BMI, kg/m^2	27.5 ± 7.0	27.2 ± 7.1	28.2 ± 6.8	.26
CAD	110 (35)	92 (44)	18 (16.5)	**<.001**
CHF	68 (21)	52 (24.9)	16 (14.7)	**.04**
HTN	260 (82)	184 (88)	76 (69.7)	**<.001**
HLD	182 (57)	134 (64.1)	48 (44)	**.001**
DM	268 (84)	175 (84)	93 (85)	.14
Current smoker	93 (31)	59 (26.2)	43 (35.5)	.07
COPD	28 (8.8)	21 (10.1)	7 (6.4)	.28
CKD (eGFR <60 mL/min/1.72 m^2)	117 (37)	88 (42.1)	29 (26.6)	**.007**
Dialysis required	55 (17)	45 (21.5)	10 (9.2)	**.006**
Prior stroke	45 (14)	37 (17.7)	8 (7.3)	**.01**
Antiplatelet	236 (69)	180 (81.1)	56 (46.7)	**<.001**
Anticoagulation	53 (16)	46 (20.8)	7 (5.9)	**<.001**
Prior minor amputation on index foot	207 (67.9)	124 (64.3)	83 (74.1)	.08

BMI, Body mass index; *CAD*, coronary artery disease; *CHF*, congestive heart failure; *CKD*, chronic kidney disease; *COPD*, chronic obstructive pulmonary disease; *DM*, diabetes mellitus; *eGFR*, estimated glomerular filtration rate; *HLD*, hyperlipidemia; *HTN*, hypertension; *TMA*, transmetatarsal amputation.
Data presented as mean (range), mean ± standard deviation, or number (%).
Boldface *P* values represent statistical significance.

Supplementary Table II (online only). Specific index revascularization procedures performed (n = 185)

Procedure	No. (%)
Endovascular only	102 (55.1)
Iliac	8
Stented	6
Angioplasty only	2
SFA	43
Stented	25
Angioplasty only	18
Popliteal	28
Stented	7
Angioplasty only	21
Tibial	68
Stented	6
Angioplasty only	62
Open only	74 (40)
Inflow procedure	17
Aorta–femoral	3
Femoral–femoral	2
Axillofemoral	3
Femoral endarterectomy	9
Infrainguinal bypass procedure	72
Femoral–popliteal	14
Femoral–ATA	12
Femoral–PT	25
Femoral–peroneal	5
Popliteal–pedal	14
Other	2
Hybrid	9 (4.9)
Femoral endarterectomy + iliac stent	2
Femoral–popliteal bypass +iliac stent	1
Femoral endarterectomy + SFA stent	3
Femoral–peroneal bypass + SFA stent	1
Femoral endarterectomy + tibial PTA	1

ATA, anterior tibial artery; *PT,* posterior tibial artery; *PTA,* percutaneous transluminal angioplasty; *SFA,* superficial femoral artery.

Supplementary Table III (online only). Multivariable model of factors associated with transmetatarsal amputation (TMA) healing for patients with peripheral artery disease (PAD) undergoing revascularization procedures

Predictor of TMA healing	OR (95% CI)	*P* value
Age	0.98 (0.95-1.0)	.29
Active smoking	1.4 (0.55-3.5)	.48
On dialysis	0.51 (0.23-1.2)	.1
GLASS infrapopliteal score 4	0.46 (0.21-1)	.05
Open or hybrid revascularization	2.8 (1.3-5.9)	**.007**

CI, Confidence interval; *GLASS,* global limb anatomic staging system; *OR,* odds ratio.
Boldface *P* values represent statistical significance.

Supplementary Table IV (online only). Multivariable model of factors associated with community ambulation after transmetatarsal amputation (TMA) for patients with peripheral artery disease (PAD) undergoing revascularization procedures

Predictors of ambulation	OR (95% CI)	*P* value
Age	1 (0.98-1.03)	.75
Female gender	1.8 (0.81-4.1)	.14
BMI	1 (0.96-1.04)	.95
Prior stroke	0.75 (0.32-1.7)	.48
COPD	0.17 (0.04-0.65)	**.01**
Open or hybrid revascularization	2.9 (1.5-5.7)	**.001**

BMI, Body mass index; *CI,* confidence interval; COPD, chronic obstructive pulmonary disease; *OR,* odds ratio.
Boldface *P* values represent statistical significance.