Outcomes Following Severe Distal Tibial, Ankle, and/or Mid/Hindfoot Trauma

Comparison of Limb Salvage and Transtibial Amputation (OUTLET)

Major Extremity Trauma Research Consortium (METRC)*

Background: Selecting the best treatment for patients with severe terminal lower-limb injury remains a challenge. For some injuries, amputation may result in better outcomes than limb salvage. This study compared the outcomes of patients who underwent limb salvage with those that would have been achieved had they undergone amputation.

Methods: This multicenter prospective observational study included patients 18 to 60 years of age in whom a Type-III pilon or IIIB or C ankle fracture, a Type-III talar or calcaneal fracture, or an open or closed blast/crush foot injury had been treated with limb salvage (n = 488) or amputation (n = 151) and followed for 18 months. The primary outcome was the Short Musculoskeletal Function Assessment (SMFA). Causal effect estimates of the improvement that amputation would have provided if it had been performed instead of limb salvage were calculated for the SMFA score, physical performance, pain, participation in vigorous activities, and return to work.

Results: The patients who underwent limb salvage would have had small differences in most outcomes had they undergone amputation. The most notable difference was an improvement in the SMFA mobility score of 7 points (95% confidence interval [CI] = 2.0 to 10.7). Improvements were largest for pilon/ankle fractures and complex injury patterns.

Conclusions: Amputation should be considered a treatment option rather than a last resort for the most complex terminal lower-limb injuries.

Level of Evidence: Therapeutic Level II. See Instructions for Authors for a complete description of levels of evidence.

The decision to attempt lower-limb salvage or perform an amputation for terminal limb injuries, including pilon, ankle, and mid/hindfoot injuries, is a clinical conundrum. While salvage procedures for complex injuries of the foot and ankle may be technically feasible, treatment decisions should be informed by the expected quality of life and function of the patient.

Lower Extremity Assessment Project (LEAP)[1] investigators reported that limb salvage and amputation provided similar functional outcomes. However, in a subgroup of participants with severe pilon, hindfoot, or ankle injury, outcomes of salvage procedures that required a free flap and/or ankle arthrodesis were worse than those of early amputation[2]. These results, coupled with a small but growing body of literature from military centers, suggested that, for certain terminal lower-limb injuries, early amputation may result in a better outcome than limb salvage[3-5]. These studies are limited in size, scope, and analytic rigor, and their authors uniformly recommended a large prospective study to definitively address differences in outcomes for these patients. Without more compelling evidence, trauma teams have difficulty counseling an injured patient.

Conducting a randomized trial would be challenging because patients likely have strong treatment preferences. Therefore, we designed an observational study to compare outcomes of patients who underwent limb salvage for a severe pilon, ankle, and/or mid/hindfoot injury with the outcomes that they would have experienced had they instead undergone an early amputation. We hypothesized that, on average, there would no appreciable difference in measures of self-reported function,

*A list of the Major Extremity Trauma Research Consortium (METRC) members is provided in a Note at the end of the article.

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A **data-sharing statement** is provided with the online version of the article (http://links.lww.com/JBJS/G528).

physical performance, return to work, or participation in vigorous activities. However, it was anticipated that patients with the highest injury burden would have had appreciably better outcomes had they undergone a transtibial amputation.

Materials and Methods

For this analysis, data were drawn from 2 institutional review board-approved, multicenter, prospective studies conducted by the Major Extremity Trauma Research Consortium (METRC)[6-8]. OUTLET was an observational study, conducted at 31 U.S. level-I trauma centers and 3 military treatment facilities, designed to address the main hypotheses stated above. Due to a lower-than-expected number of early amputations, the study sample was supplemented with participants in the Transtibial Amputation Outcomes Study (TAOS), which randomized patients to receive a transtibial amputation with or without tibiofibular synostosis. Participants in the TAOS were treated at 25 METRC centers, 22 of which also participated in the OUTLET study. The 2 studies were consistent regarding collection of baseline patient characteristics, non-study-injury characteristics, and outcomes.

Patients included in the OUTLET study were 18 to 60 years of age and had ≥1 of the following: Type-III pilon (OTA/AO 43) or IIIB or C ankle fracture (OTA/AO 44), Type-III talar or calcaneal fracture (OTA/AO 81 or 82), or open or closed crush/blast injury to the mid/hindfoot[9,10]. When a patient had multiple fractures, the principal study injury was defined as the one at greatest risk for poor outcomes according to the treating surgeon. All injuries were adjudicated for eligibility using anteroposterior and lateral radiographs and photographs of the wound. Injury characteristics that were collected included the OTA/AO open fracture classification[9], the presence of plantar degloving, the need for and location of a flap, and contralateral and ipsilateral injuries at the pelvis and below. An early amputation was defined as a transtibial or Syme amputation performed within 3 months after the injury. Of the 581 patients enrolled, 84% underwent limb salvage and 16% underwent early amputation (Fig. 1). Of the limb salvage procedures, 17 involved partial foot amputations and 10 were followed by late amputation.

We included 58 TAOS patients with a unilateral transtibial amputation within 3 months after major limb trauma who had sustained the injury within 18 months before the time of analysis. While these patients did not have an OUTLET-eligible injury, their outcomes are relevant because it can be assumed that once the injury was removed with the amputation it ceased to impact outcome. In total, 151 patients who had undergone early transtibial amputation were included.

Patients who underwent salvage were similar to those who underwent amputation with regard to preinjury health status, engagement in vigorous activity, presence of comorbidities, and body mass index (BMI). There were modest differences in socioeconomic characteristics. Most patients had an isolated musculoskeletal injury; 11% had an Injury Severity Score (ISS) of >17. A contralateral limb injury was present in 23% of the patients, and there was an ipsilateral limb injury proximal to the study injury in 14% (Table I).

Of the patients who underwent limb salvage, 38% had a Type-III pilon or IIIB or C ankle fracture, 24% had a Type-III talar or calcaneal fracture, and 37% had another severe foot injury (Table II). Approximately 75% of the patients who underwent salvage had a complex injury pattern, defined as requiring a tissue flap, a severe articular fracture (including OTA/AO 43B or C, 81B or C, or 82B or C), and/or substantial bone loss (>2 cm).

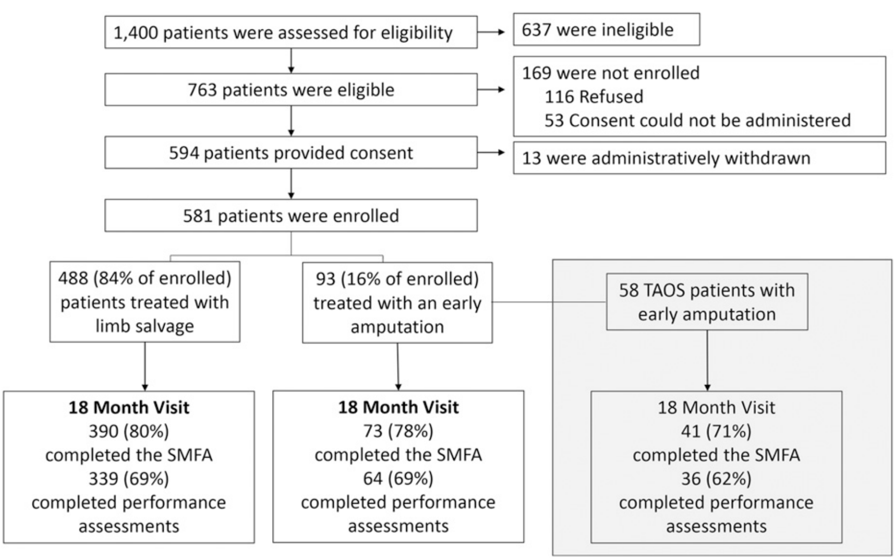

Fig. 1

CONSORT (Consolidated Standards of Reporting Trials) diagram. *The study included 58 TAOS patients who underwent a unilateral transtibial amputation within 3 months after major limb trauma that occurred within 18 months before the analysis was conducted. These patients did not have an OUTLET-eligible injury.

TABLE I Participant Characteristics

		Limb Salvage				
	Overall (N = 639)	All (N = 488)	No Flap, Severe Articular Fracture, or Severe Bone Loss (N = 131)	Flap, Severe Articular Fracture, and/or Severe Bone Loss (N = 357)	Amputation within 3 Mo of Injury (N = 151)	P Value*
Age† *(yr)*	38.4 (12.3)	37.7 (12.1)	35.8 (12.0)	38.4 (12.1)	40.6 (12.8)	0.010
Female *(%)*	32	36	41.2	34.7	18	<0.001
Race/ethnicity *(no. [%])*						0.520
White, non-Hispanic	440 (69)	329 (67)	94 (72)	235 (66)	111 (74)	
Non-White, non-Hispanic	122 (19)	96 (20)	22 (17)	74 (21)	26 (17)	
Hispanic	72 (11)	58 (12)	15 (11)	43 (12)	14 (9)	
Other	4 (1)	4 (1)	0	4 (1)	0	
Missing	1 (<1)	1 (<1)	0	1 (<1)	0	
Education *(no. [%])*						0.020
<High school	109 (17)	87 (18)	26 (20)	61 (17)	22 (15)	
High school/GED	219 (34)	151 (31)	40 (31)	111 (31)	68 (45)	
>High school	301 (47)	240 (49)	61 (47)	179 (50)	61 (40)	
Missing	10 (2)	10 (2)	4 (3)	6 (2)	0	
Working preinjury *(no. [%])*						0.506
Yes	499 (78)	374 (77)	106 (81)	268 (75)	125 (83)	
No	133 (21)	107 (22)	21 (16)	86 (24)	26 (17)	
Missing	7 (1)	7 (1)	4 (3)	3 (1)	0	
Active-duty military *(no. [%])*	11 (2%)	7 (1%)	3 (2%)	4 (1%)	4 (3%)	0.316
Health insurance *(no. [%])*						0.087
Medicaid	75 (12)	63 (13)	15 (11)	48 (13)	12 (8)	
Other insurance‡	429 (67)	318 (65)	90 (69)	228 (64)	111 (74)	
None	134 (21)	107 (22)	26 (20)	81 (23)	27 (18)	
Missing	1 (<1)	0	0	0	1 (1)	
BMI† *(kg/m^2)*	29.9 (7.5)	30.2 (8)	30.2 (8.4)	30.2 (7.8)	29 (5.7)	0.082
Self-reported health *(no. [%])*						0.278
Excellent	186 (29)	141 (29)	40 (31)	101 (28)	45 (30)	
Very good	219 (34)	157 (32)	38 (29)	119 (33)	62 (41)	
Good	158 (25)	129 (26)	37 (28)	92 (26)	29 (19)	
Fair/poor	67 (10)	52 (11)	11 (8)	41 (11)	15 (10)	
Missing	9 (1)	9 (2)	5 (4)	4 (1)	0	
Tobacco use *(no. [%])*						0.085
Never/former smoker	371 (58)	293 (60)	71 (54)	222 (62)	78 (52)	
Current smoker	259 (41)	186 (38)	56 (43)	130 (36)	73 (48)	
Missing	9 (1)	9 (2)	4 (3)	5 (1)	0	
Major comorbidity§ *(no. [%])*						0.922
None	362 (57)	278 (57)	82 (63)	196 (55)	84 (56)	
1	157 (25)	120 (25)	26 (20)	94 (26)	37 (25)	
≥2	120 (19)	90 (18)	23 (18)	67 (19)	30 (20)	
Preinjury participation in vigorous activity# *(no. [%])*	189 (30)	141 (29)	34 (26)	107 (30)	48 (32)	0.540
Injury Severity Score (ISS)						0.022
≤17	559 (87)	424 (87)	114 (87)	310 (87)	135 (89)	
>17	68 (11)	60 (12)	16 (12)	44 (12)	8 (5)	
Missing	12 (2)	4 (1)	1 (<1)	3 (1)	8 (5)	

continued

TABLE I (*continued*)

		Limb Salvage				
	Overall (N = 639)	All (N = 488)	No Flap, Severe Articular Fracture, or Severe Bone Loss (N = 131)	Flap, Severe Articular Fracture, and/or Severe Bone Loss (N = 357)	Amputation within 3 Mo of Injury (N = 151)	P Value*
Contralateral limb injury *(no. [%])*						0.467
Yes	148 (23)	111 (23)	25 (19)	86 (24)	37 (25)	
No	479 (75)	373 (76)	105 (80)	268 (75)	106 (70)	
Missing	12 (2)	4 (1)	1 (<1)	3 (1)	8 (5)	
Ipsilateral limb injury (above zone of injury) *(no. [%])*						0.241
Yes	89 (14)	73 (15)	16 (12)	57 (16)	16 (11)	
No	538 (84)	411 (84)	114 (87)	297 (83)	127 (84)	
Missing	12 (2)	4 (1)	1 (<1)	3 (1)	8 (5)	

*P values for the comparison of all salvages with amputations. †The values are given as the mean and standard deviation. ‡Other insurance included private, Medicare, Tricare, or any other form of public insurance. §Major comorbidities included diabetes, cardiac disease, vascular disease, pulmonary disease, or psychiatric conditions. #As determined with the Paffenbarger Physical Activity Questionnaire (PPAQ). Vigorous activity was defined as reporting at least 1 leisure or recreational activity associated with a metabolic equivalent score (MET) of ≥6.

The injuries among the patients who underwent early amputation in the OUTLET study were mainly foot crush and blast injuries (53%) and were more severe with respect to the domains of the AO/OTA Open Fracture Classification than the injuries that were treated with limb salvage.

Outcomes

Outcomes were assessed at 18 months after injury. The primary outcome measure was the Short Musculoskeletal Function Assessment (SMFA)[11]. Scores were determined for the dysfunction index and domains of mobility, daily activities, and emotional function. Physical performance was assessed using the Four Square Step Test[12,13], Illinois Agility Test[14,15], 5× Sit to Stand Test[16,17], Timed Stair Ascent[18], and 40-m Shuttle Run[19]. Additional secondary outcomes included pain as measured by the Brief Pain Inventory (BPI)[20], participation in vigorous activities as measured by the Paffenbarger Physical Activity Questionnaire (PPAQ)[21], and return to work (by those working prior to injury). In addition to these outcomes, participant interviews provided hospital readmission data.

The Orthotic and Prosthetics Users' Survey (OPUS)[22] was used to characterize patients' satisfaction with their device after amputation.

Statistical Analysis

The main goal of this study was to compare the outcomes for salvage-treated pfatients at 18 months with the outcomes that these patients would have experienced had they undergone early amputation. For this causal analysis (see Appendix), we assumed that, after adjusting for baseline patient characteristics (i.e., age, sex, race/ethnicity, education, preinjury work status, health insurance, BMI, self-reported health status, tobacco use, and presence of comorbidities) and non-study-injury characteristics (i.e., contralateral injury, injuries to other body systems as measured by the ISS, and ipsilateral injury above the transtibial amputation level zone), the decision to amputate was independent of the potential outcome of the amputation; study-injury characteristics below the level of amputation were assumed to not impact this potential outcome because the injury was removed with the amputation. These assumptions imply that the distribution of the potential outcomes of amputation for salvage-treated patients with baseline covariates x (excluding study-injury characteristics) is equal to the distribution of outcomes for amputees with the same covariates x.

For each outcome, the estimation procedure involved (1) simulating the outcomes that salvage-treated patients would have had if they had undergone amputation and (2) comparing the distribution of the observed outcomes of patients treated with salvage with the distribution of their simulated amputation outcomes[23,24]. Conceptually, the simulation of the amputation outcome for a salvage-treated patient with covariates x involves 2 steps. First, the percentile (p) of the salvage-treated patient's outcome is calculated based on the distribution of salvage outcomes among salvage-treated patients who share covariates x. Second, the salvage-treated patient's potential outcome had an amputation been performed is simulated by calculating the pth quantile of the distribution of the outcomes for amputees who share covariates x. To illustrate: if a salvage-treated patient (Case 1) has an SMFA score of 38, corresponding to the 44th percentile in the distribution of SMFA scores among salvage-treated patients with the same covariates as Case 1, then the outcome of amputation is simulated as the 44th quantile of the distribution of SMFA outcomes among amputees with the same covariates as Case 1.

TABLE II Principal Injury Characteristics of OUTLET Study Participants*

		Limb Salvage				
	Overall (N = 581)	All (N = 488)	No Flap, Severe Articular Fracture†, or Severe Bone Loss (N = 131)	Flap, Severe Articular Fracture†, and/or Severe Bone Loss (N = 357)	Amputation (N = 93)	P Value‡
Principal study injury *(no. [%])*						<0.001
Type-III pilon/IIIB or C ankle	221 (38)	196 (40)	1 (1)	195 (55)	25 (27)	
Type-III talar/calcaneal	141 (24)	126 (26)	27 (21)	99 (28)	15 (16)	
Other foot injury	215 (37)	166 (34)	103 (79)	63 (18)	49 (53)	
Traumatic amputation	4 (1)	0	0	0	4 (4)	
Gustilo type *(no. [%])*						<0.001
Open/closed crush/blast	87 (15)	65 (13)	46 (35)	19 (5)	22 (24)	
IIIA	296 (51)	282 (58)	65 (50)	217 (61)	14 (15)	
IIIB	135 (23)	100 (20)	0	100 (28)	35 (38)	
IIIC	16 (3)	0	0	0	16 (17)	
Closed	43 (7)	41 (8)	N = 99	21 (6)	2 (2)	
Missing (traumatic amputation)	4 (1)	0	0	0	4 (4)	
Heel-pad degloving *(no. [%])*	105 (18)	54 (11)	27 (21)	27 (8)	51 (55)	<0.001
Open OTA/OA classification (only for open injuries)	N = 519	N = 434		N = 335	N = 85	
Contamination *(no. [%])*						<0.001
None/minimal	134 (26)	123 (28)	27 (27)	96 (29)	11 (13)	
Surface	244 (47)	211 (49)	46 (46)	165 (49)	33 (38)	
Imbedded	139 (27)	98 (23)	24 (24)	74 (22)	41 (48)	
Missing	2 (<1)	2 (<1)	2 (1)	0	0	
Skin damage *(no. [%])*						<0.001
Can be approximated	291 (56)	269 (62)	71 (72)	198 (59)	22 (26)	
Cannot be approximated	106 (20)	84 (19)	13 (13)	71 (21)	22 (26)	
Degloving	121 (23)	80 (18)	14 (14)	66 (20)	41 (48)	
Missing	1 (<1)	1 (<1)	1 (1)	0		
Muscle damage *(no. [%])*						<0.001
None/minimal	208 (40)	198 (46)	52 (53)	146 (44)	10 (12)	
Damaged but functional	211 (41)	189 (44)	39 (39)	150 (45)	22 (26)	
Damaged and not functional	99 (19)	46 (11)	7 (7)	39 (12)	53 (62)	
Missing	1 (<1)	1 (<1)	1 (1)			
Bone loss *(no. [%])*						<0.001
None	178 (34)	156 (36)	68 (69)	88 (26)	22 (26)	
Some contact	240 (46)	214 (49)	26 (26)	188 (56)	26 (31)	
≤2 cm	36 (7)	27 (6)	4 (4)	23 (7)	9 (11)	
>2 cm	64 (12)	36 (8)	0	36 (11)	28 (33)	
Missing	1 (<1)	1 (<1)	1 (1)	0	0	
Arterial damage *(no. [%])*						<0.001
No injury	378 (73)	336 (77)	79 (80)	257 (77)	42 (49)	
Without ischemia	102 (20)	85 (20)	17 (17)	68 (20)	17 (20)	
With ischemia	38 (7)	12 (3)	2 (2)	10 (3)	26 (31)	
Missing	1 (<1)	1 (<1)	1 (1)	0	0	

*Injury characteristics were not collected for patients in the TAOS study. †Articular injuries were defined as OTA 43B or C, 81B or C, or 82B or C fractures. ‡P values for the comparison of all salvages with amputations.

Overall causal effect estimates (difference in means for SMFA, difference in medians for performance, and odds ratios [ORs] for vigorous activity and return to work) are presented together with estimates by principal injury (pilon/ankle, talar/calcaneal, or other foot injury) and whether the injury pattern was complex (as defined above). In the analysis of performance outcomes, patients unable to perform a given test due to physical limitations were assigned the worst rank.

Bootstrapping was used to characterize uncertainty of the causal effect estimates through the construction of 90% and 95% confidence intervals (CIs). Multiple imputation was used to handle missing baseline covariates. All analyses were conducted using R software[25].

In the absence of a well-defined minimal clinically important difference (MCID), the equivalence margin for the causal effects for SMFA was prespecified as a difference of ±6 points. Equivalence was tested by evaluating whether 90% CIs for the causal effects fell within the equivalence margins. Superiority (inferiority) was tested by evaluating whether the lower (upper) 95% confidence limit was greater (less) than zero (for the SMFA, pain, and performance outcomes) or 1 (for the vigorous activities and return-to-work outcomes)[26]. No adjustments for multiple testing were employed.

Results

The final study visit occurred 19 months following injury, on average. Overall, 79.2% of the participants were followed and completed an SMFA and a smaller proportion (68.7%) returned to complete the physical performance tests (Fig. 1). Salvage-treated patients with outcome data tended to be older (mean age, 38 versus 35 years) than those without outcome data, more were female (40% versus 23%), more were college educated (53% versus 38%), and more had an ipsilateral injury (17% versus 8%); there were no appreciable differences in other factors, including those accounted for in our analysis as well as characteristics of the injury below the knee. Amputees with outcome data tended to be comparable with those without outcome data with respect to the factors accounted for in our analysis; we assume that characteristics of the injury below the knee are unrelated to amputation outcomes and thus differences with respect to those factors are irrelevant (see Appendix Tables 1a through 2b).

The mean SMFA scores were poor for both the amputation and the limb-salvage-treated patients, with scores across all domains (except arm and hand function) well above population norms (see Appendix Table 3). With the exception of dysfunction, the equivalence hypotheses for SMFA are not supported by our analysis (Table III). It was estimated that the SMFA mobility score for the salvage-treated patients would have been improved by 7 points (95% CI = 2.0 to 10.7) had they undergone amputation. The evidence of improvement in SMFA mobility scores was consistent across all subgroups. The estimated causal differences in SMFA scores (for all domains) favored amputation and were highest for the subgroup of pilon/ankle fractures and for previously defined complex injuries.

The percentage of salvage-treated patients unable to complete performance testing due to physical impairment ranged from 16% to 25% compared with 14% to 20% of the amputees (see Appendix Table 4). Physical performance assessments indicated high levels of impairment, but improvements in outcome had amputation been performed were not as large as those for self-reported function on the SMFA. Although coupled with high levels of uncertainty, the largest estimated effects of amputation were observed for the Illinois Agility Test and the 40-m Shuttle Run, especially among those with pilon/ankle fractures or complex injuries (Table III).

While it was estimated that the salvage-treated patients would have had some improvement in pain-severity and interference scores had they undergone amputation, these differences were small (0.57 for severity and 0.62 for interference) and not clinically meaningful (Table III).

The odds of salvage-treated patients performing vigorous activities had amputation been performed were equivalent to the observed odds in the salvage group, overall and by subgroup. The estimated overall odds of salvage-treated patients returning to work would have been 25% lower had they undergone amputation. However, the results are consistent with the equivalence hypothesis (Table III).

Seventy percent of the salvage-treated patients reported at least 1 hospital readmission, compared with 50% of the amputees. Twenty-three percent of salvage-treated patients and 11% of the amputees reported ≥3 admissions.

Of 114 amputees with final outcome data, 107 (94%) had a prosthesis. Although the overall OPUS satisfaction scores were acceptable (average, 61.7 of a possible 100 points), only 47% agreed with the statement that wearing the prosthesis was pain-free and 63% agreed that the prosthesis was comfortable to wear throughout the day. SMFA mobility scores were highly correlated with device satisfaction (mean scores of 43.4, 25.8, and 13.7 for low, medium, and high satisfaction, respectively).

Discussion

This analysis sought to answer the question: "What would have been the outcomes for patients treated with limb salvage had they undergone amputation?" Our results suggest that patients with Type-III pilon, Type-IIIB or C ankle, or Type-III mid/hindfoot injuries would have had, at 18 months after injury, better self-reported mobility (measured with the SMFA) but equivalent participation in vigorous activities and return to work had they received an amputation. The differences observed for pain severity and interference were not clinically relevant[27], and great uncertainty was associated with assessment of physical performance. However, except for return to work, differences consistently favored amputation. Differences were most notable for patients with a pilon/ankle fracture and those with the most complex injuries (i.e., requiring tissue flaps, severe articular fractures, and/or substantial bone loss).

The results are consistent with recent studies of severe combat-related ankle and calcaneal fractures. A study of 102 U.S. military personnel with an open calcaneal fracture showed that those who underwent amputation had higher activity levels than those who underwent limb salvage[3]. A British study of 77 patients who had sustained a hindfoot injury in combat showed that amputation resulted in better function than reconstruction[5]. Our results are also consistent with a subgroup

TABLE III Predicted Improvement, According to Principal Study Injury and Injury Severity, for Salvage-Treated Patients Had They Undergone Amputation ➤

	Principal Study Injury					
	All Limb Salvages (N = 390)		Type-III Pilon/IIIB or C Ankle (N = 161)		Type-III Talar/Calcaneal (N = 97)	
	Observed After Salvage	Improvement with Amputation	Observed After Salvage	Improvement with Amputation	Observed After Salvage	Improvement with Amputation
SMFA*† (pop. norm)						
Dysfunction (12.5)	28.80	3.38 (0.15, 5.90) (−0.40, 6.39)	32.31	3.88 (0.66, 6.87) (0.13, 7.38)	27.27	3.85 (0.40, 7.16) (−0.05, 7.79)
Mobility (13.6)	38.62	6.99 (2.78, 10.14) (2.02, 10.68)	42.51	7.96 (3.26, 11.47) (2.56, 11.99)	38.07	7.30 (2.85, 11.18) (2.07, 11.88)
Daily activities (11.8)	33.91	4.03 (−0.12, 7.58) (−0.67, 8.22)	39.19	5.65 (1.47, 9.90) (0.81, 10.54)	31.52	3.35 (−0.58, 7.61) (−1.38, 8.70)
Emotional (20.5)	37.20	3.49 (−0.91, 7.08) (−1.49, 7.74)	40.17	3.94 (−0.31, 7.64) (−1.03, 8.25)	35.36	2.84 (−1.11, 7.47) (−2.12, 8.42)
Pain*						
Severity	3.58	0.57 (0.15, 0.98) (0.08, 1.05)	3.89	0.64 (0.19, 1.03) (0.12, 1.11)	3.26	0.53 (0.13, 1.01) (0.06, 1.10)
Interference	3.83	0.62 (0.13, 1.12) (0.02, 1.21)	4.31	0.67 (0.14, 1.22) (0.08, 1.32)	3.29	0.63 (0.12, 1.23) (0.00, 1.29)
Activity and return to work‡ *(%)*						
Vigorous activity	16.7	1.05 (0.57 1.67) (0.52, 1.75)	10.3	1.09 (0.58, 2.08) (0.52, 2.33)	18.8	1.05 (0.57, 1.67) (0.52, 1.82)
Return to work	53.4	0.75 (0.51, 1.15) (0.47, 1.23)	47.5	0.78 (0.54, 1.18) (0.51, 1.28)	65.8	0.71 (0.45, 1.11) (0.41, 1.19)
Performance tests§						
Four Square Step Test *(s)*	12.5	0.0 (−3.0, 1.0) (−3.5, 1.5)	14.0	0.5 (−3.0, 2.0) (−4.0, 3.0)	11.8	−0.3 (−3.0, 1.0) (−3.5, 1.3)
Illinois Agility Test# *(s)*	58.5	11	65	14	59.0	13
5× Sit to Stand Test *(s)*	14.0	1.5 (−1.5, 3.0) (−2.5, 3.0)	16.5	3.5 (−0.5, 4.5) (−1.5, 5.0)	13.3	1.25 (−2.0, 2.8) (−3.0, 3.0)
Timed Stair Ascent *(s)*	8.5	0.0 (−5.0, 0.5) (−5.5, 1.0)	11.0	1.5 (−5.5, 4.0) (−23.0, 5.0)	8.0	−0.5 (−5.0, 0.5) (−5.5, 1.0)
Shuttle Run *(m/s)*	1.09	0.17 (−0.11, 0.38) (−0.15, 0.43)	0.9	0.21 (−0.01, 0.47) (−0.11, 0.64)	1.2	0.11 (−0.18, 0.42) (−0.25, 0.55)

*The values are given as means. Improvement with amputation is represented as the difference in the means, with the 90% CI in parentheses followed by the 95% CI in parentheses; positive differences favor amputation. †The observed SMFA arm and hand function scores are included in Appendix Table 3. ‡The values are given as ORs. Improvement with amputation is represented as ORs with the 90% CI in parentheses followed by the 95% CI in parentheses; ORs of >1 favor amputation. §The values are given as medians. Improvement with amputation is represented as the difference in the medians with the 90% CI in parentheses followed by the 95% CI in parentheses; positive differences favor amputation. #It was not possible to calculate CIs because medians with either salvage or amputation indicated "could not perform" for more than 5% of the bootstrapped samples. The percentages of bootstrapped samples favoring amputation were: overall (81.6%); open pilon/ankle fracture (82.8%); open talar/calcaneal fracture (78.8%); other foot injury (75.9%); no flap, articular fracture, or severe bone loss (70.8%); and flap, articular fracture, and/or severe bone loss (84.2%).

analysis of 174 LEAP participants with similar injuries that showed that those who underwent limb reconstruction requiring a flap or ankle arthrodesis performed worse than those treated with transtibial amputation[2].

These studies and others demonstrated that plantar wounds, large wounds, comminuted fractures, and coexisting calcaneal, pilon, and hindfoot fractures were associated with the poorest outcomes from limb salvage[3,5,28,29]. In the current study, the estimated improvement in the SMFA mobility score derived with amputation was greatest for patients with a pilon/ankle fracture and those with complex injuries. However, the causal differences reflect only small-to-medium size effects.

Importantly, regardless of treatment, the SMFA outcomes overall were poor at 18 months. The SMFA scores across all domains (except arm and hand function) were well above age-appropriate norms, replicating results of other studies[1,3-5].

TABLE III (*continued*)

Severity					
Other Foot Injuries (N = 132)		No Flap, Severe Articular Fracture, or Severe Bone Loss (N = 101)		Flap, Severe Articular Fracture, and/or Severe Bone Loss (N = 289)	
Observed After Salvage	Improvement with Amputation	Observed After Salvage	Improvement with Amputation	Observed After Salvage	Improvement with Amputation
25.64	2.41 (−1.37, 4.52) (−2.01, 5.04)	25.04	2.64 (−1.67, 4.54) (−2.33, 5.00)	30.11	3.63 (0.50, 6.53) (0.07, 7.17)
34.27	5.58 (1.59, 8.67) (0.83, 9.18)	33.48	5.43 (0.80, 8.20) (0.02, 8.84)	40.41	7.53 (3.31, 11.12) (2.54, 11.52)
29.23	2.55 (−2.05, 5.81) (−2.91, 6.30)	28.72	2.64 (−2.43, 6.02) (−3.48, 6.79)	35.72	4.52 (0.51, 8.40) (−0.03, 8.99)
34.93	3.42 (−1.44, 6.78) (−2.54, 7.33)	34.13	2.17 (−2.08, 6.66) (−2.98, 7.28)	38.27	3.95 (−0.49, 7.45) (−1.21, 8.05)
3.44	0.53 (0.08, 0.95) (0.01, 1.02)	3.38	0.54 (0.05, 0.94) (−0.03, 1.02)	3.65	0.59 (0.18, 1.01) (0.11, 1.10)
3.65	0.56 (0.04, 1.04) (−0.05, 1.15)	3.16	0.55 (0.00, 1.00) (−0.09, 1.09)	4.07	0.65 (0.16, 1.18) (0.06, 1.28)
22.9	1.03 (0.55, 1.45) (0.50, 1.52)	18.0	1.04 (0.57, 1.64) (0.50, 1.75)	16.3	1.05 (0.57, 1.67) (0.52, 1.79)
54.1	0.72 (0.48, 1.15) (0.45, 1.23)	60.2	0.71 (0.45, 1.15) (0.43, 1.23)	52.3	0.75 (0.52, 1.15) (0.49, 1.23)
11.0	−1.0 (−3.5, 0.5) (−4.0, 1.0)	10.5	−1.5 (−3.5, 0.5) (−4.8, 1.0)	12.5	−0.5 (−2.5, 1.0) (−3.5, 1.5)
52.5	9	53.3	9.3	61.5	13.5
13.0	1.5 (−2.5, 2.0) (−3.5, 2.5)	13.0	1.0 (−2.3, 3.0) (−3.5, 3.3)	14.5	2.0 (−1.5, 3.0) (−2.5, 3.5)
7.5	−0.5 (−3.5, 0.5) (−5.0, 0.5)	7.3	−0.3 (−4.0, 0.5) (−5.0, 1.0)	9.0	0.0 (−5.5, 1.0) (−6.0, 1.5)
1.26	0.06 (−0.21, 0.26) (−0.26, 0.36)	1.09	0.17 (−0.09, 0.38) (−0.28, 0.49)	1.05	0.19 (−0.06, 0.37) (−0.12, 0.41)

Physical performance was also poor. The median observed time on the Timed Stair Ascent was comparable with that shown by older adults (8.9 seconds)[30], whereas the median observed time on the Four Square Step Test was slower than that shown by older adults (8.7 seconds) but similar to that of individuals with vestibular disorders (13.6 seconds)[13,31]. The times for the 5× Sit to Stand Test were slower than those of healthy older adults (9.9 seconds) and older adults with knee osteoarthritis (13.3 seconds)[13,30].

The patients' satisfaction with their prosthetic device after amputation was variable, but there was a strong negative correlation between the SMFA mobility and OPUS scores, suggesting that improving the quality and fit of prostheses could yield larger effects favoring amputation. At the same time, mounting evidence suggests that outcomes following limb salvage may be improved with use of custom, energy-storing carbon-fiber ankle-foot orthoses (AFOs)[32-35]. Only 38 patients with limb salvage (10%) reported use of any orthotic device and, of those, only 4 were in the military, in which the dynamic AFO was available. If dynamic AFOs had been more widely used, the differences between the results of limb salvage and amputation found in this study could be smaller. Overall, improving the fit and comfort of prosthetic devices while simultaneously making dynamic AFOs available for those undergoing limb salvage in both the military and the civilian populations could improve outcomes and result in more comparable results.

Strengths of this study include its multicenter approach, the adjudication of eligibility criteria, and the evaluation of multiple outcomes at 18 months postinjury. We also applied a rigorous counterfactual methodology to understand how salvage-treated patients would have recovered had their injured limb been amputated.

The study also has weaknesses. There was a less-than-optimal participant follow-up (79%), a frequent challenge in prospective trauma research. We cannot rule out that bias may have been introduced due to unmeasured factors (e.g., pre-injury self-efficacy) that differed between those with and those without outcome data. As with any causal analysis of observational data, our inferences rely on strong modeling assumptions, which, if violated, can yield biased results. Fundamental to the causal analysis is the conceptualization that counterfactual outcomes of amputation can be defined for each salvage. However, many salvage-treated patients in the study sample were not considered candidates for amputation. Our ability to identify a small-to-moderate improvement in SMFA score with amputation is also tempered by the recognition that there are no validated data to define an MCID for the SMFA score. Inclusion of amputees from the TAOS may have also introduced bias. However, we assumed, for the patients in both cohorts, that once amputation is performed, the characteristics of the injury that led to the amputation become irrelevant. While we believe that this is a reasonable assumption, it may fail to hold because the TAOS patients may have had some injury characteristics that were not removed by amputation. Therefore, we expect their outcomes to be worse than those for the amputees in the OUTLET study. Because we included the amputation-treated patients from the TAOS, our inferences are likely underestimates of the improvement that would have been obtained had the salvage-treated patients undergone amputation.

While this study does not provide definitive evidence for use in treatment decisions for trauma patients, its conclusions suggest that, for the most complex terminal injuries of the lower limb, amputation should be considered a treatment option rather than a last resort. If limb salvage is judged to be a possibility, the surgeon and patient must personalize the treatment plan, incorporating all relevant cofactors that influence the patient's outcome with a guiding principle that reconstruction should provide an outcome at least as good as a best-level amputation. Patient preferences may be an important factor driving treatment decisions and challenge an algorithmic approach to treatment selection. As highlighted in the recent American Academy of Orthopaedic Surgeons Clinical Practice Guideline, studies are needed to examine the dynamics of treatment decision-making to inform the development of tools to help both surgeons and patients navigate this shared decision-making process[36]. To this end, researchers need to investigate the long-term impact of these treatments on health and function as amputation-treated patients may become more adept with their prosthetic device and salvage-treated patients might experience increased impairment related to the development of posttraumatic arthritis.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G489). ■

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