Association of Specific Lower Extremity Injuries With Delayed Amputation

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ABSTRACT Introduction: Despite medical interventions to preserve viability and functionality of injured limb(s) among combat-injured service members, delayed amputations may occur. The goal of this study was to determine whether specific lower extremity (LE) injuries were associated with delayed amputations. Methods: The Expeditionary Medical Encounter Database was queried for combat-related LE injuries between 2003 and 2015. The Abbreviated Injury Scale (AIS) was used to categorize LE injuries by severity. Injury episodes with a maximum LE AIS of 1 or amputation on the day of injury were excluded. The final sample included 2,996 service members with at least one LE injury with an AIS ≥2. The frequencies of specific LE fractures and nerve and vessel injuries were determined. Logistic regression with paired independent variables was performed to examine the impact of multiple LE injuries on the odds of delayed amputation. Results: Delayed LE amputation was identified in 308 (10.3%) service members in the sample. The delayed and no amputation groups did not differ in age and service branch. The majority of injury episodes were blast-related and with an Injury Severity Score ≥9. The most frequent fractures were tibia (34.4%) and fibula (29.3%), but the highest rates of delayed amputation were in those with navicular (36.2%), talus (30.0%), or calcaneus (28.1%) fractures. Odds of amputation were highest among service members with the calcaneus fracture and LE nerve injury (odds ratio [OR]: 41.74; 95% confidence interval [CI], 14.70, 118.55; $p < 0.001$), calcaneal fracture and LE vessel injury (OR: 17.99; 95% CI: 10.53, 30.74; $p < 0.001$), and calcaneus and tibia fractures (OR: 15.12; 95% CI: 9.54, 23.96; $p < 0.001$) combinations. Conclusions: Odds of delayed amputation increased substantially with specific injury combinations. These findings may guide clinical decision-making in the acute care period.

INTRODUCTION

Extremity injuries comprised the largest proportion of injuries in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF), with published estimates ranging from 41% to 54% of all combat injuries.[1–4] Compared with civilians, severe extremity injuries in combat-deployed military personnel are more likely to result in amputations, in part because these injuries are often blast-related with higher injury severity and polytrauma.[5] Despite medical interventions to preserve the viability and functionality of injured limb(s), known as limb salvage procedures, delayed amputations and long-term impairments may occur. Functional limitations after limb salvage procedures in military personnel can result in medical retirement,[6,7] poor clinical outcome,[8] and poor self-reported health status.[9] Reported rates of delayed amputation in those with combat-related extremity injuries ranged from 11% to 77% depending on location and type of fracture (open vs. closed), presence of other injuries (e.g., vascular, nerve, or soft tissue damage), and subsequent complications (e.g., infection or flap failure).[10–15]

Previous research has examined specific extremity injuries amenable to limb salvage procedures and subsequent prevention of later amputation.[7,10,13,15,16] Fractures of the tibia and/or hindfoot were the primary injury of interest in these studies. Sheean *et al* found that open tibia fractures accompanied by vascular injuries were more likely to require immediate amputation, whereas nerve injuries were more likely associated with delayed amputations. Huh *et al* examined a cohort of patients with open tibia fractures and vascular injuries resulting in limb salvage, amputation within the first 12 weeks, or amputation greater than 12 weeks postinjury. They found that those who underwent amputation within 12 weeks of injury were more likely to require a vascular repair, and those with amputations after 12 weeks postinjury had at least one complication (e.g., infection) at the time of amputation.

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Outcomes of blast-related foot and ankle injuries have also been investigated. In a small sample of service members with lower limb injuries, 26 of the 89 injured limbs were amputated. Of these, 13 amputations occurred during acute care, and 6 were amputated an average of 18.5 months after injury because of chronic pain.[10] Factors independently associated with later or delayed amputation were hindfoot injury, vascular injury, and open fracture. Ramasamy *et al* found a higher rate of amputation in open versus closed calcaneal fractures (69.6% vs. 11.8%, respectively). In a sample of open calcaneal fractures, Dickens *et al* found that failed limb salvage was associated with concurrent forefoot fracture, talus fracture, large wound size, and wound infection.

Additional studies examined specific injury severity scales for their ability to predict amputation.[5,8,16,17] The Mangled Extremity Severity Score (MESS) combines an individual's age, systolic blood pressure, vascular status, and soft tissue injury in patients with open tibia fractures. The MESS has demonstrated poor sensitivity (0.35–0.44) but good specificity (0.88 to above 0.90) in predicting amputation.[5,16] In contrast, the Foot and Ankle Severity Scale (FASS) was developed by a panel of expert clinicians from the American Orthopaedic Foot and Ankle Society to categorize lower leg injuries by severity on a scale from 1 to 6.[17] A FASS score ≥4 (severe injury) demonstrated excellent sensitivity (100%) in predicting amputation, but poor specificity (42.9%).[8]

When defining delayed amputation, most published work uses the 90-day mark as a delineation between early and delayed amputation,[18–21] but this is not consistent across all studies.[7,11] In addition, there seems to be no data-driven evidence supporting the selection of these categories. The current work aims to address this deficit in the literature.

Early injury factors that may predict the risk of amputation in a seriously injured extremity are also not clearly delineated. To the best of our knowledge, there is no comprehensive, systematic examination of both location and type of lower extremity (LE) fractures in combination with nerve and vessel injuries in combat-injured military personnel. The purpose of this study was to examine the association of specific LE injuries with delayed amputations, as well as the timing of the amputation. This study was approved by the Naval Health Research Center (NHRC) Institutional Review Board.

METHODS

The study sample was identified from the Expeditionary Medical Encounter Database (EMED), which is maintained by NHRC in San Diego, CA, USA.[22] The EMED contains information completed by military medical providers at forward-deployed treatment facilities in the combat zone nearest to the point of injury. These records are linked with inpatient and outpatient medical record information and tactical, personnel, operational, and deployment-related data obtained from other US Department of Defense databases. The injury medical records are reviewed by expert clinical staff and assigned clinical diagnosis codes (*International Classification of Diseases, 9th Revision, Clinical Modification*) and standardized injury severity measures (Abbreviated Injury Scale [AIS] and Injury Severity Score [ISS]).[23]

Between January 2002 and September 2015, there were 9,570 service members with a combat-related LE injury documented in the EMED. Since delayed amputation (defined as any amputation occurring more than 24 hours after injury) was the target outcome, service members with an amputation within the first 24 hours after injury were excluded (n = 1,031). During preliminary analysis, it was determined that a maximum LE AIS of 1 (minor injury) was not associated with delayed amputation. Those service members with a maximum LE AIS of 1 were excluded (n = 5,543), resulting in 2,996 service members for analysis. Service member demographics (i.e., age and service branch) and injury circumstances (i.e., mission, injury mechanism, position, and ISS) were ascertained for each injury episode. ISS was analyzed as a continuous variable and categorized into two severity levels (moderate [ISS 4–8] and serious to severe [ISS ≥ 9]).[24,25] Specific LE fractures (i.e., femur, tibia, fibula, calcaneus, talus, and navicular) and LE nerve and vessel injuries were identified by AIS code. The presence of a delayed amputation and the number of days from injury to delayed amputation was determined from the EMED. Service members were categorized into early (<90 days) or late delayed amputation (>90 days).

Statistical Analysis

Means and standard deviations were reported for age and ISS, and frequency and percentages were reported for mission (OEF or OIF), injury mechanism (blast or non-blast), position (mounted or dismounted), and ISS category (ISS 4–8 or ≥9). Comparisons were made between the delayed amputation and no amputation groups using χ^2 tests for categorical variables and t tests for continuous variables.

The frequency and percentage of LE fractures, nerve injuries, and vessel injuries were calculated. Comparisons were made between no amputation and delayed amputation categories for each LE injury, including the fracture types. Logistic regression models were built using the LE injuries as unique independent variables with delayed amputation versus no amputation as the outcome. Multinomial logistic regression was utilized with early and late delayed amputation categories verses no amputation as the outcome. Continuous ISS, mission, injury mechanism, and position were used as covariates based on the descriptive analysis results. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported, and p-values were adjusted for multiple comparisons within each type of regression model. A p-value of <0.004 was considered significant for the single injury logistic regression models and a p-value of <0.002

was considered significant for the multinomial logistic regression models.

The Hosmer–Lemeshow goodness-of-fit test did not show a good fit for regression models containing more than one injury as an independent variable, most likely because of co-occurring injuries. Additional regression modeling was conducted using a combination of the LE injuries to control for the influence of co-occurring injuries on the odds of amputation. Of the original fracture variables, only open fractures (no open fracture as reference category) were assessed because of the strength of the association in the initial analyses. The combinations analyzed were: (1) open tibia and open fibula fractures; (2) open calcaneus and open tibia fractures; (3) open calcaneus and open talus fractures; (4) open calcaneus and open navicular fractures, vessel, and nerve injuries; (5) open tibia fracture and vessel injury; (6) open tibia fracture and nerve injury; (7) open calcaneus fracture and vessel injury; and (8) open calcaneus fracture and nerve injury. Each of these combinations was analyzed at four levels: no injury (reference category), first injury, second injury, and both injuries.

RESULTS

The study population included 2,996 service members with a combat-related LE injury with a maximum LE AIS ≥2. Demographics and injury characteristics by amputation group are displayed in Table I. There were no significant differences between the groups based on age or service branch. The delayed amputation group had a significantly higher mean ISS (14.9 vs. 11.7; $p < 0.001$). Although blasts were the most common injury mechanism overall, there was a significantly higher proportion of blast injuries in the delayed amputation group compared with the no amputation group. Physical position (mounted or dismounted) at the time of injury was reported for 2,060 (68.7%) of service members. Of these, a larger proportion in the delayed amputation group were in a mounted position rather than dismounted when injured (61.3% vs. 38.7%, respectively). In comparison, service members in the no amputation group were equally distributed in the mounted and dismounted positions (49.5% vs. 50.5%, respectively). There was a slight significant difference between the amputation groups on mission, with more delayed amputations resulting from the OIF conflict compared with OEF (54.2% vs. 44.8%, respectively; $p = 0.01$).

Lower Extremity Injury and Delayed Amputation Rates

The overall rate of delayed amputations was 10.3%, with 14.9% in service members with at least one fracture. Tibia fractures were the most common (34.4%) followed by fibula fractures (29.3%). Overall, those with open calcaneus, open talus, or open navicular fractures resulted in the highest rates of delayed amputation (41.5%, 45.4%, and 42.5%, respectively) (see Fig. 1). The lowest rate of delayed amputation was in service members with open femur fractures (15.0%). Vessel injuries were more common than nerve injuries overall (14.8% vs. 11.4%, respectively) and among those with delayed amputation (26.1% vs. 18.1%, respectively).

Odds of Delayed Amputation

The odds of delayed amputation in service members with any fracture were 10.10 (95% CI: 6.24, 16.37; $p < 0.001$). Multivariate logistic regression showed that all closed and open fractures (with the exception of closed tibia fractures), and nerve and vessel injuries, were significantly associated with delayed amputation, after controlling for continuous ISS, mission, position, and injury mechanism (Table II). The odds of delayed amputation were significantly higher in open than closed fractures at all sites except for the femur. Odds of delayed amputation were highest for open calcaneal (OR: 9.61; 95% CI: 7.00, 13.20; $p < 0.001$) and open talus fractures (OR: 9.50; 95% CI: 6.55, 13.79; $p < 0.001$).

The association of injury type and timing of amputation were examined using multinomial logistic regression with no amputation as the reference outcome and early (<90 days) and late delayed (>90 days) amputations as the outcomes of interest (Table II). Similar trends in the associations between injuries and delayed amputations were observed when the timing of amputation was categorized compared with uncategorized results. The majority of the ORs were higher in the early delayed amputation outcome compared with late delayed amputation outcome, but the odds of early delayed amputation were substantially greater than the odds of late delayed amputation for open calcaneus fractures (early delayed OR: 14.68; 95% CI: 9.67, 22.30, $p < 0.001$; late delayed OR: 6.61; 95% CI; 4.38, 9.98, $p < 0.001$) and open talus fractures (early delayed OR: 16.71; 95% CI: 10.55, 26.46; $p < 0.001$; late delayed OR: 5.41; 95% CI; 3.25, 9.01; $p < 0.001$).

Injury Combinations

Independent variables were paired to assess the association between the combined effect of specific open fractures and vessel and nerve injuries with delayed amputation. All injury combinations shown in Table III were significantly associated with delayed amputation. Open calcaneal fractures demonstrated the highest odds of delayed amputation when paired with other injuries, specifically open talus fracture (OR: 13.14; 95% CI: 8.52, 20.29; $p < 0.001$) and nerve injury (OR: 41.74; 95% CI: 14.70, 118.55; $p < 0.001$).

DISCUSSION

This study is one of the first to comprehensively examine whether service members with specific combat-related LE injuries and combinations of these injuries have higher odds

TABLE I. Demographic and Injury Characteristics by Lower Extremity Amputation Status

Characteristics	No Amputation (n = 2,688)	Delayed Amputation (n = 308)	p-Value
Age (year), mean (SD)	26.0 (5.8)	25.7 (5.6)	0.40
ISS, mean (SD)	11.7 (8.7)	14.9 (10.8)	<0.001
Mission, n (%)			0.01
OIF	1,251 (46.5)	167 (54.2)	
OEF	1,426 (53.0)	138 (44.8)	
Service branch, n (%)			0.64
Army	1,698 (63.2)	207 (67.2)	
Marine Corps	880 (32.7)	92 (29.9)	
Navy	78 (2.9)	7 (2.3)	
Air Force	30 (1.1)	2 (<1)	
Injury mechanism, n (%)			<0.001
Blast	1,897 (70.6)	259 (84.1)	
Non-blast	791 (29.4)	49 (15.9)	
Position, n (%)			0.01
Mounted	919 (34.2)	125 (40.6)	
Dismounted	937 (34.9)	79 (25.6)	
Unknown	832 (30.9)	104 (33.8)	
ISS, n (%)			<0.001
Moderate (4–8)	998 (37.1)	58 (18.8)	
Serious to severe (≥9)	1,690 (62.9)	250 (81.2)	
Femur fracture, n (%)	453 (16.8)	87 (28.2)	<0.001
Tibia fracture, n (%)	845 (31.4)	185 (60.1)	<0.001
Fibula fracture, n (%)	705 (26.2)	173 (56.2)	<0.001
Calcaneus fracture, n (%)	358 (13.3)	140 (45.4)	<0.001
Talus fracture, n (%)	231 (8.6)	99 (32.1)	<0.001
Navicular fracture, n (%)	97 (3.6)	55 (17.9)	<0.001
Vessel injury, n (%)	329 (12.2)	116 (37.7)	<0.001
Nerve injury, n (%)	280 (10.4)	62 (20.1)	<0.001

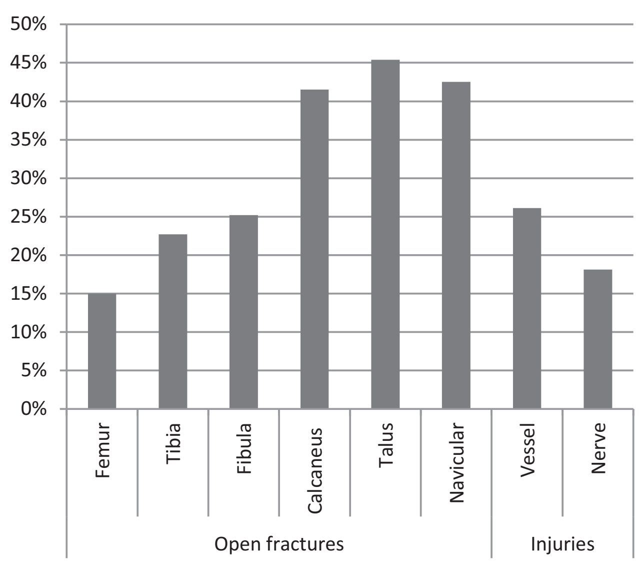

FIGURE 1. Percent of delayed amputation by injury type.

of delayed amputation. Fractures of the femur, tibia, fibula, calcaneus, talus, and navicular, as well as LE nerve and vessel injuries, were specifically examined because of the severity of these injuries and the known risk of viability of the injured limb.[7,10,13,15,16] The results of the present study provide new information and confirm previous observations regarding which traumatic injuries convey the greatest risk of amputation more than 24 hours after the point of injury.

The overall rate of delayed amputation in the study population was 10.3%, which is lower than rates reported in previous studies.[10–15] This difference is most likely because of the broader definition of LE injury for this study. When we examined rates by specific fracture type, findings were similar to previous research, which primarily used study samples with one injury type or location. Additionally, the present study included service members with at least moderate LE injuries (in terms of severity), whereas other studies focused on only severe injuries.[10–15] Although tibia fracture was the most common injury overall, a greater proportion of delayed amputations were associated with calcaneal, talus, and navicular fractures. Altogether, these results highlight the frequency of LE fractures and the resulting risk in delayed amputations below the knee.

Service members with open fractures of the hindfoot (calcaneus and talus) had more than nine times higher odds of delayed amputation compared with those without. Odds of delayed amputation were even greater when considering these injuries in combination with other injuries, specifically LE nerve injury. This finding is consistent with previous literature on calcaneus fractures[7,10,15] and could be explained by the complexities of these injuries. Even with optimal initial treatment, calcaneal fractures often result in a myriad of postinjury complications, such as osteoarthrosis, iatrogenic neuromas, soft tissue impingement, reflex sympathetic dystrophy, compartment syndrome, compromise of the peroneal tendon, and altered tibiotalar mechanics.[26]

The definition most frequently used for delayed amputation in the literature has been greater than 90 days, and it is the definition most consistently used in studies comparing functional outcomes of subjects with amputations versus limb reconstruction.[18–21] In studies examining prediction factors for amputation, the definition of delayed amputation is less clearly delineated.[7,11] This analysis focused on delayed amputations, defined as those occurring at least 24 hours after the point of injury and beyond. Delayed amputation was further delineated by defining early delayed (<90 days postinjury) and late delayed (>90 days postinjury) to further examine whether injuries may drive timing of amputation. For the majority of the injuries examined, the odds of early delayed amputation were higher than the odds of late delayed amputation. In service members with open calcaneus or talus fractures, the odds of early delayed amputation were more than double those of late delayed amputations. This difference in odds of amputation between early and late delayed amputation may be explained by the decreasing influence of acute injuries on amputation over time. The higher odds of early delayed amputation may also be due to a limb that was never viable, but the amputation occurred beyond 24 hours after injury because of extenuating

TABLE II. Percentage and Odds of Delayed Lower Extremity Amputation by Injury Type

Injury Type[a]	Delayed Amputation[c] (n = 308)			Early Delayed Amputation[c] (n = 134)			Late Delayed Amputation[c] (n = 174)		
	n (%)	OR (95% CI)	p-Value	n (%)	OR (95% CI)	p-Value	n (%)	OR (95% CI)	p-Value
Femur fracture									
Closed	26 (8.4)	1.81 (1.13, 2.90)	0.01	13 (9.7)	2.46 (1.29, 4.69)	0.006	13 (7.5)	1.42 (0.76, 2.66)	0.27
Open	61 (19.8)	1.80 (1.31, 2.48)	<0.001[b]	32 (23.9)	2.28 (1.47, 3.53)	<0.001[b]	29 (16.7)	1.47 (0.95, 2.27)	0.08
Tibia fracture									
Closed	35 (11.4)	1.38 (0.92, 2.06)	0.12	13 (9.7)	1.30 (0.69, 2.45)	0.41	22 (12.6)	1.42 (0.85, 2.35)	0.18
Open	150 (48.7)	3.86 (2.96–5.03)	<0.001[b]	69 (51.5)	4.17 (2.84, 6.11)	<0.001[b]	81 (46.5)	3.64 (2.59, 5.13)	<0.001[b]
Fibula fracture									
Closed	38 (12.3)	1.60 (1.08, 2.37)	0.02	17 (12.8)	1.82 (1.03, 3.23)	0.04	21 (12.1)	1.45 (0.87, 2.41)	0.15
Open	135 (43.8)	4.32 (3.30, 5.65)	<0.001[b]	60 (44.8)	4.56 (3.09, 6.72)	<0.001[b]	75 (43.1)	4.15 (2.95, 5.85)	<0.001[b]
Calcaneus fracture									
Closed	42 (13.6)	2.94 (1.98, 4.37)	<0.001[b]	12 (9.0)	2.47 (1.27, 4.82)	0.01	30 (17.2)	3.13 (1.97, 4.98)	<0.001[b]
Open	98 (31.8)	9.61 (7.00, 13.20)	<0.001[b]	56 (41.8)	14.68 (9.67, 22.30)	<0.001[b]	42 (24.1)	6.61 (4.38, 9.98)	<0.001[b]
Talus fracture									
Closed	35 (11.4)	2.67 (1.76, 4.04)	<0.001[b]	10 (7.5)	2.19 (1.08, 4.43)	0.03	25 (14.4)	2.88 (1.78, 4.67)	<0.001[b]
Open	64 (20.8)	9.50 (6.55, 13.79)	<0.001[b]	41 (30.6)	16.71 (10.55, 26.46)	<0.001[b]	23 (13.2)	5.41 (3.25, 9.01)	<0.001[b]
Navicular fracture									
Closed	21 (6.8)	4.12 (2.39, 7.09)	<0.001[b]	13 (9.7)	7.48 (3.81, 14.70)	<0.001[b]	8 (4.6)	2.35 (1.08, 5.13)	0.03
Open	34 (11.0)	6.92 (4.31, 11.10)	<0.001[b]	21 (15.7)	10.91 (6.18, 19.26)	<0.001[b]	13 (7.5)	4.39 (2.30, 8.38)	<0.001[b]
Vessel injury	116 (37.7)	2.56 (1.86, 3.52)	<0.001[b]	62 (46.3)	2.55 (1.62, 3.99)	<0.001[b]	54 (31.0)	2.57 (1.71, 3.88)	<0.001[b]
Nerve injury	62 (20.1)	4.52 (3.44, 5.95)	<0.001[b]	28 (20.9)	6.13 (4.20, 8.95)	<0.001[b]	34 (19.5)	3.50 (2.44, 5.01)	<0.001[b]

[a]No injury was the reference category for each injury type.
[b]Statistically significant after Bonferroni correction for multiple analyses ($p < 0.004$).
[c]All regression models controlled for continuous ISS, mission, position, and injury mechanism. No amputation was the reference category for the dependent variable (amputation status).

circumstances that may sometimes exist in a combat zone. Further study into more specific reasons for an amputation would help to clarify these theories.

Previous literature has examined varying injury patterns in open (e.g., dismounted) versus closed (e.g., mounted) blast environments.[7,27,28] Specifically, Ramasamy *et al* found that more LE fractures occurred in a closed rather than open environment, purportedly because of the blast energy under the vehicle and subsequent axial loading to the LE. Likewise, our study found a larger proportion of delayed amputations related to injuries received by service members in a mounted compared with a dismounted vehicle position. These differences in blast injuries in open versus closed environments may be explained by blast physics. Typically, blast energy decreases as it moves outward from the source of the blast, and, in a closed environment, such as a vehicle, the blast wave effects are intensified because of reverberations against walls and other rigid objects.[28] Further work in this area would be valuable as it could help guide the development or enhancement of combat vehicles and personal protective equipment.

The limitations of this study include the focus on specific LE injuries. It is likely that other injuries (e.g., substantial soft tissue injury), complications (e.g., infections, nonunion/malunion of fractures), and comorbid conditions also influence the likelihood of delayed amputation. The additive effect of these conditions, in addition to factors related to rehabilitation, will be important to examine in order to identify other risk factors involved in delayed amputation. Nevertheless, it is important to note that acute injuries provide the earliest and most distinguishable postinjury evidence to inform surgical decisions on amputation or limb salvage. The strengths of this analysis include the large cohort of service members with combat-related LE injuries, which were coded by expert clinical staff. Further, we used an extensive set of relevant control variables, such as injury severity and circumstances. This study also included more LE injuries compared with previous analyses focused only on one fracture location and type.[7,10,13,15,16]

CONCLUSIONS

Service members with combat-related fractures below the knee are at risk of delayed amputations, especially those with open fractures of the calcaneus, in conjunction with concomitant vessel or nerve injury. These results provide important information to consider in the decision-making process between clinicians and service members on whether an injured limb should be amputated during the reconstruction phase of care. Understanding the risks of delayed amputation, the potential course of reconstructive surgeries, and individual attributes, such as psychological and social support of the service member, should all play a role in the decision for a reconstructive or amputation-based treatment strategy. Future studies should further investigate the timing of delayed amputations in relation to these acute injuries, as well as the role that other co-occurring injuries and complications may have in the odds of delayed amputations. It is

TABLE III. Odds of Delayed Lower Extremity Amputation by Lower Extremity Injury Combinations

	Delayed Amputation[c]	
Lower Extremity Injury Combinations[a]	OR (95% CI)	*p*-Value
Open tibia and open fibula fractures		
Tibia only	2.79 (1.92, 4.04)	<0.001[b]
Fibula only	3.37 (2.19, 5.21)	<0.001[b]
Both fractures	5.60 (4.15, 7.55)	<0.001[b]
Open calcaneus and open tibia fractures		
Calcaneus only	11.35 (7.60, 16.95)	<0.001[b]
Tibia only	4.08 (3.03, 5.50)	<0.001[b]
Both fractures	15.12 (9.54, 23.96)	<0.001[b]
Open calcaneus and open talus fractures		
Calcaneus only	6.20 (4.20, 9.15)	<0.001[b]
Talus only	5.63 (2.88, 11.01)	<0.001[b]
Both fractures	13.14 (8.52, 20.29)	<0.001[b]
Open calcaneus and open navicular fractures		
Calcaneus only	7.00 (4.98, 9.84)	<0.001[b]
Navicular only	2.57 (0.94, 7.00)	0.06
Both fractures	13.59 (7.70, 23.99)	<0.001[b]
Nerve and vessel injury		
Nerve only	1.63 (0.99, 2.68)	0.05
Vessel only	3.95 (2.86, 5.44)	<0.001[b]
Both injuries	7.24 (4.74, 11.06)	<0.001[b]
Open tibia fracture and vessel injury		
Tibia only	3.69 (2.69, 5.05)	<0.001[b]
Vessel only	4.67 (3.15, 6.92)	<0.001[b]
Both injuries	10.66 (7.35, 15.47)	<0.001[b]
Open calcaneus fracture and vessel injury		
Calcaneus only	10.55 (7.38, 15.07)	<0.001[b]
Vessel only	5.21 (3.76, 7.19)	<0.001[b]
Both injuries	17.99 (10.53, 30.74)	<0.001[b]
Open tibia fracture and nerve injury		
Tibia only	4.96 (3.78, 6.49)	<0.001[b]
Nerve only	2.49 (1.62, 3.84)	<0.001[b]
Both injuries	9.61 (5.38, 17.18)	<0.001[b]
Open calcaneus fracture and nerve injury		
Calcaneus only	8.06 (5.82, 11.18)	<0.001[b]
Nerve only	2.71 (1.89, 3.89)	<0.001[b]
Both injuries	41.74 (14.70, 118.55)	<0.001[b]

[a]No injury was the reference category for each injury type.
[b]Statistically significant after Bonferroni correction for multiple analyses ($p < 0.002$).
[c]All regression models controlled for continuous ISS, mission, position, and injury mechanism. No amputation was the reference category for the dependent variable (amputation status).

also necessary to examine outcomes, such as long-term health effects, career performance, and quality of life, in order to develop effective treatment and rehabilitation strategies for service members with combat-related LE injuries and delayed amputations.

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REFERENCES

1. Zouris JM, Walker GJ, Dye J, Galarneau M: Wounding patterns for U. S. Marines and sailors during Operation Iraqi Freedom, major combat phase. Mil Med 2006; 171(3): 246–52.

2. Owens BD, Kragh JF Jr, Macaitis J, Svoboda SJ, Wenke JC: Characterization of extremity wounds in Operation Iraqi Freedom and Operation Enduring Freedom. J Orthop Trauma 2007; 21(4): 254–7.
3. Owens BD, Kragh JF Jr, Wenke JC, Macaitis J, Wade CE, Holcomb JB: Combat wounds in Operation Iraqi Freedom and Operation Enduring Freedom. J Trauma 2008; 64(2): 295–9.
4. Eskridge SL, Macera CA, Galarneau MR, et al: Injuries from combat explosions in Iraq: injury type, location, and severity. Injury 2012; 43(10): 1678–82.
5. Doucet JJ, Galarneau MR, Potenza BM, et al: Combat versus civilian open tibia fractures: the effect of blast mechanism on limb salvage. J Trauma 2011; 70(5): 1241–7.
6. Cross JD, Stinner DJ, Burns TC, Wenke JC, Hsu JR. Skeletal Trauma Research Consortium (STReC): Return to duty after type III open tibia fracture. J Orthop Trauma 2012; 26(1): 43–7.
7. Ramasamy A, Hill AM, Phillip R, Gibb I, Bull AMJ, Clasper JC: The modern "deck-slap" injury—calcaneal blast fractures from vehicle explosions. J Trauma 2011; 71(6): 1694–8.
8. Ramasamy MA, Hill AM, Phillip R, Gibb I, Bull AMJ, Clasper JC: FASS is a better predictor of poor outcome in lower limb blast injury than AIS: implications for blast research. J Orthop Trauma 2013; 27(1): 49–55.
9. Mackenzie EJ, Bosse MJ, Pollak AN, et al: Long-term persistence of disability following severe lower-limb trauma. Results of a seven-year follow-up. J Bone Joint Surg Am 2005; 87(8): 1801–9.
10. Ramasamy A, Hill AM, Masouros S, et al: Outcomes of IED foot and ankle injuries. J Bone Joint Surg Am 2013; 95(5): e25.
11. Gwinn DE, Tintle SM, Kumar AR, Andersen RC, Keeling JJ: Blast-induced lower extremity fractures with arterial injury: prevalence and risk factors for amputation after initial limb-preserving treatment. J Orthop Trauma 2011; 25(9): 543–8.
12. Casey K, Demers P, Deben S, Nelles ME, Weiss JS: Outcomes after long-term follow-up of combat-related extremity injuries in a multidisciplinary limb salvage clinic. Ann Vasc Surg 2015; 29(3): 496–501.
13. Huh J, Stinner DJ, Burns TC, Hsu JR. Late Amputation Study Team: Infectious complications and soft tissue injury contribute to late amputation after severe lower extremity trauma. J Trauma 2011; 71(1 Suppl): S47–51.
14. Sheean AJ, Krueger CA, Hsu JR: Return to duty and disability after combat-related hindfoot injury. J Orthop Trauma 2014; 28(11): e258–62.
15. Dickens JF, Kilcoyne KG, Kluk MW, Gordon WT, Shawen SB, Potter BK: Risk factors for infection and amputation following open, combat-related calcaneal fractures. J Bone Joint Surg Am 2013; 95(5): e24.
16. Sheean AJ, Krueger CA, Napierala MA, Stinner DJ, Hsu JR. Skeletal Trauma and Research Consortium (STReC): Evaluation of the mangled extremity severity score in combat-related type III open tibia fracture. J Orthop Trauma 2014; 28(9): 523–6.
17. Manoli A, Prasad P, Levine RS: Foot and ankle severity scale (FASS). Foot Ankle Int 1997; 18(9): 598–602.
18. Stinner DJ, Burns TC, Kirk KL, Scoville CR, Ficke JR, Hsu JR: Prevalence of late amputations during the current conflicts in Afghanistan and Iraq. Mil Med 2010; 175(12): 1027–9.
19. Melcer T, Sechriest VF, Walker J, Galarneau M: A comparison of health outcomes for combat amputee and limb salvage patients injured in Iraq and Afghanistan wars. J Trauma Acute Care Surg 2013; 75(2): S247–54.
20. Doukas WC, Hayda RA, Frisch M, et al: The Military Extremity Trauma Amputation/Limb Salvage (METALS) study: outcomes of amputation versus limb salvage following major lower-extremity trauma. J Bone Joint Surg Am 2013; 95(2): 138–45.
21. Krueger CA, Rivera JC, Tennent DJ, Sheean AJ, Stinner DJ, Wenke JC: Late amputation may not reduce complications or improve mental health in combat-related, lower extremity limb salvage patients. Injury 2015; 46: 1527–32.
22. Galarneau MR, Hancock WC, Konoske P, et al: The Navy-Marine Corps Combat Trauma Registry. Mil Med 2006; 171(8): 691–7.
23. Gennarelli T, Wodzon E: The Abbreviated Injury Scale – 2005. Barrington, IL, Association for the Advancement of Automotive Medicine, 2005.
24. Copes WS, Champion HR, Sacco WJ, Lawnick MM, Keast SL, Bain LW: The Injury Severity Score revisited. J Trauma 1988; 28(1): 69–77.
25. Linn S, Linn R, Sheps S, et al: Injury severity scoring and length of stay in hospital of war casualties – demonstration of an association and possible selection bias. Int J Epidemiol 1993; 22(5): 905–10.
26. Myerson M, Quill GE Jr.: Late complications of fractures of the calcaneus. J Bone Joint Surg Am 1993; 75(3): 331–41.
27. Ramasamy A, Masouros SD, Newell N, et al: In-vehicle extremity injuries from improvised explosive devices: current and future foci. Philos Trans R Soc Lond B Biol Sci 2011; 366(1562): 160–70.
28. DePalma RG, Burris DG, Champion HR, Hodgson MJ: Blast injuries. N Engl J Med 2005; 352(13): 1335–42.

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14. ABSTRACT
Background: Despite medical interventions to preserve viability and functionality of injured limb(s) among combat-injured service members, delayed amputations may occur. The goal of this study was to determine whether specific lower extremity (LE) injuries were associated with delayed amputations.
Methods: The Expeditionary Medical Encounter Database was queried for combat-related LE injuries between 2003 and 2014. The Abbreviated Injury Scale (AIS) was used to categorize LE injuries by severity. Injury episodes with a maximum LE AIS = 1 or amputation on the day of injury were excluded. The final sample included 2,996 service members with at least one LE injury with an AIS ≥ 2. The frequencies of specific LE fractures and nerve and vessel injuries were determined. Logistic regression with paired independent variables was performed to examine the impact of multiple LE injuries on the odds of delayed amputation.
Results: Delayed LE amputation was identified in 308 (10.3%) service members in the sample. The delayed and no amputation groups did not differ in age and service branch. The majority of injury episodes were blast-related and with an Injury Severity Score ≥ 9. The most frequent fractures were tibia (34.4%) and fibula (29.3%), but the highest rates of delayed amputation were in those with navicular (36.2%), talus (30.0%), or calcaneus (28.1%) fractures. Odds of amputation were highest among service members with the calcaneus fracture and LE nerve injury (odds ratio [OR], 41.74; 95% confidence interval [CI], 14.70–118.55; $p < 0.001$), calcaneal fracture and LE vessel injury (OR, 17.99; 95% CI, 10.53–30.74; $p < 0.001$), and calcaneus and tibia fracture (OR, 15.12; 95% CI, 9.54–23.96; $p < 0.001$) combinations.
Conclusions: Odds of delayed amputation increased substantially with specific injury combinations. These findings may guide clinical decision making in the acute care period.

15. SUBJECT TERMS
Combat injury; delayed amputation; fracture; lower extremity injury

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