Infectious Complications and Soft Tissue Injury Contribute to Late Amputation After Severe Lower Extremity Trauma

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Background: Although most combat-related amputations occur early for unsalvageable injuries, >15% occur late after reconstructive attempts. Predicting which patients will abandon limb salvage in favor of definitive amputation has not been explored. The purpose of this study was to identify factors contributing to late amputation for type III open tibia fractures sustained in combat.

Methods: Operative databases were reviewed to identify all combat-related type III open diaphyseal tibia fractures from March 2003 to September 2007. Patients were categorized based on their definitive treatment: group I, limb salvage; group II, early amputation (<12 weeks postinjury); group III, late amputation (≥12 weeks postinjury). Injury, treatment, and complication data were extracted from medical records and compared across groups.

Results: We identified 213 consecutive fractures, including 166 (77.9%) treated definitively with limb salvage, 36 (16.9%) with early amputation, and 11 (5.2%) with late amputation. There was no difference in fracture severity among the three groups. Before amputation, group III was more likely to use autograft and bone morphogenic protein (27.3%), compared with group I (4.8%) and group II (0%), and was more likely to undergo rotational flap coverage (45.5%), compared with group II (0%). Group III patients had the highest average number of revision surgeries and rate of deep soft tissue infection and were more likely to have osteomyelitis (54.5%) before amputation compared with group I (13.9%) and group II (16.7%).

Conclusion: Patients definitively managed with late amputation were more likely to have soft tissue injury requiring flap coverage and have their limb salvage course complicated by infection.

Key Words: Late amputation, Delayed amputation, Limb salvage, Combat.

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The ongoing conflicts in Afghanistan and Iraq have made management of complex high-energy lower extremity trauma common in the military.[1] Current battlefield doctrine urges against primary amputation when possible to afford patients and their stateside orthopedic team the greatest number of definitive treatment options.[2] Mobile, forward-deployed assets provide sophisticated medical and surgical care to stabilize casualties on the battlefield for rapid evacuation to tertiary medical centers in the United States. This expedited care has given numerous patients the opportunity to undergo reconstructive efforts toward limb salvage for injuries that might have otherwise resulted in primary amputation during previous conflicts.

Embarking on a course of limb salvage, however, does not preclude the possibility of proceeding to eventual amputation. Compared with primary amputation, limb salvage has been associated with significantly higher rates of rehospitalization, greater number of surgical procedures, and higher rates of complications.[3,4] These factors highlight why a delayed or late amputation may be required or requested by the patient during the course of limb salvage.

Although much attention has surrounded the debate between limb salvage versus amputation following severe lower extremity injuries, the concept of the late amputee has not been as heavily discussed or reviewed. As a result, definitions of late and delayed amputation have varied in the literature, resulting in wide discrepancies in reported rates, ranging between 9% and 40%.[4–8] Defining late amputation as occurring after the initial hospitalization, the Lower Extremity Assessment Project (LEAP) Study Group reported a 3.9% late amputation rate after 2 years.[3]

As the current conflicts continue and more limb salvage patients enter rehabilitation, the military has encountered increasing numbers of these nonacute or late amputations. In a recent review of all amputee soldiers who had a combat-related lower extremity amputation, Stinner et al.[9] found that 15.2% were performed late, which was defined as occurring >12 weeks after injury. Our available literature indicates that scoring systems have not been useful to help guide surgeons in the decision of whether to acutely amputate or salvage a severely mangled lower extremity; there is even less scientific evidence available to identify injuries that will proceed to late amputation.[10,11] The purpose of this study was to identify factors contributing to late amputation (>12 weeks after injury) after initial attempts at limb reconstruction in patients who sustained type III open tibia fractures during combat operations.

MATERIALS AND METHODS

This retrospective study was conducted under a protocol approved by each institutional review board and in ac-

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cordance with good clinical practices. Operative databases from three tertiary military medical facilities (Brooke Army Medical Center, Walter Reed Army Medical Center, and National Naval Medical Center) were reviewed to identify all Gustilo and Anderson (G/A) type III open diaphyseal tibia fractures sustained in combat by US military personnel from March 2003 to September 2007. Diaphyseal fractures were defined as those fractures that did not extend within 5 cm of the tibial plateau or tibial plafond.[12]

Using inpatient and outpatient medical records and radiographs, the following data were extracted: patient demographics, mechanism of injury, treatment course, and complications. Patients were categorized into groups based on their definitive treatment at the end of the review period (March 1, 2009). Group I (limb salvage group) consisted of subjects who were treated definitively with limb salvage; group II (early amputation group) consisted of subjects who underwent amputation within 12 weeks of injury; group III (late amputation group) consisted of subjects who underwent amputation >12 weeks after injury. We used the 12-week time point to define late amputation as a previous large prospective study showed statistically different patient outcomes using these time periods,[13] and this allowed adequate time for interventions aimed at limb reconstruction.[9]

Fracture severity was classified according to the Orthopaedic Trauma Association fracture classification.[14] The severity of soft tissue defect was recorded based on the Gustilo and Anderson classification.[15–17] Potential factors contributing to late amputation were identified using injury, treatment, and complication data. A deep soft tissue infection was defined as any soft tissue infection that was not successfully treated by antibiotics alone and required operative intervention. Osteomyelitis was defined as a deep infection with positive intraoperative bone cultures.

Statistical analyses were performed with SAS 9.1 (Cary, NC) to assess for differences across groups with regard to patient demographics, injury characteristics, treatment course, and complications. Descriptive statistical analysis for demographic data included the means and standard deviations. Continuous variables and scores were compared via the Wilcoxon test for nonparametric and score data and Student's t test for parametric data. Dichotomous variables were compared using the χ^2 test or Fisher's exact test, as appropriate. All reported p values are two tailed, with an $\alpha \leq 0.05$ representing statistical significance.

RESULTS

Our study cohort consisted of a total of 213 combat-related type III open diaphyseal tibia fractures. Of these, 77.9% were definitively treated with limb salvage (group I), 16.9% with early amputation (group II), and 5.2% with late amputation (group III) (Fig. 1). Average follow-up after injury was 26.7 months (range, 5–56 months). There were no detectable differences between groups with respect to age or mechanism of injury (Table 1).

Injury characteristics for each group are listed in Table 2. For all groups, the majority of fractures were classified as type C according to the Orthopaedic Trauma Association system. There was a significant difference in associated soft tissue injuries according to the G/A classification across groups. The limb salvage group had the highest proportion of less complex soft tissue injuries (G/A type IIIA; $p < 0.0001$). Patients in the early amputation group were more likely to have an associated vascular injury requiring repair (G/A type

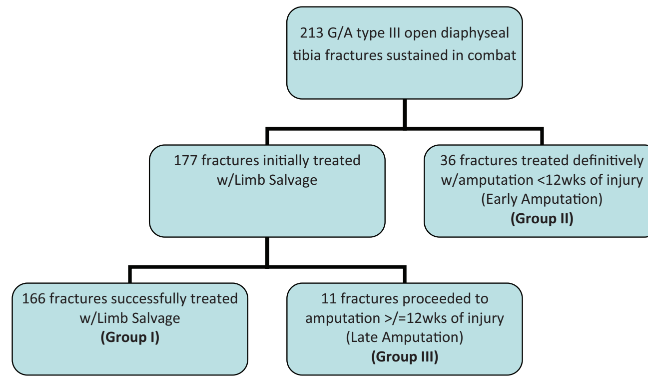

Figure 1. Breakdown of combat-related type III open tibia fractures based on definitive treatment.

TABLE 1. Distribution of Patient Characteristics

	Group I, Limb Salvage (N = 166)	Group II, Early Amputees (N = 36)	Group III, Late Amputees (N = 11)	p
Patient characteristics				
Mean age (range), yr	25 (18–54)	23 (20–34)	25 (19–42)	0.1017
Male	100% (167)	94.0% (33)	91.0% (10)	0.0057
Mechanism of injury				
Blast	78.9% (131)	91.7% (33)	73.0% (8)	0.1674
GSW	10.8% (18)	0	18.0% (2)	0.0658
Other	10.2% (17)	8.3% (3)	9.0% (1)	1

GSW, gunshot wound.

TABLE 2. Distribution of Injury Characteristics

	Group I, Limb Salvage (N = 166)	Group II, Early Amputees (N = 36)	Group III, Late Amputees (N = 11)	p
Fracture classification				
OTA type A	18.1% (30)	8.3% (3)	9.1% (1)	0.2928
OTA type B	30.1% (50)	16.7% (6)	36.4% (4)	0.2197
OTA type C	51.8% (86)	75.0% (27)	54.5% (6)	0.0395
Soft tissue classification				
G/A type IIIA	60.8% (101)	16.7% (6)	45.5% (5)	<0.0001
G/A type IIIB	34.9% (58)	36.1% (13)	45.5% (5)	0.7786
G/A type IIIC	4.2% (7)	47.2% (17)	9% (1)	<0.0001
Associated injuries				
Nerve injury	16.9% (28)	22.2% (8)	36.3% (4)	0.2171

G/A, Gustilo-Anderson; OTA, Orthopaedic Trauma Association.

TABLE 3. Distribution of Treatment Course

	Group I, Limb Salvage (N = 166)	Group II, Early Amputees (N = 36)	Group III, Late Amputees (N = 11)	*p*
Bone Graft				
Autograft	12.7% (21)	0	9.1% (1)	0.0520
BMP	34.9% (58)	2.8% (1)	27.3% (3)	0.0008
Autograft and BMP	4.8% (8)	0	27.3% (3)	0.0095
Other	4.2% (7)	0	9.1% (1)	0.3286
Flap coverage				
Free flap	4.2% (7)	5.6% (2)	18.2% (2)	0.1117
Rotational flap	30.7% (51)	0% (0)	45.5% (5)	0.0003
Revision surgeries				
Average number of revision surgeries (range)*	1.44 (0–10)	1.85 (1–11)	3.18 (1–11)	0.0002

* Not including debridement and irrigation procedures.
BMP, bone morphogenic protein.

TABLE 4. Distribution of Complications

Complications*	Group I, Limb Salvage (N = 166)	Group II, Early Amputees (N = 36)	Group III, Late Amputees (N = 11)	*p*
Deep infection	20.5% (34)	41.7% (15)	72.7% (8)	<0.0001
Osteomyelitis	13.9% (23)	16.7% (6)	54.5% (6)	0.0056
Flap failure	1.2% (2)	5.6% (2)	18.2% (2)	0.0072

* Complications related to limb salvage effort, prior to definitive amputation.

IIIC) (47.2%) compared with those in the limb salvage group (4.2%; $p < 0.0001$) and late amputation group (9.0%; $p = 0.063$). There was no statistically significant difference across the groups with respect to initial nerve injury.

All open tibia fractures in our cohort were treated initially in the theater of operations with external fixation following wound debridement. Treatment characteristics for each group are illustrated in Table 3. Patients who eventually underwent late amputation were more likely to have both autograft and bone morphogenic protein used (27.3%) compared with the limb salvage group (4.8%; $p = 0.04$) and early amputation group (0%; $p = 0.02$). Similarly, the late amputation patients were more likely to undergo rotational flap coverage (45.5%) before amputation compared with early amputation patients (0%) ($p < 0.0001$). The average number of revision surgeries, not including debridement and irrigation procedures, was higher for the late amputation group ($p = 0.0002$).

Complications encountered in each group before definitive treatment are shown in Table 4. For those with a late amputation, the mean time interval between injury and amputation was 13.1 months (range, 3–23.4 months). At the time of amputation, all late amputees had at least one complication. Patients in the late amputation group had the highest rate of deep soft tissue infection ($p < 0.0001$). They were also more likely to have osteomyelitis (54.5%) before amputation compared with those in the limb salvage (13.9%; $p = 0.006$) and early amputation groups (16.7%; $p = 0.04$). Two of the seven late amputation patients (18.2%) who underwent flap coverage had failure of their flaps because of infection (a free latissimus flap and a local rotational flap). This rate of failure was significantly higher than what was observed in the limb salvage group (1.2%) ($p = 0.04$).

DISCUSSION

During reconstructive efforts to salvage a mangled extremity, the potential for eventual amputation still exists. Most of the debate and literature surrounding management of severe lower extremity injuries focuses on limb salvage versus primary amputation.[4,16–19] Nonacute amputation occurring after limb salvage, although recognized, is not as thoroughly reviewed in the literature. No consistent timeframes for defining secondary amputations have been established and range from 24 hours postinjury to >1 year postinjury.[13,20,21] This lack of consensus helps explain the wide discrepancy among reported late amputation rates, ranging from 9% to 40%.[4–8]

Of the limited literature that is available on late amputations, most attention has been given to outcomes and complications. In addition to having worse 2-year functional outcomes,[13] limb salvage patients who eventually go on to have a late amputation are known to require more days in the hospital, more surgical procedures, and overall increased expenditures compared with primary amputees.[3,20] Bondurant et al.[20] showed that a primary decision for amputation in a severe injury cuts the cost of medical care by half compared with costs incurred by secondary amputation. In 2009, the LEAP study group demonstrated a higher complication rate after late amputation compared with primary amputation and limb salvage, including most commonly wound infection (68%), osteomyelitis (40%), and residual limb complications (24%).[3] This study, however, did not comment on specific complications in the reconstructive candidates before late amputation.

Thus, despite awareness of the poor prognosis of secondary amputations, the challenging question remains: what leads some patients to abandon salvage efforts and pursue late amputation over others?

In this study, we found that patients with type III open diaphyseal tibia fractures definitively managed with an amputation >12 weeks after their initial injury were more likely to require a soft tissue coverage procedure and had higher rates of infectious complications. The majority of late amputees in our study had at least one major unresolved complication that threatened future limb viability, including deep wound infection (72.7%), osteomyelitis (54.5%), and flap failure (18.2%). The rate of these particular complications was significantly higher in the late amputee group compared with the limb salvage and early amputee groups.

Similar complications have been cited in the literature as precursors to late amputation. In a retrospective study of 24 type III open tibia fractures, Fairhurst[6] defined late amputations as those occurring >11 months from injury and found that among a total of 8 late amputations, 5 were performed due to recurrent osteomyelitis.

The current study made it a point to distinguish "early" from "late" amputations because they are different entities that stem from different factors. Thiagarajan et al. in 1999 described different factors leading to secondary amputation, depending on how far out the amputation was performed from injury. In their review of 49 late amputations, they attributed amputations performed within 1 month of injury to vascular reasons, those performed between 1 month and 1 year to persistent sepsis, and those performed after 1 year to chronically infected nonunions.[21] This is consistent with our data.

From their findings, the LEAP Study Group concluded that emphasis needs to be given to postacute care services that address secondary conditions that may inhibit or delay optimal recovery.[3,16,19] The military has established a strong model of postacute care services for our soldiers who have sustained limb threatening trauma in combat. Limb salvage programs have been established at the major military treatment facilities receiving casualties with limb threatening injuries. Also, centralized institutions for amputee care at Walter Reed Medical Center, Brooke Army Medical Center, and Naval Medical Center San Diego were created. At these state-of-the-art centers, centralized teams of surgeons, physiatrists, physical therapists, prosthetists, nurses, peer mentors, and behavioral medicine specialists work to progress the injured soldier from wound closure to reintegration within civilian life or return to active duty depending on the service member's goals.[22] The influence of peers and other amputees on outcome of amputation has been recognized;[23] however, their influence on limb salvage patients in the decision to pursue "elective" amputation to our knowledge has not been studied.

This study has several limitations. First, this is a retrospective analysis and carries the shortcomings inherent to the study design. Although fracture, wound, and complication management principles were consistently similar, specific treatment, particularly for infection (i.e., antibiotic type and length of treatment), was not necessarily standardized among patients, surgeons, or institution. Second, our study population was limited to open type III diaphyseal tibia fractures. Other lower extremity injuries may also result in late amputation after an initial attempt at salvage, such as those involving the foot and articular surfaces of the tibia. Finally, our findings are representative only of combat-inflicted injuries sustained by active duty service members treated in a military medical system and may not be generalizable to the civilian centers.

In conclusion, patients definitively managed with late amputation were more likely to have severe soft tissue injury requiring flap coverage and have their limb salvage course complicated by infection. Although these objective factors seem to be influential in the decision to pursue late amputation, the decision is undoubtedly multifactorial.

This review serves as a pilot study and provides a glimpse at some of the injury, treatment, and complication factors contributing to the decision to pursue late amputations for severe tibia injuries sustained in combat. Although reports evaluating primary amputee outcomes and long-term performance are available from previous conflicts,[24,25] currently no data exist comparing outcomes of early versus late amputations in our combat wounded. Given the known poor functional, medical, and economic prognoses of late amputation, further research is warranted to explore other potentially controllable variables influencing the decision. The Late Amputation Study Team is a multicenter, multidisciplinary team that was established to address this challenge and look into the predictive factors and outcomes of the late amputee.

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