Copyright © 2019 by The Journal of Bone and Joint Surgery, Incorporated

The Military Extremity Trauma Amputation/Limb Salvage (METALS) Study

Outcomes of Amputation Compared with Limb Salvage Following Major Upper-Extremity Trauma

Stuart L. Mitchell, MD, Roman Hayda, MD, Andrew T. Chen, MD, MPH, Anthony R. Carlini, MS, James R. Ficke, MD, and Ellen J. MacKenzie, PhD, on behalf of the METALS Study Group*

Investigation performed at Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Background: Severe upper-extremity injuries account for almost one-half of all extremity trauma in recent conflicts in the Global War on Terror. Few long-term outcomes studies address severe combat-related upper-extremity injuries. This study's objective was to describe long-term functional outcomes of amputation compared with those of limb salvage in Global War on Terror veterans who sustained severe upper-extremity injuries. Limb salvage was hypothesized to result in better arm and hand function scores, overall functional status, and quality of life, with similar pain interference.

Methods: This retrospective cohort study utilized data from the Military Extremity Trauma Amputation/Limb Salvage (METALS) study for a subset of 155 individuals who sustained major upper-extremity injuries treated with amputation or limb salvage. Participants were interviewed by telephone 40 months after injury, assessing social support, personal habits, and patient-reported outcome instruments for function, activity, depression, pain, and posttraumatic stress. Outcomes were evaluated for participants with severe upper-extremity injuries and were compared with participants with concomitant severe, lower-extremity injury. The analysis of outcomes comparing limb salvage with amputation was restricted to the 137 participants with a unilateral upper-extremity injury because of the small number of patients with bilateral upper-extremity injuries (n = 18).

Results: Overall, participants with upper-extremity injuries reported moderate to high levels of physical and psychosocial disability. Short Musculoskeletal Function Assessment (SMFA) scores were high across domains; 19.4% screened positive for posttraumatic stress disorder (PTSD), and 12.3% were positive for depression. Nonetheless, 63.6% of participants were working, were on active duty, or were attending school, and 38.7% of participants were involved in vigorous recreational activities. No significant differences in outcomes were observed between patients who underwent limb salvage and those who underwent amputation.

Conclusions: Severe, combat-related upper-extremity injuries result in diminished self-reported function and psychosocial health. Our results suggest that long-term outcomes are equivalent for those treated with amputation or limb salvage. Addressing or preventing PTSD, depression, chronic pain, and associated health habits may result in less disability burden in this population.

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

*The members of the Military Extremity Trauma Amputation/Limb Salvage (METALS) Study Group included Roman Hayda, MD, William C. Doukas, MD, H. Michael Frisch, MD, Romney C. Andersen, MD, John J. Keeling, MD, Michael T. Mazurek, MD (deceased), Paul F. Pasquina, MD, Harold J. Wain, PhD, Anthony R. Carlini, MS, James R. Ficke, MD, and Ellen J. MacKenzie, PhD.

Disclosure: This study was funded in part by a grant from the U.S. Department of Defense, Military Amputee Research Program of the United States Army Medical Research Acquisition Activity (USAMRAA) (Contract Number: W81XWH-06-1-0361), and by a grant from the National Institutes of Health (T32 AR067708). On the **Disclosure of Potential Conflicts of Interest** forms, *which are provided with the online version of the article*, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work and "yes" to indicate that the author had other relationships or activities that could be perceived to influence, or have the potential to influence, what was written in this work (http://links.lww.com/JBJS/F370).

Upper-extremity injuries are common among combat casualties, most often resulting from high-energy explosives such as improvised explosive devices. Extremity injuries accounted for 39% to 54%[1-3] of all combat wounds sustained by injured U.S. service members in the Global War on Terror[4], among which 41% to 52% of wounds were to the upper extremities[5,6]. Between 2001 and 2011, there were 2,037 traumatic major amputations (i.e., at, or proximal to, the radiocarpal or tibiotalar joint) sustained by service members during these conflicts[7], with 14% to 25% involving the upper extremities[8-12]. The remaining severe upper-extremity injuries were surgically reconstructed.

The upper extremity is generally thought to be less prone to complications with reconstruction, and when amputation is performed, prosthetics often cannot fully replicate upper-extremity function despite continuing advances in technology[9,12-15]. Consequently, reconstruction is attempted in most mangled upper-extremity trauma injuries, although amputation may be selectively indicated. In other limited circumstances, typically those limited to civilian-type injuries, replantation may be feasible[14-17].

There have been few studies showing long-term outcomes of combat-related, major trauma to the upper extremity[13,18-20]. Without outcomes data, health services lack information to perform evidence-based decision-making and counseling while resource allocation is made difficult. A few studies of severe upper-extremity injury outcomes have been performed in civilian populations[15,17,21-24]. However, with differences in military and civilian injuries and the advances in prosthetic technology and surgical care available to service members, the civilian results may not be generalizable to military populations.

The objective of this study was to describe long-term functional outcomes among service members who sustained major upper-extremity injuries in combat during the Global War on Terror by comparing differences between patients who underwent limb salvage and those who underwent amputation. We hypothesized that limb salvage would result in better arm and hand function scores, overall functional status, and quality of life and that pain interference would be similar because of chronic pain in patients who underwent limb salvage and prosthesis-related discomfort or phantom limb pain in patients who underwent amputation.

Materials and Methods

This retrospective cohort study utilized data from a subset of individuals from the Military Extremity Trauma Amputation/Limb Salvage (METALS) study[25]. In their study, Doukas et al.[25] analyzed outcomes following lower-extremity trauma; the current study focuses on patients who sustained major upper-extremity trauma.

Study Population

Active-duty personnel and reservists who sustained major limb trauma while deployed in Iraq or Afghanistan between 2003 and 2007 were eligible for participation in the METALS study. Major limb trauma was defined as an injury at, or proximal to, either the hindfoot or radiocarpal joint that resulted in an amputation or required reconstruction that included revascularization, bone-grafting or transport, local or free-flap coverage, repair or treatment of a major nerve deficit, or treatment for compartment syndrome. Patients with persistent brain injury (Glasgow Coma Scale score of <15 points at discharge) or spinal cord injury resulting in paraplegia or quadriplegia were excluded.

The overall METALS study included 429 participants with complete medical records who consented to the study. Of the initial 868 initial patients screened, 519 (59.8%) were located and agreed to be interviewed, 202 (23.3%) declined to participate, and 147 (16.9%) did not respond. Of those who agreed to participate, 69 were ineligible and 21 had incomplete records. More detailed patient selection has been described previously[25]. This study focuses on 155 individuals who sustained METALS-eligible upper-extremity injuries.

Characterizing Patients and Injuries

Information obtained from the interviews was used to characterize participant demographic characteristics, social support (Multidimensional Scale of Perceived Social Support[26]), branch of military service and grade (highest while on active duty), combat experiences (Combat Experiences Questionnaire[27]), and health habits (tobacco and alcohol use[28]).

Injuries were classified using medical record documentation of a stateside military treatment facility. Amputations were categorized by anatomic level. Fractures of salvaged limbs were classified by bone segment. Additional injuries were also documented, including segmental bone loss, skin defect, burns, extent of muscle and/or tendon injury, and location and severity of all neurovascular injuries.

Measurement of Outcomes

Participants were interviewed by telephone and completed self-reported outcome measures[25] including the Short Musculoskeletal Function Assessment (SMFA)[29], Paffenbarger Physical Activity Questionnaire[30-32], Center for Epidemiological Studies Depression Scale Revised (CESDR)[33,34], PTSD (Posttraumatic Stress Disorder) checklist (PCL)[35,36], and Chronic Pain Grade (CPG)[37] (see Appendix 1 for outcomes measurement tools). Major role activity participation was assessed by standard questions pertaining to involvement in usual activities in the past week.

Data Analysis

Outcomes were evaluated first for all patients with any upper-extremity injury and then separately for those with or without a concomitant METALS-eligible lower-extremity injury. Analysis comparing limb salvage with amputation was restricted to the subjects with a unilateral upper-extremity injury because of the small number with bilateral upper-extremity injuries.

Multiple regression techniques were used to examine differences in outcomes associated with limb salvage compared with amputation while adjusting for patient characteristics and their injuries, together with the time since the injury. Continuous outcomes were modeled using linear regressions, and

the probability of dichotomous outcomes was modeled using logistic regressions. Significance was set at $\alpha = 0.05$. Statistical analyses were performed using SAS, version 9.1 (SAS Institute).

Results

Characteristics of the Participants

Participants with major trauma to ≥1 upper extremity had a mean age of 30 years (range, 22 to 55 years), and the majority were male (98.1%), non-Hispanic white (81.1%), married (50.3%), and senior enlisted (53.5%) (Table I). At the time of the injury, participants were most commonly active-duty Army (68%), Marines (20%), or reservists (8%). There were no significant differences between the limb salvage group and the amputation group with regard to the distribution of participants' age, sex, race or ethnicity, education, social support, combat experiences, or highest military rank. Participants were interviewed at a mean of 40 months (range, 12 to 70 months) after the injury.

Characteristics of the Injuries

Overall, 137 participants sustained METALS-eligible injuries to 1 upper extremity (104 salvages; 33 amputations) and 18 participants sustained METALS-eligible injuries to both upper extremities (11 bilateral salvage, 4 bilateral amputation, and 3 salvage and amputation), for a total of 173 limb injuries. All amputations took place within 9 days of the initial injury

TABLE I Characteristics of METALS Study Participants with Major Upper-Extremity Injuries by Presence of Bilateral Injury and by Amputation Compared with Limb Salvage for Those with Unilateral Injuries

		Unilateral Upper-Extremity Injuries		
	All Participants (N = 155)	Salvage (N = 104)	Amputation (N = 33)	Bilateral Upper-Extremity Injuries* (N = 18)
Age†				
18 to 24 years	24.5%	23.1%	24.2%	33.3%
25 to 29 years	33.6%	35.6%	33.3%	22.2%
≥30 years	41.9%	41.4%	42.4%	44.4%
Male sex†	98.1%	99.0%	97.0%	94.4%
Race or ethnicity†				
Non-Hispanic white	81.1%	83.5%	81.8%	64.7%
Non-Hispanic black	8.5%	5.8%	18.2%	5.9%
Hispanic	7.8%	7.8%	0.0%	23.5%
Other	2.6%	2.9%	0.0%	5.9%
High school graduate or less†	34.8%	38.5%	27.3%	27.8%
Marital status at time of injury†				
Married	50.3%	51.0%	51.5%	44.4%
Never married	42.6%	44.2%	39.4%	38.9%
Living with a partner	0.7%	0.0%	0.0%	5.6%
Separated, divorced, widow	6.4%	4.8%	9.1%	11.1%
Social support†				
Low (0 to 70)	29.0%	28.9%	33.3%	22.2%
Moderate (71 to 80)	39.4%	44.2%	30.3%	27.8%
High (81 to 100)	31.6%	26.9%	36.4%	50.0%
Military rank†				
Junior enlisted (E1 to E4)	34.2%	31.7%	39.4%	38.9%
Senior enlisted (E5 to E9)	53.5%	57.7%	39.4%	55.6%
Officers	12.3%	10.6%	21.2%	5.6%
No. of combat experiences†				
0 to 5	13.6%	15.4%	3.0%	22.2%
6 to 8	21.3%	18.3%	42.4%	0.0%
9 to 11	29.0%	31.7%	27.3%	16.7%
12 to 17	36.1%	34.6%	27.3%	61.1%

*Bilateral upper-extremity injuries included 11 cases of bilateral limb salvage, 4 cases of bilateral amputation, and 3 cases of combined amputation and limb salvage (i.e., 1 of each type of treatment). †The values are given as the percentage of patients.

TABLE II METALS Eligibility: Characteristics of Injured Limbs

	All METALS Upper-Extremity Injuries (N = 173)	With METALS Lower-Extremity Injury (N = 56)	Without METALS Lower-Extremity Injury (N = 117)
Amputated limb level*	44	8	36
Shoulder disarticulation†	7 (15.9%)	0 (0.0%)	7 (19.4%)
Transhumeral†	14 (31.8%)	3 (37.5%)	11 (30.6%)
Transradial†	19 (43.2%)	5 (62.5%)	14 (38.9%)
Wrist disarticulation†	4 (9.1%)	0 (0.0%)	4 (11.1%)
Salvaged limb injuries and/or procedures*‡	129	48	81
Bone graft or bone transport for segmental bone defect†	54 (41.9%)	19 (39.6%)	35 (43.2%)
Complete deficit of major nerve†	47 (36.4%)	15 (31.3%)	32 (39.5%)
Local or free flap coverage†	43 (33.3%)	14 (29.2%)	29 (35.8%)
Compartment syndrome or muscle loss requiring fasciotomy†	30 (23.3%)	15 (31.3%)	15 (18.5%)
Revascularization†	11 (8.5%)	3 (6.3%)	8 (9.9%)

*The values are given as the number of patients. †The values are given as the number of patients, with the percentage in parentheses. ‡The numbers will not add to the number of patients because some patients met multiple criteria.

(mean [and standard deviation], 1 ± 2 days [range, 0 to 9 days]). The majority of amputations were at the transradial level (19 [43.2%] of 44) or the transhumeral level (14 [31.8%] of 44) (Table II). Among the 129 salvaged limbs, 70.5% (91 limbs) had ≥1 fracture of the radius and/or ulna and 33.3% (43 limbs) had ≥1 humeral fracture. The 3 most common METALS-eligible injuries and/or procedures in salvaged limbs were bone-grafting or transport for a segmental defect (41.9%), complete deficit of a major nerve (36.4%), and local or free-flap coverage (33.3%). Fifty participants (32.3%) had 56 associated METALS-eligible lower-extremity injuries.

TABLE III Unadjusted Outcomes of METALS Participants with Any Upper-Extremity Injury at the Time of Interview

		Unilateral Upper-Extremity Injuries		
	All Participants	Salvage	Amputation	Bilateral Upper-Extremity Injuries
No. of participants	155	104	33	18
Mean SMFA scores* *(points)*				
Total dysfunction	26.9	27.3	24.0	29.1
Daily activities	25.2	27.7	23.4	31.9
Emotional status	44.1	46.4	38.2	41.1
Arm and hand function	21.8	20.1	23.5	28.6
Mobility†	19.7	22.0	14.2	17.1
Engaged in vigorous sports or recreational activities	38.7%	41.4%	39.4%	22.2%
With depressive symptoms	40.0%	41.4%	36.4%	38.9%
With possible or probable depression	12.3%	13.5%	6.1%	16.7%
Screened positive for PTSD	19.4%	19.2%	21.2%	16.7%
Working or on active duty at time of interview	44.8%	47.6%	39.4%	38.9%
Working, on active duty, or in school at time of interview	63.6%	63.1%	69.7%	55.6%
Mean pain intensity within 4 weeks prior to interview	50.9	50.7	53.4	47.2
With pain interfering with activity	18.2%	18.5%	18.2%	16.7%

*Higher SMFA scores represent worse function in a given domain. †The comparison of the unilateral salvage group and amputation group was significant at $p < 0.05$. The mean difference was 7.8 (95% confidence interval, 0.06 to 15.4).

TABLE IV Tobacco Smoking and Alcohol Drinking Status at the Time of Interview in Participants with Any Upper-Extremity Injury

	All Participants (N = 155)	Unilateral Upper-Extremity Injuries		Bilateral Upper-Extremity Injuries (N = 18)
		Salvage (N = 104)	Amputation (N = 33)	
Current smoking status				
No smoking in past 4 weeks	71.1%	65.7%	75.0%	94.4%
Current tobacco smoking				
<20 cigarettes per day	21.7%	25.5%	21.9%	0.0%
≥20 cigarettes per day	7.2%	8.8%	3.1%	5.6%
Current drinking status				
No drinks in past 4 weeks	18.7%	18.3%	15.5%	27.8%
Current alcohol intake				
≤3 drinks per week	47.1%	50.0%	36.4%	50.0%
4 to 13 drinks per week	23.2%	22.1%	33.3%	11.1%
≥14 drinks per week	11.0%	9.6%	15.2%	11.1%
CAGE score				
0 (no drinking problem)	74.2%	76.9%	63.6%	77.8%
1 (possible drinking problem)	11.6%	8.7%	18.2%	16.7%
≥2 (probable drinking problem)	14.2%	14.4%	18.2%	5.6%

Outcomes at Follow-up

Overall, participants with any METALS-eligible upper-extremity injury reported moderate to high levels of physical and psychosocial disability (Table III). In all domains of the SMFA except mobility, subjects scored significantly higher (worse function) than population norms (norms: 12.7 for total dysfunction, 13.6 for mobility, 11.8 for daily activities, 20.5 for emotional status, and 6.0 for arm and hand function)[38]. Notably, more dysfunction was reported for arm and hand function (21.8) and emotional status (44.1). Nonetheless, 38.7% reported engaging in vigorous sports or recreational activities, and 63.6% were working, were on active duty, or were attending school. Eighteen percent reported having pain that interfered with their normal activities, compared with 16% in the general population. Only 9.1% reported being pain-free (42% in the general population)[39]. Depressive symptoms were reported by 40.0% of participants, with 12.3% screening positive for possible or probable depression and 19.4% screening positive for PTSD. Additionally, 28.9% reported current tobacco smoking and 25.8% had self-reported drinking that indicated a possible

TABLE V Regression Results: Effect of Upper-Extremity Amputation Status on SMFA Scores of Participants with Unilateral Upper-Extremity Injuries (N = 137)

	Total Dysfunction*	Mobility Subscore*	Daily Activities Subscore*	Emotional Subscore*	Arm and Hand Subscore*
Upper-extremity amputation	−2.95 (−8.78 to 2.87)	−5.47 (−12.1 to 1.13)	−1.53 (−9.23 to 6.16)	−7.68 (−16.1 to 0.78)	2.23 (−5.32 to 9.79)
METALS lower-extremity injury	7.03† (1.70 to 12.37)	19.6‡ (13.5 to 25.6)	4.61 (−2.43 to 11.65)	5.25 (−2.49 to 12.99)	−2.46 (−9.37 to 4.45)
Age	0.73‡ (0.34 to 1.12)	0.61‡ (0.16 to 1.05)	0.57† (0.05 to 1.09)	0.84‡ (0.27 to 1.41)	0.97‡ (0.46 to 1.48)
Months to interview	−0.23† (−0.42 to −0.05)	−0.20 (−0.41 to 0.01)	−0.39‡ (−0.64 to −0.15)	−0.19 (−0.46 to 0.08)	−0.11 (−0.35 to 0.13)
Rank					
Junior enlisted	Reference	Reference	Reference	Reference	Reference
Senior enlisted	−5.14 (−10.9 to 0.64)	−1.47 (−8.00 to 5.07)	−5.62 (−13.2 to 2.00)	−8.00 (−16.4 to 0.38)	−6.16 (−13.6 to 1.33)
Commissioned officer	−7.79 (−17.0 to 1.44)	−6.71 (−17.2 to 3.73)	−5.55 (−17.7 to 6.63)	−15.4† (−28.8 to −2.01)	−5.14 (−17.1 to 6.82)
No. of combat experiences	1.04‡ (0.38 to 1.70)	0.88† (0.14 to 1.63)	0.72 (−0.15 to 1.59)	2.07‡ (1.11 to 3.02)	0.72 (−0.13 to 1.58)
Social support					
Low (≤70)	Reference	Reference	Reference	Reference	Reference
Moderate (71 to 80)	−7.46† (−13.4 to −1.49)	−5.34 (−12.1 to 1.41)	−6.22 (−14.1 to 1.66)	−14.5‡ (−23.2 to −5.87)	−5.20 (−12.9 to 2.54)
High (>80)	−7.94† (−14.4 to −1.44)	−5.28 (−12.6 to 2.07)	−9.65† (−18.2 to −1.07)	−15.8‡ (−25.2 to −6.33)	−1.94 (−10.4 to 6.49)
R^2	0.27	0.36	0.17	0.30	0.15

*The values are given as the regression coefficient, with the 95% confidence interval in parentheses; higher SMFA scores represent worse function in a given domain. †Significant at $p < 0.05$. ‡Significant at $p < 0.01$.

TABLE VI Regression Results: Adjusted Odds of Depression, PTSD, Role Participation, Engagement in Vigorous Sports, and Pain Interference for Participants with Unilateral Upper-Extremity Injuries (N = 137)

	Screens Positive for Depression*	Screens Positive for PTSD*	Currently Working, Active Duty, or in School*	Engaged in Vigorous Sports*	Pain Interferes with Activity*
Upper-extremity amputation	0.28 (0.04 to 1.76)	1.32 (0.40 to 4.38)	1.29 (0.50 to 3.31)	0.89 (0.37 to 2.16)	1.05 (0.35 to 3.16)
METALS lower-extremity injury	1.77 (0.51 to 6.06)	0.71 (0.23 to 2.25)	1.27 (0.54 to 2.96)	1.57 (0.71 to 3.46)	0.75 (0.27 to 2.08)
Age	1.07 (0.99 to 1.17)	1.10† (1.01 to 1.20)	0.95 (0.90 to 1.01)	1.02 (0.96 to 1.08)	1.06 (0.99 to 1.14)
Months to interview	0.99 (0.94 to 1.03)	1.01 (0.98 to 1.06)	1.06† (1.03 to 1.10)	1.01 (0.99 to 1.04)	0.99 (0.96 to 1.03)
Rank					
Junior enlisted	Reference	Reference	Reference	Reference	Reference
Non-commissioned officer	0.43 (0.10 to 1.77)	0.35 (0.11 to 1.19)	1.17 (0.47 to 2.91)	1.72 (0.72 to 4.08)	1.33 (0.42 to 4.18)
Commissioned officer	0.22 (0.02 to 3.07)	0.03† (0.00 to 0.56)	3.91 (0.76 to 20.3)	5.70† (1.38 to 23.6)	0.64 (0.09 to 4.33)
No. of combat experiences	1.25† (1.03 to 1.52)	1.32‡ (1.09 to 1.59)	0.94 (0.84 to 1.05)	0.98 (0.89 to 1.09)	1.14 (0.99 to 1.31)
Social support					
Low (≤70)	Reference	Reference	Reference	Reference	Reference
Moderate (71 to 80)	0.09‡ (0.02 to 0.48)	0.23‡ (0.08 to 0.71)	0.97 (0.39 to 2.45)	1.20 (0.49 to 2.93)	0.46 (0.16 to 1.36)
High (>80)	0.23 (0.05 to 1.07)	0.08‡ (0.01 to 0.44)	2.07 (0.71 to 6.03)	1.32 (0.50 to 3.46)	0.48 (0.14 to 1.66)

*The values are given as the odds ratio, with the 95% confidence interval in parentheses. †Significantly different at $p < 0.05$. ‡Significantly different at $p < 0.01$.

(CAGE score = 1; 11.6%) or probable (CAGE score ≥ 2; 14.2%) drinking problem[28] (Table IV).

Comparison of Outcome by Treatment

Outcomes by the presence of a unilateral injury compared with a bilateral injury and by amputation compared with limb salvage are presented in Table III, and Tables V and VI summarize the results of the regressions. Covariates included in the final regression models were the presence of a major lower-extremity injury, age, time to interview, military rank, combat experiences, and perceived social support. Race or ethnicity was removed because it was not a significant predictor in any regression. Education was also removed because it correlated with military rank and could not be considered a predictor of outcome as it was assessed at the time of the interview.

After adjusting for covariates, there were no significant differences in outcomes between participants who underwent unilateral limb salvage and participants who underwent unilateral amputation, including any SMFA domain scores or rates of depression; PTSD; return to work, active duty, or school; participation in vigorous activity; or pain interference. However, several other factors were associated with the outcomes (Tables V and VI). The presence of a lower-extremity injury was associated with worse SMFA total dysfunction scores ($p < 0.05$) and mobility scores ($p < 0.01$). Older age was associated with worse SMFA scores in all domains ($p < 0.05$) and with 10% higher odds of PTSD ($p < 0.05$). Commissioned officers had better SMFA emotional scores ($p < 0.05$), were 97% less likely to screen positive for PTSD ($p < 0.05$), and were 5.7 times more likely to engage in vigorous activities ($p < 0.05$). More combat experience was correlated with worse SMFA total dysfunction scores ($p < 0.01$), mobility scores ($p < 0.05$), and emotional scores ($p < 0.01$) and increased the likelihood of depression by 25% ($p < 0.05$) and the likelihood of PTSD by 32% ($p < 0.01$). More social support was associated with a lower likelihood of PTSD ($p < 0.01$) and improved SMFA emotional and activity scores ($p < 0.05$).

Discussion

This study presents the first comparison of long-term outcomes following major upper-extremity trauma sustained by U.S. military personnel in the Global War on Terror treated with limb salvage or amputation. Like patients with lower-extremity injuries in the METALS study[25], moderate to high levels of physical and psychosocial disability were reported by participants with upper-extremity injuries compared with general population norms. Although unique functional limitations specific to the site of injury exist, similar, significant rates of overall disability persisted in this population regardless of whether the upper or lower extremity was involved and irrespective of treatment by amputation or salvage.

Although basic surgical principles may be similar when managing severe upper-extremity or lower-extremity injury, functional and anatomic differences must be considered when deciding whether to perform limb salvage or amputation. Motion, dexterity, and sensibility, which are believed to be critical in the upper extremity, cannot be fully replicated by a prosthesis[14]. Tintle et al. suggested that a "bad hand" may be more functional than a "good amputation" in the upper extremity, but this difference may not be as important in the lower extremity[14]. The limitations of prosthetic technology may make limb salvage more attractive than amputation in the upper extremity[12,14]. However, despite the hypothesis favoring limb salvage over amputation, our results did not demonstrate any significant differences in outcomes for those undergoing limb salvage compared with amputation following a unilateral, major upper-extremity injury.

To our knowledge, there have been no prior studies directly comparing long-term outcomes of reconstruction with

amputation after upper-extremity injuries in military or civilian populations; however, there have been a few studies in civilian populations comparing replantation with amputation[15,17,23]. The destructive mechanisms of war injury usually preclude replantation, and resources required for a replantation surgical procedure are usually lacking in the battle zone. Nonetheless, revascularization, nerve and tendon repair, and complex osteosynthesis were components of reconstruction in our cohort, making civilian replantation reports the closest counterpart for comparison. In a cohort of 44 patients with major traumatic amputations (50% replantation cases) at a mean follow-up of 7.3 years, patients who underwent a replantation had better function than those treated with amputation[17]. Similarly, patient-reported function was compared following major traumatic amputations treated with either replantation (n = 9) or amputation (n = 22) at a mean follow-up of 10.0 years[15], finding that successful replantation was more favorable than amputation. A systematic review of transradial, elbow disarticulation, or transhumeral traumatic amputations compared functional and psychological outcomes among 301 patients who underwent replantation and 172 patients who underwent revision amputation from 41 observational studies[23]. The authors concluded that replantation had good functional results and higher satisfaction, independent of objective functional outcome. These civilian studies suggest that upper-extremity replantation leads to improved outcomes over amputation with prosthetic fitting, in contrast to the results of our study. These differences suggest that data from civilian trauma populations may not be directly applicable to military populations given the unique mechanisms of injury and likely differences in immediate care, social support, and access to rehabilitation and prosthetic devices.

The comparable outcomes that we found may be explained by several factors related to improved amputee care. Military amputees have access to the best prosthetic technology available with few financial restrictions. Modern prosthetic devices capable of complex tasks and with many degrees of freedom such as myoelectric limbs were also routinely available to this cohort[13]. Reiber et al.[40] showed that military personnel who have undergone upper-extremity amputation take advantage of the newest prosthetic technologies, with each patient receiving nearly 5 different prosthetic devices, on average, since amputation. However, Gajewski and Granville[41] suggested that focused rehabilitation for up to a year or even longer and the dedication of physiatrists, therapists, and patients improve functional outcomes in military amputees. Lastly, robust social support services for amputees likely also play an important role.

The rates of depression and PTSD among injured veterans in this study were concerning. In prior studies of Global War on Terror veterans, the rates of depression and PTSD varied substantially depending on definitions, method of diagnosis (e.g., self-report or formal evaluation), and population studied (military operation and armed service branch). Using the same criteria as the current study, the prevalence of major depression has been reported to be 9.3% to 9.6% and the prevalence of PTSD has been reported to be 12.0% to 23.9% among injured soldiers, which is similar to the 12.3% of soldiers with possible or probable depression and 19.4% of soldiers who screened positive for PTSD found in this study[42,43]. Alcohol use and misuse by this cohort were higher than national figures: 81.3% of participants were current drinkers compared with 68.8% for adults who were 18 to 44 years of age[44]. Additionally, 25.8% screened positive for a possible alcohol-related problem (CAGE score ≥ 1), compared with 19.4% of participants in the Millennium Cohort Study with combat exposure[45]. Surprisingly, the mean pain intensity score reported was lowest for patients with bilateral upper-extremity injuries, and only 16.7% reported pain interfering with their normal activities, compared with 16% in the general population[39]. Our findings indicate that, although these service members have access to extensive physical and occupational therapy and mental health support, additional work is needed to optimize outcomes in upper-extremity reconstruction and amputation.

The limitations of the present investigation included those inherent to any retrospective, observational study, including limitations related to the time since the injury, the use of self-reported measures, and the potential for selection bias as described in the previous METALS study[25]. The modest overall METALS participation rate of 59.8% and the differential rate between the participants who underwent amputation (64%) and those who underwent limb salvage (55%) were a potential source of bias. Although attempts were made at controlling differences between the treatment groups, there may be unmeasured differences between the 2 groups that could result in confounding. However, further analysis of the METALS study cohort has found that there are no major differences between the patients who participated in the study and those who did not consent or could not be located, reducing concerns about potential differences between the participants in each group and generalizability of results[46].

Surgical techniques for limb salvage and amputation continue to evolve, as has prosthetic technology since the subjects' injuries were treated. More refined use of nerve conduits, allograft[47], targeted reinnervation[48], and others may reduce the sequela of severe nerve injury and may provide improved prosthetic function. Enhanced myoelectric prostheses have the potential for greater dexterity and functionality, particularly if coupled with targeted reinnervation. Osseointegrated prostheses, although not approved in the United States, have the potential of obviating socket fit issues, enhancing function of upper-extremity amputees[49]. These technological and surgical advances in the treatment of severe upper-extremity injury are important and may influence outcomes in an incremental fashion. They should be studied and improved further, but such advances have not fully restored normal function after these complex, multidimensional injuries.

Severe, combat-related upper-extremity injuries are debilitating in terms of self-reported function and psychosocial health. Our results suggest that there is no difference in outcomes between those treated by amputation or limb salvage. The results of this study do not prescribe treatment by salvage or amputation, but rather point to significant long-term challenges

incurred by all severely injured patients. Surgeons must consider each injury in the context of patient needs and the resources available. Developing means of addressing or preventing PTSD, depression, chronic pain, and associated health habits may result in less disability in war casualties with severe upper-extremity injuries.

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/F371). ■

NOTE: The authors thank the service members and veterans who generously gave their time to participate in the METALS study. They also thank them and all our troops for the sacrifice they make for our country. In addition, the authors thank all of the medics, corpsmen, doctors, nurses, and therapists who cared for the participants in the METALS study. The authors specifically thank those who directly contributed to this research effort, including Major Adam Groth, Commander Robert Beer, Major Travis Burns, Major Anton Lacap, Colonel Charles Scoville (retired), Dr. Timothy McHenry, and Captain Dana C. Covey. The authors also thank the data abstractors (Caren C. Swift, Selina P. Doncevic, Davina Murphy Jeter, Caroline A. Eiteljorge, Patricia Horgas, and Sheila Menagh); Vivian Luu, who assisted in developing the METALS database; and Patti Ephraim, who provided important direction and coordination for the study early in its development. Finally, the authors especially thank their late colleague and METALS coinvestigator and study group author, Commander Michael Mazurek, who died before the current study was completed.

Stuart L. Mitchell, MD[1,2]
Roman Hayda, MD[3]
Andrew T. Chen, MD, MPH[4]
Anthony R. Carlini, MS[2]
James R. Ficke, MD[1]
Ellen J. MacKenzie, PhD[2]

[1]Department of Orthopaedic Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

[2]Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

[3]Department of Orthopaedic Surgery, Brown University Warren Alpert School of Medicine, Providence, Rhode Island

[4]Department of Orthopaedic Surgery, University of North Carolina School of Medicine, Chapel Hill, North Carolina

E-mail address for R. Hayda: roman_hayda@brown.edu

ORCID iD for S.L. Mitchell: 0000-0001-9066-1088
ORCID iD for R. Hayda: 0000-0003-0061-155X
ORCID iD for A.T. Chen: 0000-0001-8662-5295
ORCID iD for A.R. Carlini: 0000-0003-1419-4515
ORCID iD for J.R. Ficke: 0000-0002-0275-4223
ORCID iD for E.J. MacKenzie: 0000-0002-5480-8502

References

1. Belmont PJ Jr, McCriskin BJ, Hsiao MS, Burks R, Nelson KJ, Schoenfeld AJ. The nature and incidence of musculoskeletal combat wounds in Iraq and Afghanistan (2005-2009). J Orthop Trauma. 2013 May;27(5):e107-13.

2. Schoenfeld AJ, Dunn JC, Bader JO, Belmont PJ Jr. The nature and extent of war injuries sustained by combat specialty personnel killed and wounded in Afghanistan and Iraq, 2003-2011. J Trauma Acute Care Surg. 2013 Aug;75(2):287-91.

3. Hoencamp R, Vermetten E, Tan EC, Putter H, Leenen LP, Hamming JF. Systematic review of the prevalence and characteristics of battle casualties from NATO coalition forces in Iraq and Afghanistan. Injury. 2014 Jul;45(7):1028-34. Epub 2014 Feb 15.

4. U.S. Department of Defense. Defense Casualty Analysis System. Conflict casualties. https://dcas.dmdc.osd.mil/dcas/pages/casualties.xhtml. Accessed 2019 Apr 17.

5. 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 Apr;21(4):254-7.

6. Schoenfeld AJ, Dunn JC, Belmont PJ. Pelvic, spinal and extremity wounds among combat-specific personnel serving in Iraq and Afghanistan (2003-2011): a new paradigm in military musculoskeletal medicine. Injury. 2013 Dec;44(12):1866-70. Epub 2013 Aug 11.

7. Armed Forces Health Surveillance Center (AFHSC). Amputations of upper and lower extremities, active and reserve components, U.S. Armed Forces, 2000-2011. MSMR. 2012 Jun;19(6):2-6.

8. Tennent DJ, Wenke JC, Rivera JC, Krueger CA. Characterisation and outcomes of upper extremity amputations. Injury. 2014 Jun;45(6):965-9. Epub 2014 Feb 15.

9. Krueger CA, Wenke JC, Ficke JR. Ten years at war: comprehensive analysis of amputation trends. J Trauma Acute Care Surg. 2012 Dec;73(6)(Suppl 5):S438-44.

10. Belisle JG, Wenke JC, Krueger CA. Return-to-duty rates among US military combat-related amputees in the global war on terror: job description matters. J Trauma Acute Care Surg. 2013 Aug;75(2):279-86.

11. Stinner DJ, Burns TC, Kirk KL, Ficke JR. Return to duty rate of amputee soldiers in the current conflicts in Afghanistan and Iraq. J Trauma. 2010 Jun;68(6):1476-9.

12. Stansbury LG, Lalliss SJ, Branstetter JG, Bagg MR, Holcomb JB. Amputations in U.S. military personnel in the current conflicts in Afghanistan and Iraq. J Orthop Trauma. 2008 Jan;22(1):43-6.

13. Tintle SM, Baechler MF, Nanos GP, Forsberg JA, Potter BK. Reoperations following combat-related upper-extremity amputations. J Bone Joint Surg Am. 2012 Aug 15;94(16):e1191-6.

14. Tintle SM, Baechler MF, Nanos GP 3rd, Forsberg JA, Potter BK. Traumatic and trauma-related amputations: part II: upper extremity and future directions. J Bone Joint Surg Am. 2010 Dec 15;92(18):2934-45.

15. Pet MA, Morrison SD, Mack JS, Sears ED, Wright T, Lussiez AD, Means KR, Higgins JP, Ko JH, Cederna PS, Kung TA. Comparison of patient-reported outcomes after traumatic upper extremity amputation: replantation versus prosthetic rehabilitation. Injury. 2016 Dec;47(12):2783-8. Epub 2016 Oct 19.

16. Larson JV, Kung TA, Cederna PS, Sears ED, Urbanchek MG, Langhals NB. Clinical factors associated with replantation after traumatic major upper extremity amputation. Plast Reconstr Surg. 2013 Oct;132(4):911-9.

17. Graham B, Adkins P, Tsai TM, Firrell J, Breidenbach WC. Major replantation versus revision amputation and prosthetic fitting in the upper extremity: a late functional outcomes study. J Hand Surg Am. 1998 Sep;23(5):783-91.

18. Woodruff SI, Galarneau MR, Sack DI, McCabe CT, Dye JL. Combat amputees' health-related quality of life and psychological outcomes: a brief report from the Wounded Warrior Recovery Project. J Trauma Acute Care Surg. 2017 Mar;82(3):592-5.

19. Krueger CA, Wenke JC, Cho MS, Hsu JR. Common factors and outcome in late upper extremity amputations after military injury. J Orthop Trauma. 2014 Apr;28(4):227-31.

20. Rivera JC, Glebus GP, Cho MS. Disability following combat-sustained nerve injury of the upper limb. Bone Joint J. 2014 Feb;96-B(2):254-8.

21. Paryavi E, Pensy RA, Higgins TF, Chia B, Eglseder WA. Salvage of upper extremities with humeral fracture and associated brachial artery injury. Injury. 2014 Dec;45(12):1870-5.

22. Mattiassich G, Rittenschober F, Dorninger L, Rois J, Mittermayr R, Ortmaier R, Ponschab M, Katzensteiner K, Larcher L. Long-term outcome following upper extremity replantation after major traumatic amputation. BMC Musculoskelet Disord. 2017 Feb 10;18(1):77.

23. Otto IA, Kon M, Schuurman AH, van Minnen LP. Replantation versus prosthetic fitting in traumatic arm amputations: a systematic review. PLoS One. 2015 Sep 4;10(9):e0137729.

24. Märdian S, Krapohl BD, Roffeis J, Disch AC, Schaser KD, Schwabe P. Complete major amputation of the upper extremity: early results and initial treatment algorithm. J Trauma Acute Care Surg. 2015 Mar;78(3):586-93.

25. Doukas WC, Hayda RA, Frisch HM, Andersen RC, Mazurek MT, Ficke JR, Keeling JJ, Pasquina PF, Wain HJ, Carlini AR, MacKenzie EJ. 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 Jan 16;95(2):138-45.

26. Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric characteristics of the Multidimensional Scale of Perceived Social Support. J Pers Assess. 1990 Winter;55(3-4):610-7.

27. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. N Engl J Med. 2004 Jul 1;351(1):13-22.

28. Ewing JA. Detecting alcoholism. The CAGE questionnaire. JAMA. 1984 Oct 12; 252(14):1905-7.

29. Swiontkowski MF, Engelberg R, Martin DP, Agel J. Short Musculoskeletal Function Assessment questionnaire: validity, reliability, and responsiveness. J Bone Joint Surg Am. 1999 Sep;81(9):1245-60.

30. Paffenbarger RS Jr, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. Am J Epidemiol. 1978 Sep;108(3):161-75.

31. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC, Kriska A, Leon AS, Marcus BH, Morris J, Paffenbarger Jr RS, Patrick K, Pollock ML, Rippe JM, Sallis J, Wilmore JH. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA. 1995 Feb 1;273(5): 402-7.

32. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc. 2000 Sep;32(9)(Suppl):S498-504.

33. Eaton WW, Smith C, Ybarra M, Muntaner C, Tien A. Center for Epidemiologic Studies Depression Scale: Review and Revision (CESD and CESD-R). In: Maruish ME, editor. The use of psychological testing for treatment planning and outcomes assessment. 3rd ed, vol 3, Instruments for adults. Mahwah: Lawrence Erlbaum Associates; 2004. p 363-77.

34. Schulberg HC, Saul M, McClelland M, Ganguli M, Christy W, Frank R. Assessing depression in primary medical and psychiatric practices. Arch Gen Psychiatry. 1985 Dec;42(12):1164-70.

35. Forbes D, Creamer M, Biddle D. The validity of the PTSD checklist as a measure of symptomatic change in combat-related PTSD. Behav Res Ther. 2001 Aug;39(8): 977-86.

36. Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW. Prevalence of mental health problems and functional impairment among active component and National Guard soldiers 3 and 12 months following combat in Iraq. Arch Gen Psychiatry. 2010 Jun;67(6):614-23.

37. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. Pain. 1992 Aug;50(2):133-49.

38. Engelberg R, Martin DP, Agel J, Swiontkowski MF. Musculoskeletal function assessment: reference values for patient and non-patient samples. J Orthop Res. 1999 Jan;17(1):101-9.

39. Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA. The course of chronic pain in the community: results of a 4-year follow-up study. Pain. 2002 Sep; 99(1-2):299-307.

40. Reiber GE, McFarland LV, Hubbard S, Maynard C, Blough DK, Gambel JM, Smith DG. Servicemembers and veterans with major traumatic limb loss from Vietnam war and OIF/OEF conflicts: survey methods, participants, and summary findings. J Rehabil Res Dev. 2010;47(4):275-97.

41. Gajewski D, Granville R. The United States Armed Forces Amputee Patient Care Program. J Am Acad Orthop Surg. 2006;14(10 Spec No.):S183-7.

42. Hoge CW, McGurk D, Thomas JL, Cox AL, Engel CC, Castro CA. Mild traumatic brain injury in U.S. soldiers returning from Iraq. N Engl J Med. 2008 Jan 31;358(5): 453-63. Epub 2008 Jan 30.

43. Grieger TA, Cozza SJ, Ursano RJ, Hoge C, Martinez PE, Engel CC, Wain HJ. Posttraumatic stress disorder and depression in battle-injured soldiers. Am J Psychiatry. 2006 Oct;163(10):1777-83; quiz 1860.

44. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: National Health Interview Survey, 2012. Vital Health Stat 10. 2014 Feb;10(260): 1-161.

45. Wells TS, LeardMann CA, Fortuna SO, Smith B, Smith TC, Ryan MA, Boyko EJ, Blazer D; Millennium Cohort Study Team. A prospective study of depression following combat deployment in support of the wars in Iraq and Afghanistan. Am J Public Health. 2010 Jan;100(1):90-9.

46. Frey K, Mitchell S, Pugh MJ, Amuan E, Brooke B, Rivera J, Carlini A, Johnson A, Hadya R, Ficke J, Bosse M, Potter B, MacKenzie E. Selection bias in military cohort studies: an analysis of differences between participants and non-participants in a study of service members with severe limb trauma. Poster #055 2018 Military Health System Research Symposium; 2018 Aug 20-23; Kissimmee, FL.

47. Eberlin KR, Ducic I. Surgical algorithm for neuroma management: a changing treatment paradigm. Plast Reconstr Surg Glob Open. 2018 Oct 16;6(10):e1952.

48. Kuiken T. Targeted reinnervation for improved prosthetic function. Phys Med Rehabil Clin N Am. 2006 Feb;17(1):1-13.

49. Cancio JM, Ikeda AJ, Barnicott SL, Childers WL, Alderete JF, Goff BJ. Upper extremity amputation and prosthetics care across the active duty military and veteran populations. Phys Med Rehabil Clin N Am. 2019 Feb;30(1):73-87. Epub 2018 Oct 31.