Award Number: W81XWH-14-2-0165

TITLE: GWOT Vascular Injury Study 2 Supplemental Project: Impact of Prophylactic Fasciotomy

PRINCIPAL INVESTIGATOR: Dr. Thomas Walters

CONTRACTING ORGANIZATION: The Geneva Foundation
917 Pacific Ave., Ste. 600
Tacoma, WA 98402

REPORT DATE: OCT 2018

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

X Approved for public release; distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
OCT 2018	Annual	29SEP2017 - 28SEP2018

4. TITLE AND SUBTITLE
GWOT Vascular Injury Study 2 Supplemental Project: Impact of Prophylactic Fasciotomy

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-14-2-0165

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Dr. Thomas Walters

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The Geneva Foundation
917 Pacific Ave., Ste. 600
Tacoma, WA 98402

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
US Army MEDICAL RESEARCH AND MATERIEL COMMAND
Ft Detrick, MD 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The majority of battlefield injures involve the extremities and encompasses either isolated or a combination of vascular injury, penetrating trauma, crush, blunt trauma, burns, and fractures. Each of these injuries places the wounded Service members at risk for developing acute extremity compartment syndrome (ACS). Under far forward surgical conditions the policy is to manage these at-risk patients with prophylactic fasciotomies. The objective of this study is to determine the impact of the widespread use of fasciotomies on a mortality, delayed amputation, fasciotomy related morbidities, and fasciotomy wound management.

15. SUBJECT TERMS NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE	Unclassified	13	USAMRMC
Unclassified	Unclassified	Unclassified			19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents Page

INTRODUCTION:

This is a retrospective analysis of a cohort of US service members included in the wartime vascular injury database. Information regarding service members with a lower extremity vascular injury will be used to determine fasciotomy rates, wound management, and iatrogenic complications. The impact of injury and fasciotomy on the service members' return-to-duty and long-term disability will also be examined.

KEYWORDS:

Vascular Injury
Compartment Syndrome
Extremity
Fasciotomy

ACCOMPLISHMENTS:

What were the major goals of the project?
The overall goal is to determine the impact of the widespread use of fasciotomies on current medical/surgical practices, management guidelines, medical needs, as well as future research direction. The specific aims are:

- Aim 1. Characterization of patients-demographics, injury, fasciotomy.
- Aim 2. Characterize the morbidities associated with fasciotomy.
- Aim 3. Determine the impact of fasciotomy on delayed amputation rate.
- Aim 4. Characterize fasciotomy wound management.

100% of all charts in the database have been reviewed. Characterization and analysis of data has started, but is still pending.

What was accomplished under these goals?

- FaVIO database developed and data collection is complete. The final database contains 384 fasciotomy patients and 186 non-fasciotomy patients after excluding those with only minor vascular injuries or limited injury documentation.
- This database now represents the most complete existing fasciotomy outcomes data base currently available for military extremity trauma. Furthermore it represents the most complete extremity vascular injury outcomes database for military trauma.
- All data analysis has been completed and we are currently writing the manuscripts.

What opportunities for training and professional development has the project provided?
Under the mentorship of LTC David Kauvar, MD presentations have been made and manuscripts are being prepared by residents in the BAMC Vascular Service as part of their professional development using the FaVIO data base. To date 2 vascular surgery residents have co-authored papers (Piper and Schechtman), and 1 has presented at a vascular surgery conference (Excelsior Surgical Society).

How were the results disseminated to communities of interest?
Medical Journals; Military and Civilian Medical/Surgical Conferences

What do you plan to do during the next reporting period to accomplish the goals?

The following manuscripts will be submitted during the next reporting period:

- Kauvar DS, Piper LC, Riveria JC, Miller DL, Propper B, Walters TJ. Outcomes of Lower Extremity Fasciotomy in Wartime Vascular Injury. *JAMA Surg.*
- Thomas SB, Schechtman DW, Walters TJ, Kauvar DS. Predictors and Timing of Amputations in Military Lower Extremity Arterial Injury. *J Trauma.*

IMPACT:

Nothing to report

What was the impact on the development of the principal discipline(s) of the project?
The reporting of the preliminary results of this project at medical conferences and during JPC-6/CCCRP Forward Surgical En Route Critical Care Portfolio In-Progress Review has contributed to the recongnition for a need to develop diagnostic devices to aid in the diagnosis of extremity compartment syndrome when wounded Service members face prolonged patient hold and delayed evacuation (Prolonged Field Care). This has contributed to the decision by JPC-6/CCCRP to fund a multi-center clinical trial to test near-infrared spectroscopy for diagnosis of extremity compartment syndrome. Additionally, a topic area for the most recent round of proposals by the Per Reviewed Orthopaedic Research Program (PRORP) was prompted in part from the presentation of our results.

What was the impact on other disciplines?
Nothing to report

What was the impact on technology transfer?
Nothing to report

What was the impact on society beyond science and technology?
Nothing to report

CHANGES/PROBLEMS:

A No Cost Extension request has been approved

Changes in approach and reasons for change
Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them
Nothing to report

Changes that had a significant impact on expenditures
Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to report

PRODUCTS:

Publications, conference papers, and presentations

Journal publications.

- Kauvar DS, Miller D, Walters TJ. Tourniquet use is not associated with limb loss following military lower extremity arterial trauma. *The journal of trauma and acute care surgery.* Sep 2018;85(3):495-499.

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers, and presentations.

- Piper LC, Kauvar DS, Propper B, Miller DL, Rivera JC, Walters TJ. Outcomes of Lower Extremity Fasciotomy in Wartime Vascular Injury. Excelsior Surgical Society; October 22-26, 2017; San Diego, CA.

- Kauvar DS, Walters TJ. Tourniquet Use is Not Associated with Limb Loss Following Military Lower Extremity Arterial Trauma. Military Health Services Research Symposium; Aug 20, 2018; Kissammee, FL

Website(s) or other Internet site(s)

Nothing to report\

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other Products

Nothing to report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

What individuals have worked on the project?

Name: Thomas Walters
Project Role: PI
Nearest person month worked: 2.4
Contribution to Project: Dr. Walters is a research physiologist and Chief of the Department of Expeditionary Critical Care at the U.S Army Institute of Surgical Research, San Antonio, TX and Capability Area Manager for Prolonged Field Care. His research focus is on the treatment and detection of acute compartment syndrome and related issues involving combat related muscle trauma. He is experienced in conducting retrospective studies involving battlefield extremity trauma from the wars in Iraq and Afghanistan. He is the chair of Combat Casualty Care Research Program Integrated Product Team tasked with identifying technologies to aid in the diagnosis of extremity compartment syndrome. Dr. Walters provides the necessary scientific leadership, administrative oversight, and support for all aspects of the study, and ensure personnel and departmental resources are properly aligned to achieve the scope of work.

Name: LTC David S. Kauvar, MD, FACS
Project Role: AI
Nearest person month worked: 2.4

Contribution to Project: LTC Kauvar is a board certified vascular surgeon and active duty military officer with multiple deployments to Iraq and Afghanistan. He currently oversees the vascular surgery residency program at Brooke Army Medical Center; Vascular Surgery Service. Additionally he is an Associate Professor of Surgery at the Uniformed Services University of the Health Sciences, Bethesda, Maryland. Dr. Kauvar is currently responsible for all data analysis of the deidentified data for the project and manuscript preparation, either directly or through the oversight of surgical fellows. Dr. Kauvar's experience as a military vascular surgeon coupled with his experience in retrospective data analysis and publication will ensure accurate data interpretation and publication.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
With the completion of data extraction and data entry all members of the support staff and left the project.

What other organizations were involved as partners?
Organization Name:
None

Location of Organization: *(if foreign location list country)*
Partner's contribution to the project (identify one or more)

- Financial support;
- In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);
- Facilities (e.g., project staff use the partner's facilities for project activities);
- Collaboration (e.g., partner's staff work with project staff on the project);
- Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and
- Other

SPECIAL REPORTING REQUIREMENTS:

Quad Chart: Attached

APPENDICES:

Kauvar DS, Walters TJ. Tourniquet Use is Not Associated with Limb Loss Following Military Lower Extremity Arterial Trauma. Military Health Services Research Symposium; Aug 20, 2018; Kissammee, FL

Tourniquet use is not associated with limb loss following military lower extremity arterial trauma

David S. Kauvar, MD, Diane Miller, MSN, MPH, *and* **Thomas J. Walters, PhD**, *Fort Sam Houston, Texas*

BACKGROUND:	The effect of battlefield extremity tourniquet (TK) use on limb salvage and long-term complications following vascular repair is unknown. This study explores the influence of TK use on limb outcomes in military lower extremity arterial injury.
METHODS:	The study database includes cases of lower extremity vascular injury from 2004 to 2012 with data recorded until discharge from military service. We analyzed all limbs with at least one named arterial injury from the femoral to the tibial level. Tourniquet (TK) and no TK (NTK) groups were identified. Univariate analyses were performed with significance set at $p \leq 0.05$.
RESULTS:	A total of 455 cases were included, with 254 (56%) having a TK for a median of 60 minutes (8–270 minutes). Explosive injuries (53%) and gunshot wounds (26%) predominated. No difference between TK and NTK was present in presence of fracture, level of arterial injury, type of arterial repair, or concomitant venous injury. More nerve injuries were present in the TK group, and Abbreviated Injury Scale extremity and Mangled Extremity Severity Score tended toward greater injury severity. Amputation and mortality rates did not differ between groups, but the incidence of severe edema, wound infection, and foot drop was higher in the TK group. Vascular above-knee amputation, arterial repair complication, and severe edema were higher in the TK group also ($p = 0.10$). Tourniquet duration of 60 minutes or longer was not associated with increased amputations, but more rhabdomyolysis was present.
CONCLUSION:	Field TK use is associated with wound infection and neurologic compromise but not limb loss. This may be due to a more severe injury profile among TK limbs. Increased TK times may predispose to systemic, but not limb, complications. (*J Trauma Acute Care Surg.* 2018;85: 495–499. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)
LEVEL OF EVIDENCE:	Therapeutic/care management, level IV.
KEY WORDS:	Military trauma; vascular injury; tourniquet; limb salvage; fasciotomy; extremity trauma.

The lower extremity is the most frequent site of arterial injury in modern combat trauma.[1–4] During Operations Iraqi and Enduring Freedom (OIF and OEF), lower extremity vascular injuries were identified as a major source of preventable battlefield mortality and extremity tourniquets were developed, tested, and fielded for battlefield-expedient lower limb hemorrhage control.[5–8] Tourniquets placed in the field before surgical care have been associated with decreased hemorrhage-associated mortality but are not without potential risks.[5,9–12]

Most of the published data regarding the use of combat-related lower extremity tourniquet use examines shock and survival outcomes rather than limb-specific outcomes. The published outcomes of military arterial injury focus to a greater extent on limb loss and functional parameters, but these reports have historically had very short follow-up periods limited to in-theater measures. The purpose of this study was to use a military lower extremity vascular injury database with long-term follow-up to study the influence of tourniquet use on long-term limb outcomes following arterial injury.

METHODS

This research was approved by the United States Army Medical Research and Materiel Command Institutional Review Board and was exempt from informed consent owing to the de-identified nature of the data use. This was a retrospective cohort study using data from the Fasciotomy and Vascular Injury Outcomes (FaVIO) database, a vascular injury limb salvage database with cases compiled from the Joint Theater Trauma Registry, Department of Defense Trauma Registry. Additional patient information was attained from the Medical Evaluation Board; the Physical Evaluation Board; the Theater Medical Data Store database; the Transportation Command Regulating and Command and Control Evacuation System information system; the Patient Administration Systems and Biostatistics Activity database; the Web Interface for Scanned Patient Records; and the Defense Enrollment Eligibility Reporting System database. The FaVIO database includes casualties having sustained lower extremity arterial, venous, or combined injuries (iliac through tibial) between 2004 and 2012 and who underwent at least one limb salvage procedure in the OIF or OEF theaters of operations. Data regarding the surgical management of lower extremity injuries and follow-up data regarding limb complications and outcomes are obtained from review of Department of Defense electronic clinical records. Follow-up data are available in this database from the time of injury until the casualty was discharged from military service. Casualties sustaining traumatic amputations and those with vascular injuries

Submitted: May 16, 2018, Revised: June 14, 2018, Accepted: June 18, 2018, Published online: July 17, 2018.

From the Vascular Surgery Service, San Antonio Military Medical Center, San Antonio, Texas (D.S.K.); Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, Maryland (D.S.K.); and Department of Tactical Combat Casualty Care Research, United States Army Institute of Surgical Research, Fort Sam Houston, Texas (D.M., T.J.W.).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

Address for reprints: Thomas J Walters, PhD, United States Army Institute of Surgical Research, 3551 Roger Brooke Drive, Fort Sam Houston, TX 78234; email: thomas.j.walters 22.civ@mail.mil.

DOI: 10.1097/TA.0000000000002016

managed with amputation at the index operation are excluded, as are superficial venous and unnamed arterial branch injuries. Data in FaVIO are included on a limb (rather than a patient) basis; and in the event of bilateral lower extremity vascular injuries, the more severely injured limb is included.

For this study, FaVIO was queried for limbs sustaining at least one arterial injury to the common, superficial, or deep femoral, popliteal, or tibial arteries. Limbs that arrived at the first level of surgical care with a tourniquet in place were classified as TK limbs, while those without one comprised the no tourniquet (NTK) group. The FaVIO data set does not include the precise presurgical setting of tourniquet placement (i.e., in the field or during evacuation). Tourniquet time was the time from placement in the field to removal at the first surgical level of care (Role 2 or Role 3). The Injury Severity Score and the Abbreviated Injury Scale extremity were used to quantify global and limb injury severity, respectively. Both are reported in FaVIO, as is the Mangled Extremity Severity Score, which is calculated retrospectively based on reported injury characteristics from primary records. In addition to the primary arterial injury, associated limb tissue injuries and treatment characteristics were obtained.

The primary outcome of this study was delayed amputation, defined as surgical amputation performed for any reason at any time following the initial surgical limb salvage attempt. Secondary outcomes included limb-specific neurologic, infectious, and vascular repair complications as well as patient-level systemic complications. The inclusion of complications in the database was based on their documentation in the patient's medical record. The specific clinical, radiographic, or biochemical characteristics leading to the diagnosis are not recorded; and no specific attempt was made to make additional complication diagnoses when constructing the data set. Statistical analysis was performed using SPSS Statistical Software version 24 (IBM, Armonk, NY). Chi-squared or Fisher exact test and Student *t*-test or Wilcoxon-Mann-Whitney test was used where appropriate. Statistical significance was defined at a $p < 0.05$.

RESULTS

There were 455 limbs meeting the inclusion criteria in the FaVIO database. Of these, 254 (56%) were in the TK group, with tourniquets being increasingly used over the years of the study (Fig. 1). The causes of injury for the TK and NTK groups

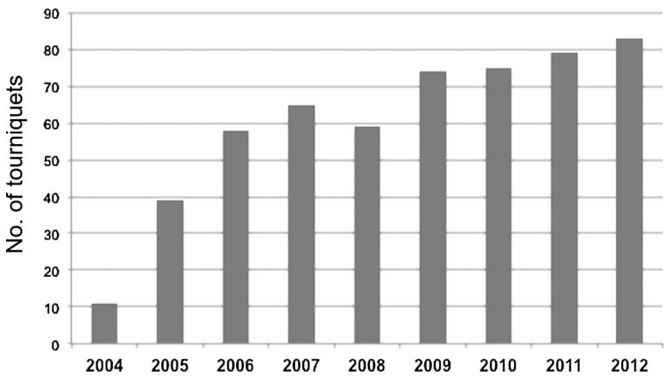


Figure 1. The number of tourniquets used over the period of study (2004–2012).

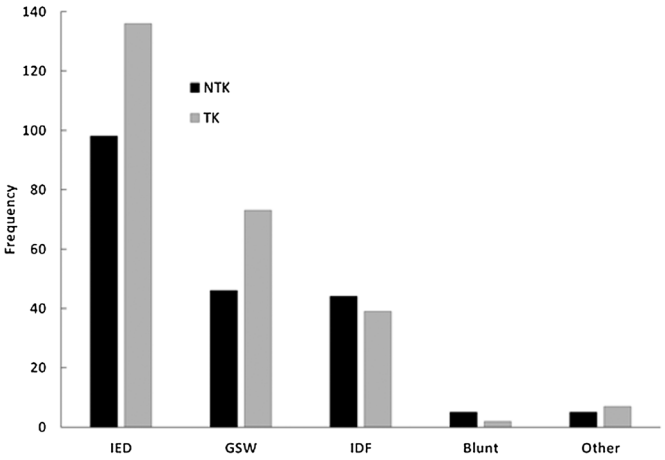


Figure 2. Cause of injury among tourniquet (TK, n = 254) and no tourniquet (NTK, n = 201) limbs. *IED*, Improvised explosive device; *GSW*, gunshot wound; *IDF*, indirect fire (includes mortar, artillery, rocket-propelled grenade); blunt includes motor vehicle and aircraft crashes.

are presented in Figure 2. Blast-related causes predominated in both groups, followed by gunshot wounds; and there were no statistical differences. Table 1 contains the injury and initial treatment characteristics for the TK and NTK groups. Somewhat more NTK casualties received their initial surgical care at a Role 2 facility. Packed red blood cells and/or whole blood transfusions were given to 44 (17%) of TK and 40 (20%) of NTK patients through their care at Role 3. No difference was seen in the overall transfusion amounts between the groups. The TK and NTK

TABLE 1. Demographic, Injury, and Surgical Treatment Characteristics

	TK (n = 254)	NTK (n = 201)	*p*
Army	173 (68)	125 (62)	
Marine Corps	65 (26)	65 (32)	
Navy/Air Force	16 (6.3)	11 (5.5)	
Age	27 ± 7	26 ± 6	NS
ISS	17 ± 9	16 ± 10	NS
AIS extremity*	3 (3–4)	3 (3–3.5)	0.02
MESS*	6 (5–7)	6 (5–7)	0.006
Role 2	112 (44)	115 (57)	0.005
Whole blood + PRBC	31 ± 26	25 ± 19	NS
Resuscitation adjunct	48 (19)	22 (11)	0.02
Fracture	153 (60)	112 (56)	NS
Nerve injury	144 (57)	91 (45)	0.015
Vascular injury AK	145 (57)	109 (54)	NS
Venous injury	50 (20)	43 (21)	NS
Arterial shunt	54 (21)	30 (15)	0.08
Arterial bypass	122 (48)	92 (46)	NS
Fasciotomy	195 (77)	134 (67)	0.02

*Median (range), Mann-Whitney U test.
Data presented as mean ± SD, and median (IQR). Data presented as n (percent).
AIS, Abbreviated Injury Scale; AK, above knee; ISS, Injury Severity Score; MESS, Mangled Extremity Severity Score; PRBC, packed red blood cells.

groups had similar global injury severity, but the distributions of Abbreviated Injury Scale extremity and Mangled Extremity Severity Score scores indicated overall greater limb injury severity in TK than NTK limbs (Figures, Supplemental Digital Contents 1 and 2, http://links.lww.com/TA/B189) Nerve injuries were more frequent in TK than NTK limbs, but the incidences of fracture and combined arterial and venous injury and the level of the highest arterial injury were similar between the groups.

An arterial bypass (as opposed to primary repair, patch angioplasty, or ligation) was the eventual formal vascular repair in similar proportions of TK and NTK limbs as was the use of an arterial shunt before definitive repair. Fasciotomy was performed more frequently in TK than NTK limbs. Adjuncts to fluid and blood resuscitation (recombinant factor VIIa and/or transexamic acid) were used more frequently in casualties with a TK, suggesting more severe shock in this cohort.

Despite greater limb injury severity in the TK group, the primary outcome of amputation following the initial limb salvage attempt was equally likely in TK (25%) as NTK (20%) limbs ($p = 0.22$). Amputations were performed at a median of 6 days (interquartile range, 2–17 days) in the TK group and 12 days (3–114 days) in the NTK group ($p = 0.317$). The distributions of amputation time in each group were heavily skewed to the left, with 18% of TK and 38% of NTK amputations performed after 30 days. Limbs undergoing amputation in the TK group had a higher proportion of early (within 48 hours) amputations (TK, 36% vs NTK, 20%), but the difference did not reach statistical significance ($p = 0.075$). Table 2 presents the limb and patient-level outcomes in the TK and NTK groups. No difference in the incidence of sensory loss, muscle contracture, or severe edema was noted between the groups. Despite similar arterial injury level, amputation above the knee was twice as likely in the TK than the NTK group, although the difference was not significant ($p = 0.10$). Severe limb edema and complications related to the vascular reconstruction were more frequently seen in TK than NTK limbs, but these differences were also not significant. Wound infection and foot drop were significantly more frequent in TK than NTK limbs. Deep venous thrombosis within the study limb developed in a greater percentage of TK (8%) than NTK (6%) limbs, but the difference was not significant ($p = 0.35$).

The mortality rate was 3% overall, with no difference between the TK and NTK groups. Rhabdomyolysis was diagnosed in 10% of casualties, again, with no difference seen between the groups. Despite equivalent proportions of deep venous thrombosis, the incidence of pulmonary embolism was significantly higher in the TK (7%) than NTK (2.5%) group.

The duration of tourniquet application was unavailable for 58 (23%) of the TK limbs. Among the remaining 77% of TK limbs, the mean tourniquet time was 72 ± 47 minutes (median, 60 minutes; range, 8–270 minutes). When TK limbs with tourniquet application times of 60 minutes or greater were compared with those with shorter durations, no difference was found in the rate of amputation (25% vs 23%, $p = 0.80$) or vascular reconstruction complication (20% vs 16%, $p = 0.39$). There was, however, a higher incidence of rhabdomyolysis among casualties with 60 minutes or greater tourniquet time (15% vs 6.2%, $p = 0.04$).

TABLE 2. Limb and Systemic Outcomes

	TK (n = 254)	NTK (n = 201)	*p*
Limb complications			
Amputation	63 (25)	40 (19)	NS
Amputation AK	28 (11)	11 (5.4)	0.11
Vascular repair	51 (20)	27 (13)	0.06
Wound infection	79 (31)	41 (20)	0.01
Contracture	21 (8.3)	11 (5.5)	NS
Foot drop	70 (28)	35 (17)	0.011
Sensory deficit	67 (26)	63 (31)	NS
Severe edema	108 (43)	70 (35)	NS
DVT	21 (8.3)	12 (6.0)	NS
Systemic complications			
Mortality	8 (3.2)	8 (4.0)	NS
Rhabdomyolysis	26 (10)	18 (9.0)	NS
Pulmonary embolism	18 (7.1)	5 (2.5)	0.026

Data presented as n (%).
AK, above knee; DVT, deep venous thrombosis.

DISCUSSION

In this analysis of data from an OIF/OEF lower extremity vascular injury database, we have demonstrated that tourniquet use before initial surgical care in limbs with arterial injury was not associated with eventual amputation despite somewhat greater limb injury severity among TK limbs. Tourniquet use was associated with the development of foot drop and wound infections and may have been associated with vascular repair complications, however.

Although there have been many publications supporting the potential lifesaving benefits of prehospital tourniquets in modern combat trauma, the association of tourniquet use with long-term limb outcomes has been unreported until now.[9–12] The observed overall amputation rate of approximately 20% in this study is comparable to that reported by Kragh et al. in an in-theater study of tourniquet use.[9] Given the longer-term follow-up in our study, this equivalence suggests that a successful initial limb salvage attempt with vascular repair is associated with long-term limb salvage whether or not a tourniquet is used to control hemorrhage before surgical care can be reached. These results speak well for the multidisciplinary limb salvage efforts of the United States combat casualty care system. Our results regarding tourniquets and amputation are also comparable to those from a recent study of extremity arterial trauma from the ongoing conflict in Syria. Longer-term follow-up was available for the casualties in this study, and tourniquet use was also not associated with eventual limb loss.[3]

We observed no difference in amputation rates between TK and NTK limbs. This is an encouraging finding in the sense that tourniquet use in the presence of an arterial injury that is surgically repaired did not predispose the affected limb to amputation. Previous comparative studies of military tourniquet use have reported on all extremity injury patterns (including traumatic amputations), while our study contained only intact limbs with arterial injuries. One possible explanation for our observed equivalence in the amputation rate between the TK and NTK groups is that, by virtue of having an arterial injury, all

limbs in both groups had some degree of distal ischemia. The additional tourniquet-induced ischemia in the TK group may have presented a relatively smaller metabolic burden for distal limb tissues compared to that in previous reports in which only some of the limbs had an arterial injury and many tourniquets were placed on limbs that had sustained traumatic amputations.[9] Our finding of a lack of association of a tourniquet use duration of over 1 hour with amputation is also comparable to that reported in the Kragh study, which reported increased amputations only after 2 hours of tourniquet time.[9] The increase in rhabdomyolysis among casualties with longer duration tourniquet times seems to be a novel finding and may result from our longer-term period of follow-up and the fact that all limbs in our study underwent attempted salvage, therefore inviting the potential for ischemia-reperfusion injury. Interestingly, the rate of rhabdomyolysis in our study was markedly less than the 31% rate reported by Stewart et al.[13] for casualties injured during the same period in Iraq and Afghanistan.

Complications following repair of combat-related lower extremity arterial injuries have been reported in a number of clinical series with short-term follow-up from OIF and OEF. Such complications can include graft or native arterial stenosis or thrombosis and anastomotic dehiscence, pseudoaneurysm, or arteriovenous fistula. These complications have typically been reported in 5% to 10% of cases and have been associated with early amputation.[2,4,14,15] Our observed incidence of repair-related complications exceeds this benchmark, likely resulting from the capture among our data of complications that arose following evacuation out of the combat theater. Tourniquet use has not previously been identified as a risk factor for arterial repair complications, and although not statistically significant, we did observe a higher rate of such complications among TK limbs, with one-fifth of TK limbs having at least one. With the unique long-term limb complication follow-up available in the FaVIO database, we are able to suggest that the increased arterial repair complications seen in TK limbs may be related to coexisting limb complications such as infection.

As our findings indicate, tourniquets are not risk-free interventions; and in this study, their use was associated with increased wound infections and the neurologic complication of foot drop. The association between tourniquet use and wound infection in lower extremity combat trauma has been previously reported as has an association with the use of fasciotomy.[16,17] As has previously been reported, the use of fasciotomy was greater in tourniquet than nontourniquet limbs, and it is possible that the wound infection rate was influenced by the increased wound burden present in limbs with fasciotomy.[18] Increased foot drop among tourniquet-treated lower extremities with arterial repairs has not previously been reported, but tourniquet use has been associated with transient nerve palsies in combat casualties, and ischemia-reperfusion has been demonstrated to impact neuromuscular functional recovery in large and small animal hemorrhage models.[9,19–21] Additionally, tourniquet-induced neural injury is well documented following surgical use of tourniquets[22] and is thought to be caused by compression injury induced by the sheer force under the tourniquet.[23,24] Although the nerve injury rate was higher in tourniquet limbs in the current study, we cannot definitively discern whether the association with foot drop resulted from the use of the tourniquet or from a primary motor nerve injury.

This study has several limitations. Foremost among them is the retrospective nature of the data contained in the parent FaVIO database. Point-of-care records from combat theaters are notoriously sparse, and it is possible that key pieces of information regarding the primary injury patterns and initial care procedures are missing from our data. Additionally, the timing of specific procedures cannot be reliably ascertained from the data available for analysis. Finally, when examining long-term limb outcomes with potentially imperfect initial injury data, it can be impossible to determine whether a specific intervention (such as a tourniquet) was responsible for an observed outcome. This may particularly be the case with chronic nerve deficits, which can result from direct wounding of a nerve in proximity to a blood vessel, limb ischemia-reperfusion injury caused by arterial injury or shock, or by a surgical or other intervention such as the tourniquet or incomplete fasciotomy.[19,25]

CONCLUSION

In combat-related lower extremity trauma with arterial injury, tourniquet use before initial surgical care was not associated with early or eventual limb loss despite increased limb injury severity. Tourniquet use was associated with some eventual adverse limb outcomes, however, indicating that tourniquets should continue to be used for well-defined indications and rapid surgical control of limb hemorrhage should remain a priority during modern military operations.

ACKNOWLEDGMENTS

The authors express their sincere gratitude to Ms Julie E Cutright and Ms Leslie M Dubois for efforts performing patient data extraction and data entry.

This research was funded by grant number W81XWH-14-2-0165 from the US Army Medical Research Materiel Command to TJW through the Geneva Foundation.

DISCLOSURE

The authors declare no conflicts of interest.

The assertions and opinions contained herein are solely those of the authors and do not represent those of the US Army, the Department of Defense, or any other official entity.

This study was conducted under a protocol reviewed and approved by the US Army Medical Research and Materiel Command Institutional Review Board and in accordance with the approved protocol.

The authors acknowledge the Department of Defense Trauma Registry (DoDTR) and the Patient Administration Systems and Biostatistics Activity (PASBA) for providing data for this study.

REFERENCES

1. Markov NP, DuBose JJ, Scott D, Propper BW, Clouse WD, Thompson B, Blackbourne LH, Rasmussen TE. Anatomic distribution and mortality of arterial injury in the wars in Afghanistan and Iraq with comparison to a civilian benchmark. *J Vasc Surg*. 2012;56:728–736.
2. Peck MA, Clouse WD, Cox MW, Bowser AN, Eliason JL, Jenkins DH, Smith DL, Rasmussen TE. The complete management of extremity vascular injury in a local population: a wartime report from the 332nd Expeditionary Medical Group/Air Force Theater Hospital, Balad Air Base, Iraq. *J Vasc Surg*. 2007;45:1197–1204; discussion 1204–1195.
3. Şişli E, Kavala AA, Mavi M, Sarıosmanoğlu ON, Oto Ö. Single centre experience of combat-related vascular injury in victims of Syrian conflict: retrospective evaluation of risk factors associated with amputation. *Injury*. 2016; 47:1945–1950.

4. Clouse WD, Rasmussen TE, Peck MA, Eliason JL, Cox MW, Bowser AN, Jenkins DH, Smith DL, Rich NM. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. *J Am Coll Surg*. 2007;204:625–632.
5. Kragh JF, O Neill ML, Beebe DF, Fox CJ, Beekley AC, Cain JS, Parsons DL, Mabry RL, Blackbourne LH. Survey of the indications for use of emergency tourniquets. *J Spec Oper Med*. 2011;11:30–38.
6. Kragh JF Jr, Walters TJ, Westmoreland T, Miller RM, Mabry RL, Kotwal RS, Ritter BA, Hodge DC, Greydanus DJ, Cain JS, et al. Tragedy into drama: an American history of tourniquet use in the current war. *J Spec Oper Med*. 2013;13:5–25.
7. Kragh JF Jr, Dubick MA, Aden JK, McKeague AL, Rasmussen TE, Baer DG, Blackbourne LH. U.S. Military use of tourniquets from 2001 to 2010. *Prehosp Emerg Care*. 2015;19:184–190.
8. Walters TJ, Wenke JC, Kauvar DS, McManus JG, Holcomb JB, Baer DG. Effectiveness of self-applied tourniquets in human volunteers. *Prehosp Emerg Care*. 2005;9:416–422.
9. Kragh JF Jr, Walters TJ, Baer DG, Fox CJ, Wade CE, Salinas J, Holcomb JB. Practical use of emergency tourniquets to stop bleeding in major limb trauma. *J Trauma*. 2008;64(Suppl 2):S38–S49; discussion S49–50.
10. Kragh JF, Walters TJ, Baer DG, Fox CJ, Wade CE, Salinas J, Holcomb JB. Survival with emergency tourniquet use to stop bleeding in major limb trauma. *Ann Surg*. 2009;249:1–7.
11. Kragh JF Jr, Nam JJ, Berry KA, Mase VJ Jr, Aden JK 3rd, Walters TJ, Dubick MA, Baer DG, Wade CE, Blackbourne LH. Transfusion for shock in US military war casualties with and without tourniquet use. *Ann Emerg Med*. 2015;65:290–296.
12. Beekley AC, Sebesta JA, Blackbourne LH, Herbert GS, Kauvar DS, Baer DG, Walters TJ, Mullenix PS, Holcomb JB, 31st Combat Support Hospital Research Group. Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes. *J Trauma*. 2008; 64(Suppl 2):S28–S37 discussion S37.
13. Stewart IJ, Faulk TI, Sosnov JA, Clemens MS, Elterman J, Ross JD, Howard JT, Fang R, Zonies DH, Chung KK. Rhabdomyolysis among critically ill combat casualties: associations with acute kidney injury and mortality. *J Trauma Acute Care Surg*. 2016;80:492–498.
14. Woodward EB, Clouse WD, Eliason JL, Peck MA, Bowser AN, Cox MW, Jones WT, Rasmussen TE. Penetrating femoropopliteal injury during modern warfare: experience of the Balad Vascular Registry. *J Vasc Surg*. 2008;47:1259–1264; discussion 1264–1255.
15. Fox CJ, Perkins JG, Kragh JF Jr, Singh NN, Patel B, Ficke JR. Popliteal artery repair in massively transfused military trauma casualties: a pursuit to save life and limb. *J Trauma*. 2010;69(Suppl 1):S123–S134.
16. Brown KV, Murray CK, Clasper JC. Infectious complications of combat-related mangled extremity injuries in the British military. *J Trauma*. 2010; 69(Suppl 1):S109–S115.
17. Clasper JC, Brown KV, Hill P. Limb complications following pre-hospital tourniquet use. *J R Army Med Corps*. 2009;155:200–202.
18. Kragh JF Jr, Wade CE, Baer DG, Jones JA, Walters TJ, Hsu JR, Wenke JC, Blackbourne LH, Holcomb JB. Fasciotomy rates in Operations Enduring Freedom and Iraqi Freedom: association with injury severity and tourniquet use. *J Orthop Trauma*. 2011;25:134–139.
19. Hancock HM, Stannard A, Burkhardt GE, Williams K, Dixon P, Cowart J, Spencer J, Rasmussen TE. Hemorrhagic shock worsens neuromuscular recovery in a porcine model of hind limb vascular injury and ischemia-reperfusion. *J Vasc Surg*. 2011;53:1052–1062; discussion 1062.
20. Walters TJ, Kragh JF, Kauvar DS, Baer DG. The combined influence of hemorrhage and tourniquet application on the recovery of muscle function in rats. *J Orthop Trauma*. 2008;22:47–51.
21. Walters TJ, Kragh JF, Baer DG. Influence of fiber-type composition on recovery from tourniquet-induced skeletal muscle ischemia-reperfusion injury. *Appl Physiol Nutr Metab*. 2008;33:272–281.
22. Mohler LR, Pedowitz RA, Lopez MA, Gershuni DH. Effects of tourniquet compression on neuromuscular function. *Clin Orthop Relat Res*. 1999; 213–220.
23. Nitz AJ, Matulionis DH. Ultrastructural changes in rat peripheral nerve following pneumatic tourniquet compression. *J Neurosurg*. 1982;57: 660–666.
24. Ochoa J, Fowler TJ, Gilliatt RW. Anatomical changes in peripheral nerves compressed by a pneumatic tourniquet. *J Anat*. 1972;113:433–455.
25. Ritenour AE, Dorlac WC, Fang R, Woods T, Jenkins DH, Flaherty SF, Wade CE, Holcomb JB. Complications after fasciotomy revision and delayed compartment release in combat patients. *J Trauma*. 2008;64(Supp 2l): S153–S161; discussion S161–152.

GWOT Vascular Injury Study 2 Supplemental Project: Impact of Prophylactic Fasciotomy

BAA Log Number 13180003

W81XWH-14-2-0165

PI: Thomas J. Walters, Ph.D. **Org:** USAISR/The Geneva Foundation **Award Amount:** $791,101

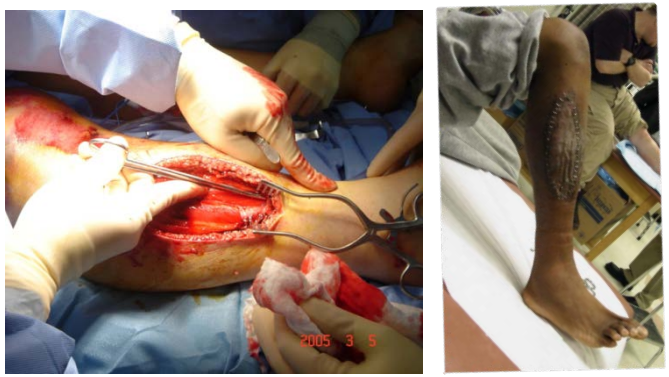
Study/Product Aim(s)

•Specific Aim 1: Identify patients that received fasciotomies and characterize the data relating to demographics, mortality, primary injury, complications, return-to-duty, long-term disabilities.

•Specific Aim 2: Determine the incidence of morbidities associated with fasciotomy; 3) assess the impact of fasciotomy on delayed amputation; and 4) characterize fasciotomy wound management.

Approach

This study will involve a retrospective analysis of a cohort of US Service members included in the GWOTVII database. Information regarding fasciotomy wound management and iatrogenic complications of fasciotomy will be obtained from individual patient records. Information specific for return to duty and long-term disability will be obtained from the Physical Evaluation Board Liaison Office for each branch of service.



(Left) Fasciotomy of the anterior compartment of the lower leg. (Right) The need to close fasciotomy wound with skin graft suggests that muscle swelling was sufficient to induce compartment syndrome. This project will examine the complications and morbidities associated with fasciotomy wounds.

Timeline and Cost

Activities	Year 1	Year 2	Year 3
Obtain IRB/HRPO approval, Hire Staff and FaVIO database development			
Extract data from GWOTVII database			
Conduct Chart Reviews			
Data Analysis and Reporting			
Estimated Budget ($791K)	**$339K**	**$452K**	**$000K**

Updated: 11 July 2018

Goals/Milestones

CY14 Goal – Protocol/Staffing

☑Write and submit protocol to IRB

☑Hire project manager

CY15 Goals – Data Collection

☑Obtain IRB and HRPO approval

☑Complete staff hiring

☑Extract data

☑Conduct chart reviews

CY16 Goals – Data Collection & Analysis

☑Conduct chart reviews (89% of 851 records reviewed)

☑Analyze data (in progress)

❑Submit results for publication (pending results)

Comments/Challenges/Issues/Concerns

- Currently PI and AI working on analysis and publication

Budget Expenditure as of 29 June 2018

Projected Expenditure: $791,101

Actual Expenditure: $740,139