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TITLE: Joint Global War on Terror (GWOT) Vascular Injury Study 2

PRINCIPAL INVESTIGATOR: LTC Zachary Arthurs, MD

RECIPIENT: The Geneva Foundation
Tacoma, WA 98402

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14. ABSTRACT The objective of the proposed study is to initiate a large-scale investigation of patient based outcomes following extremity vascular injury in the wars in Afghanistan and Iraq. This study proposes to link acute injury and clinical management information from the Joint Theater Trauma Registry (JTTR) to authentic patient-based outcomes years following injury. In this effort, the study aims to provide novel information on amputation and return to duty rates as well as to characterize the relationship between eventual quality of limb and psychological recovery or well-being.					
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1. INTRODUCTION:

The objective of the proposed study is to initiate a large-scale investigation of patient based outcomes following extremity vascular injury in the wars in Afghanistan and Iraq. This study proposes to link acute injury and clinical management information from the Joint Theater Trauma Registry (JTTR) to authentic patient-based outcomes years following injury. In this effort, the study aims to provide novel information on amputation and return to duty rates as well as to characterize the relationship between eventual quality of limb and psychological recovery or well-being. Finally, this program aims to characterize and compare the physical and emotional burden in large cohorts of US service personnel having had successful limb salvage or amputation in the years following extremity vascular injury. An updated vascular study is needed to evaluate long-term outcomes and lifelong follow-up of the injured Service Member with vascular injury.

2. **KEYWORDS:** extremity vascular injury, extremity, vascular injury, vascular trauma, vascular injury management, survey, OIF, OEF, Iraq, Afghanistan, Iraq, deployment, training

3. ACCOMPLISHMENTS:

What were the major goals of the project?

- **Study Phase I (Acute and Mid-Term Data Collection):**
 - Several databases, including the JTTR, WISPR, PASBA, JPTA, AHLTA, DEERS, etc., will be searched to identify Service Members who incurred vascular injury in theater.
 - To augment data on acute injury characteristics and management strategies, a retrospective review of the medical records of those in the cohort will be performed.
- **Study Phase II (Patient Based Outcomes):**
 - Service Members identified via the database established in Phase I will be contacted to obtain status information to include the most recent date of vascular follow-up.
- **Study Phase III (Analysis):**
 - Information from Phase I and Phase II will be analyzed to provide comprehensive descriptive information on the patient cohort pertaining to demographics, injury information and management strategies.

What was accomplished under these goals?

Phase I & II- Project was awarded on February 2013. At the beginning of Study Phase I, we developed the surveillance program design and identified Service Members who incurred vascular injury. Two research nurse coordinators, one research fellow, one technical writer and one biostatistician were hired in support of the award. The GWOT 2 Wartime Vascular Injury Study is an ongoing effort, therefore, the number injured continues to grow contingent upon additional potential subjects that are added to the database from yearly queries derived from the Department of Defense Trauma Registry (DoDTR). The Principal Investigator, Col Todd Rasmussen, changed duty stations, and he is now at Fort Detrick in Combat Casualty Care.

LTC Zachary Arthurs was selected to be the incoming PI of this effort by Col Rasmussen and has taken leadership of the protocol. HRPO approval was obtained September 9, 2014.

4,193 potential subjects have been identified with 3,725 records verified. Of those records, 1,574 did not meet criteria for inclusion, 1,418 were successfully contacted by the research staff, and 686 consented to be included in the survey. From the consented subgroup, 518 health surveys and 380 vascular surveys have been returned. For the 2015 reporting year, 524 new patients were added to the database however, many did not

meet the inclusion criteria. 226 contact attempts were made for the new inclusions with 14 surveys returned. During IRB protocol review delays, the research staff reviewed all past records for quality control purposes and found updated contact information for 55 existing records. New attempts were made to contact the 55 patients with updated contact information resulting in 6 completed surveys. Also during this reporting period, attempts were made to scan and enter in data from the Vietnam Vascular Registry. 167 records were manually scanned from the VVR files.

On the regulatory side, Annual Continuing Review was completed and conditionally approved on 1 Jul 2015. After stipulations were met, full approval was received on 15 Jul 2015. After extended work, IRB approved Amendment 30 in July 2015. A minor amendment 31, primarily for staffing changes, was approved in January 2016. IRB Continuing Review approved 13JUL2016 and USAISR Protocol Audit Passed 22SEPT2016. After approval of a NCE in January 2016, RNCs continued to work on adding records to the database. Of note during this reporting period is the large drop off in new potential subjects. The team continued to screen incoming potential subjects, contact, consent and include in the study with some limited success.

As of 31JAN2017, 22 additional records have been verified in the GWOT database to bring the total to 3795. Of those, 14 records did not meet criteria bring the excluded total to 1,615. 7 new extremity injuries were identified for a new total of 1,585. 5 new subjects were contacted successfully but unfortunately, there was no increase in survey consents which remains at 689. 525 SF36 (Quality of Life) surveys have been completed with 380 vascular surveys completed.

Phase III – After the initial data collection through Phase I and II, we completed the initial demographic, outcome measure, and quality of life metric manuscripts. Citations are listed below. While we had met the primary aim of the study and were impressed with new long term war time injury data, we were troubled by the low rate of response to follow-up. It was our position that young injured soldiers would be willing to provide survey data; however, we had a greater than 50% non-response rate. We collectively felt that this was the missing link to understanding the long-term impact on wartime injuries. Based on historical data from Vietnam Registries, we knew that mental health, suicide, and early death were concerns in battle field injuries. We set out to identify this non-response cohort as we felt they may be soldiers that sustained the greatest injury burden.

As a first measure, we re-reviewed all non-responders and confirmed that they were called 3 times by research nurses, emailed and or mailed research questionnaires. In addition, we searched social media for updated contact information and queried the global network for new contact information. If emergency contacts were available on record, we queried those individuals. Once this was complete, we felt that all efforts were exhausted. As a next step, we opened discussions with the Audie Murphy Veteran's Administration Hospital. This initiative was titled VAVIS, VA Vascular Injury Study. The goal was to sync GWOT injury data with VA follow-up files nationally. This would solve a lot of our difficulties with the non-response rate. Most of the patients tracked may have moved or changed their contact numbers after discharge from service, and many would have different emergency contact information. All of them however would receive benefits from the VA administration. Over the course of a year, we met with the VA as well as the Institute of Surgical Research in San Antonio to fill this gap and create an amendment. Ultimately, this initiative was denied. Today, we still believe that the non-responders hold an important piece of this research area.

Final Draw Down – Toward the end of 2017, focus turned to database quality control in preparation for study draw down. In November of 2016, staff began investigating the possibility of preserving the GWOT2 data after study conclusion to allow access by future researchers.

GWOT2 study team met with Joint Trauma System (JTS) representatives who were willing to investigate transfer of GWOT2 data to JTS for future management and preservation. After budget analysis, it was determined that adequate funds remained to apply for a final NCE. The NCE would allow enough time for the database transfer to JTS custody and any final protocol modifications deemed necessary. Application for

NCE was submitted in January 2017.

GWOT2 was approved for a no cost extension of the project until 30 JUN 2017 in January of 2017. After successful meetings with Joint Trauma System, a technical review of the GWOT database determined that transfer to JTS should be relatively straightforward. In April 2017, we received verbal agreement from IRB that a de-identified version of the GWOT database would be approved for transfer to JTS for custody and preservation. Data base was successfully transferred to JTS by May 2017.

The GWOT study provided real world data on battlefield vascular injuries. This study provided direct patient outcomes via research driven follow-up endpoints, patient directed questionnaires, and quality of life outcome surveys. During the initial phase, patients were enrolled following point of injury care, revascularization, and limb salvage. Patients were queried and tracked across the entire Department of Defense. The results from this study provided critical long term volume up on practice patterns to include temporary shunting of vascular injuries, fasciotomy utilization, and tibial artery revascularization outcomes. In addition, one of the most important findings included the impact of socioeconomic status and its inter-relationship with limb related outcomes to include functional status. Our results provided a 360-degree view of the injured vascular patient and what is critical for them to achieve a functional result. A final understanding included a first-time evaluation of mental illness in patients following vascular injuries.

What opportunities for training and professional development has the project provided?

The GWOT2 Project provided professional development opportunities for its research staff as well as new research opportunities for surgical residents focusing on vascular research at SAMMC/USAISR.

How were the results disseminated to communities of interest?

We aimed at disseminating and promoting the GWOT 2 Wartime Vascular Injury Study to the research community through national civilian and military academic conferences/or meetings. Details are included in Section 6 of report. Additionally, once we complete manuscripts, these will be submitted to peer-reviewed journals for publishing.

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

Nothing to report.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Vascular injury represents a common cause of morbidity and mortality not only during wartime but also in the civilian trauma sector in the US. Historically, advances in the management of civilian disease and injury have resulted from wartime experience in the areas of burn care, resuscitation, infectious diseases and vascular surgery. What is learned from the mid and long- term follow up provided by this study will undoubtedly impact the management of age-related vascular disease in the United States. Additionally, the management of vascular injury in the civilian setting stands to benefit from the activities of this study. Given the minimal published data on host national vascular injuries, any information in this arena would be of potential benefit to developing proven management strategies. Lastly, understanding of vascular injury including limb ischemia and reperfusion is relevant to other vascular distributions including the coronary and cerebro-vascular circulations which are also prone to ischemic insult.

For the first time, this study proposes a mixed methods approach to link data from the time of injury, the subsequent medical record, and real-time patient-based outcomes assessment years after injury. In this context, the proposed study encompasses the entire timeline from point of battlefield injury to eventual perceived physical and psychological recovery. Findings from this study stand to characterize the physical

and psychological impact of extremity vascular injury and guide military providers, patients and their families as they cope with recovery from extremity injury. Finally, in characterizing the relationship between the SMFSA and the SF-36 surveys, this study promises to provide novel insight in to a long suspected, but never quantified, relationship between quality of limb and quality of life; a finding that would impact the management of military and civilian extremity injury worldwide.

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?

The GWOT data provided insight beyond the vascular injury and limb injury. The project provided areas of weakness in current rehab medicine, and areas of weakness on long-term care. This has impacted civilian providers approach to similar injury patterns.

5. CHANGES/PROBLEMS:

Nothing to report.

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.

Significant changes in use or care of human subjects

Nothing to report.

6. PRODUCTS:

• **Publications, conference papers, and presentations**

- Mid-term, amputation free survival and patient based outcomes following wartime vascular injury-The American Association for the Surgery of Trauma 18- 21 September 2014, podium presentation
- REBOA-Clinical Use and Update for Vascular Wartime Injuries-Trauma Rounds and Symposium at the Aberdeen Royal Infirmary, 7 November 2013
- Use of the Short Musculoskeletal Function Assessment for Assessing Limb- Specific Outcomes Following Extremity Vascular Injuries-Society for Military Vascular Surgery and Peripheral Vascular Surgery Society, 30 January 2014, podium presentation
- Mental health co-morbidities of service members with extremity vascular injuries acquired in Iraq and Afghanistan, Society for Trauma Nurse, 2-4 April 2014, poster presentation
- Vascular discharge education and follow-up care subsequent to wartime vascular trauma; Presented in San Antonio, TX, May 2014

- **Journal publications.**

1. Alarhayem AQ, Cohn SM, Cantu-Nunez O, Eastridge BJ, Rasmussen TE. Impact of time to repair on outcomes in patients with lower extremity arterial injuries. *J Vasc Surg.* 2018 Nov 26. pii: S0741-5214(18)32221-3. doi: 10.1016/j.jvs.2018.07.075.
2. **Rasmussen T**, Stockinger Z, Antevil J, White C, Fernandez N, White J, White P. Wartime **Vascular** Injury. *Mil Med.* 2018 Sep 1;183(suppl_2):101-104. doi: 10.1093/milmed/usy138.
3. Patel JA, White JM, White PW, Rich NM, Rasmussen TE. A contemporary, 7-year analysis of **vascular** injury from the war in Afghanistan. *J Vasc Surg.* 2018 Dec;68(6):1872-1879. doi: 10.1016/j.jvs.2018.04.038. Epub 2018 Jun 23.
4. Perkins ZB, Yet B, Glasgow S, Marsh DWR, Tai NRM, Rasmussen TE. Long-term, patient-centered outcomes of lower-extremity **vascular** trauma. *J Trauma Acute Care Surg.* 2018 Jul;85(1S Suppl 2):S104-S111. doi: 10.1097/TA.0000000000001956.
5. Rich NM, Elster EA, Rasmussen TE. The Vietnam **Vascular** Registry at 50 years: An historical perspective and continuing legacy. *J Trauma Acute Care Surg.* 2017 Jul;83(1 Suppl 1):S4-S8. doi: 10.1097/TA.0000000000001545.
6. Cannon JW, Hofmann LJ, Glasgow SC, Potter BK, Rodriguez CJ, Cancio LC, Rasmussen TE, Fries. Dismounted Complex Blast Injuries: A Comprehensive Review of the Modern Combat Experience. CA, Davis MR, Jezior JR, Mullins RJ, Elster EA. *J Am Coll Surg.* 2016 Oct;223(4):652-664.e8. doi: 10.1016/j.jamcollsurg.2016.07.009. Epub 2016 Jul 30. Review.
7. Shireman PK, Rasmussen TE, Jaramillo CA, Pugh MJ. VA **Vascular** Injury Study (VAVIS): VA-DoD extremity injury outcomes collaboration. *BMC Surg.* 2015 Feb 3;15:13. doi: 10.1186/1471-2482-15-13.
8. Scott DJ, Arthurs ZM, Stannard A, Monroe HM, Clouse WD, Rasmussen TE. Patient-based outcomes and quality of life after salvageable wartime extremity **vascular** injury. *J Vasc Surg.* 2014 Jan;59(1):173-9.e1. doi: 10.1016/j.jvs.2013.07.103. Epub 2013 Sep 13.
9. Scott DJ, Watson JD, Heafner TA, Clemens MS, Propper BW, Arthurs ZM. Validation of the Short Musculoskeletal Function Assessment in patients with battlefield-related extremity vascular injuries. *J Vasc Surg.* 2014 Dec;60(6):1620-6. doi: 10.1016/j.jvs.2014.08.060. Epub 2014 Sep 19.
10. Watson JD, Houston R 4th, Morrison JJ, Gifford SM, Rasmussen TE. A retrospective cohort comparison of expanded polytetrafluorethylene to autologous vein for **vascular** reconstruction in modern combat casualty care. *Ann Vasc Surg.* 2015;29(4):822-9. doi: 10.1016/j.avsg.2014.12.026. Epub 2015 Feb 28.
11. Villamaria CY, Morrison JJ, Fitzpatrick CM, Cannon JW, Rasmussen TE. Wartime **vascular** injuries in the pediatric population of Iraq and Afghanistan: 2002-2011. *J Pediatr Surg.* 2014 Mar;49(3):428-32. doi: 10.1016/j.jpedsurg.2013.10.002. Epub 2013 Oct

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

Nothing to report.

- **Other publications, conference papers, and presentations.**

Nothing to report.

- **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.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Col Todd E. Rasmussen, MD, FACS
 Project Role: PI
 Nearest person month worked: 2
 Contribution to Project: Col Todd E. Rasmussen is the former PI of the award.

Name: LTC Zachary M. Arthurs, MD
 Project Role: PI
 Nearest person month worked: 16
 Contribution to Project: LTC Zachary M. Arthurs is the current PI of the award

Name: Thomas Evans
 Project Role: Research Nurse
 Nearest person month worked: 36
 Contribution to Project: Mr. Evans assisted in developing the surveillance program design and continues to identify Service Members who incurred vascular injury. Mr. Evans also worked as lead on the VVR data scanning project.

Name: Joe Holguin
 Project Role: Research Nurse Coordinator
 Nearest person month worked: 11
 Contribution to Project: Mr. Holguin assisted in developing the surveillance program design and identified Service Members who incurred vascular injury

Name: Shawn Dalle Lucca
 Project Role: Technical Writer
 Nearest person month worked: 9
 Contribution to Project: Ms. Dalle Lucca provided technical writing expertise to GWOT Wartime Vascular Injury staff.

Name: Kira Long, MD
 Project Role: Research Fellow
 Nearest person month worked: 8
 Contribution to Project: Dr. Kira Long assisted in developing the surveillance program design and identified Service Members who incurred vascular injury. She has left the study.

Name: Andrea Russell
 Project Role: Research Nurse
 Nearest person month worked: 36
 Contribution to Project: Ms. Andrea Russell assisted in developing the surveillance program design and continues to identify Service Members

who incurred vascular injury for inclusion in the study. Ms. Russell also oversees all regulatory records and submissions.

Name: Lee Ann Zarzabal
Project Role: Biostatistician
Nearest person month worked: 1
Contribution to Project: Ms. Zarzabal provided biostatistician and data analysis expertise to GWOT Wartime Vascular Injury staff

Name: Diane Miller
Project Role: Research Nurse
Nearest person month worked: 6
Contribution to Project: Diane Miller assisted in developing the surveillance program design and identified Service Members who incurred vascular injury. She departed to join another research study.

Name: Irma McNamee
Project Role: Research Nurse
Nearest person month worked: 36
Contribution to Project: Irma McNamee assisted in developing the surveillance program design and continues to identify Service Members who incurred vascular injury for inclusion in the study.

Name: Julie Cutright
Project Role: Research Nurse Coordinator
Nearest person month worked: 6
Contribution to Project: Assisted in reviewing Service Member records for inclusion in the study.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

The first Principal investigator, Col Todd Rasmussen, changed duty stations and he is now at Fort Detrick in Combat Casualty Care. MAJ Zachary Arthurs was selected to be the incoming PI of this effort by Col Rasmussen and took leadership of the protocol and award. Additionally, Maj Brandon Propper assisted MAJ Zachary Arthurs to lead the program. Both are vascular surgeons at SAMMC. Geneva sent a request for PI change from Col Todd Rasmussen to MAJ Zachary Arthurs to sponsor on 20 Feb 2014. Dr. Rose Ramos and COL Lorne Blackbourne are no longer working in support of this award. MAJ Zachary Arthurs assumed the role of PI after award PI change approval.

What other organizations were involved as partners?

Organization Name: USAF 59MDW/ST Chief Scientist's Office

Location of Organization: 2200 Bergquist Dr. Ste 1., JBSA Lackland AFB, TX 78236

Partner's contribution to the project: Facilities-project staff use the partner's facilities for project activities

Organization Name: United States Institute of Surgical Research

Location of Organization: 3698 Chambers Pass, JBSA Fort Sam Houston, Tx 78234-6315

Partner's contribution to the project: Facilities-project staff use the partner's facilities for project activities; Collaboration-Support for Ms. Andrea Russell's time in support of award.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: N/A

9. APPENDICES: None