

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE (DD-MM-YYYY) 23 03 2012		2. REPORT TYPE Final Report		3. DATES COVERED (From - To) 2009-2012	
The Impact of Prophylactic Fasciotomy following porcine limb ischemia/reprofusion injury			5b. GRANT NUMBER		
			5c. PROGRAM ELEMENT NUMBER		
			5d. PROJECT NUMBER FWH20090165A		
Capt Thomas J. Percival, MD; CPT Shimul Patel; Capt Nickolay P. Markov, MD; Jerry R. Spencer RVT; Capt Gabriel E. Burkhardt, MD; Col Todd E. Rasmussen, MD			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
			8. PERFORMING ORGANIZATION REPORT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Wilford Hall Ambulatory Surgical Center 2200 Bergquist Dr. Bldg 4430 Lackland AFB TX 78236			10. SPONSOR/MONITOR'S ACRONYM(S)		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)			11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT Distribution Statement A. Approved for public release: distribution unlimited.					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF: UNCLASSIFIED			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES 2	19a. NAME OF RESPONSIBLE PERSON Todd E. Rasmussen
a. REPORT	b. ABSTRACT X	c. THIS PAGE			19b. TELEPHONE NUMBER (include area code) 210-539-0936

The Impact of Prophylactic Fasciotomy Following Porcine (*Sus scrofa*) Hind Limb Ischemia/reperfusion Injury

CAPT Thomas J. Percival MD^{1,2}, CPT Shimul Patel², CAPT Nickolay P. Markov MD^{1,2},
Jerry R Spencer RVT¹, CAPT Gabriel E. Burkhardt MD¹, COL Todd E. Rasmussen,
MD^{1,2,3}

¹Wilford Hall USAF Medical Center and Genesis Concepts & Consultants
Lackland Air Force Base, Texas

²The US Army Institute of Surgical Research, Fort Sam Houston, Texas

³The Norman M. Rich Department of Surgery
F. Edward Hebert School of Medicine
The Uniformed Services University of the Health Sciences,
Bethesda, Maryland

Keywords: Vascular injury, Extremity, Ischemia-reperfusion, Therapeutic reperfusion, Statin, Recovery, Neuromuscular, Functional, Fasciotomy

Reprint requests:

Corresponding author:

Todd E. Rasmussen MD FACS

Col United States Air Force, MC

Deputy Commander

US Army Institute of Surgical Research

3400 Rawley E. Chambers/ Suite B

Fort Sam Houston, Texas 78236

Office: 210-916-5181

Email: todd.rasmussen@amedd.army.mil

Background: Prophylactic fasciotomy has been used as an adjunct to alleviate the compartment syndrome after an ischemia reperfusion injury. It has been purposed that prophylactically treating compartment syndrome will improve neuromuscular recovery of the limb therefore improving functional limb outcome. The purpose of this study is to quantify the neuromuscular recovery of prophylactic fasciotomy in a porcine model of hind limb ischemia.

Method: Swine (*Sus Scrofa*; 76 +/-6kg) were randomly assigned to no fasciotomy or prophylactic fasciotomy after ischemia via external iliac artery occlusion and arteriotomy. Class III shock was induced via a 35% blood volume variable rate hemorrhage and external iliac artery repair was achieved after 0, 3, or 6 hours of ischemia. Prophylactic fasciotomy of the anterior compartment was performed at the time of reperfusion. Compound motor action potential, sensory nerve action potential, nerve conduction velocity and gait testing was evaluated during the 14-day survival period to calculate the composite physiologic model of recovery (PMR). Necropsy was performed for evaluation of nerve and muscle histology.

Results: In hemorrhage alone, according to the PMR the recovery was 94+/-28%, 63+/-37% and 55+/-44% at 0, 3 and 6 hours of ischemia respectively. A significant difference was noted between 0 and 6 hours of ischemia ($p<0.05$). With fasciotomy, a recovery of 97+/-72%, 98+/-80% and 42+/-39% was noted after 0, 3 and 6 hours of ischemia. Compound motor action potential showed the greatest decrement with ischemic insult. Histologic analysis is currently on going.

Conclusion: This study demonstrates the feasibility of fasciotomy in a porcine model. It validates the previous model of functional limb outcome with hemorrhage in a porcine model and shows an apparent trend towards improved functional limb outcome if vascular repair and prophylactic fasciotomy are performed within 3 hours of ischemic time.



The Impact of Prophylactic Fasciotomy Following Porcine Hind Limb Ischemia/Reperfusion Injury

Capt Thomas Percival MD, CPT Shimul Patel MD, Capt Nickolay Markov MD, Jerry Spencer RVT,
Capt Gabriel Burkhardt MD, COL Lorne Blackbourne MD FACS, Col Todd Rasmussen MD FACS
United States Army Institute of Surgical Research, Fort Sam Houston, TX 78234-6315



Introduction

Vascular injury is five times the rate of previously reported wars, with the majority of those injuries taking place in the extremities¹. Recent research has shown the ischemic threshold of 6 hours has been decreased to < 6 hours in the absence of hemorrhage² and < 3 hours in the presence of hemorrhage³. Prophylactic fasciotomy has been used to extend the ischemic threshold by alleviating compartment syndrome after ischemia reperfusion injury. The functional improvement after prophylactic fasciotomy has yet to be investigated in a translatable large survival model. The objective of this study is to establish a model of extremity compartment syndrome following vascular injury, hemorrhage and ischemia/reperfusion. An additional objective is to determine the effect of fasciotomy on measures of neuromuscular recovery. We hypothesize that prophylactic fasciotomy will improve functional outcome through the alleviation of compartment syndrome.

Methods

Thirty five female yorkshire swine (75+/-5kg) underwent 35% blood volume hemorrhage, followed by 1, 3 and 6 hours of ischemia via a right retroperitoneal iliac artery occlusion followed by standardized repair with dacron patch angioplasty and reperfusion (n=17; 1HR, 3HR, 6HR). A second cohort (n=18) underwent prophylactic fasciotomy of the anterior compartment of the hind limb following the blood volume hemorrhage and arterial repair, (1HR-F, 3HR-F, 6HR-F). Compartment pressures and measures of electromyographic (EMG) recovery were performed pre-operative, post-operative and on POD 1, 2, 7 and 14. The EMG variables were combined and compared to baseline to create the Physiologic Model of Recovery (PMR). On day 14, necropsy was performed and histologic analysis of the peroneus tertius and peroneal nerve was performed.

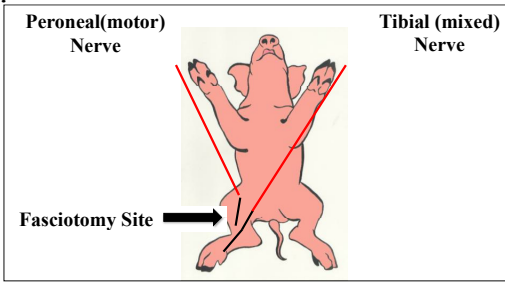


Figure. Location of Anterior Compartment Fasciotomy and Nerves evaluated for EMG. The peroneal nerve and peroneus tertius muscle are located within the anterior compartment.

Results

Compartment Pressures

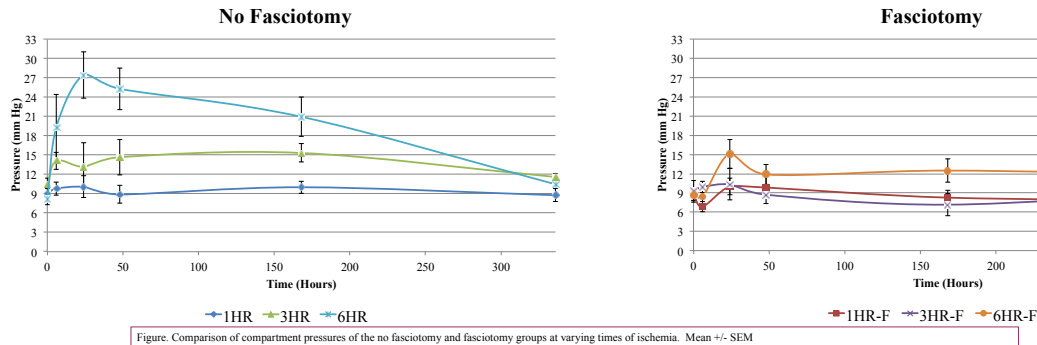


Figure. Comparison of compartment pressures of the no fasciotomy and fasciotomy groups at varying times of ischemia. Mean +/- SEM

Histologic Results

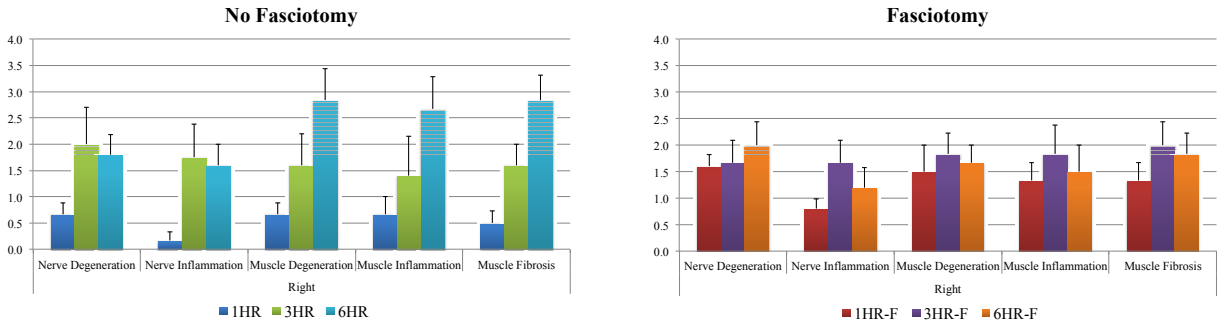


Figure. Comparison between the histologic grades of the peroneal nerve and peroneus tertius muscle between the fasciotomy and no fasciotomy groups. Mean +/- SEM
Y-Axis Scale: Muscle Score 0 = No Involvement 1 = 1-25% 2 = 26-50% 3 = 51-75% 4 = 76 - 100%, Nerve Score 0 = No Involvement 1 = Mild 2 = Moderate 3 = Severe Degeneration, Inflammation/Fibrosis 1 = Minimal 2 = Mild 3 = moderate 4 = Severe

Physiologic Model of Recovery

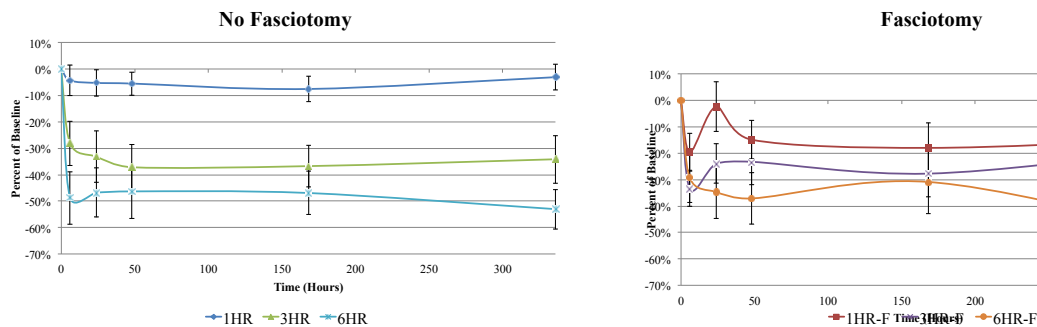


Figure. Physiologic model of recovery (combination of Compound Motor Action Potential (CMAP), Sensory Nerve Action Potential (SNAP) and Nerve Conduction Velocity (NCV)) comparison between groups. Mean +/- SEM

Variables Means (SE)	1 HR N=6	3 HR N=5	6 HR N=6	p-value	1 HR-F N=6	3HR-F N=6	6HR-F N=6	p-value
CMAP [mV]	10.3 (1.0)	5.8 (1.5)	3.2 (1.4)	<0.001	4.5 (0.3)	4.9 (1.3)	1.5 (0.7)	0.03
SNAP [uV]	15.0 (2.1)	8.1 (1.5)	5.0 (0.9)	0.04	11.5 (1.0)	11.3 (1.1)	5.1 (1.4)	0.005
AST [U/L]	44 (6)	45 (4)	52 (4)	0.65	50 (8)	45 (9)	50 (6)	0.80
Myoglobin [ng/mL]	63 (32)	39 (7)	39 (6)	0.42	48 (9)	23 (7)	21 (2)	0.36
Flows [cm/s]	59.8 (5.1)	68.3 (6.3)	61.1 (6.8)	0.08	64.2 (10.6)	44.5 (7.8)	65.1 (5.4)	0.10

Table. Characteristics at day 14.
One way ANOVA revealed a statistical difference among groups. Further analysis with post-hoc T-Tests revealed that CMAP and SNAP for the no fasciotomy group, 3 and 6 hours of ischemia were similar. These groups were different than 1 hour of ischemia. For the fasciotomy group, 1 and 3 hours of ischemia were similar, which was different that 6 hours of ischemia.
Duplex flow velocity and laboratory values to include, myoglobin, lactate, potassium, creatinine kinase, were not found to be different at the conclusion of the study.

Observations

- Compartment pressure had a statistically significant rise between all groups (1HR, 3HR & 6HR)
- Fasciotomy released compartment pressure in a statistically significant manner at 3 and 6 hours of ischemia.
- Increasing intervals of ischemia without fasciotomy showed worsening muscle damage that was mitigated by fasciotomy.
- Fasciotomy did not improve recovery at 6 hours of ischemia, 6HR 47 +/- 8% vs. 6HR-F 52 +/- 11%
- Fasciotomy at 3 hours of ischemia improved recovery, 3HR 66 +/- 9% vs. 3HR-F 81 +/- 9%

Conclusions

- Elevated compartment pressures can be obtained in a translatable model of ischemia/reperfusion injury.
- Fasciotomy successfully reduces compartment pressures and reduces the result for further damage caused by compartment syndrome.
- After 6 hours of ischemia in the presence of hemorrhage, fasciotomy does not improve the functional outcome of the limb
- Although not statistically significant, fasciotomy at 3 hours of ischemia with hemorrhage trended towards improved functional outcome.
- Fasciotomy moves the ischemic threshold from less than 3 hours to 3 to 6 hours.

Acknowledgements

The veterinary staff at the USAISR for the tireless efforts to help complete this protocol.

References

1. White JM, Stannard A, Burkhardt GE, et al. The epidemiology of vascular injury in the wars in Iraq and Afghanistan. Ann Surg. 2011 Jun;253(6):1184-9.
2. Burkhardt GE, Gifford SM, Propper B, et al. The impact of ischemic intervals on neuromuscular recovery in a porcine (Sus scrofa) survival model of extremity vascular injury. J Vasc Surg. 2011 Jan;53(1):165-73. Epub 2010 Oct 20.
3. Hancock HM, Stannard A, Burkhardt GE, et al. Hemorrhagic shock worsens neuromuscular recovery in a porcine model of hind limb vascular injury and ischemia-reperfusion. J Vasc Surg. 2011 Apr;53(4):1052-62; discussion 1062. Epub 2011 Jan 20.