Research on Tourniquet Related Injury for Combat Casualty Care[1]

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ABSTRACT

The tourniquet has been used for over 300 years for effective hemorrhage control during surgery and trauma. However, tourniquets are far from benign, causing a host of complications collectively known as tourniquet injury. A tremendous body of clinical experience and scientific research has resulted in principles of safe use and advances in tourniquet design, minimizing tourniquet injury under clinical conditions. Unfortunately, battlefield conditions preclude adherence to these safe principles and the use of surgical tourniquets. The United States Army Institute of Surgical Research (USAISR) has developed an integrated program designed to address the unique nature of tourniquet use under combat conditions with the goal of increasing the rate of limb salvage and saving lives.

1.0 INTRODUCTION

Since the tourniquet was introduced in 1674 on the battlefield by the French military surgeon, Moral, it has been routinely used to control bleeding during surgery or following extremity trauma involving severe vascular damage. While properly applied tourniquets are extremely effective in controlling hemorrhage, their use is far from benign. Tourniquet-related injury consists of compression injury to the underlying skin, nerve, and muscle, as well as ischemia/reperfusion injury (I/R) to the underlying and distal muscle and nerve [3, 4]. When tourniquets applied for long durations are removed, a severe systemic inflammatory response leading to damage to remote organs can take place, in some cases resulting in fatality [5]. This understanding has led to clinical practices and advances in tourniquet design that have minimized the risk of these complications during surgery. Specifically, minimizing tourniquet application duration to less than 2 hours and the use of wide, pneumatic tourniquets that minimize tissue compression, have led to safe and practically complication-free use [3].

Unfortunately, the circumstances that dictate the use of tourniquets on the battlefield typically exclude compliance with safety principles and tactical constraints often violate the 2-hour safe period. The duration of trauma tourniquet application is usually controlled by the length of time it takes to evacuate the soldier to a far-forward medical treatment facility for definitive vascular repair, a delay that often exceeds 2 hours. While it is well recognized that extended tourniquet application often results in the loss of muscle function or limb amputation, it has been generally accepted that the priority is “life over limb.”

[1] The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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Design is another major distinction between surgical and trauma tourniquets. The wide, pneumatic tourniquets popular in surgery today are not practical on the battlefield. Specifically, they are too large to carry. Because life-threatening extremity arterial wounds are often near the groin or auxiliary regions, the width of a surgical tourniquet may preclude effective placement for these wounds. Finally, concerns over the inherent propensity of pneumatic bladders to leak have led to their dismissal as impractical on the battlefield. As a result, the military has seen virtually no advancement in reducing tourniquet injury. Even the newly fielded one-handed tourniquet [9], while effective for hemorrhage control, does not resolve the tourniquet-related injury observed on the battlefield over 300 years ago.

It is the goal of our program to advance tourniquet design and to optimize limb salvage by integrating the relevant scientific, clinical, and military medical literature supported by our own laboratory studies to produce: 1) tourniquet guidelines; 2) medical treatments; and 3) new tourniquet designs to optimize limb salvage.

2.0 MILITARY TOURNIQUET EXPERIENCE

Although the scientific literature contains little research on the consequences of tourniquets during trauma, the pre-Vietnam military medical literature contains a wealth of relevant information based on thousands of cases involving tourniquet application. The majority of these reports document cases during WWII [10]. This information constitutes a resource virtually unknown to modern day military medical personnel, unavailable in medical reference databases. Currently, a major effort is underway to unearth this literature for future publication in the form of a review article.

What is an appropriate combat tourniquet? When is it appropriate to use a tourniquet? When and by whom should a tourniquet be removed? Under what conditions should a tourniquet not be released or removed? What are the most effective ways to increase limb salvage while using a tourniquet? These questions and concerns among soldiers, medics, and military medical officers were addressed by a panel of experts who convened at the 2003 Advanced Technology Applications for Combat Casualty Care Conference. Recommendations were made and published [8].

3.0 SMALL ANIMAL STUDIES

3.1 Characterizing Tourniquet Injury In An Animal Model.

Research to characterize tourniquet injury in an animal model at the United States Army of Surgical Research (USAISR) was initiated three years ago with the development of a rat model of tourniquet injury. Using a pneumatic tourniquet system, we have explored a range of durations of tourniquet application for which we have assessed animals at 2 hr, 2 d, or 2 wk following tourniquet release. These time points were chosen as they characterize the acute injury (2 hr), the peak of the injury process (2 d), and the intermediate stage of muscle recovery and regeneration (2 wk). Muscle injury is determined primarily by examining muscle function using an *in situ* preparation, as well as standard histology and vital staining. Muscle edema and atrophy are determined using wet weights and wet-to-dry weight ratios.

The most conspicuous response to tourniquet release is profound edema (Fig. 1). The affected limb is paralyzed, with no response to painful stimuli for at least 2 days. *In-situ*, muscles do not respond to electrical stimulation of the motor nerve. However, direct stimulation of the muscle does elicit force production, although it is well below that produced by the corresponding contralateral muscle. Taken together these observations indicate both nerve and muscle injury (Fig.2). At day 14, peak force production is similar regardless of whether the muscle is stimulated directly or via the motor. However, force production is significantly reduced compared with the contralateral control muscle [7].

Figure 1: Rat model. Representative photograph demonstrating the extreme level of edema 2 days after 4 hours of tourniquet application. The lack of toe spreading in the affected left limb indicates neural injury.

The magnitude of the injury depends on the muscle examined. The plantaris, a predominantly fast-twitch (type II) muscle is significantly more vulnerable to tourniquet injury than the predominantly slow-twitch (type I) soleus muscle. (Fig. 3)[6, 7]. A hallmark of aerobic training is a shift in the metabolic profile to that characterized by type I muscle fibers, e.g., high mitochondrial content and capillary density [2]. Thus, fitness level prior to injury may be an important mediator in determining the extent of tourniquet injury. Regardless, a better understanding of the specific reasons for these differences should help in the development of treatments that can reduce the magnitude of the injury and hasten recovery.

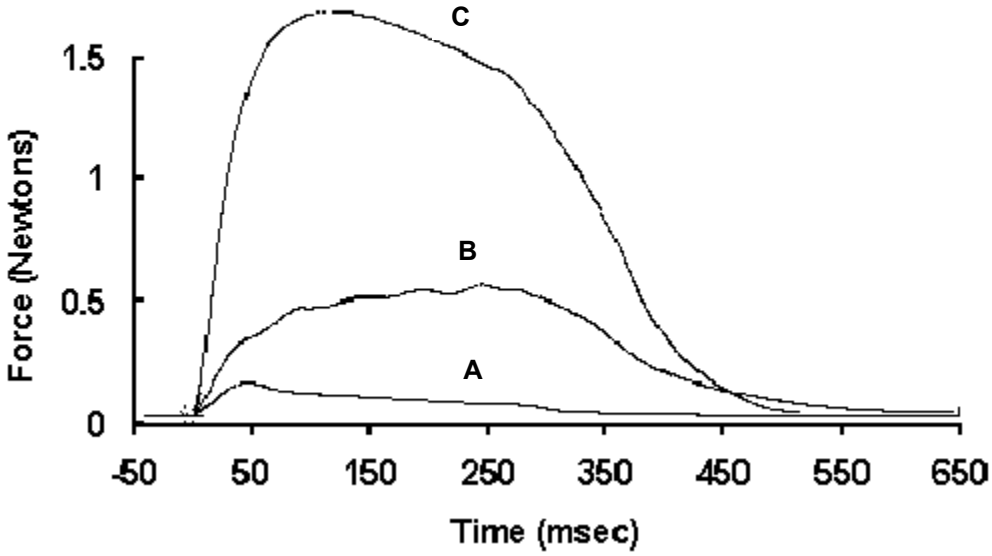

Figure 2: Force traces. Stimulation of the motor nerve resulted in little force production (A). Direct stimulation of the muscle resulted in greater force (B), demonstrating injury to motor nerve. Regardless, force is significantly reduced compared to the contralateral control (C). This pattern occurred in all animals tested on day 2 independent of muscle (soleus or plantaris) or tourniquet duration (2 or 4 hr).

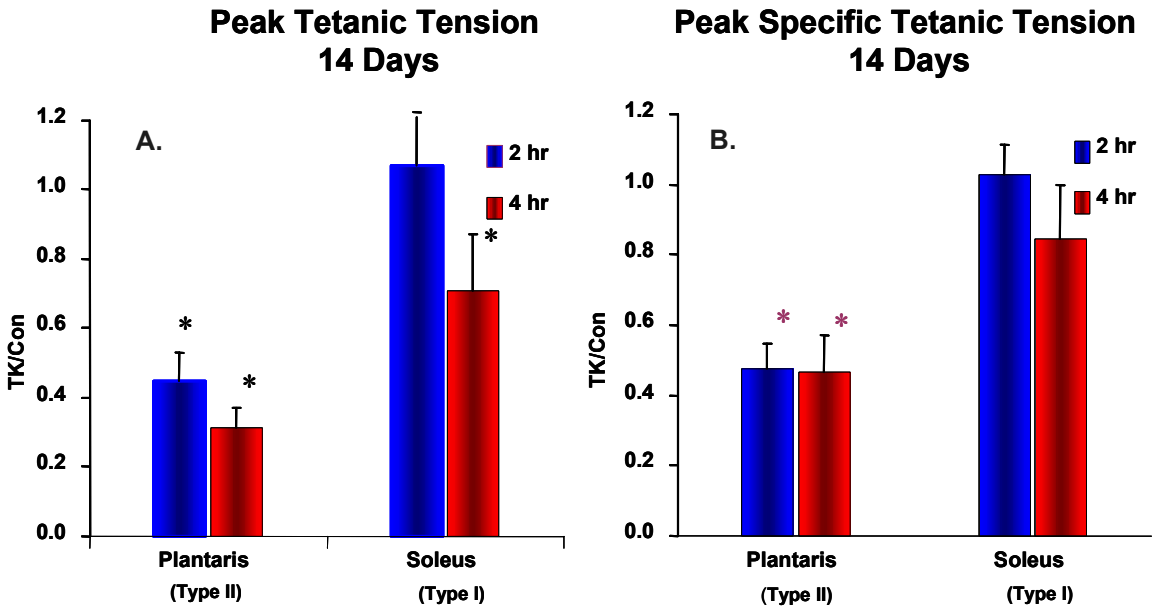

Figure 3: A) Ratio of tetanic tension of treatment/contralateral control muscles. Significant reductions took place for all muscles and treatments with the exception of the soleus at 2 hr tourniquet (TK). B) Ratio of normalized (muscle wt.) tetanic tension of treatment/contralateral control muscles. Significant reductions took place only in the plantaris, indicating an increase in non-contractile elements, probably fibrotic tissue. In contrast the reduction in force for the soleus reflects atrophy and/or fiber loss. *Different from contralateral control ($p < 0.05$).

3.2 Effect of Hemorrhage Induced Hypotension on Tourniquet Injury

Clinically, tourniquets are used to create a bloodless surgical field. In contrast, a trauma tourniquet is preceded by severe hemorrhage. We are currently addressing the question of whether hemorrhage-induced hypotension impacts the extent of tourniquet injury. In these studies animals undergo a hemorrhage of approximately 30-35% of their total blood volume, followed immediately by tourniquet application for 4 hours. These animals are then compared to appropriate groups that have undergone a sham hemorrhage. These studies are currently in progress and will be of importance in determining the injury pattern from tourniquet use after trauma-induced blood loss.

3.3 Remote Injury

Tourniquets are known to cause injury to remote organs [1, 5]. The extent of the injury is related to the duration of tourniquet application. This is of minimal clinical concern in civilian surgery, however, the extended period of time between tourniquet application on the battlefield and removal of the tourniquet at far-forward medical treatment, make it a significant concern for combat casualty care. We have done preliminary studies of the damage to all major organ systems following 3 hr of tourniquet application. A biochemical

maker of cellular stress, 3-nitrotyrosine (3-NT), was significantly elevated in the lung and liver following 3 hr of tourniquet application in our rat model (Fig.4). These responses were rather modest. However, this was not unexpected as the magnitude of systemic responses may be significantly affected by the mass of the directly injured tissue, i.e., the rather modest responses observed may be a function of the relatively small muscle mass involved within the rat model. Furthermore, while military applications dictate tourniquet use for hemorrhage control; hemorrhage *per se* has been associated with increases in nitrosative stress. We are therefore currently investigating the effects of both the mass of the injured muscle, as well as tourniquet application in combination with hemorrhage, on systemic nitrosative stress. In addition to nitrosative stress, ongoing studies are examining a number of indicators to quantify the systemic inflammatory response.

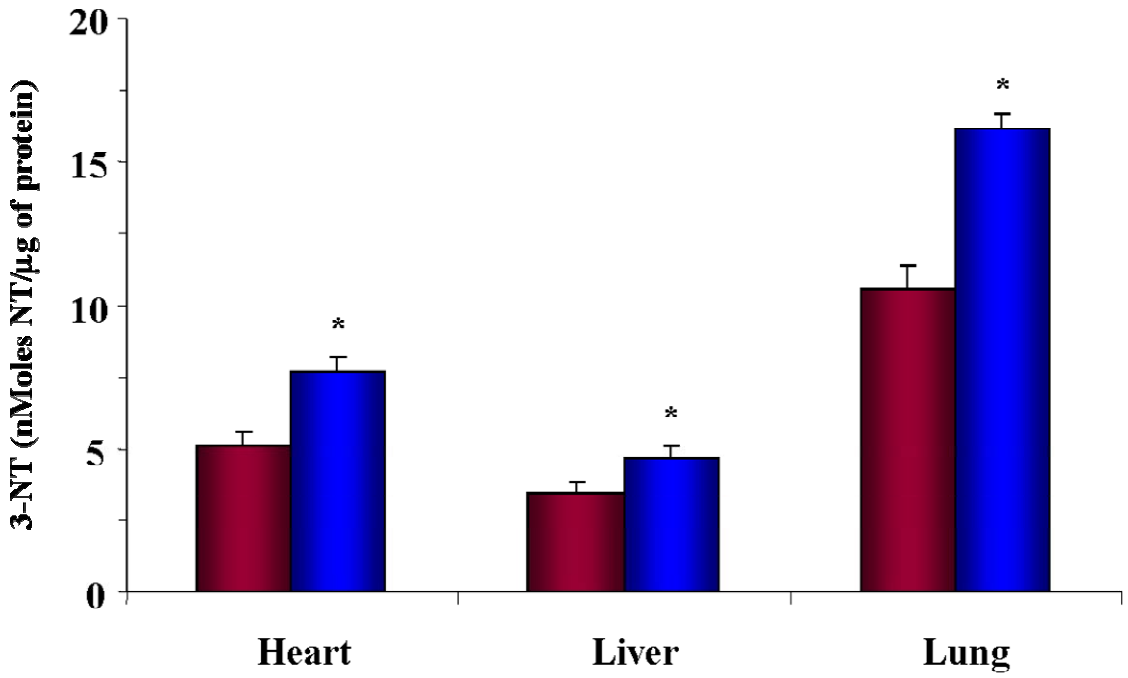

Fig. 4 3-NT levels in heart, liver and lung following 3 hrs of TK application and 2 hrs of reperfusion. *p ≤ 0.05 compared with control (CTL) value. 3-NT is an indicator of tissue damage caused by protein nitration.

3.4 Gene Expression Profiles

The reduction of tourniquet injury through the development of pharmacological interventions requires an understanding of the response of muscle to both the ischemic and reperfusion phases of injury. The most efficient method for assessing the response of a cell or tissue to injury or a drug is with gene expression analysis with cDNA microarrays. The gene expression profile of skeletal muscle in response to I/R is currently unknown so we are using this technique to characterize I/R injury in skeletal muscle using our rat

tourniquet model. An understanding of the genetic response to both ischemia and reperfusion may lead to pharmacological interventions and therapies that can address both components of this injury, leading to greater tissue salvage and ultimately saving limbs.

4.0 HUMAN STUDIES

4.1 Reducing Duration of Tourniquet Use

Many of the injurious effects of tourniquets cannot be avoided. Regardless of advances in tourniquet engineering and treatments to reduce the injury process, biophysical limits will always exist. However, recent development and fielded hemostatic agents and polymeric wound dressings can be used in conjunction with a tourniquet to reduce the required duration of tourniquet application. This scenario involves initial prompt application of a tourniquet to a severely bleeding extremity by the injured soldier or a buddy. When the tactical situation allows, a medic would then apply an appropriate wound dressing (convert), release (not remove) the tourniquet and then observe for effectiveness of the wound treatment. If hemorrhage is not adequately controlled, the tourniquet would again be tightened. Successful control of hemorrhage by a wound dressing would obviously reduce tourniquet injury, which results from physical compression. Additionally, it would reduce I/R by allowing reperfusion of the limb by the remaining patent collateral circulation. Together these factors would greatly increase the chances of limb salvage.

The preceding scenario requires a tourniquet that can be rapidly applied and easily released, and easily re-applied if required. Our lab is currently screening a number available trauma tourniquets in human subjects to determine which tourniquets best meet these requirements. This effort is composed of both laboratory and field testing. The purpose of laboratory testing is primarily to confirm that a candidate tourniquet is effective, i.e., it is capable of occluding arterial blood flow. This is assessed using Doppler auscultation. All candidates that are determined to be effective will then be field tested by combat medics. Ultimately, a multifactor selection matrix will be used to determine the best tourniquet for fielding.

5.0 PRODUCT DEVELOPMENT

5.1 Advanced Tourniquet Design

Dr. Jan Gooch, a National Research Council Senior Fellow at the USAISR, has focused on designing and engineering the initial models of the next generation of military trauma tourniquets. Ongoing interaction with Special Operation Force medics assures the design parameters meet the requisite flexibility and cube constraints required for the battlefield. As discussed above, concerns regarding inherent leaking and the bulky nature of pneumatic orthopedic tourniquets have kept these devices from being fielded for combat use. However, the appreciation of the superiority of a pneumatic design was recognized by far-forward military personal over 60 years ago [1]. Considering all of these concerns, Dr. Gooch's current prototype is a self-contained narrower version of an orthopedic tourniquet. By employing a self-inflating system equipped with a servo system to monitor and maintain a prescribed pressure, the system averts the problem of leaking. Additionally, in the event of a catastrophic leak, the system can be used in the manner of a traditional strap-and- buckle tourniquet. Formal testing of these systems on phantoms, followed by human subjects is planned for the next year.

6.0 CONCLUDING REMARKS

We have presented a description our program that takes an integrated approach to reducing tourniquet-related injury. Scientific research and military experience will produce new treatments, procedures, guidelines and devices aimed at a single goal, to change the axiom "saving life over limb" to "saving life and limb".

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