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Morbidity and mortality associated with ischemia-reperfusion injury after prolonged tourniquet use: A wartime single-center treatment algorithm

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BACKGROUND:	The evolving warfare tactics used by near-peer adversaries are expected to increase the incidence of severe extremity injuries and delayed evacuations. Initial reports from combat in Ukraine suggest high complication rates associated with prolonged tourniquet use. This study aimed to evaluate the systemic effects of limb reperfusion following tourniquet application lasting 4 hours or more in patients with isolated extremity injuries. Patients were treated according to an evidence-based protocol designed to mitigate ischemia-reperfusion injuries.
METHODS:	This retrospective review was conducted at a forward surgical facility in Ukraine during combat operations from May 2023 to February 2024. Patients with tourniquets in place for at least 4 hours were included, while those with contraindications to limb salvage or significant confounding injuries were excluded. Short-term outcomes assessed included limb salvage, organ failure, and survival rates.
RESULTS:	Of the 1,945 casualties screened, 90 (4.6%) met the inclusion criteria. After excluding 16 patients, outcomes were analyzed for 74 males, with an average age of 41.6 ± 8.5 years and a mean tourniquet duration of 7.1 ± 2.9 hours. Among these, 19 patients (25.67%) had vascular injuries, and compartment syndrome was present in all cases. Hemodialysis was required for 58 patients (70.8%), while 27 (36.3%) needed a delayed limb amputation, and 5 patients (6.7%) died. Patients requiring dialysis underwent an average of 3 ± 2 sessions to recover kidney function. Longer tourniquet times increased the need for dialysis, which increased the likelihood of patient death.
CONCLUSION:	We used a standardized ischemia-reperfusion algorithm to reduce the systemic effects of ischemia and reperfusion during attempts to salvage limbs following 4 hours or more of tourniquet time. Preliminary outcomes indicate that survival is probable, kidney function may improve with brief periods of dialysis, and limb salvage is possible in most cases. (<i>J Trauma Acute Care Surg.</i> 2025;99: S79–S85. Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)
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Explosion-related extremity injuries resulting in multiple amputations have become a hallmark of the wars during the Global War on Terror (GWOT). Tactical Combat Casualty Care

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guidelines universally train all deployed troops in the early application of tourniquets to control life-threatening extremity hemorrhage. With access to surgical care within 2 hours during the GWOT era, tourniquets were widely used with relatively few complications.^{1,2} However, changing warfare tactics used by near-peer adversaries, which favor denied air superiority, high-explosive munitions, and drone-delivered bombs, are expected to create a burden of severe extremity injuries requiring tourniquets and delayed evacuation that exceeds those seen in Vietnam, Iraq, and Afghanistan.^{3,4}

Since the onset of the Russo-Ukraine War, casualty volumes often exceed 100 per day at Role 2 facilities⁵ (Oral communication. Nov 14, 2024. MD). Survivors of large-scale engagements in such remote settings may face prolonged tourniquet application, as the lack of air superiority inhibits expedited evacuation to definitive care.⁶ Further compounding this problem is the direct intentional targeting of medical personnel by enemy forces,⁷ leading to most tourniquets being managed by nonmedical personnel (Oral communication. June 17, 2024. MD). Early reports of tourniquet use emerging from combat in Ukraine demonstrate a high rate of complications from tourniquets applied for 4 hours or more.^{4,8,9}

Data collected by the US military during the GWOT demonstrated the lifesaving potential of appropriately applied

tourniquets and the relative safety of their use when limb perfusion could be restored within 2 hours.^{10,11} Less is known about the effects of longer periods of tourniquet use. Most guidelines suggest that tourniquets should be applied for no longer than 6 hours if limb salvage is contemplated.^{4,12} Despite the GWOT experience of rapid transport of casualties to a facility with surgical capabilities, future wars may not have this advantage, requiring Prolonged Casualty Care (PCC).^{13,14} Similarly, Ukrainian combat casualty care providers have faced the need to provide care under fire for hours or days before reaching a surgical facility. Given the concern for life-threatening ischemia-reperfusion injury, most military surgeons would advise against the removal of a tourniquet that has been in place for 6 hours or more.⁴ Animal models illustrate that limb ischemia may be tolerated for even shorter periods when additional factors compound the extremity injury.^{15,16} The systemic impact of limb reperfusion between 4 and 6 hours remains uncertain; therefore, there is little guidance on managing these patients.

Our study aimed to characterize the systemic impact of limb reperfusion after 4 hours or more of tourniquet time in patients with isolated extremity injuries managed by a forward surgical team (FST) in Ukraine. This team employed an evidence-based protocol to mitigate ischemia-reperfusion injuries under PCC conditions.

PATIENTS AND METHODS

Overview

This is an institutional review board-exempt retrospective review of patients treated at a single Ukrainian austere surgical care facility in support of combat operations, equivalent to a US Role 2 FST. De-identified data were collected by patient care providers who had access to the surgical records. Charts of patients treated at a single FST in eastern Ukraine from May 2023 to February 2024 were reviewed. Patients with an extremity tourniquet in place for 4 hours or longer were included in the analysis. Patients were excluded if they had contraindications to limb salvage (traumatic amputation, severely mangled extremity, or a nonsalvageable extremity characterized by rigidity of the limb and joints) or confounding injuries (defined as major concomitant traumatic injury with an Abbreviated Injury Scale score of >3 in any other region). Patient demographics, injury characteristics (including the duration of tourniquet application), vital signs, laboratory markers of ischemia, and short-term clinical outcomes data were collected. Outcomes of interest included survival, limb salvage, and organ failure. Additional outcomes data collected included the presence of compartment syndrome and the duration of dialysis when required. The presence of compartment syndrome was determined by the presence of edematous, bulging muscle in affected compartments during fasciotomy, as documented in the surgical record. All patients were followed until discharged from the Role 3 facility. Data are reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology) checklist (Supplemental Digital Content, Supplementary Data 1, <http://links.lww.com/TA/E538>).

Care Environment

Role 2 FST staffing included two surgeons, two anesthetists, and up to 20 auxiliary staff, with two operating tables, each equipped with mechanical ventilators. Type O-negative blood was available. Facility limitations included the absence of laboratory analysis, no x-ray or computed tomography capabilities, and no holding capacity.

Patients arrived at the facility after initial lifesaving interventions had been performed (e.g., tourniquet placement, wound packing, pleural space decompression) per Tactical Combat Casualty Care guidelines.¹⁷ The facility was often overwhelmed by the number of casualties, necessitating the triage of patients based on available resources (e.g., prioritizing life over limb). The closest higher level of care was a Role 3 equivalent facility, located 2.5 hours away by ground. Vascular surgery, imaging, laboratory studies, dialysis, blood, and an intensive care unit were available at the Role 3 facility.

Therapeutic Approach

The FST patient care providers developed the following therapeutic approach based on a selective literature review, expert input, and clinical experience (Fig. 1). This management algorithm was applied to all described cases.

Upon arrival, all patients underwent an initial trauma assessment consisting of a physical examination, vital signs monitoring (heart rate, blood pressure, and SpO₂), an extended focused assessment with sonography for trauma ultrasound, urinalysis testing, and placement of intravenous access. Necessary stabilizing interventions were performed (e.g., resuscitation, intubation), followed by assessing potential limb salvage. It is important to note that, to preserve FST resources and mitigate immediate metabolic complications if a limb was deemed obviously non-salvageable by any of the previously listed criteria, the patient was transferred to the Role 3 facility for amputation with the tourniquet still in place.

Those patients eligible for tourniquet removal and reperfusion were then prepared for surgery at the Role 2. All patients received a peripheral nerve block and total intravenous sedation/analgesia for their procedures. After anesthesia was achieved, preparation for reperfusion began by administering medications and fluids designed to offset the expected cardiac instability resulting from the return of ischemic metabolites and the redistribution of blood volume into the dilated capillary beds of the affected limb (see “Medications/Fluids for Potential Reperfusion” box inset into Fig. 1).

Before reperfusion, a complete fasciotomy was performed, with a full assessment of the muscles. Tissue viability was assessed clinically using the “4 C’s”: contraction, consistency, color, and capillary bleeding. To evaluate the final “C” of capillary bleeding, the tourniquet was slowly released while the patient’s electrocardiogram was continuously monitored.

Concurrent with reperfusion, every patient received treatment with mannitol and crystalloid to reduce the effects of pigment-induced nephropathy (see “Reperfusion Treatment” box inset into Fig. 1).

Ligation or shunting of vascular injuries was performed as clinically indicated. After the procedure was completed, urine output replacement to maintain a net-even fluid balance continued until arrival at the Role 3 facility. The effectiveness of

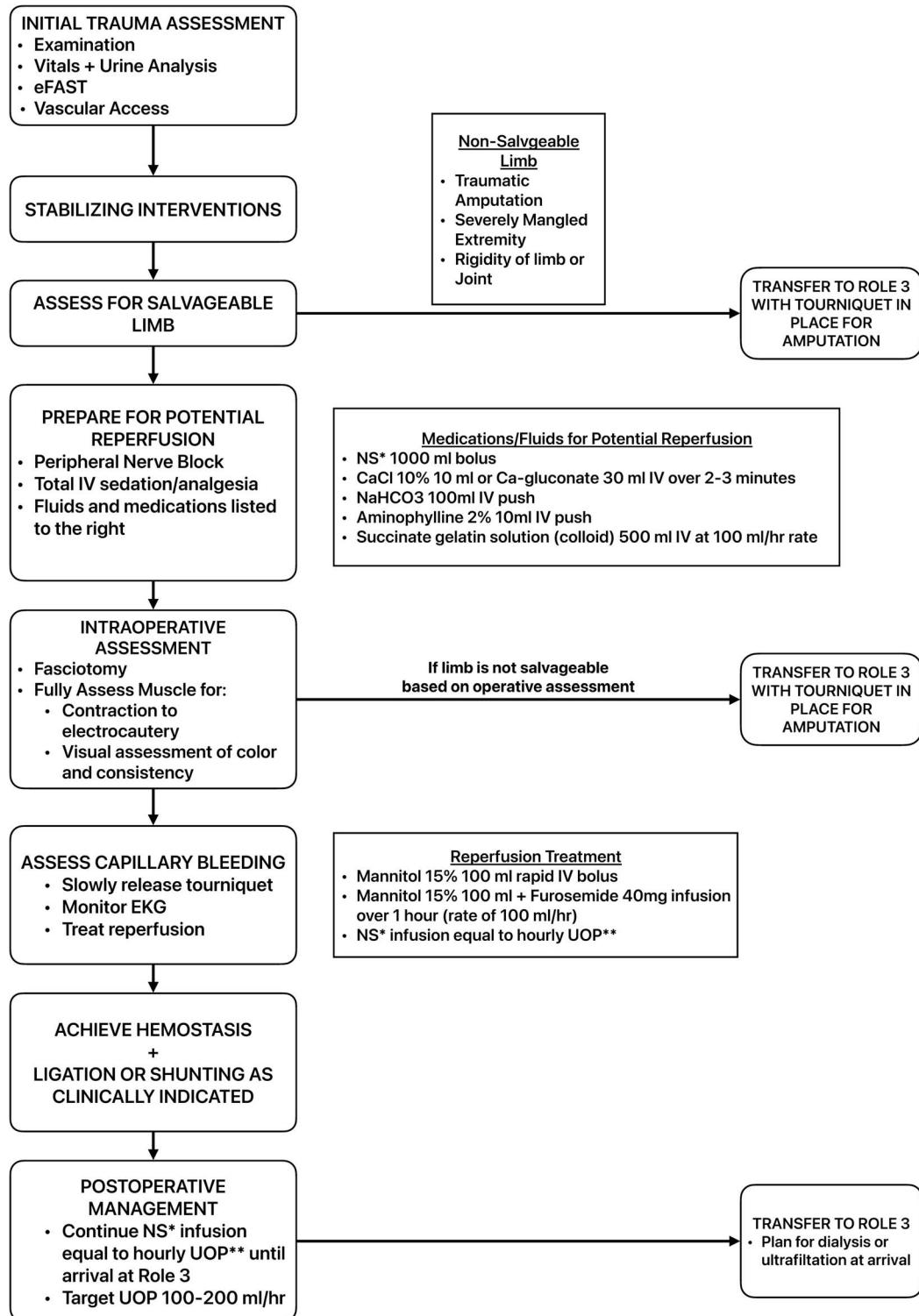


Figure 1. Treatment algorithm for the assessment and management of limbs with tourniquets in place for 4 hours or more. *NS, normal saline or NaCl 0.9%; **UOP, urine output.

resuscitation was assessed by achieving a target hourly urine output of 100 to 200 mL. Dialysis or ultrafiltration was accomplished if needed at the Role 3 facility.

Statistical Analysis

Where possible, data were tested for normality using the Shapiro-Wilk test. Data are presented as the mean with standard

error of the mean for normally distributed data and as the median with interquartile ratio for nonnormally distributed data. To examine the relationships between the tourniquet time and the complications of post-tourniquet syndrome, nonparametric statistical data analyses were performed using Friedman's two-way analysis of variance by ranks with an asymptotic significance (two-sided) level of 0.050.

RESULTS

Over the 9-month period, 1,945 casualties were treated at a single FST. Ninety patients (4.6%) met the inclusion criteria, having an extremity tourniquet in place for 4 hours or more. Sixteen patients with contraindications to limb salvage or confounding injuries were excluded, resulting in a cohort of 74 patients (3.8%) in the analysis (Fig. 2).

Summary statistics are presented in Table 1, with injury characteristics and outcomes data broken down by binned tourniquet application times. All 74 patients included in the analysis were males, with an average age of 41.6 ± 8.5 years and a mean tourniquet duration of 7.1 ± 2.9 hours. Eighteen patients (24.3%) had tourniquets in place for 4 to 5 hours, 40 patients (54.1%) for 5 to 6 hours, and 16 patients (21.6%) for more than 6 hours. Arterial injury was identified as the major source of bleeding

in 19 (25.7%) of the patients. All patients manifested compartment syndrome. The incidence of patients developing multiple complications increased with increasing tourniquet time. Patients with tourniquets in place for more than 4 hours but less than 5 hours commonly had compartment syndrome (100%) and one other complication of post-tourniquet syndrome (17 of 18), most commonly the need for temporary dialysis. Patients with tourniquets in place for longer were more likely to have compartment syndrome, the need for dialysis, and delayed amputation or death.

Nonparametric analysis using Friedman's two-way analysis of variance by ranks demonstrated a statistically significant relationship between tourniquet time and vascular injury, compartment syndrome, need for amputation, and dialysis resulting from tourniquet placement ($p < 0.02$). Significant pairwise comparisons included confirmed greater tourniquet time resulted in increased likelihood of compartment syndrome ($p < 0.04$) and the increased likelihood of death when the patient had compartment syndrome ($p < 0.001$) or dialysis ($p < 0.01$).

The urine of the first 15 injured individuals was analyzed at the Role 2 facility to detect hemoglobinuria, which was present in all cases. Hemoglobinuria increased during treatment at the Role 2 facility, reaching its peak after a 15% mannitol solution bolus was administered and slightly decreasing 30 minutes before evacuation to Role 3.

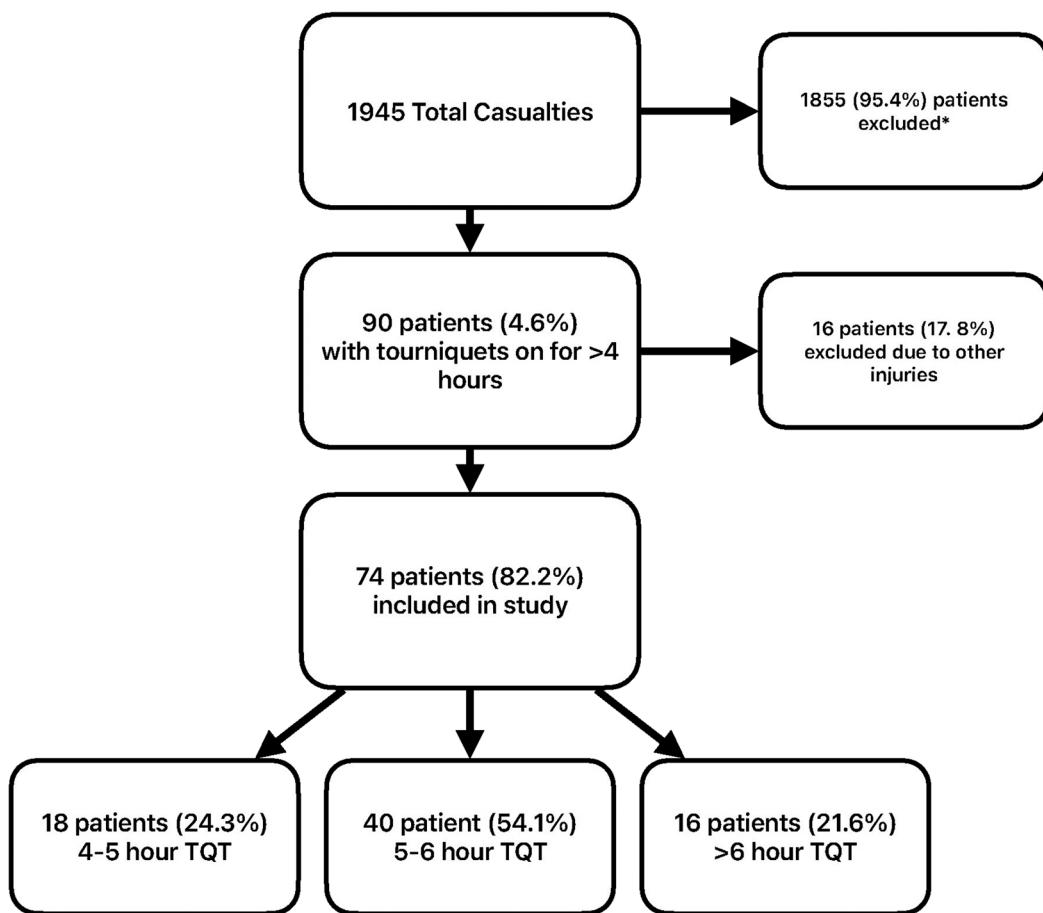


Figure 2. Distribution of study population presenting to a single FST. *Exclusion criteria: if patients had contraindications to limb reperfusion or major concomitant traumatic injury with an Abbreviated Injury Scale score of >3 in any other region. TQT, tourniquet time (duration prior to arrival).

TABLE 1. Population Demographics and Outcomes Following Prolonged Tourniquet Use

Tourniquet Time, h	Subjects, n	Arterial Injury	Incidence of PTS					
			74	19	Compartment Syndrome	Amputation	Dialysis	Major PTS
4 < 5	18	6 (33%)		18 (100%)		5 (28%)	11 (61%)	1 (5.6%)
5 < 6	40	9 (23%)		40 (100%)		16 (40%)	33 (82%)	2 (5.0%)
>6	16	4 (25%)		16 (100%)		6 (38%)	14 (88%)	2 (13%)

Significance equals $p < 0.05$. * "Major PTS" represents the combined incidences of amputation, dialysis, and death for each time bin. Significant pairwise comparisons confirmed greater tourniquet time resulted in increased likelihood of compartment syndrome ($p < 0.04$), and the increased likelihood of death when the patient had compartment syndrome ($p < 0.001$) or dialysis ($p < 0.01$). PTS, post-tourniquet syndrome.

Since Role 2 had no holding capacity, transfer to the Role 3 facility was prioritized, with only damage control interventions provided at Role 2. Within 90 minutes of arrival, all patients were evacuated by ground with paramedic support to the Role 3 hospital. All patients were treated according to the previously described algorithm and arrived at the Role 3 facility in stable condition.

Upon admission to the Role 3 hospital, all patients had elevated creatinine and urea levels (32.13 ± 8.0 mmol/L and 8.36 ± 2.8 mmol/L, respectively). Serum potassium levels were elevated (5.48 ± 0.43 mmol/L), and serum lactate level was 1.98 ± 0.58 mmol/L. All patients exhibited subcompensated metabolic acidosis: pH of 7.33 ± 0.05 , HCO₃ of 20.68 ± 2.36 mmol/L, and PaCO₂ of 40.2 ± 0.32 mm Hg. In addition, all patients experienced hypoproteinemia (45.7 ± 6.66 g/L), which normalized throughout treatment (Table 2). The rest of the patient's serum abnormalities improved over 2 days.

During Role 3 treatment, which averaged 3 ± 2 days, 58 individuals (70.8%) required acute hemodialysis, 27 patients (36.3%) required limb amputation, and 5 individuals (6.7%) died. The need for acute dialysis was based on Kidney Disease: Improving Global Outcomes (2012) and Acute Kidney Injury Network guidelines. The average number of hemodialysis sessions required at Role 3 was 3 ± 2 . The cause of death for the five casualties was unable to be obtained because of the military policy of all mortality cases being classified.

DISCUSSION

The changing landscape of the modern battlefield, with ubiquitous drone warfare and more accurate artillery, has resulted in casualty evacuation times to a surgical facility that are much longer than those seen in other recent conflicts. Adverse

tactical circumstances can result in prehospital times of 6 to 12 hours or longer.⁴ During this prolonged interval, the casualty may be under the care of a very junior medic or even nonmedical personnel. These delays to reach surgical care have resulted in many instances of prolonged tourniquet application. Tourniquets are lifesaving when indicated, but even when indicated, they can result in life-threatening metabolic derangements when left on for prolonged periods.¹⁸ Furthermore, many applied tourniquets are being found (in hindsight) not to have been indicated in the first place, thus risking the potential loss of limb or life for an intervention that was not required, as was the case for nearly 75% of the patients in this cohort. Finally, tourniquets are too often not being reassessed at the 2-hour point or before and are not being converted to a nontourniquet mode of hemorrhage control when possible.¹⁸ This results in unnecessary tourniquet ischemia. The FST in this study developed a treatment algorithm designed to counteract the systemic sequelae generated from prolonged ischemia. In our cohort, short-term outcomes demonstrate that survival was likely at 93.3%, although morbidity was high with an amputation rate of 36.6%, a 70.8% rate of dialysis, and a 100% rate of fasciotomy. Nonetheless, kidney injury improved after short periods of only 3 ± 2 sessions, and limb salvage was possible in most cases.

The management of patients with prolonged tourniquet application syndrome has not been standardized. The algorithm included in this article is an attempt to standardize the approach to managing patients with tourniquets in place for 4 hours or more, considering the tactical and operational limitations of providing care in a PCC environment. Several military guidelines assist in the management of these patients and their ischemic complications, including the Joint Trauma System Clinical Practice Guidelines for (1) Hyperkalemia and Dialysis in the Deployed Setting (CPG ID: 52), (2) Acute Extremity Compartment Syndrome and the Role of Fasciotomy in Extremity War Wounds (CPG ID: 17), and Crush Syndrome—Prolonged Field Care (CPG ID: 58).^{19–21} While data are lacking for direct comparison, outcomes using this approach at the FST appear generally favorable with a high rate of survival, limb salvage, and recovery from kidney injury.

We found that successful reperfusion could not have been accomplished without appropriately trained and prepared medical personnel with surgical resources, even when no arterial injury was identified. Universally, fasciotomy was required, and in most cases, dialysis was needed. When arterial injury was encountered, surgical capabilities were necessary to reestablish distal perfusion with damage control interventions, such as shunting. Obtaining vascular control while the tourniquet was

TABLE 2. Trend in Blood Laboratory Values Within Role 3 Setting for Revascularized Patients After Prolonged Tourniquet Use

Time	Day 1	Day 3	Change
Urea, mmol/L	8.36 ± 2.8	6.65 ± 1.59	-1.71
Creatinine, mmol/L	32.13 ± 8.0	13.8 ± 2.57	-18.33
Potassium, mmol/L	5.48 ± 0.43	4.59 ± 0.52	-0.89
pH	7.33 ± 0.05	7.39 ± 0.03	0.06
HCO ₃ , mmol/L	20.68 ± 2.36	24.89 ± 2.6	4.21
PaCO ₂ , mm Hg	40.2 ± 0.32	35.8 ± 0.48	-4.4
Lactate, mmol/L	1.98 ± 0.58	1.28 ± 0.3	-0.7
Total protein, g/L	45.7 ± 6.66	55.4 ± 5.5	9.7

in place minimized blood loss, although blood transfusion was sometimes necessary.

The anesthesia provider served two roles: providing adequate analgesia and sedation to facilitate surgery and providing critical care interventions for ischemia-reperfusion injury. Prolonged soft-tissue ischemia-induced physiological changes secondary to reperfusion result in the release of the following:

- Creatine phosphokinase and myoglobin, which caused pigmentary-induced nephropathy, acute tubular necrosis, and acute kidney injury;
- Potassium, at levels that could induce immediate life-threatening cardiac arrhythmias;
- Lactic acid, resulting in severe metabolic acidosis that can induce respiratory failure and cardiac collapse and interfere with vasopressor function;
- Redistribution of previously stagnant circulating blood volume that can lead to cardiac collapse and multi-organ failure.

Anticipating these consequences, being adequately prepared with appropriate medications, and having access to transport to a higher level of care with dialysis and intensive care unit resources were paramount for patient survival. Avoiding volatile anesthetics improved hemodynamic stability and facilitated rapid patient selection for limb salvage, saving time with limited resources and overwhelming casualties. In contrast to typical civilian practice, total intravenous anesthesia and regional anesthesia with sedation have become standards in the Ukrainian armed forces. This approach is especially valuable when managing multiple casualties with fewer resources. Patients could often be managed entirely without intubation or mechanical ventilation.

Leaving the tourniquet in place allowed the surgeons to perform fasciotomies with minimal blood loss and assess for muscle viability before releasing the tourniquet. This approach also enabled the anesthesia provider to prepare the patient for reperfusion. Resuscitative fluids and medications to enhance resistance to ischemia-reperfusion injury and promote hemodynamic stability were selected for inclusion in the FST's treatment algorithm. In preparation for tourniquet release, this protocol used intravenous administration of NaCl, CaCl or Ca-gluconate, NaHCO₃, aminophylline, and a colloid solution of succinate gelatin.²² This combination was theorized to maintain stability throughout the redistribution of circulating blood volume during limb reperfusion. Aminophylline treatment was added for renal protection because it improved renal function and indexes of renal inflammation in prior studies.²³ In addition, aminophylline has numerous anti-inflammatory effects.²⁴ When limb salvage was not possible, the applied tourniquet was left in place and delayed the development of life-threatening complications from reperfusion injury, and no ill consequence came from the prophylactic medications. Following reperfusion, the infusion of mannitol 15% was used for osmotic diuresis to add to renal protection against pigment-induced nephropathy.²⁵ Cardio-protective effects of mannitol have also been described for managing ischemia-reperfusion injury associated with cardiac surgery.²⁶ The more prolonged infusion of mannitol and furosemide was used to eliminate the products of metabolism from ischemic tissues.²⁷ Finally, mannitol is an antioxidant substance that may scavenge oxygen free radicals, protecting cells from their damage.²⁸ Continued replacement of urine output by crystalloid infusion was used

to maintain intravascular volume throughout diuresis. Limitations in cold-chain storage precluded the use of insulin and glucose as a mitigating strategy for hyperkalemia. Future advances in medical logistics may enable additional adjuncts to be included in the medical management of post-tourniquet syndrome that could further reduce the need for dialysis. Similarly, management of hypothermia was limited to passive rewarming because of equipment limitations and operational constraints associated with distributed dismounted combat.

Unsurprisingly, we found that the length of tourniquet time influenced patient outcomes. Notably, longer tourniquet times increased the need for dialysis, which increased the likelihood of patient death. Our findings underscore the critical need to establish guidance for early tourniquet conversion and to proactively mitigate post-tourniquet syndrome. While the efforts of this article focused primarily on mitigating the physiologic impact of ischemia-reperfusion injury, reducing complications from tourniquets requires a multifaceted approach.⁴ Numerous military and civilian studies have shown that, in hindsight, many wounds may not have needed a tourniquet.¹¹ We, too, found evidence of limbs lost secondary to tourniquets applied to extremities that lacked major vascular injury. Improved education and training regarding appropriate indications for tourniquet use are needed to reduce unnecessary tourniquets. Tactical Combat Casualty Care guidelines, used in the United States and Ukraine, have already been updated to reflect the need to reevaluate the appropriateness of tourniquet application as soon as tactically feasible.²⁹ Tourniquet conversion and replacement, using lower-risk hemorrhage control options such as packing and pressure dressings, is emphasized when possible.⁴ Early reevaluation for tourniquet removal, conversion, or relocation nearer the wound will need to be able to be performed by nonmedical personnel and not just professional medics. A decision support algorithm to guide tourniquet assessment by nonmedical personnel has been developed by our NATO working group and is being published separately. A presentation with educational material designed to highlight the Prolonged Tourniquet Application Syndrome problem in Ukraine has been developed and is being disseminated. This information will help military personnel recognize what types of bleeding are truly life-threatening and to emphasize the need for early tourniquet conversion whenever possible.¹⁸ Finally, efforts to reduce the time between injury and definitive care will continue to be required.

To optimize medical care for the wounded, continuous efforts are required to collect, maintain, and analyze performance data. Information regarding the mechanism of injury, injury characteristics, treatments rendered throughout the echelons of care, and longitudinal outcomes data is needed. As the use of this algorithm expands to other FSTs and follow-up information becomes available, our group will reevaluate outcomes to validate our findings. Together with the ongoing efforts of an associated NATO committee geared toward reducing the complications of tourniquets, we anticipate a reduction in limb loss.

This study is limited by the complexities of conducting research and gathering clinical data in a war zone. As such, it is a single-center, retrospective study with no comparison group for ethical reasons. Patients with other significant injuries were excluded. This choice limits confounding variables and allows for a better assessment of the protocol used, but it also limits generalizability to different patient populations. Because of

operational security issues, no long-term outcomes assessing limb function or other details could be obtained. More granular details regarding the patients' injury characteristics and causes of death could not be disclosed because of their classified nature.

CONCLUSION

Prolonged tourniquet application of 4 hours or more in isolated extremity injuries is a significant cause of morbidity in the Russo-Ukrainian War and can be life-threatening. Reducing the use of unindicated tourniquets is essential to minimize unnecessary loss of life and limb. Our proposed treatment algorithm aims to minimize the systemic effects of ischemia-reperfusion during attempts at limb salvage. Although direct comparative data are lacking, preliminary outcomes suggest that survival is probable, kidney function improves after short periods of dialysis, and limb salvage is achievable in most cases.

AUTHORSHIP

W.C.D., J.B.H., T.M.P., and F.K.B. contributed in the conception and study design. All authors contributed in the literature review. V.L. contributed in the data acquisition. All authors contributed in the data analysis and interpretation. R.M.R., W.C.D., J.B.H., S.A., S.P., and O.L. contributed in the drafting of the manuscript. All authors contributed in the critical revision.

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DISCLOSURE

Conflicts of Interest: Author Disclosure forms have been supplied and are provided as Supplemental Digital Content (<http://links.lww.com/TA/E539>). I, Rachel Russo, attest on behalf of all authors that we had full access to the data of the study, conducted all data analyses independently from the funding entity, and take complete responsibility for the integrity and accuracy of the data reported in the manuscript. The opinions and assertions expressed herein are those of the author(s) and do not reflect the official policy or position of the Medical Forces of the Armed Forces of Ukraine, Uniformed Services University of the Health Sciences, or the Department of Defense.

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