Battlefield Extracorporeal Cardiopulmonary Resuscitation for Out-of-Hospital Cardiac Arrest

A Feasibility Study During Military Exercises

Viktor A. Reva, MD, PhD[1]; Alexander A. Pochtarnik, MD[2]; Daniil A. Shelukhin, MD, PhD[3]; Andrey E. Skvortzov, MD, PhD[4]; Evgeny A. Semenov, MD, PhD[5]; Alexander A. Emelyanov, MD[6]; Artem M. Nosov, MD, PhD[7]; Konstantin N. Demchenko, MD, PhD[8]; Oleg N. Reznik, MD, PhD[9]; Igor M. Samokhvalov, MD, PhD[10]; Joseph J. DuBose, MD[11]*

ABSTRACT

Purpose: To evaluate the feasibility of prehospital extracorporeal cardiopulmonary resuscitation (E-CPR) in the military exercise setting. **Methods:** Three 40kg *Sus scrofa* (wild swine) underwent controlled 35% blood loss and administration of potassium chloride to achieve cardiac arrest (CA). During CPR, initiated 1 minute after CA, the animals were transported to Role 1. Femoral vessels were cannulated, followed by E-CPR using a portable perfusion device. Crystalloid and blood transfusions were initiated, followed by tactical evacuation to Role 2 and 4-hour observation. **Results:** All animals developed sustained asystole. Chest compressions supported effective but gradually deteriorating blood circulation. Two animals underwent successful E-CPR, with restoration of perfusion pressure to 80mmHg (70–90mmHg) 25 and 23 minutes after the induction of CA. After transportation to Role 2, one animal developed abdominal compartment syndrome as a result of extensive (9L) fluid replacement. The other animal received a lower volume of crystalloids (4L), and no complications occurred. In the third animal, multiple attempts to cannulate arteries were unsuccessful because of spasm and hypotension. Open aortic cannulation enabled the circuit to commence. No return of spontaneous circulation was ultimately achieved in either of the remaining animals. **Conclusion:** Our study demonstrates both the potential feasibility of battlefield E-CPR and the evolving capability in the care of severey injured combat casualties.

KEYWORDS: *combat trauma; extracorporeal membrane oxygenation; endovascular; battlefield; cardiac arrest; cardiopulmonary resuscitation*

Introduction

The avoidance of early mortality remains the primary focus of combat surgeons around the world. The main causes of potentially preventable deaths—hemorrhage, airway obstruction, and tension pneumothorax—have been aggressively addressed by TCCC and advanced resuscitative care (ARC) protocols to minimize mortality.[1–3] Although a variety of solutions has been proposed to prevent death, resuscitation in the setting of traumatic cardiac arrest (TCA) after combat injury remains an almost universally fatal endeavor, with no optimal intervention having been identified to support salvage of these casualties.

An 11-year database analysis of the UK Joint Theatre Trauma Registry previously reported on 424 casualties (4.6% of all registered patients) with CA caused mostly by explosive or gunshot injuries.[4] The authors found that 10.6% of casualties who arrested after arrival at the Role 3 medical treatment facility (MTF) survived to discharge, with most of them (80%) presenting with injuries consistent with major hemorrhage. Resuscitative thoracotomy was the only performed life-saving surgical procedure attempted in this series, but this heroic intervention did not affect survival.

As combat medical providers continue to strive to improve outcomes for critically unstable casualties and TCA victims, newer life-saving techniques have been proposed to expediently restore systemic and central circulation. These novel interventions include resuscitative endovascular balloon occlusion of the aorta (REBOA),[5,6] selective aortic arch perfusion,[7,8] emergency preservation and resuscitation,[9] and extracorporeal membrane oxygenation (ECMO).[10,11] Many of these techniques are now extensively used in select civilian trauma centers and have also been investigated for field implementation.[12,13]

*Correspondence to vreva@mail.ru
[1]**LTC Reva** serves in the Russian Army, MC, Department of War Surgery, Kirov Military Medical Academy, and Department of Polytrauma, Dzhanelidze Research Institute of Emergency Medicine, Saint Petersburg, Russian Federation. [2]**LT Pochtarnik** serves in the Russian Army, MC, Department of War Surgery, Kirov Military Medical Academy. [3]**Dr Shelukhin** is affiliated with the Department of Anesthesiology and Reanimatology, Nikiforov Russian Center of Emergency and Radiation Medicine of EMERCOM, Saint Petersburg. [4]**Dr Skvortzov** is affiliated with the Department of Organ Donation and Transplantation, Dzhanelidze Research Institute of Emergency Medicine, and Pavlov First Saint Petersburg State Medical University, Saint Petersburg. [5]**CPT Semenov** serves in the Russian Army, MC, Department of War Surgery, Kirov Military Medical Academy, Saint Petersburg. [6]**LTC Emelyanov** serves in the Russian Army, MC, Department of Anesthesiology and Reanimatology, Kirov Military Medical Academy. [7]**CPT Nosov** serves in the Russian Army, MC, Scientific Laboratory of War Surgery, Kirov Military Medical Academy. [8]**MAJ Demchenko** serves in the Russian Army, MC, Scientific Laboratory of War Surgery, Kirov Military Medical Academy. [9]**Dr Reznik** is affiliated with the Department of Organ Donation and Transplantation, Dzhanelidze Research Institute of Emergency Medicine, and Pavlov First Saint Petersburg State Medical University. [10]**COL Samokhvalov** served in the Russian Army, MC (Ret.), Department of War Surgery, Kirov Military Medical Academy. [11]**Col DuBose** serves in the USAF, MC, R Adams Cowley Shock Trauma Center, University of Maryland Medical System, Baltimore, MD.

While venoarterial (V-A) ECMO is increasingly being used in the setting of cardiogenic shock and CA (E-CPR) at select civilian centers, the utility of artificial circulation for hemorrhagic shock and TCA remains a matter of active investigation. Recent experience from leading trauma centers has demonstrated success in the effective use of V-A ECMO for saving severely polytraumatized patients by appropriately trained and configured teams.[10,14] To date, however, no examination of the feasibility of this intervention in an austere military environment has been reported.

Our present report outlines the results of a feasibility study conducted in the context of military exercise setting. A scenario of out-of-hospital/battlefield TCA, followed by combat casualty care and staged forward resuscitative care, was designed to simulate circumstances in which E-CPR might be potentially employed during military conflict.

Methods

Overview

This study was performed during the May 2018 and June 2019 iterations of the annual military medical exercises held at the educational center of the Kirov Military Medical Academy, Saint Petersburg, Russian Federation. For the purpose of training and investigation, we generated a specific experimental CA four-stage protocol consisting of animal preparation, induction of CA, resuscitation including ECMO initiation, and tactical evacuation on ECMO (Figure 1). All animal live-tissue training and investigations during the military exercises are conducted under annual protocols reviewed and approved by the local ethical committee. This study, spanning a 2-year period, was approved by the ethical committee of the Kirov Military Medical Academy (protocol No. 203, 20 March 2018).

Experimental Protocol

Animal preparation

Sus scrofa (wild swine) study subjects weighing 40kg each were housed in quarantine at the animal facility for 14 days. After initial sedation with 400mg tiletamine and zolazepam (Zoletil; Virbac, France), an ear vein was cannulated for primary drug administration, and the left carotid artery was exposed for placement of a 6-Fr retrograde sheath. This sheath was then used to facilitate a controlled hemorrhage, blood pressure monitoring, and blood sampling. The animal was then placed on an outdoor litter close to a simulated Role 1 MTF, consisting of a field tent facility with an operating table, a ventilator, and a basic kit of surgical instruments.

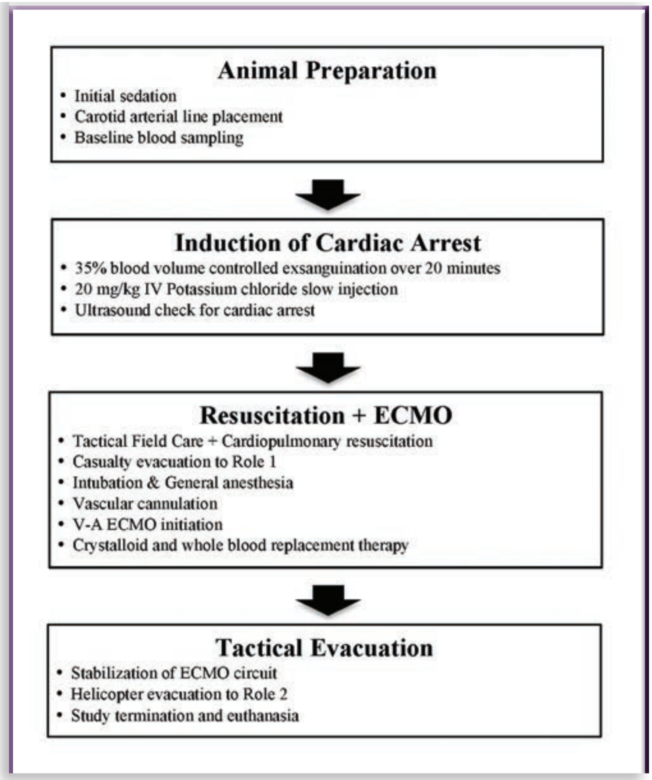
Induction of CA

We chose a combined (hemorrhage-induced plus nontraumatic) mechanism of CA for our study protocol. After controlled removal of 35% of total blood volume (stored using 1000IU of heparin per unit), 20mg/kg potassium chloride was administered. We then used ultrasound (Sonoscape S6, China) and electrocardiography to document loss of heart contractility.

CPR and ECMO Protocol

One minute after documented CA, a Lucas2 chest compression system (Jolife, Sweden) was applied over the animal's chest for ongoing CPR. During CPR, the animal was transported to a tent (Role 1) and placed on a surgical table (Figure 2).

FIGURE 1 *Experimental protocol.*



ECMO = extracorporeal membrane oxygenation; IV = intravenous; V-A = venoarterial.

FIGURE 2 *The animal admitted to a Role 1 medical treatment facility on ongoing cardiopulmonary resuscitation. Surgical cricothyrotomy is performed, and femoral vessels are explored for subsequent cannulation.*

Along with surgical cricothyroidotomy, 50IU/kg heparin was administered and emergency cannulation was performed. Both the femoral artery and vein were exposed and instrumented with 12-Fr 7.5–9" and 17- to 18-Fr short (12") or long (30") cannulae, respectively, for emergent V-A ECMO–E-CPR. Cannulae were reliably secured to the body and connected to a perfusion device. Pump flow was initiated at blood flow rate (BFR) of 600mL/min and increased slowly to 1500 to 2500mL/min. As early as 10 minutes after the ECMO procedure was initated, the animals were resuscitated with whole blood. To avoid severe hypocalcemia, small boluses of 10% calcium chloride were administered. Epinephrine was used to correct critical hypotension.

Blood samples were taken for gas analisys (i-Stat, Abbott Laboratories, IL) at the following timepoints: baseline, 5 minutes after CA (pre-ECMO), 1 hour after ECMO initiation (on-ECMO), and on admission to Role 2 before study termination (terminal-ECMO). Mean arterial pressure (MAP), flow, and saturation parameters were monitored throughout the study. The primary endpoint was the adequate level of perfusion pressure on admission to Role 2.

One experienced anesthetist-perfusionist responsible for ECMO augmented a Role 1 team consisting of an anesthetist, a military surgeon, and a scrub nurse. The air critical care transport team consisted of another anesthetist, the anesthetist-perfusionist joining the transport, and two anesthetist nurses equipped with a dedicated trauma care package. The military surgeon experienced in performing REBOA and other basic endovascular interventions in human and animals, but having no experience in large cannulae insertion, performed all cannulations in our study. No additional training for ECMO in animals was undertaken before the study began.

Field ECMO Equipment

For the ECMO circuit, we used a lightweight (3kg) portable perfusion system, Ex-Stream (TransBiotech, Ltd., Skolkovo, Russian Federation). The whole ECMO kit, weighing approximately 3–4kg (total kit dimensions, 50 × 40 × 25cm), also includes an oxygenator (Affinity Pixie, Medtronic, Fridley, MN), venous (access) and arterial (return) cannulae, a spare ECMO circuit, connectors, tubes, sterile scissors, and tubing clamps. The ECMO circuit was primed and prepared. Bio-Medicus and DLP pediatric cannulae were used for semi-Seldinger and open cannulation, respectively (all Medtronic).

Evacuation Protocol

Once the ECMO circuit was stabilized, the animal underwent immediate evacuation by a rotary wing platform to a Role 2 MTF deployed in fast adjustable pneumatic modules within the distance of a 15-minute flight (Figure 3). A single, dedicated, high-capacity Mil Mi-8 helicopter equipped with a standard medical transportation module was used for the flights.

FIGURE 3 *Tactical evacuation of the animal to Role 2 during extracorporeal cardiopulmanory resuscitation (V-A ECMO) using the portable Ex-Stream device (TransBiotech, Ltd, Skolkovo, Russian Federation).*

V-A = venoarterial.

Study Termination and Euthanasia

After delivery to the Role 2, animals were checked for MAP and possible return of spontaneous circulation (ROSC). If indicated, the swine underwent additional appropriate intervention for stabilization and continuous monitoring, such as abdominal compartment syndrome (ACS) release or/and additional vascular cannulation. If no ROSC was achieved after these procedures, death was confirmed, the study was terminated, and the ECMO circuit stopped. No postmortem examination was undertaken.

Results

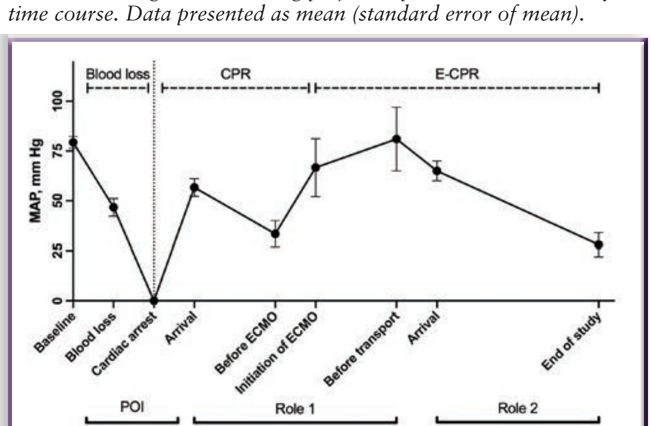
Overview

Three sedated animals underwent induction of CA at a distance of 100–150 m from the Role 1 facility and developed sustained asystole. On the scene, care providers initated intraosseus fluid replacement (200mL Ringer solution) and CPR within 1.4 minutes (range, 1–2 minutes), followed by immediate ground transportation to the Role 1, which took 5 minutes. Because of low oxygen saturations (<60%) upon admission, surgical cricothyroidotomy was performed with high-flow 100% oxygen administered via a tracheostomy tube. Lucas chest compressions supported effective but gradually deteriorating blood circulation, confirmed by decreasing MAP from initial values of 55mmHg (range, 50–65mmHg) to 40mmHg (range, 20–40mmHg) prior to ECMO initiation (Figure 4). Two of three animals underwent immediate successful cannulation and ECMO initiation, resulting in restoration of perfusion pressure to 80mmHg (range, 70–90mmHg). We ultimately evacuated these two animals to the Role 2, followed by additional surgical interventions and study termination. The arteries of animal No. 3 were unable to be cannulated after multiple attempts over an hour because of spastic small-caliber vessels. In this latter animal, the protocol was ultimately discontinued due to futility. No ROSC was ultimately achieved in either of the remaining study animals.

Successful Role 1 E-CPR

Two animals underwent a complete protocol of ECMO initiation under ongoing CPR. Cannulation of femoral vessels was performed within 20 and 18 minutes after arrival to Role 1, respectively, and restoration of flow was achieved 25 and 23

FIGURE 4 *Diagram illustrating perfusion pressure over the study time course. Data presented as mean (standard error of mean).*



CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; E-CPR = extracorporeal cardiopulmonary resuscitation; MAP = mean arterial pressure; POI = point of injury.

minutes after the induction of CA. As soon as ECMO was initiated, we stopped the external compressions. In animal No. 1, both short cannulae (a 12-Fr 9" arterial and an 18-Fr 12" venous) were inserted into the left femoral vessels using an open cutdown exposure. In animal No. 2, ultrasound-guided percutaneous access was initially attempted to achieve venous and arterial sheath placement (a 12-Fr 7.5" arterial and a 17-Fr 30"). Body movements during the CPR and small-caliber vessels hindered the ability to achieve a stable needle position, however, so access was rapidly transitioned to a semi-Seldinger technique that involved cutdown to expose the anterior vessel walls for direct needle puncture of both the femoral artery and vein.

After connection to the ECMO circuit, E-CPR was initiated with a BFR of 2.0–2.5L/min, and the ventilator was disconnected. The two study animals were initially resuscitated with 9L and 4L of crystalloids, respectively. This was followed by the infusion of 1L of stored whole blood and 10mg of calcium chloride. Thereafter, the two animals were transported with ongoing ECMO by helicopter to the Role 2 facility. After a 15-minute flight to the Role 2 and 3 hours after CA, animal No. 1 developed ACS due to severe blood loss (hemoglobin level decreased from 10.2 to 1.3g/dL), shock (MAP decreased from 97 to 34mmHg), and extensive fluid replacement. The resulting ACS contributed to inferior vena cava compression and inadequate blood drainage via the short-access venous cannula, which resulted in a drop of the ECMO circuit BFR to 400mL/min. An emergent decompressive laparotomy was subsequently peformed at the Role 2, restoring the BFR to 1.5L/min.

Animal No. 2 received a lower volume of crystalloids and developed no complications en route to the Role 2, although a similar drop in measured hemoglobin level was observed (9.5 to 1.5g/dL). Despite effective blood drainage and return, this second study animal continued to deteriorate and developed progressive shock (MAP decrease from 65 to 22mmHg). Additional carotid artery cannulation was attempted to restore BFR at the Role 2 via the addition of two arterial return cannulae, with no notable effect.

Perfusion of both animals was artifically maintained during the experimental protocol in its entirety. The protocol was terminated in both study animals after 4 hours without ROSC. We recorded no access-related complications in either of the two study animals.

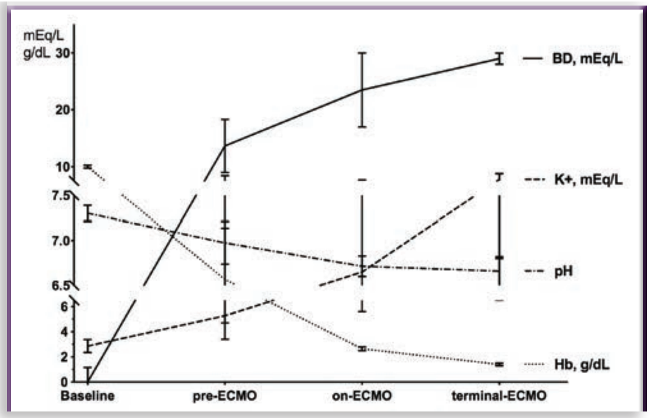
Role 1 E-CPR Failure

In animal No. 3, open femoral vein cannulation (an 18-Fr 12" cannula) was successfully achieved 17 minutes after the induction of CA. Arterial access via cutdown of the femoral, carotid, and even iliac arteries (a 12-Fr 9" cannula) was not able to be achieved, however, because of profound spasm and hypotension. Open aortic cannulation via laparotomy ultimately enabled the circuit to commence at a BFR of 1L/min. The arterial cannulae at this location were not able to be appropriately secured for transport, however. Because of these challenges and extensive bleeding from the aortic cannulation sites, the protocol for the third animal was discontinued due to futility.

Laboratory Values

Blood tests taken from all animals demonstrated a dramatic progression of metabolic acidosis because of blood loss and extensive fluid replacement therapy. The base deficit gradually increased from 0 (–2 to +2) to 29 (28 to 30), and the pH level gradually decreased from 7.25 (7.18 to 7.48) to 6.66 (6.50 to 6.82) during the time course (Figure 5). Despite resuscitation, ECMO, and blood replacement, rapidly developing hyperkalemia was observed in the two study animals. In these study subjects, the potassium level increased from 2.8mmol/L (2.0–3.8mmol/L) to 7.8mmol/L (6.8–8.8mmol/L). In addition, these two study animals demonstrated a dramatic and progressive decrease in hemoglobin levels to the end of the study (Figure 5). No blood samples were taken from animal No. 3 after aortic cannulation and initiation of ECMO.

FIGURE 5 *Blood gases analysis summarizing three study animals that underwent extracorporeal cardiopulmonary resuscitation. Data presented as mean (standard error of mean).*



BD = base deficit; Hb = hemoglobin (g/dL) level; K^+ = potassium (mmol/L), pH level.

Discussion

Extensive combat trauma is a leading cause of prehospital and in-hospital mortality in the warfare environment. Exsanguination leading to blood volume depletion remains an ever-present potential challenge. Despite advances in TCCC, ARC, far-forward damage-control surgery, and resuscitation, there remains a need to evaluate the utility of further emerging techniques capable of supporting and restoring circulation in casualties with TCA. E-CPR (V-A ECMO during CA), already shown to be an effective tool in the rescue from cardiogenic CA in select patients,[10,14] warrants examination in this regard. However, E-CPR for acute trauma remains a controversial topic requiring additional study. Although ongoing hemorrhage is considered to be a traditional contraindication for ECMO due to the typically required systemic heparinization, some civilian trauma centers have already demonstrated the potential for saving lives using this technique, even for polytraumatized patients.[14]

Early hospital-based use of V-A ECMO has already been found to be effective for refractory nontraumatic CA.[15] In order to explore the potential value of this adjunct as early after arrest as possible, the use of V-A ECMO has also been pushed forward for potential prehospital applications.[16] These investigations have shown that the interval between CA and restoration of circulation (the low-flow period) is inversely associated with optimal neurologic and clinical outcome after E-CPR.[17] To optimize out-of-hospital care and reduce the low-flow time period, special ECMO teams have been developed in some countries.[16,18] ECMO experience in austere military circumstances is, however, limited.

ECMO was rarely perfomed during the recent combat operations and mostly at higher echelons of care for patients sustaining acute respiratory distress syndrome.[19–23] Turner et al[19] reported only three ECMO procedures documented at Role 3 MTFs during 15 years of combat operations in Iraq and Afghanistan. Ten US casualties (four of them cannulated in the war zone) were also successfully treated with either venovenous ECMO or pumpless extracorporeal lung assist and underwent strategic evacuation.[20,23] These isolated reports represent the only description of ECMO or E-CPR cases in a combat zone that to date have been published in the literature.

The present work demonstrates the technical feasibility of E-CPR for use on the modern battlefield. During the field exercises, simulated out-of-hospital CA was achieved in austere settings, followed by staged care. Two animals were transported to Role 2 with adequate levels of perfusion pressure without access-related complications. Although nominally admitted alive (normal-range MAP on admission to Role 2), both animals had artificial circulation and were progressively deteriorating with uncontrolled acidosis and anemia. To support circulation, large volumes of crystalloids were used; however, early blood replacement has a potential for use in E-CPR. In a study investigating TCA in animals, Barnard et al.[8] demonstrated that animals that had undergone selective aortic arch perfusion and been resuscitated with fresh whole blood had higher rates of ROSC and survival than did those resuscitated with Ringer lactate or that underwent REBOA without an additional perfusion modality. Because of the high serum concentration of potassium administered to initiate CA in our study, ROSC was unlikely to be achieved and hence was not considered to be a primary endpoint. Although additional study is required, these findings suggest that ECMO for very select patients may avoid mortality and support transfer to Role 3, where more comprehensive resuscitative care can be provided.

It is important to note that ECMO remains a highly technical and technology-dependent intervention. Tisherman et al.[18] recently raised critical questions related to development of an effective system to integrate E-CPR in a continuum of care, including such important factors as selection of patients, the experience and skills of personnel, and equipment.

Combat wounded are a unique cohort of patients. Effective TCCC protocols provide the best chances for the combat wounded to survive, but the value of battlefield CPR remains a matter of active debate. Present TCCC doctrine does not advocate the use of prehospital CPR when no pulse, ventilation, or other signs of life are appreciated.[24] These guidelines suggest that CPR may be attempted during tactical evacuation only if transportation time is minimal and the casualty has no obviously fatal wounds. In accordance with sound prehospstial combat casualty practice, the obvious sources of hemorrhage must be primarily controlled and other immediately life-threatening conditions addressed.

Exploration of the value of E-CPR in the combat setting will require judicious consideration of the potential role of anticoagulation early after control of obvious hemorrhage sources. Although some leading centers have initiated ECMO for trauma without systemic anticoagulation,[10] optimal practice in this regard is not well elucidated. Modern heparin-bonded cannulae and circuits may play a particularly valuable role in the trauma setting.

Trained, experienced personnel are also absolutely necessary for successful ECMO implementation. Many formal hospital-based ECMO teams consist of providers from an array of different specialties, including cardiac surgeons and cardiac anesthetists, perfusion services, intensive care nursing, and others.[25,16] For battlefield ECMO, Macku et al.[26] previously proposed a larger group of specialists, including a cardiac and vascular surgeon. The team used for the present report consisted of four members: two anesthetists, a military (trauma) surgeon, and a nurse. The optimal configuration of a potential austere E-CPR team will require additional study, however, because several studies have also demonstrated that nonsurgeons with appropriate training can safely perform vascular cannulation and initiate ECMO.[16,27] Additional vascular training is likely very important to support expediency with both cannulation and coping with potential vascular-access complications.

Although cannulation procedures and ECMO are typically performed at facilties with capabilities substantially greater than those in the typical Role 1 setting, only hand-carried devices (i.e., ECMO machine, ventilator, gas cylinder) were used by the personnel augmenting this stage of care in the present report. This expanded prehospital military capability goes along with the current paradigm of special operations surgical/resuscitative teams that have evolved to provide surgical capability farther forward to the battlefield.[28,29] Among the vascular access procedures described on the study animals, surgery was attempted in one animal to achieve more proximal access because of the failure of femoral cannulation. The surgeons in this study protocol persisted with vascular access alternatives despite recurrent challenges, but this practice might not prove feasible in a real-world casualty care event. In that context, such persistent failure to achieve access would demand an earlier shift in focus toward other life-saving techniques and interventions.[30]

The specific equipment to facilitate E-CPR continues to evolve. At present, ECMO requires an appropriate perfusing machine, additional oxygen supply, and cannulae. The portable perfusion device used in the present study satisfies the portability and functionality needs for prehospital scenarios. To reduce weight, a portable oxygen concentrator or generator might be potentially used, but because it was unavailable in this instance, an additional oxygen gas cylinder was used. The choice of a draining (i.e., venous) cannula in the present study was found to be critical because a short cannula was unable to adequately drain blood from the inferior vena cava compressed by elevated abdominal compartment pressure. Further, the inability to cannulate the femoral artery in animal No. 3 demonstrates the need to have an enlarged kit containing cannulae of different sizes and lengths to meet the anatomic configurations encountered.

Equipment for adjunctive CPR in a harsh military setting is another issue for consideration. The Lucas compression device used in the present study is not currently familiar in the modern battlefield and may be too large to be included in a typical combat medic kit. It may, however, improve the ability to deliver required hands-free compression, as supported by the finding here that one-third of closed CPR time was required en route. Effective CPR for these durations by hand compression is unlikely to be as effective as that of device-assisted CPR, thereby potentially worsening an outcome.

This feasibility report has important limitations that must be acknowledged. First, this is a pilot, small-sample-size study primarily evaluating the field logistics and feasibility of the procedure rather than state-of-the-art care. Second, this study lacks stringent monitoring and laboratory-guided resuscitation capabilities. Although during closed CPR the utilized MAP monitoring demonstrated an adequate initial perfusion, continuous monitoring during transportation could not be used to exclude undocumented episodes of hypoperfusion. Hemodilution and acidosis were clearly demonstrated by point-of-care testing results but are likely largely attributable to the more liberal use of crystalloids than would have occurred in actual contemporary practice. It is likely that modern whole blood resuscitation strategies as outlined in the ARC protocols[2] would result in more consistent laboratory results in future study animals. The present study did, however, use the implementation of CPR in accordance with current basic and advanced life support recommendations. This resulted in a temporary elevation of MAP, which permitted effective transportation to a location where more advanced resuscitatieve and hemorrhage control techniques might be available.

Despite these limitations, the present work is the first to demonstrate the potential feasibility of V-A ECMO use during far-forward resuscitative care to support casualties with TCA who would otherwise be considered unsalvageable. The potential role for battlefield E-CPR, however, requires additional examination. It might warrant consideration at Role 2 facilities with more robust surgical capability for casualties admitted in extremis with impending CA but not frank arrest. In this fashion, E-CPR might serve to expediently support (rather than substitute) a casualty's circulation. However, as required technology continues to evolve (an ECMO machine and kit can be carried in a rucksack now), and as concurrent improvements in skills training and rapid casualty transport develop, E-CPR may soon become an option in the armamentarium of specific care providers even closer to the point of injury. The effective implementation of early E-CPR in the forward military setting seems to be logistically, mentally, and technically challenging, but in the future, it may become a bridge from "killed in action" to "returned to duty."

Conclusion

The present study in a porcine model demonstrates the feasibility of V-A ECMO for use during TCCC and forward resuscitative care at Role 1 or 2. CPR (closed and then extracorporeal) may play a potential role in improving survival in future warfare. Further investigations are warranted to determine indications, optimal training, equipment, and utilization protocols required to facilitate the effective integration of ECMO into military forward-care capabilities.

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Disclaimer

The views expressed are solely those of the authors and do not reflect the official policy or position of the Ministry of Defense of the Russian Federation or the U.S. Air Force.

Conflict of Interest

All products and instruments described and discussed in this manuscript were either purchased by authors or provided by their units, except the portable perfusion device that was supplied for free by the manufacturer.

Author Contributions

VAR, DAS, ONR, IMS, and JJD conceived the study design. VAR, AAP, DAS, EAS, AMN, and KND performed the experiments. VAR, AES, and AAE collected and analyzed the data. VAR, DAS, AES, and ONR interpreted the data. VAR and JJD wrote the first draft. IMS and ONR critically revised the manuscript, and all authors read and approved the final manuscript.

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