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Prehospital extracorporeal cardiopulmonary resuscitation for refractory out-of-hospital cardiac arrest in goat with severe primary blast lung Injury-a pilot study

Zheng-Bin Wu¹, Yao-Li Wang¹ and Shi-Feng Shao^{1*}

Abstract

Background Although extracorporeal cardiopulmonary resuscitation (ECPR) has shown promise for refractory out-of-hospital cardiac arrest (CA), limited data exist regarding its application in cases involving severe primary blast lung injury (PBLI). This study evaluated the feasibility, indications, complications, and early management of ECPR for refractory out-of-hospital CA in goats with severe PBLI.

Methods Twenty adult goats (30.47 ± 4.74 kg) were randomly divided into five groups based on their distance from an 8 kg TNT-equivalent explosive: 2.5 m ($n=3$), 3 m ($n=5$), 4 m ($n=4$), 5 m ($n=4$), and 6 m ($n=4$). Goats were positioned in concentric circles and fixed in special iron frames in the same direction (with the right chest facing the core of the explosion). Following detonation, all animals were transported 500 m to a field rescue unit. Cardiopulmonary resuscitation (CPR) was initiated 1 min after CA. Two of the twenty goats were used for gross lung pathology assessment. Four goats underwent neck vessel cannulation and venoarterial extracorporeal membrane oxygenation (VA-ECMO). Crystalloid and blood transfusions were administered, and animals were monitored for 4 h.

Results All goats within 3 m suffered severe lung damage and CA after the explosion. Despite effective chest compression support, six of the eight goats within 3 m of the explosion died due to progressive circulatory failure. Four goats received ECPR. Among them, two were successfully resuscitated using VA - ECMO, with perfusion pressures restored to 65 mmHg (range: 60–70 mmHg) at 25 and 30 min post-CA. In the remaining two, large thrombi in the carotid arteries prevented effective flow initiation. No complications such as hemorrhage or failed vascular access were observed during cannulation. The ECMO circuit was established via an open carotid artery and the jugular vein cannula started, leading to the return of spontaneous circulation in the two successfully treated animals. All goats in the 4-, 5-, and 6-meter groups survived.

Conclusions Prehospital ECPR improved the restoration of spontaneous circulation and hemodynamic stability in goats with severe PBLI-induced CA. These findings demonstrate the feasibility and early efficacy of ECPR in austere

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conditions. Further investigations in larger animal cohorts and human trials are warranted to validate its potential as a life-saving intervention for blast-induced CA.

Keywords Primary blast lung injury, Extracorporeal membrane oxygenation, Cardiac arrest, Cardiopulmonary resuscitation, Field

Background

Major blast injuries pose significant challenges for critical care teams, with the lungs bearing the brunt of the blast wave. Pulmonary blast injury (PBLI) is usually the main cause of death among blast injury patients. Severe PBLI constitutes a complex form of blunt chest trauma that remains difficult to manage. Timely and effective support of respiratory and circulatory functions is key to improving the treatment outcome and reducing the mortality rate [1, 2]. Reducing early mortality remains the primary focus of prehospital critical care around the world. The leading causes of potentially preventable deaths (hemorrhage, airway obstruction, and tension pneumothorax) have been aggressively addressed by advanced resuscitative care to minimize mortality [3]. Although multiple strategies have been proposed to prevent death after PBLI, no optimal resuscitation technique has been identified to improve outcomes in subjects with traumatic cardiac arrest (CA) induced by severe PBLI.

An 11-year database analysis of the UK Joint Theatre Trauma Registry previously reported 424 casualties (4.6% of all registered patients) with CA, predominantly caused by blast injuries [4]. Most battlefield casualties succumbed to their injuries before reaching a surgical team. Given that most deaths occurring before reaching a medical treatment facility (MTF) are considered, reducing the time between the point of injury and surgical intervention is critical [5]. To improve outcomes in critically unstable patients, including those with traumatic CA, combat medical teams have introduced advanced life-saving techniques aimed at restoring systemic and central circulation. These novel interventions include emergency resuscitative thoracotomy, hybrid emergency room system (HERS), and extracorporeal membrane oxygenation (ECMO) [6, 7]. These techniques are now widely adopted in trauma and critical care centers and are under investigation for battlefield use. Extracorporeal cardiopulmonary resuscitation (ECPR), defined as the rapid initiation of venoarterial extracorporeal membrane oxygenation (VA-ECMO) during cardiopulmonary resuscitation (CPR), is used in patients who experience sudden and unexpected pulseless conditions due to the cessation of cardiac mechanical activity. VA-ECMO is being increasingly used in the setting of cardiogenic shock and CA [8, 9]. Empirical success with VA-ECMO has been observed in cardiogenic shock and severely polytraumatized patients at the Army Medical Center, where the present authors are based. Successful ECPR depends on

early initiation following CA, availability of appropriate equipment, trained personnel, and coordinated team response [10, 11]. However, no studies have evaluated the feasibility of artificial circulatory support in cases of PBLI-related CA.

To address this critical gap, the present study investigates the feasibility, indications, complications, and early management of ECPR for refractory CA in goats with severe PBLI. Artificial scenarios of refractory out-of-hospital CA were created to simulate circumstances in which ECPR could be applied in battlefield settings.

Methods

Overview

This study was conducted from July to August 2021 during military medical training exercises at the Army Medical University in Chongqing, China. A structured four-stage experimental protocol was developed to investigate CA and ECPR in a controlled animal model. The protocol included the following phases: animal preparation, induction of CA, resuscitation with ECMO initiation, and early management of ECMO. The choice between the percutaneous or surgical cannulation of the femoral vessels was determined based on the skill and preference of the clinician. Central cannulation outside of an operating theatre was performed with proper planning and the availability of adequate equipment and resources. All animal anatomical observations and investigations during the military exercises were conducted under annual protocols reviewed and approved by the local ethical committee. The two-week study was approved by the ethical committee of the Daping Hospital Medical Academy.

Animal preparation

Goat subjects, each weighing approximately 30 kg, were housed under quarantine conditions at the animal facility for 14 days.

Sedation was achieved through intramuscular injection of phenobarbital sodium (Fujian Mindong Lijiexun Pharmaceutical Co., LTD, China) and midazolam (Jiangsu Nhwa Pharmaceutical Co., LTD., China), followed by intravenous injection of propofol injectable emulsion (Xi'an Libang Pharmaceutical Co., LTD, China) and desocine (Yangtze River Pharmaceutical Group, China) through a catheter placed in the left marginal ear vein. The right carotid artery was exposed for insertion of a 7-Fr (12") central venous catheter (B. Braun Melsungen

AG, Germany), which was used for continuous arterial pressure monitoring and blood sampling.

Induction of refractory CA caused by PBLI

A model of refractory CA induced by PBLI was established for the experimental protocol. Twenty goats were exposed to an explosive charge equivalent to 8 kg of trinitrotoluene (TNT), positioned in concentric circles at varying distances to generate graded blast exposure. The animals were fixed at 2.5 m ($n=3$), 3 m ($n=5$), 4 m ($n=4$), 5 m ($n=4$) and 6 m ($n=4$) to induce CA caused by severe PBLI (Fig. 1).

CPR and ECMO protocol

Chest compressions were initiated one minute after confirmation of CA. During chest compressions, the animal was transported to the MTF and placed on a surgical table. The MTF consisted of a total of 8 field tents and was equipped with seven operating tables, a ventilator (Aeonmed Shangrila510), an electrocardiograph (Reward 3000, China), a cardiac monitor (Mindray, China), an ultrasound machine (Mindray, China), a portable radiographic system, a blood-warming transfusion device, and a standard set of surgical instruments. Aseptic techniques were strictly followed during intubation and the early phase of ECMO management. Sterile procedures included the use of single-use surgical fenestrated sheet (Kangmin, Xinxiang City, China), Iodophors (Sichuan Huatian Technology Industrial Co., LTD), Disinfecting paper towels LIRCON (Shandong LIRCON Medical Technology Co., LTD). Prophylactic antibiotics administered included Vancocin (Eli Lilly Japan K.K, Seishin Laboratories) and Meropenem (Sumitomo Dainippon Pharma Co., Ltd).

After tracheal intubation, 200 IU/kg heparin was administered. Both the carotid artery and vein were exposed and instrumented with 15-Fr (5.0 mm, 3/8", CB96570-015, Medtronic Inc., U.S.A) and 19-Fr (6.3 mm,

3/8", CB96670-019, Medtronic Inc., U.S.A) cannulae, respectively, to establish ECPR. Cannulae were fixed to the animal and connected to the ECMO perfusion device. Pump flow was initiated at a blood flow rate (BFR) of 600mL/min and increased to a target range of 1500 to 2500mL/min. As early as 10 min after the ECMO procedure was initiated, the animals were resuscitated with whole blood. To avoid severe hypocalcemia, small boluses of 10% calcium chloride were administered. Prophylactic antibiotics were administered throughout the procedure to prevent septic complications (Fig. 2).

Laboratory investigations (arterial pH value and serum lactate levels)

Blood samples were collected for gas analysis (i-STAT, Abbott Laboratories, IL) at the following time points: baseline (pre-explosion), 5 min after CA, 1 h after ECMO initiation, and before study termination. Mean arterial pressure, blood flow rates (BFR), and saturation parameters were monitored throughout the study.

The primary endpoint was the achievement of adequate levels of perfusion pressure in MTF. The critical care team consisted of a chief physician, an experienced attending doctor physician with a dedicated trauma care package, and an experienced resident-perfusionist responsible for ECMO. All cannulation procedures were performed by the chief and attending physicians. No additional training for ECMO in animals was implemented before the study began.

Field ECMO equipment

The ECMO circuit was established using the Ex-Stream perfusion system (MAQUET, Germany). The ECMO kit included an oxygenator (MAQUET, Germany), venous (access) and arterial (return) cannulae, a spare ECMO circuit, a centrifugal pump (Scrin group Italia S.r.l, Italy), connectors, tubes, sterile scissors, and tubing clamps. The ECMO circuit was primed and prepared. Bio-Medicus

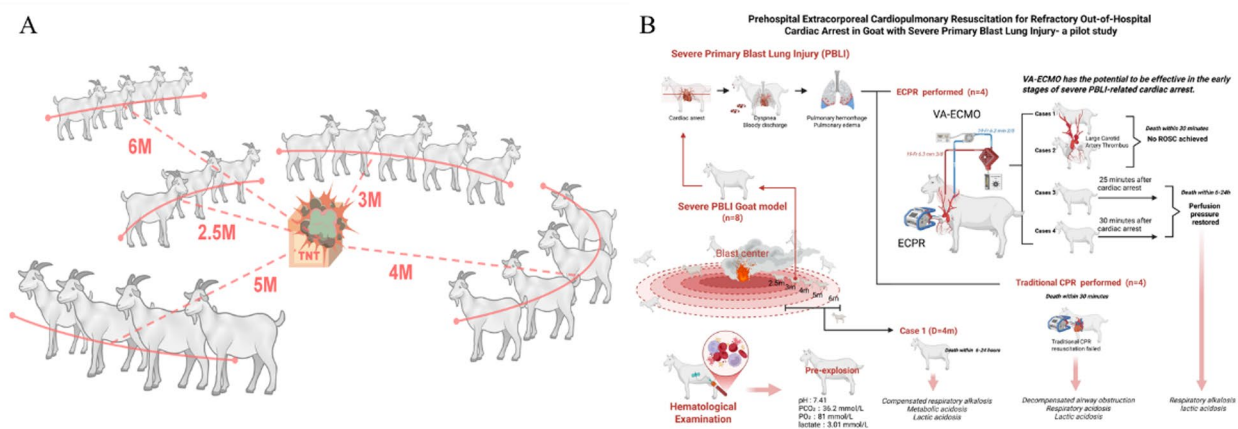


Fig. 1 Explosion protocol. (A) Induction of refractory cardiac arrest caused by primary explosive lung injury. (B) Overview of the experimental workflow

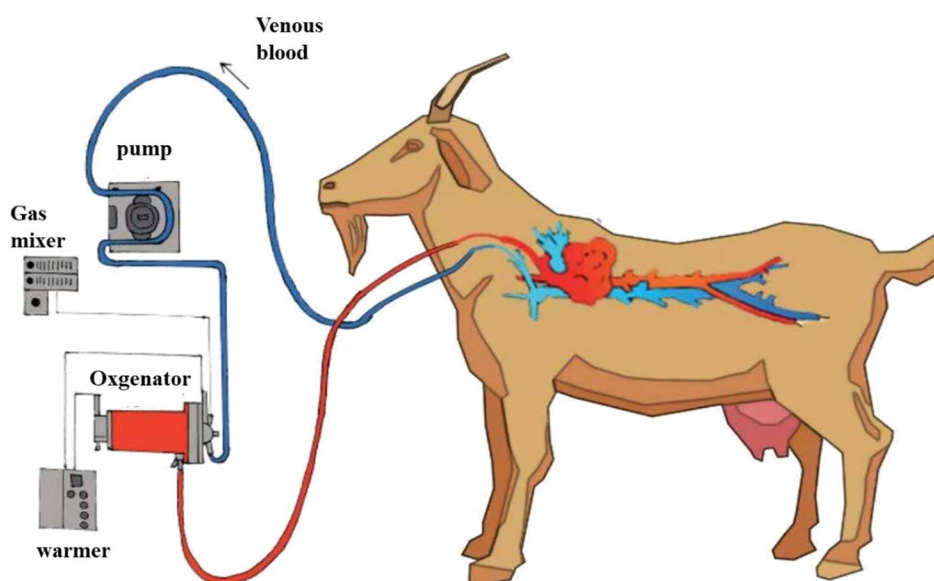


Fig. 2 Four animals were admitted to a Role 1 medical treatment facility for ongoing cardiopulmonary resuscitation. Tracheal intubation was performed, and neck vessels were explored for subsequent cannulation

and DLP pediatric cannulae were used for semi-Seldinger and open cannulation, respectively (all from Medtronic).

ECPR experimental protocol

ECPR was initiated as early as possible following the onset of CA. In many cases, the procedure was cancelled during transportation or at the CA site due to the return of spontaneous circulation (ROSC) or failure to meet the inclusion criteria for ECPR. All relevant data, including the number of ECPR attempts, location and timing of intervention, and reasons for cancellation, were systematically recorded. Once the ECMO circuit was stabilized, assessments were conducted to evaluate ECMO vascular access, bypass time, record catheter placement time, anticoagulant dose, blood gas analysis, coagulation function, and the incidence of complications.

The prognostic assessment of goats undergoing ECPR was based on a combination of physical examination (pupil diameter and brain stem reflexes), imaging (Chest X-ray), grey-white matter ratio (GWR) and laboratory investigations (arterial pH value and serum lactate levels).

Post-ECPR management

After delivery to the MTE, early management of prehospital ECMO in goats with PBLI-related CA focused on monitoring mean arterial pressure (MAP) and assessing the potential for ROSC. When indicated, additional appropriate interventions were performed to stabilize the animals, followed by continuous monitoring during a four-hour observation period. Study termination and euthanasia were carried out at the end of the observation period if stabilization was achieved. If no ROSC was

achieved after these procedures, death was confirmed, the study was terminated, and the ECMO circuit was discontinued. No postmortem examination was performed.

Blood source

Whole blood was autologously collected from each animal approximately 14 days prior to injury. Around 200 mL of blood was drawn from each goat, labeled individually, and stored in accordance with laboratory animal regulations. Blood collection and storage were carried out under standardized conditions within the animal facility. Following injury, autologous transfusion was prioritized. In cases requiring additional transfusion, cross-matching was performed by pairing the recipient goat's plasma with the donor goat's red blood cells to ensure compatibility.

Results

Overview

A goat model of severe PBLI was successfully established. Among the eight goats positioned within 3 m of the explosion (including both the 2.5-meter and 3-meter groups, which exhibited comparable injury severity and were collectively analyzed as the "within 3 meters" group), six died due to progressive circulatory collapse despite receiving effective chest compressions. Most goats within the 3-meter explosion range suffered severe PBLI and subsequently succumbed to CA. In contrast, all twelve goats positioned at 4, 5, and 6 m from the blast survived.

After the explosion, goats positioned three meters from the blast source developed dyspnea and showed bloody

discharge from the mouth and nose (Fig. 3). All goats at this distance died within 30 min after the explosion. The cause of death was identified as acute severe pulmonary edema, with bronchial lumens filled with thrombi and large volumes of pink, foamy sputum. Massive pulmonary hemorrhage and pulmonary edema caused Type II respiratory failure, resulting in death. Conventional CPR was unsuccessful in restoring circulation (Fig. 4 and Supplementary Fig. 1).

VA-ECMO was initiated in four goats following PBLI-induced CA. Large thrombi were observed in the CA of two goats, preventing the establishment of an effective flow rate. The other two goats underwent successful E-CPR, with perfusion pressure restored to 65 mmHg at 25 and 30 min after CA. There are no bleeding or unsuccessful vascular catheterization complications. No complications related to bleeding or vascular access were noted. The ECMO circuit was initiated via open cannulation of the carotid artery and jugular vein, ultimately leading to the return of spontaneous circulation in both cases. Four goats underwent induction of PBLI-related CA at a distance of 400–500 m from the MTF and developed sustained asystole. Ground transportation to the MTF required approximately 5 min. On the MTF, critical care providers initiated central venous catheter fluid replacement (500mL ringer solution) and CPR within 3 min. Due to severe hypoxemia from acute pulmonary edema, surgical cricothyroidotomy was performed with, followed by administration of high-flow 100% oxygen via

tracheostomy tube and subsequent mechanical ventilation. Chest compressions supported circulation, but progressive hemodynamic deterioration occurred prior to ECMO initiation.

Arterial cannulation in ECPR Case No. 1 was achieved only after multiple attempts over a 30-minute period due to severe vasospasm and spastic small-caliber vessels. In ECPR Case No. 2, the protocol was ultimately discontinued due to futility. No ROSC was ultimately achieved in either of the study animals (ECPR No. 1 and ECPR No. 2), likely due to a hypercoagulable state associated with severe PBLI. In contrast, ECPR Cases No. 3 and No. 4 underwent immediate and successful cannulation followed by prompt ECMO initiation, resulting in restoration of perfusion pressure to 65mmHg. Both cases subsequently received additional pharmacologic interventions and proceeded to study termination.

MTF ECPR failure

In ECPR Cases No. 1 and No. 2, open neck vein cannulation (a 19-Fr 6.3 mm 3/8" cannula) was successfully achieved 20 minutes after the induction of CA. Arterial access was also established via surgical cutdown of the carotid artery (a 15-Fr 5.0 mm 3/8" cannula). However, due to the hypercoagulable state of blood, the ECMO perfusion could not be initiated at the target BFR 0.6 L/min. As a result, the protocol for the ECPR No. 1 and ECPR No. 2 goat was discontinued due to futility. Goat ECPR No. 1 received a lower volume of crystalloids.



Fig. 3 Profuse pink frothy sputum observed in the mouth and nasal cavities of goats following the explosion

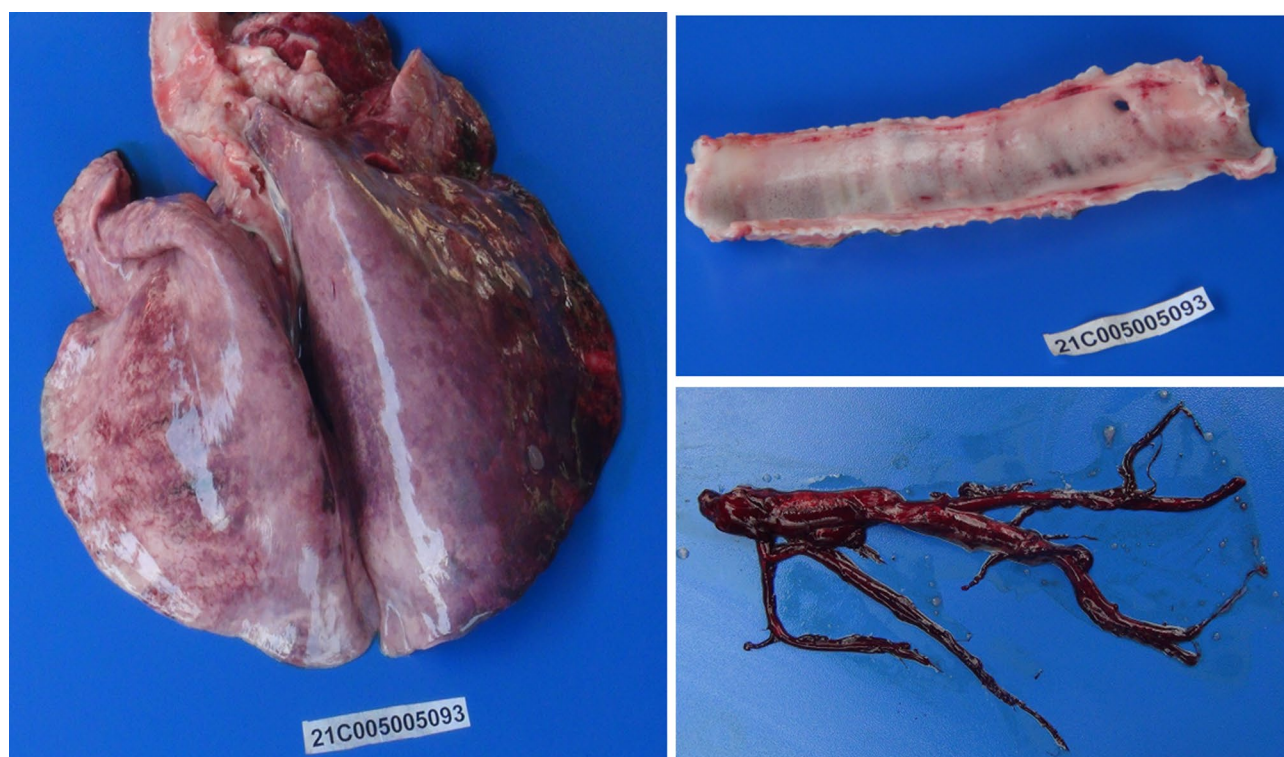


Fig. 4 Goat No. 1 Lung Anatomy which died within half an hour after the explosion

Despite effective blood drainage and return, progressive hemodynamic deterioration led to refractory shock. Additional central venous cannulation was attempted to restore BFR at the MTF via central venous cannulae, but no improvement in perfusion was observed. Artificial circulation was artificially maintained throughout the experimental period in both animals. The protocol was terminated 30 min after initiation without ROSC. Except for the large blood clotting in the carotid artery catheter, no other access-related complications were recorded in either animal.

Successful MTF E-CPR

Goat No. 3 and No. 4 underwent a complete protocol of ECMO initiation under ongoing CPR. Cannulation of neck vessels was performed within 20 min after arrival to Role 1 (Supplementary Table 1), and restoration of flow was achieved at 25 and 30 min after the induction of CA, respectively. External chest compressions were discontinued immediately upon ECMO initiation. In two goats, both short cannulae (a 15-Fr 5.0 mm 3/8" arterial and a 19-Fr 6.3 mm 3/8" venous) were inserted into the right neck vessels using an open cutdown exposure. Body movements during the CPR and small-caliber vessels hindered the ability to achieve a stable needle position. Vascular 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 neck artery and vein. After connection to the ECMO circuit, ECPR was initiated at a BFR of 0.6–0.8 L/min, and the ventilator was disconnected. Initial resuscitation included the administration of 1 L and 2 L of crystalloids in the two animals, respectively, followed by the infusion of 0.5 L of stored whole blood. BFR was subsequently increased to 1.5 L/min (Figs. 5 and 6.). Full ECPR support was achieved within 30 min.

Laboratory values

Blood tests from No. 1, No. 2 and ECPR No.4 goats demonstrated a dramatic progression of metabolic acidosis secondary to PBLI (Supplementary Tables 2 and Supplementary Table 3). The base deficit gradually increased from 0 (−3 to +3) to 20 (28 to 30), and the pH level gradually decreased from 7.40 (7.38 to 7.48) to 6.72 (6.50 to 6.82) over the course of the study. Despite resuscitation, ECMO, and blood replacement, rapid development of hyperlactemia was observed in the two study animals. In these study subjects, the lactic acid level increased from 11.4 mmol/L to 19.8 mmol/L. No blood samples were collected from goats No. 1, No. 2 and No. 3 after initiation of ECMO via aortic cannulation.

Table 1 illustrates the progression of metabolic acidosis in PBLI, highlighting the inability of ECPR to reverse severe lactic acidosis despite adequate oxygenation. Discrepancies between pH and lactate levels in ECPR 4 (e.g., pH 7.57 with Lac 19.81) suggest respiratory



Fig. 5 The ECMO catheter was successfully placed, and the dark red blood slowly flowing out of the vein can be seen. The ECMO centrifugal pump turned bright red, but the flow rate was very low due to high blood coagulation, and the establishment of the ECMO model of goat explosion injury failed (Goat No. 3 and No. 4)



Fig. 6 The ECMO catheter was successfully placed and heparinized with heparin 200 IU/kg. The dark red blood can be seen quickly flowing out of the vein. The ECMO centrifugal pump turned bright red, and the goat blast injury ECMO model was successfully established (goat No. 3 and No. 4).CPR= cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; E-CPR= extracorporeal cardiopulmonary resuscitation; MAP= mean arterial pressure; POI=point of injury

Table 1 Blood gas analysis results

Goat No.	Time Point	pH	PCO ₂ (mmol/L)	PO ₂ (mmol/L)	Lac(mmol/L)	HCO ₃ ⁻ (mmol/L)	BE (mmol/L)	SO ₂ (%)
No.1	Post-explosion (before death)	6.72	121.8	19	17.7	15.8	−20	8
No.2	Pre-explosion	7.41	36.2	81	3.01	22.9	−2	96
No.2	0.5 h post-explosion	7.46	27	82	7.76	19.3	−5	97
No.2	3 h post-explosion	7.48	18	72	14.2	13.4	−10	96
No.2	6 h post-explosion	7.5	18.7	68	12.48	14.6	−9	95
No.4	3 h post-explosion	7.3	39.9	254	11.42	19.7	−7	100
No.4	6 h post-explosion	7.57	8.9	406	19.81	8.1	−14	100

alkalosis, potentially masking the underlying metabolic disturbance.

Goat No.1, positioned three meters from the source of the explosion, died within 30 min after the explosion. The blood gas analysis result indicated decompensated airway obstruction, respiratory acidosis and lactic acidosis.

Goats No.2, located four meters from the source of the explosion, died within 6–24 h after the explosion.

Prior to the explosion, arterial blood gas analysis showed values within normal ranges: pH 7.41, PCO₂ 36.2 mmol/L, PO₂ 81 mmol/L, and lactate 3.01 mmol/L. At 30 min post-explosion, blood gas results indicated a pH of 7.46, PCO₂ decreased to 27 mmol/L, and lactate rose to 7.76 mmol/L, suggesting compensatory hyperventilation in response to emerging metabolic acidosis. At 3 h post-explosion, pH increased to 7.48 and PCO₂ dropped further to 18 mmol/L, while lactate sharply rose

to 14.2 mmol/L, reflecting a significant worsening of metabolic acidosis. By 6 h post-injury, pH reached 7.50 with PCO₂ remaining low at 18.7 mmol/L, and lactate slightly decreased to 12.48 mmol/L but remained markedly elevated. These findings indicate a state of compensatory respiratory alkalosis combined with metabolic acidosis and severe lactic acidosis, reflecting progressive acid-base imbalance and tissue hypoxia caused by blast-induced pulmonary injury, ultimately leading to death.

Goat No. 4, positioned three meters from the source of the explosion, died within 6–24 h after the explosion. Despite ECMO support leading to markedly improved oxygenation (PO₂ increased to 406 mmol/L), blood gas analysis revealed persistent and severe lactic acidosis (lactate 19.81 mmol/L). These findings indicate that although ECMO effectively sustained high arterial oxygenation, excessive ventilation contributed to pronounced

respiratory alkalosis. Simultaneously, the marked elevation in lactate levels reflected worsening metabolic acidosis, consistent with persistent tissue hypoxia or impaired cellular metabolism. The results underscore the complex pathophysiological processes underlying blast-induced lung injury, in which oxygenation support alone failed to correct the profound metabolic derangements.

Discussion

Goats in this study exhibited severe PBLI, a condition that proved refractory to conventional CPR and mechanical ventilation. For goats with severe PBLI, hypoxemia and respiratory failure were difficult to correct with conventional mechanical ventilation [2, 12]. ECPR offers a means of maintaining systemic perfusion and may serve as a “bridge-to-decision” option, allowing time for further diagnostics and treatment [3, 13, 14]. Hence, research on ECPR is critical for refining case selection and optimizing early management protocols. Extensive combat trauma is a leading cause of prehospital and in-hospital mortality in the warfare environment. Despite advances in Tactical Combat Casualty Care (TCCC) and far-forward damage control resuscitation, the need persists for advanced techniques capable of supporting and restoring circulation in casualties with TCA. Regardless of the cause, chest compressions remain the fundamental initial intervention for all kinds of cardiovascular arrests [10]. The present study aims to establish a cardiopulmonary assist model of PBLI-related CA in goats and to explore key issues in the establishment of ECPR.

Our results indicate that VA-ECMO has the potential to effectively rescue severe PBLI-related CA in the early stage. To explore the potential value of this adjunct as early as possible after arrest, tVA-ECMO has been explored for prehospital applications. Previous investigations have shown that the interval between CA and restoration of circulation (the low-flow period) is inversely associated with optimal neurologic and clinical outcomes after ECPR [15, 16]. Although ongoing hemorrhage has traditionally been considered a contraindication for ECMO due to the typically need for systemic heparinization, clinical experience in our trauma and critical care unit has shown that ECMO may still offer survival benefits even in polytraumatized patients. Early hospital-based use of VA-ECMO has already been found to be effective for refractory nontraumatic CA [15–17]. However, ECMO implementation in austere or military circumstances is limited. Its use during combat operations has been rare and typically restricted to higher levels of care for patients with acute respiratory distress syndrome (ARDS). Published reports of ECPR in combat environments remain scarce, and further exploration of VA-ECMO for PBLI-related CA is warranted. The present study demonstrated the technical feasibility of ECPR

in simulated battlefield conditions. During the field exercises, simulated out-of-hospital CA was achieved in austere settings. Two animals had adequate levels of perfusion pressure without access-related complications. Although circulation was artificially maintained, both animals exhibited progressive physiological deterioration with uncontrolled acidosis. Large volumes of crystalloids and whole blood were required to support systemic perfusion. Comparative analysis showed that goats resuscitated with fresh whole blood had higher rates of ROSC and survival than those resuscitated with Ringer lactate. Given the severity of PBLI administered to initiate CA in our study, ROSC was unlikely to be achieved by routine CPR. These findings suggest that ECMO may reduce mortality in cases of severe PBLI-related CA and suggest its role in enabling patient transfer to higher-level medical facilities where definitive care can be provided. The results align with previous ECPR clinical research results [11–19].

It should be emphasized that ECMO remains a highly technical and technology-dependent intervention. This study raised critical questions related to the development of an effective system to integrate ECPR in a continuum of care. Key considerations include appropriate subject selection, personnel experience and technical skill, maintenance of a sterile environment, and the availability of portable ECMO equipment. Current TCCC guidelines do not recommend the use of prehospital CPR in cases where no pulse, ventilation, or other signs of life are appreciated. 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 prehospital combat casualty practice, major sources of hemorrhage must be controlled first, and other immediately life-threatening conditions must be addressed. The potential application of ECPR in combat settings requires careful consideration of anticoagulation strategies, particularly after the initial control of bleeding. Although ECMO was initiated in this study for PBLI-related CA with systemic anticoagulation at a dose of 200IU/kg, the optimal anticoagulation strategy in this context remains poorly defined. Consistent with previous research on anticoagulation management, modern heparin-bonded cannulae and circuits may play a particularly valuable role in the PBLI-related CA setting [20, 21].

To optimize out-of-hospital care and reduce the low flow time period, an ECMO team was established as part of the study protocol. Successful ECMO deployment depends heavily on trained and experienced personnel. In hospital settings, ECMO teams often comprise specialists across multiple disciplines, including cardiac surgery, anesthesiology, perfusion, and intensive care. In battlefield conditions, the proposed team configuration

may require broader capabilities, potentially involving cardiac and vascular surgeons. The team used for the present report consisted of three members: a chief physician, an attending doctor, and a resident. ECMO machines were not hand-carried devices in the present report. Although cannulation procedures and ECMO are typically performed in facilities with resources exceeding those of a standard MTF setting, only hand-carried devices (i.e., ventilator, gas cylinder) were used at this stage of care. The successful implementation of our pre-hospital ECPR supports previous findings indicating that properly trained non-surgeons can safely perform vascular intubation and initiate ECMO [18, 22, 23]. However, during the actual pre-hospital ECPR implementation process, it is important to realize that additional vascular training is essential to support successful cannulation and manage potential vascular access complications. These findings support the technical feasibility of prehospital ECPR and emphasize the importance of targeted training for personnel involved in its deployment [19, 24]. Furthermore, a review of literature, including retrospective case series and controlled animal modelling studies published since 2000, revealed that PBLI accounts for 6–11% of military casualties in recent conflicts. In contrast, the incidence rises to over 90% in terrorist attacks occurring in enclosed spaces such as trains. The majority of victims require mechanical ventilation and intensive care management. Appropriate use of airway pressure release ventilation (APRV) has been associated with significant mortality-related benefits [25, 26].

Several improvements are needed to optimize prehospital ECPR technology. To reduce weight, an additional oxygen gas cylinder was used. The perfusion device used in the present study did not satisfy the portability and functionality needs for prehospital scenarios. Continued refinement of dedicated ECPR equipment remains essential. At present, successful ECMO implementation relies on a compatible perfusion machine, supplemental oxygen supply, and suitable cannulae. The choice of a draining (i.e., venous) cannula in the present study was found to be critical. Short or oversized cannulae failed to provide effective drainage from the jugular vein, highlighting the necessity of a comprehensive cannulation kit containing cannulae of various lengths and diameters to accommodate anatomical variability. Additional considerations include equipment for adjunctive CPR. Manual chest compressions over extended periods are unlikely to match the consistency and efficacy of device-assisted CPR, which may negatively impact outcomes. A portable, sterile laminar flow environment may also help reduce the incidence of bloodstream infections.

Despite these limitations, the present work is the first to demonstrate the potential feasibility of VA-ECMO use during far forward resuscitative care to support

casualties with TCA who would otherwise be considered unsalvageable. Further investigation is needed to clarify the potential role for battlefield ECPR, particularly given that primary blast injury may cause devastating injury without external signs [27–29]. The success of ECMO goats was the result of coordinated team efforts. In 2021, an interdisciplinary clinical group for extracorporeal life support was established, comprising intensivists, cardiothoracic surgeons, anesthesiologists, cardiologists, perfusionists, dietitians, physiotherapists and nurses. In this group, cardiothoracic surgeons and intensivists served as ECMO specialists. Clinical operations adhered to international standards, and a dedicated intensive care unit was established to manage ECMO cases. An ECPR kit was developed to enable rapid deployment at the point of care. The kit includes a preassembled ECMO circuit, serial dilators, cannulas of various sizes, antiseptic solutions, surgical drapes, surgical aprons, gloves, a surgical tray for vascular access, surgical blades, suture materials and ECMO consent forms. Proper planning and standard operating protocol (SOP) are essential for the improved survival of ECPR goats. The SOP, developed by the interdisciplinary team, was specifically designed to minimize downtime and facilitate timely ECPR initiation. Following ECPR, three outcomes are generally observed: death due to complication, recover or irreversible organ damage necessitating termination of ECMO support. The end of life on ECMO may represent either biological death or cessation of artificial support due to equipment failure. Therefore, training of the healthcare team is critical to optimizing outcomes from ECPR.

Previous studies have shown that chest wall and pulmonary injuries range from rib fractures to flail chest, pneumothorax to hemothorax and pulmonary contusion to tracheobronchial injuries. Following these injuries, patients may present with a simple dyspnea or even respiratory arrest [30–32]. Severity of ARDS has been correlated with higher 28-day hospital and 3-year mortality. Increased mechanical power during ventilation has also been linked to poorer outcomes, with plateau pressure and driving pressure identified as modifiable parameters associated with decreased survival [15, 33, 34]. Outcomes in cardiovascular arrest differ significantly between in-hospital and out-of-hospital settings. Out-of-hospital arrest is typically associated with a poorer prognosis, largely due to longer no-flow times (duration without perfusion), extended low-flow times (duration of inadequate perfusion), and variable resuscitation quality. Beyond failed cannulation, another major cause of ECPR failure is the inability to achieve adequate perfusion flow. In these cases, adequate volume therapy should be used. If sufficient flow cannot be achieved, the pathology underlying the resuscitation situation (e.g., aortic dissection), resuscitation trauma, and a misalignment of

the cannula or a perforation must be considered and, if possible, excluded. The eCPR (extracorporeal cardiopulmonary resuscitation) is a treatment option for a selected number of patients with refractory cardiovascular arrest if a ROSC ("return of spontaneous circulation") cannot be achieved through conventional measures. A clear indication is absolutely necessary to ensure appropriate and meaningful use of this resource-intensive intervention. Time management is crucial for the prognosis. Ideally, the interval from collapse to ECPR initiation should be less than 60 min, with a door-to-ECLS (extracorporeal life support) implantation time under 30 min. In cases of refractory hypoxemia and cardiac arrest, combining ECMO with independent lung ventilation may offer life-saving benefits [16]. The ECPR should be regarded solely as a bridging therapy. Continuous reassessment of therapeutic goals is necessary to determine whether ongoing support remains appropriate.

Limitations

Several limitations of this feasibility study must be acknowledged. First, as a pilot investigation with a small sample size, the primary objective was to assess the field logistics and feasibility of the ECPR procedure rather than state-of-the-art care. A primary limitation of the study is the small number of goats undergoing ECMO. As the experiment remains in the exploratory stage of establishing a PBLI-related CA model, the focus was placed on addressing specific technical challenges. To comply with the requirements of animal ethics and to ensure the feasibility and stability of large animal experiments, the number of subjects was intentionally limited, with a total of 20 animals included. Another limitation is the absence of comprehensive monitoring and laboratory-guided resuscitation protocols. Detailed hemodynamic assessment was not performed, and the study lacked systematic anticoagulation monitoring and metabolic monitoring indicators. Future investigations should incorporate continuous monitoring to better characterize physiological responses and guide management during ECMO support. Third, undocumented episodes of hypoperfusion could not be ruled out. Vascular injury during cannulation, aberrant placement of the cannula and unsuccessful cannulation are remarkably higher in ECPR compared with routine ECMO. Finally, as the study was specifically designed to evaluate the feasibility of ECPR in an animal model of CA induced by severe PBLI, the findings cannot be directly translated to clinical practice. Therefore, additional studies are warranted to replicate these results across diverse realistic scenarios before applying the conclusions to human patients or other forms of critical illness.

Conclusion

The present study demonstrates the feasibility and early management of prehospital ECPR for severe PBLI-related CA and forward resuscitative care at MTF. ECPR may hold significant potential to improve survival outcomes in future combat scenarios. Regular military training should be implemented to standardize ECPR technology. In addition to unsuccessful cannulation, the inability to achieve adequate circuit flow remains a key factor contributing to ECPR failure. The effective implementation of early ECPR in the forward military setting poses considerable logistical, technical, and psychological challenges, its successful implementation may ultimately serve as a critical bridge, from being classified as killed in action to returning to duty.

Abbreviations

CA	Cardiac arrest
CPR	Cardiopulmonary resuscitation
ECPR	Extracorporeal cardiopulmonary resuscitation
ECMO	Extracorporeal membrane oxygenation
OHCA	Out-of-Hospital Cardiac Arrest
ROSC	Restoration of spontaneous circulation
VA-ECMO	Veno-arterial extracorporeal membrane oxygenation
PBLI	Primary blast lung injury
SCAPE	Sympathetic Crashing Acute Pulmonary Edema
SOP	Standard operating protocol
BiPAP	Bilevel positive airway pressure
MTF	Medical treatment facility
TNT	Trinitrotoluene

Supplementary Information

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Supplementary material 1

Supplementary material 2

Supplementary material 3

Supplementary material 4

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Author contributions

Shi-Feng Shao performed the research design and the paper drafting. ZBW and YLW performed the experimental guidance and manuscript revision. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

All experimental procedures were conducted in strict accordance with the Guide for the Care and Use of Laboratory Animals established by the Animal Ethics Committee of the Army Medical University (AMUWEC20202140) and

complied with Directive 2010/63/EU of the European Parliament. The animal production license number is SCXK (Chongqing) 2017-0002, and the animal use license number is SYXK (Chongqing) 2017-0002. The care and handling of the animals were conducted in strict accordance with the guidelines outlined in the "Guide for the Care and Use of Laboratory Animals" (<https://www.nature.com/srep/journal-policies/editorial-policies#experimental-subjects>). All surgeries were performed with ketamine hydrochloride, propofol and sufentanil citrate anesthesia, and all efforts were made to minimize suffering. All methods were performed in accordance with the relevant guidelines and regulations. The study was carried out in compliance with the ARRIVE guidelines (<https://arriveguidelines.org>).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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The views expressed are solely those of the authors and do not reflect the official policy of China.

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