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The inflammatory sequelae of aortic balloon occlusion in hemorrhagic shock

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ABSTRACT

Background: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a hemorrhage control and resuscitative adjunct that has been demonstrated to improve central perfusion during hemorrhagic shock. The aim of this study was to characterize the systemic inflammatory response associated and cardiopulmonary sequelae with 30, 60, and 90 min of balloon occlusion and shock on the release of interleukin 6 (IL-6) and tumor necrosis factor alpha.

Materials and methods: Anesthetized female Yorkshire swine (*Sus scrofa*, weight 70–90 kg) underwent a 35% blood volume–controlled hemorrhage followed by thoracic aortic balloon occlusion of 30 (30-REBOA, $n = 6$), 60 (60-REBOA, $n = 8$), and 90 min (90-REBOA, $n = 6$). This was followed by resuscitation with whole blood and crystalloid over 6 h. Animals then underwent 48 h of critical care with sedation, fluid, and vasopressor support.

Results: All animals were successfully induced into hemorrhagic shock without mortality. All groups responded to aortic occlusion with a rise in blood pressure above baseline values. IL-6, as measured (picogram per milliliter) at 8 h, was significantly elevated from baseline values in the 60-REBOA and 90-REBOA groups: 289 ± 258 *versus* 10 ± 5; $P = 0.018$ and 630 ± 348; $P = 0.007$, respectively. There was a trend toward greater vasopressor use ($P = 0.183$) and increased incidence of acute respiratory distress syndrome ($P = 0.052$) across the groups.

Conclusions: REBOA is a useful adjunct in supporting central perfusion during hemorrhagic shock; however, increasing occlusion time and shock results in a greater IL-6 release. Clinicians must anticipate inflammation-mediated organ failure in post-REBOA use patients.

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1. Introduction

Hemorrhage remains the leading cause of potentially preventable death in civilian [1,2] and military [3,4] trauma, with a significant proportion occurring before hospital admission [5,6]. Hemorrhage arising from the noncompressible regions in the torso and junctional regions has been consistently identified as particularly lethal with a mortality of 18%–50% [7–9].

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Definitive hemorrhage control and resuscitation is crucial to survival from exsanguinating injury [10]. Despite advances in damage control resuscitation [11], most of the torso hemorrhage control interventions require hospital-based facilities. However, the delivery of such care is both time dependent and capability driven; a patient must survive long enough to access such facility.

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a proactive hemorrhage control adjunct designed to sustain vital perfusion until definitive hemostasis can be achieved [12,13]. In the setting of noncompressible torso hemorrhage, a balloon is inflated in the thoracic aorta. This augments cardiac afterload improving myocardial and cerebral perfusion while simultaneously controlling arterial inflow. Importantly, unlike resuscitative thoracotomy and aortic clamping, REBOA can be initiated without the need for general anesthesia and applied in resource poor environments.

Translational large animal work and early clinical series have shown REBOA to have significant promise as a bridge to definitive hemostasis [14–17]. However, this technique is known to incur a lactate penalty that is proportional to the length of occlusion. Although up to 90 min of occlusion has been demonstrated to be survivable in a swine model of hemorrhagic shock, the systemic inflammatory response and the cardiopulmonary sequelae have yet to be characterized [14]. The aim of this study was to quantify the inflammatory response to different occlusion times and their effect on cardiopulmonary function.

2. Methods

2.1. Overview

This study represents the analysis of previously unpublished data from three experimental groups (30-REBOA, $n = 6$; 60-REBOA, $n = 8$, and 90-REBOA, $n = 6$) drawn from two previously published studies [14,15]. These two studies shared a common experimental design but realized different endpoints. All experiments were conducted at a single accredited large animal facility under the supervision of an Institutional Animal Care and Use Committee supported by licensed veterinary staff. All animals were in good health and housed for at least 7 d before study enrollment to allow for acclimation.

Female Yorkshire swine (*Sus scrofa*) weighing 70–90 kg were entered into a study protocol consisting of the following five phases: animal preparation, induction of hemorrhagic shock (30 min), balloon occlusion (30, 60, or 90 min), resuscitation (6 h), and critical care (48 h) (Fig. 1). Indices of hemodynamic performance were recorded throughout the study, along with blood sampling at specific time points. Animals were euthanized at the end of the critical care phase and necropsy performed.

2.2. Animal preparation

General anesthesia was induced using intravenous ketamine and maintained following orotracheal intubation with isoflurane (range 2%–4%). Animals were ventilated using a volume-controlled mode of 6–8 mL/kg with an FiO_2 of 40%–80% sufficient to maintain an SpO_2 of >96%. Surgical exposure and cannulation of the common carotid, internal and external jugular vein was performed via a midline neck incision. This facilitated invasive blood pressure monitoring, intravenous fluid resuscitation, and the placement of a Swan-Ganz catheter. A 14F sheath was placed in the external iliac artery via a retroperitoneal surgical exposure in the 30- and 90-REBOA groups, whereas this was accomplished in the 60-REBOA group by an ultrasound-guided percutaneous technique.

A cerebral oximetry probe (LICOX; Integra LifeSciences, Plainsboro, NJ) and carotid flow probe (Transonic Systems Inc, Ithaca, NY) were also placed; the data from these devices have been reported previously and will not be discussed further.

2.3. Induction of hemorrhagic shock (30 min)

Class IV hemorrhagic shock was induced using a standardized technique previously described [18]. Over 20 min, 35% of the animal's blood volume (total porcine blood volume: 66 mL/kg) was removed from the iliac arterial sheath: half over 7 min and the remaining over 13 min. As the swine has a contractile spleen, animals underwent a further hemorrhage of 0.15 mL/kg/min for 10 min to minimize the effect of autotransfusion. Whole blood was collected in citrated bags for reinfusion during the resuscitation phase.

2.4. Balloon occlusion (30, 60, or 90 min)

Following the conclusion of the controlled hemorrhage, REBOA was performed either for 30, 60, or 90 min. A stiff Amplatz wire was passed through the 14F sheath into the thoracic aorta guided by fluoroscopy. A Coda balloon catheter (Cook Medical, Bloomington, IN) was advanced to the midpoint of the thoracic aorta using an "over the wire" technique and inflated with a mixture of saline and contrast medium observed under fluoroscopy.

2.5. Resuscitation (6 h) and critical care (48 h)

Fluid resuscitation was initiated 10 min before commencing balloon deflation at the end of the occlusion period (30, 60, or 90 min). Shed whole blood was slowly infused to raise the mean arterial pressure (MAP) by around 25%. This was to avoid precipitous cardiovascular collapse once balloon deflation was commenced, which was performed gradually over 3 min in parallel with the rapid infusion of shed whole blood. Once the balloon was fully deflated, the catheter and wire were withdrawn from the sheath.

Whole blood resuscitation continued and was titrated to an MAP of 60 mm Hg. Once these reserves were exhausted, boluses of 1.0 L of 0.9% saline were used to achieve the target blood pressure. When animals became refractory to fluid challenges, an infusion of norepinephrine was commenced at 4 μg/h and titrated to an MAP of 60 mm Hg. Animals were also transitioned from inhaled isoflurane to intravenous ketamine and midazolam sedation once considered sufficiently stable.