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Aortic balloon occlusion is effective in controlling pelvic hemorrhage

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ARTICLE INFO

Article history:
Received 11 February 2012
Received in revised form
31 March 2012
Accepted 17 April 2012
Available online 8 May 2012

Keywords:
Hemorrhagic shock
Vascular injury
Pelvic bleeding
Endovascular balloon

ABSTRACT

Background: The objective of this study was to evaluate the efficacy of resuscitative endovascular aortic balloon occlusion (REBOA) of the distal aorta in a porcine model of pelvic hemorrhage.

Methods: Swine were entered into three phases of study: injury (iliac artery), hemorrhage (45 s), and intervention (180 min). Three groups were studied: no intervention (NI, $n = 7$), a kaolin-impregnated gauze (Combat Gauze) (CG, $n = 7$), or REBOA ($n = 7$). The protocol was repeated with a dilutional coagulopathy (CG-C, $n = 7$, and REBOA-C, $n = 7$). Measures of physiology, rates of hemorrhage, and mortality were recorded.

Results: Rate of hemorrhage was greatest in the NI group, followed by the REBOA and CG groups (822 ± 415 mL/min *versus* 11 ± 13 and 0.2 ± 0.4 mL/min respectively; $P < 0.001$). MAP following intervention (at 15 min) was the same in the CG and REBOA groups and higher than in the NI group (70 ± 4 and 70 ± 11 mm Hg *versus* 5 ± 13 mm Hg respectively; $P < 0.001$). There was 100% mortality in the NI group, with no deaths in the CG or REBOA group. In the setting of coagulopathy, the rate of bleeding was higher in the CG-C *versus* the REBOA-C group (229 ± 295 mL/min *versus* 20 ± 7 mL/min, $P = 0.085$). MAP following intervention (15 min) was higher in the REBOA-C than the CG-C group (71 ± 12 mm Hg *versus* 28 ± 31 mm Hg; $P = 0.005$). There were 5 deaths (71.4%) in the CG-C group, but none in the REBOA-C group ($P = 0.010$).

Conclusion: Balloon occlusion of the aorta is an effective method to control pelvic arterial hemorrhage. This technique should be further developed as an adjunct to manage noncompressible pelvic hemorrhage.

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0022-4804/$ – see front matter Published by Elsevier Inc.
doi:10.1016/j.jss.2012.04.035

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 OCT 2012	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Aortic balloon occlusion is effective in controlling pelvic hemorrhage	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Morrison J. J., Percival T. J., Markov N. P., Villamaria C. Y., Scott D. J., Saches K. A., Spencer J. R., Rasmussen T. E.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**7**	

1. Introduction

Vascular disruption with concomitant hemorrhage is the leading cause of potentially preventable death following military and civilian trauma [1–3]. Vascular injury within the pelvis and proximal femoral region is particularly challenging as it exists within a junctional zone between the torso and the extremities [4,5]. In this anatomic location, pelvic and proximal femoral vascular injury is not readily amenable to direct pressure or tourniquet application and generally requires control to be obtained within the abdomen.

The issue of vascular control in the setting of pelvic and junctional femoral hemorrhage has become particularly relevant to surgeons treating patients injured by improvised explosive devices (IEDs) [6]. Frequently these patients have sustained bilateral high lower extremity amputations with pelvic disruption and present *in extremis* requiring significant resuscitation and immediate operation [7]. Often, the first surgical maneuver required is occlusion of the terminal aorta through a laparotomy in order to reduce bleeding and enhance central aortic pressure.

An alternative method of aortic control is the use of endovascular aortic balloon occlusion, a technique that has been used in the setting of elective and emergent aneurysm repair for many years [8,9]. When used in the trauma context, this technique has been termed resuscitative endovascular balloon occlusion of the aorta, or REBOA [10]. The technique of REBOA does not require an operating room and has been used to salvage patients with pelvic trauma who are too unstable to move from the emergency room [11]. Recently, three aortic zones have been proposed for consideration with the use of REBOA: zone I, an occlusion zone of the descending thoracic aorta; zone II, a nonocclusion zone consisting of the paravisceral aorta; and zone III, an occlusion zone of the infrarenal aorta [10]. The aim of this study is to evaluate the effectiveness of zone III REBOA in a porcine model of pelvic arterial hemorrhage.

2. Materials and methods

2.1. Study overview

This study protocol was approved by the Institutional Animal Care and Use Committee (IACUC) and was undertaken at an accredited facility (Lackland Air Force Base, San Antonio, TX) under the supervision of licensed veterinary staff. Female Yorkshire swine (*Sus scrofa*), aged between 5 and 6 mo and weighing between 75 and 100 kg, were studied. Animals were physically fit and free of pathogens, having undergone a quarantine and acclimatization phase in the facility 7 d prior to the protocol.

The study consisted of two phases, each comparing the effectiveness of the hemostatic interventions Combat Gauze (Z-Medica Corportation, Wallingford, CT) and zone III REBOA (Fig. 1). In phase I, the clotting profile was unaltered and included a control group with no intervention (NI) and a Combat Gauze (CG) and a zone III REBOA (REBOA) group. Phase II of the study was performed in the setting of an induced dilutional coagulopathy testing the effectiveness of Combat Gauze (CG-C) and zone III REBOA (REBOA-C). Following induction of anesthesia, all groups were entered into three consecutive stages of the protocol: injury (distal iliac artery injury), hemorrhage (45 s), and hemostatic intervention (180 min). Following the hemostatic intervention phase, the animals were euthanized for postmortem analysis and the terminal aorta harvested for histologic examination.

2.2. Animal preparation

Following cannulation of an ear vein, anesthesia was induced with intravenous ketamine and maintained with isoflurane (range: 2%–4%) following orotracheal intubation and mechanical ventilation. All animals underwent cannulation of the internal jugular vein and common carotid artery with a large bore cannula through a midline surgical exposure using a modified Seldinger technique. This permitted large intravenous volume infusion using a Belmont fluid infuser, and transduction of the arterial cannula enabled continuous blood pressure monitoring. Throughout the protocol, heart rate (HR), blood pressure (BP), end tidal carbon dioxide (CO_2), core temperature (rectal), and urine output (UOP) were continuously monitored. Maintenance intravenous fluid was infused through the ear vein with lactated Ringer solution at a rate of 100 mL/h as soon as practicable. Prior to commencement of the injury stage, baseline blood tests were drawn from the arterial line and physiologic measurements recorded.

2.3. Induction of dilutional coagulopathy

The technique used has been described previously [12] and was used in phase II of this study. Following preperitoneal surgical exposure, the iliac artery is cannulated with a 14 F sheath. This enables the removal of 60% of the animal's circulating volume at a rate of 60 mL/min. This is accompanied by concomitant replacement with a colloid (Hextend; Hospira, Inc, Lake Forrest, IL) at the same rate and volume. The animal does not undergo any active warming in order to exacerbate the coagulopathy. All blood tests and baseline monitoring are repeated postdilution with a target INR of between 1.4 and 1.6.

2.4. Surgical injury and hemorrhage

A standard model of noncompressible junctional pelvic arterial hemorrhage was developed. A midline incision was used to access the right-side preperitoneal space. Using blunt dissection, the distal external iliac artery was identified and controlled with silastic vessel loops. The vessel was dissected free of adventitial tissue 5 cm proximal to the distal bifurcation. Following proximal and distal control, a small arteriotomy was performed to enable the deployment of a 6-mm arterial punch to create a standard arterial defect. All clamps and loops were then removed to permit 45 s of uncontrolled arterial hemorrhage. Blood was evacuated from the wound by surgical suction applied to the periphery of the wound (so as not to disrupt any clot formation) into graduated containers to record volume.

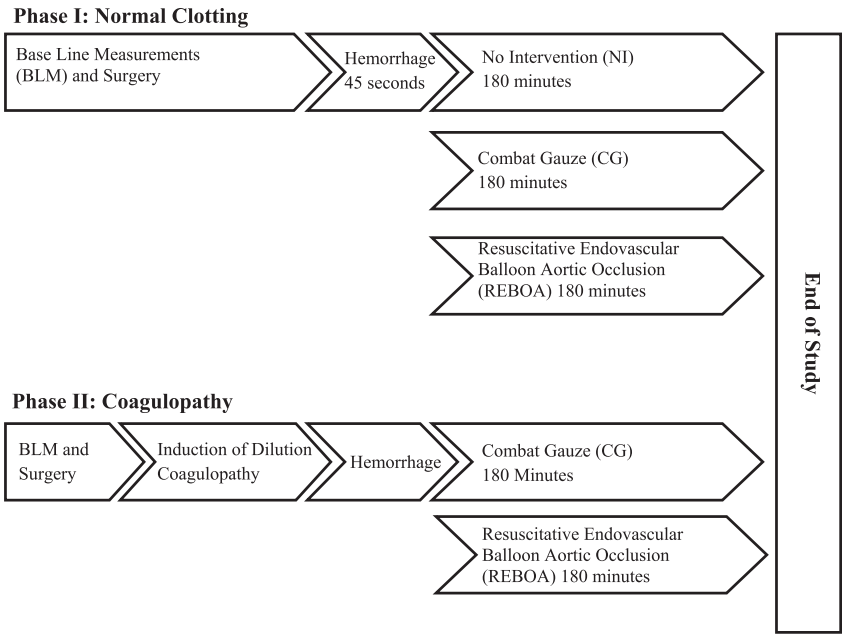

Fig. 1 – Schematic representation of experimental groups and timelines.

2.5. *Hemostatic intervention*

Common to all groups was an IV bolus of 500 mL of colloid (Hextend) following the conclusion of the hemorrhage stage. Subsequent IV fluid administration with lactated Ringer solution at 100 mL/min (to a maximum of 10 L) is triggered when the MAP is less than 65 mm Hg. Recordings of all physiologic parameters were made at 15-min intervals throughout the protocol.

The NI group underwent no further intervention.

The CG and CG-C groups underwent packing of the wound with Combat Gauze (packaged as a 3-in × 12-ft roll) and the application of pressure for 2 min. At the end of 2 min, should bleeding have persisted around or through the gauze, it was replaced with a new roll of Combat Gauze. A maximum of 2 rolls was permitted and the wound was left undisturbed after the second roll. Surgical suction was applied to the periphery of the wound to record losses.

The REBOA and REBOA-C groups had a 0.035 wire pre-positioned in the left femoral artery following an ultrasound-guided puncture and Seldinger insertion. A Coda balloon catheter (Cook Medical, Bloomington, IN) was mounted on the wire, but was not advanced beyond the skin of the animal. An angiogram was obtained to ensure correct wire position and to delineate the aortic anatomy. Following conclusion of the hemorrhage stage, the wire was advanced into the aorta and the balloon catheter delivered into the region of the terminal aorta and inflated to resistance under fluoroscopic guidance.

The experiment was concluded at 180 min post-hemorrhage, or sooner if the animal died (defined as a MAP <20 mm Hg and ET CO_2 <15 mm Hg). At the end-of-study point, final laboratory blood samples were drawn and physiologic recordings made. Total blood loss was calculated from the volume in the surgical suction reservoir and weight of surgical sponges and Combat Gauze (if used).

2.6. *Study endpoints*

The primary endpoint of the study was mortality within 180 min. Secondary endpoints were the MAP at 15, 60, and 180 min; rate of hemorrhage (mL/min); volume of resuscitation fluid; measures of acidosis and tissue ischemia (pH, base excess, and lactate); and evidence of histologic damage to the terminal aorta.

2.7. *Statistical analysis*

Data were analyzed using SPSS ver. 19.0 (SPSS, Chicago, IL). χ^2 tests were used to compare categorical data, analysis of variance (ANOVA) and *t*-tests for normally distributed continuous variables, and Mann-Whitney rank sum tests for non-normally distributed variables. Kaplan-Meier rank sum test in conjunction with survival plots was used for survival analysis.

3. Results

Thirty-eight consecutive animals were entered into the investigation: 3 model development and 35 study animals. All animals had similar pre-injury physiologic and laboratory indices (Table 1) except for weight. The animals in the NI group were heaviest, with animals in the CG group the lightest. There was no difference among groups when comparing blood volume of blood loss during the 45-s hemorrhage phase ($P = 0.366$).

In phase I (normal coagulation profile) the rate of hemorrhage (mL/min) during the intervention phase was greatest in the NI group (822 ± 415 mL/min) compared to the REBOA (9.5 ± 12.1 mL/min) and the CG groups (0.2 ± 0.4 mL/min) (Table 2). All of the animals in the NI group died within 15 min,

Table 1 – Baseline characteristics of study groups.

	NI	CG	REBOA	CG-C	REBOA-C	P value
n	7	7	7	7	7	
Weight/kg	93.1 ± 10.7	71.7 ± 7.2	74.5 ± 10.8	86.3 ± 3.9	75.9 ± 12.5	0.001
Female	7 (100%)	7 (100%)	7 (100%)	7 (100%)	7 (100%)	1.000
MAP, mm Hg	67 ± 11	61 ± 12	59 ± 7	66 ± 18	59 ± 7	0.569
HR, beats/min	85 ± 21	85 ± 17	69 ± 10	82 ± 18	81 ± 8	0.287
ET CO_2, mm Hg	35 ± 4	40 ± 2	38 ± 4	36 ± 4	37 ± 4	0.167
Temp, °C	36.0 ± 3.7	37.8 ± 0.5	36.4 ± 1.4	36.1 ± 2.1	35.8 ± 3.1	0.723
pH	7.46 ± 0.06	7.31 ± 0.04	7.45 ± 0.03	7.48 ± 0.04	7.44 ± 0.04	0.400
Base excess	1.8 ± 2.8	3.1 ± 2.5	2.6 ± 1.4	3.7 ± 2.1	6.1 ± 6.4	0.222
Lactate, mmol/L	2.0 ± 1.6	2.1 ± 1.6	1.7 ± 1.7	1.0 ± 0.3	1.6 ± 0.3	0.583
Hemoglobin, g/dL	10.2 ± 1.3	10.0 ± 0.7	10.2 ± 0.8	10.0 ± 0.5	9.0 ± 0.7	0.090
Hematocrit, %	32.0 ± 3.7	31.5 ± 2.0	32.2 ± 2.3	31.5 ± 1.7	28.7 ± 2.1	0.076
Platelet count, 10^{10}/L	271 ± 51	318 ± 72	308 ± 80	359 ± 37	312 ± 34	0.126
PT, s	13.8 ± 0.5	13.6 ± 0.3	28.5 ± 0.3	13.6 ± 0.4	14.0 ± 0.5	0.518
aPTT, s	32.7 ± 8.8	31.1 ± 3.9	31.8 ± 7.5	30.6 ± 5.0	30.0 ± 9.2	0.965
INR	1.0 ± 0.1	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.1 ± 0.0	0.070
Fibrin, mg/dL	187 ± 30	193 ± 26	210 ± 40	218 ± 24	173 ± 14	0.042

aPTT = activated partial thromboplastin time; CG = Combat Gauze; CG-C = Combat Gauze in the setting of induced dilutional coagulopathy; ET CO_2 = end tidal carbon dioxide; HR = heart rate; INR = International Normalized Ratio; MAP = mean arterial pressure; NI = no intervention; PT = prothrombin time; REBOA = resuscitative endovascular balloon aortic occlusion; REBOA-C = resuscitative endovascular balloon aortic occlusion in the setting of induced dilutional coagulopathy.

with no deaths in either the CG or AB groups (Fig. 2A). During the phase I experiments, there was no difference between the MAP (mm Hg) in the CG *versus* REBOA groups at 15 min (70 ± 4 *versus* 70 ± 11; $P = 0.955$), 60 min (71 ± 7 *versus* 63 ± 15; $P = 0.209$), or 180 min (71 ± 9 *versus* 56 ± 27; $P = 0.202$) (Fig. 3A). The REBOA group required an apparent but not significantly higher resuscitation rate and total volume during the protocol than the CG group. At the termination of the protocol the CG group had a higher base excess (5.5 ± 1.2 *versus* 2.2 ± 5.6; $P = 0.040$) and lower INR (1.0 ± 0.0 *versus* 1.2 ± 0.3; $P = 0.040$) than the REBOA group (Table 2).

Similar and effective coagulopathy during phase II of the study was confirmed with INR measurements postdilution in the CG-C (1.4 ± 0.3) and REBOA-C (1.5 ± 0.3) groups ($P = 0.507$).

Table 2 – Comparison of end-of-study laboratory values, blood loss, and mean survival length between groups.

	NI	CG	REBOA	P value*	P value†	CG-C	REBOA -C	P value‡
n	7	7	7					
pH	7.56 ± 0.04	7.48 ± 0.04	7.43 ± 0.06	0.001	0.152	7.54 ± 0.07	7.43 ± 0.05	0.008
Base excess	−2.6 ± 3.0	5.5 ± 1.2	2.2 ± 5.6	0.003	0.040	0.6 ± 2.6	1.7 ± 3.0	0.491
Lactate, mmol/L	5.5 ± 1.9	2.0 ± 1.2	3.8 ± 4.6	0.125	0.281	6.1 ± 2.5	5.6 ± 1.1	0.653
Hemoglobin, g/dL	9.2 ± 2.5	7.5 ± 1.1	5.8 ± 2.2	0.015	0.121	4.8 ± 2.6	3.5 ± 1.6	0.284
Hematocrit	29.1 ± 7.4	23.8 ± 3.2	18.9 ± 6.7	0.016	0.094	15.7 ± 7.9	11.8 ± 5.0	0.288
Platelet count, 10^{10}/L	217 ± 62	254 ± 69	203 ± 64	0.314	0.281	88 ± 32	104 ± 30	0.342
PT, s	14.5 ± 1.0	13.8 ± 0.3	15.9 ± 3.3	0.186	0.040	24.3 ± 5.7	34.3 ± 9.7	0.037
aPTT, s	24.3 ± 5.3	24.6 ± 2.4	21.2 ± 4.8	0.258	0.072	24.9 ± 12.8	43.2 ± 32.6	0.199
INR	1.1 ± 0.1	1.0 ± 0.0	1.2 ± 0.3	0.193	0.040	2.1 ± 0.6	3.3 ± 1.2	0.038
Fibrin, mg/dL	133 ± 31	158 ± 20	124 ± 38	0.119	0.054	70 ± 28	60 ± 1.9	0.401
Hemorrhage phase BL	957 ± 264	786 ± 225	1031 ± 385	0.307	0.164	943 ± 341	1043 ± 21	0.582
Intervention phase BL	3207 ± 2354	32 ± 74	1709 ± 2177	0.017	0.064	2536 ± 1234	3579 ± 1169	0.130
Blood loss, min	822 ± 415	0.2 ± 0.4	9.5 ± 12.1	<0.001	0.001	274 ± 104	20 ± 7	0.041
Total IV fluid, mL	703 ± 887	3250 ± 1841	6679 ± 4243	0.002	0.070	5359 ± 2565	8459 ± 3286	0.073
Rate of IV fluid, mL/min	133 ± 59	18 ± 10	37 ± 24	<0.001	0.066	257 ± 237	47 ± 18	0.037
Mortality, *n* (%)	7 (100%)	0	0	<0.001	n/a	5 (71.4%)	0	0.010
Length of survival, min	6.4 ± 9.2	180 ± 0	180 ± 0	<0.001	1.000	68 ± 80	180 ± 0	0.003

aPTT = activated partial thromboplastin time; CG = Combat Gauze; CG-C = Combat Gauze in the setting of induced dilutional coagulopathy; INR = International Normalized Ratio; NI = no intervention; PT = prothrombin time; REBOA = resuscitative endovascular balloon aortic occlusion; REBOA-C = resuscitative endovascular balloon aortic occlusion in the setting of induced dilutional coagulopathy.
Values are *n* or mean ± SD.
* NI *versus* CG *versus* REBOA.
† CC *versus* REBOA.
‡ CG-C *versus* REBOA-C.

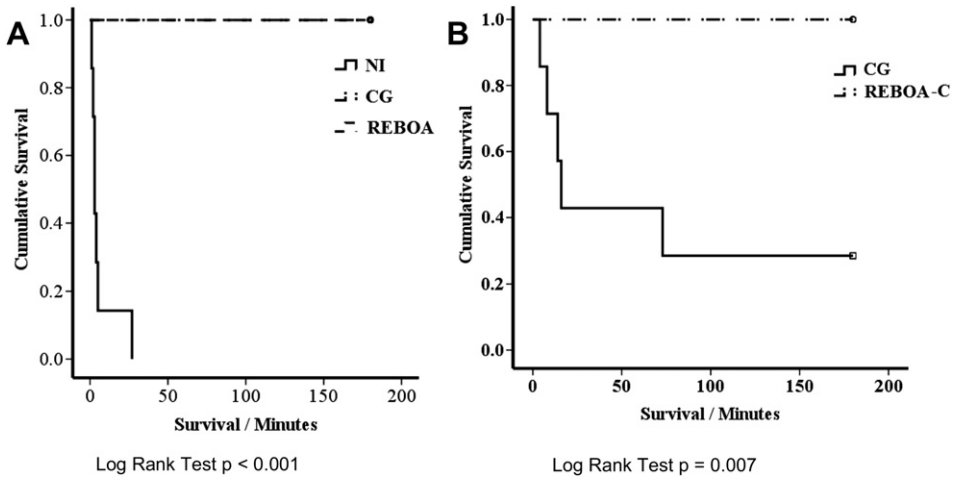

Fig. 2 – Kaplan-Meier survival curves of animals with (A) no coagulopathy, treated with either no intervention (NI), Combat Gauze (CG), or resuscitative endovascular balloon occlusion of the aorta (REBOA); and (B) dilution coagulopathy, undergoing treatment with either Combat Gauze (CG-C) or resuscitative endovascular balloon occlusion of the aorta (REBOA-C). Log rank test $P < 0.001$ and $P = 0.007$, respectively.

There were no differences between the baseline physiologic or laboratory measurements (Table 2) or the postdilution measurements (Table 3) in either the CG-C or REBOA-C groups during phase II of the study. Mortality during phase II of the study was 71.4% (5 of 7) in the CG-C group compared to 0.0% in the REBOA-C group ($P = 0.010$) (Fig. 2B). The REBOA-C group required a larger volume of IV fluid than the CG-C group ($P = 0.073$); however, when comparing the rate of administration, the REBOA-C group required a significantly lower rate of infusion (47 ± 18 ml/min *versus* 257 ± 237 ml/min; $P = 0.037$) (Table 2). During phase II of the study, the MAP at 15 min was greater in the REBOA-C (71 ± 12 mm Hg) than in the CG-C group (28 ± 31 mm Hg; $P = 0.005$), a finding that was sustained through to the end of the protocol (Fig. 3B).

There was no difference in the histologic appearance of the terminal aorta between any of the groups.

4. Discussion

This study describes a novel translatable model of pelvic vascular injury resulting in a consistent rate of hemorrhage and mortality. Findings from this study demonstrate that in the setting of normal coagulation, zone III REBOA is equally as effective at controlling hemorrhage as manual pressure with a known topical hemostatic agent (Combat Gauze) but results in greater resuscitative fluid requirements. In the setting of dilutional coagulopathy, zone III REBOA provides better hemorrhage control, improved central aortic pressure, and lower mortality than the established topical hemostatic agent. In this model, zone III REBOA was technically feasible and resulted in no adverse aortic injury.

Findings from the current study confirm and extend previous work by White *et al.*, who used a porcine model of hemorrhagic shock [13] to demonstrate the superiority of zone I REBOA to emergency thoracotomy in class IV shock [14]. Animals that underwent zone I REBOA had a higher pH, had lower lactate, and required less fluid and inotropic support during resuscitation than animals undergoing thoracotomy and aortic clamping. These findings are further supported by the recent work by Avaro *et al.* [15], who demonstrated that 40 min of zone I occlusion increased the 2-h survival of animals in hypovolemic shock compared to those treated with saline (7/16 *versus* 0/9; $P = 0.03$). All studies demonstrated an

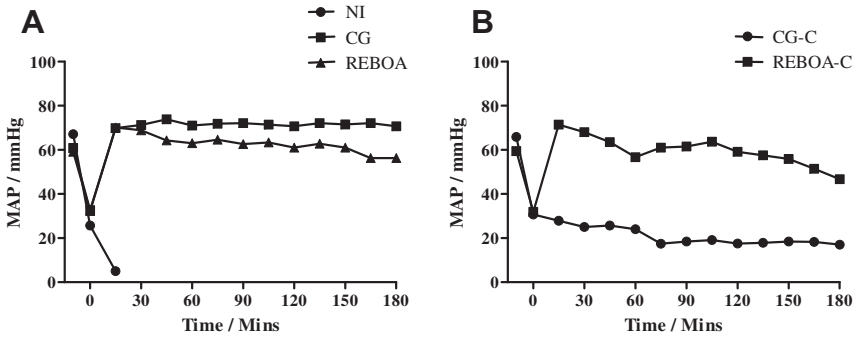

Fig. 3 – Mean MAP in animals with (A) normal coagulation, undergoing either no intervention (NI), Combat Gauze (CG), or resuscitative endovascular balloon occlusion of the aorta (REBOA); and (B) dilution coagulopathy, undergoing treatment with either Combat Gauze (CG-C) or resuscitative endovascular balloon occlusion of the aorta (REBOA-C).

Table 3 – Physiologic and laboratory indices post-induction of dilutional coagulopathy.

	CG-C	REBOA-C	P value
n	7	7	
Physiology			
MAP, mm Hg	75 ± 14	88 ± 13	0.103
HR, beats/min	101 ± 21	129 ± 28	0.055
ET CO_2, mm Hg	33 ± 3	38 ± 4	0.032
Temp, °C	35.1 ± 2.3	35.4 ± 0.3	0.737
Laboratory			
pH	7.44 ± 0.04	7.40 ± 0.02	0.058
Base excess	1.7 ± 1.8	2.0 ± 0.4	0.718
Lactate, mmol/L	6.5 ± 9.5	2.9 ± 0.4	0.383
Hemoglobin, g/dL	3.2 ± 0.7	2.9 ± 0.7	0.339
Hematocrit	10.7 ± 2.2	9.5 ± 2.3	0.358
Platelet count, 10^{10}/L	109 ± 30	79 ± 30	0.086
PT, s	17.9 ± 2.4	18.9 ± 3.0	0.507
aPTT, s	18.8 ± 2.3	17.9 ± 1.3	0.351
INR	1.4 ± 0.3	1.5 ± 0.3	0.507
Fibrin, mg/dL	89 ± 27	78.9 ± 27	0.491

aPTT = activated partial thromboplastin time; CG = Combat Gauze; ET CO_2 = end tidal carbon dioxide; PT = prothrombin time; HR = heart rate; INR = International Normalized Ratio; MAP = mean arterial pressure; REBOA = resuscitative endovascular balloon aortic occlusion; CG-C = Combat Gauze in the setting of coagulopathy; REBOA-C = Resuscitative Endovascular Balloon Occlusion of the Aorta in the setting of coagulopathy.
Values are *n* or mean ± SD.

improvement in mean blood pressure following REBOA. Importantly, the current study is the first to examine zone III occlusion in the context of a specific vascular injury model.

Interestingly, REBOA has been previously examined by studies undertaken in the 1950s and 1970s, although in a less formalized manner [16,17]. Studies undertaken in dogs found that zone I occlusion in shock was associated with a rise in central blood pressure and a reduction in traumatic abdominal hemorrhage [16,17]. However, the technique was not recommended for practice because of the high incidence of hind limb paralysis in survived subjects, although this could be eliminated with the use of hypothermia [18].

The current study also extends the findings from groups that have studied the effectiveness of the procoagulant topical hemostatic agent Combat Gauze in porcine models of femoral arterial injury [12,19–21]. Results from the current investigation demonstrate that the hemostatic effect of CG is present even in the setting of an injury to a larger artery such as the iliac. Furthermore, this study confirms the observation by Kheirabadi *et al.* that the effectiveness of CG is reduced in the setting of a dilutional coagulopathy [12]. Dilutional coagulopathy reduces all components required in the circulation to form a stable clot: red blood cells, platelets, coagulation factors, and fibrinogen (Table 2). As such, dilutional coagulopathy effectively eliminates the procoagulant action of the kaolin, which is impregnated into the CG with the intent of activating the prothrombin complex.

Importantly, the current study supports the clinical findings from a study describing the use of zone III REBOA. Martinelli *et al.* described a series of 13 patients with pelvic fracture following blunt injury who were in refractory hypovolemic shock with a mean systolic blood pressure of 41 ± 26 mm Hg [11]. Blind deployment of a balloon catheter to effect zone III REBOA resulted in a significant increase in SBP (70 mm Hg; $P = 0.001$). The cohort had a mean ISS of 48 ± 15.5 and an overall survival rate of 6/13 (46%). The clinical report from Martinelli and the current study are the first report on the specific effectiveness of zone III REBOA. However, the utility of endovascular balloon occlusion as a preemptive or resuscitation adjunct has been demonstrated in the elective and emergent repair of abdominal aortic aneurysms [8,9]. A recent technical note from this group provided a fuller description of the technique of compliant balloon selection, insertion, inflation, deflation, and removal while proposing a series of aortic zones (or landing sites) in order to better facilitate the consistent use and reporting of REBOA [10].

The current study has limitations worth noting. Foremost, the two methods of hemorrhage control used in this study, CG and REBOA, have inherent differences and may not be fully comparable. As a topical hemostatic, CG is designed to be applied with an element of manual pressure to a junctional or extremity soft tissue wound, while endovascular balloon control works under the premise of halting inflow from within the vessel proximal to the site of bleeding. The model of injury in the current study was to the distal iliac artery located within the pelvis, and was therefore not inherently suited (i.e., not directly accessible or compressible) for CG application in the clinical setting. However, because the technique of REBOA for hemorrhage control is in early stages of reevaluation and may be well suited for instances of junctional iliac or femoral injury, its comparison in this model against a known standard such as CG is sensible. In this context, REBOA and CG should not be viewed as mutually exclusive forms of hemorrhage control but instead as complementary. It is the authors' viewpoint that improvements in hemorrhage control will require not one but a combination of techniques (e.g., tourniquets, manual pressure with and without hemostatic agents, and endovascular balloon control) to manage a wide array of complex injury patterns.

Another limitation relates to the artificial nature of the induced coagulopathy. Specifically, the model of coagulopathy in this study may not be as severe as that encountered clinically following vascular injury and shock. As such, the effectiveness of REBOA in the current study may not reflect its usefulness in the setting of more profound physiologic derangement in the clinical setting. Finally, as an initial study examining the feasibility of REBOA, this study did not make observations during a survival phase. Consequently, any adverse effect of zone III REBOA on the distal circulation of the hind limbs was not accounted for in this study. Despite these limitations, this set of experiments was based on established models and demonstrated zone III REBOA to be effective compared to a recognized standard. As such, the current report provides an important foundation from which to perform additional study of this technique, including observations in a survival model.

5. Conclusion

In the setting of normal coagulation, zone III REBOA is equally effective at controlling hemorrhage as manual pressure with

a known topical hemostatic agent but results in greater resuscitative fluid requirements. In the setting of coagulopathy, zone III REBOA provides better hemorrhage control, improved central aortic pressure, and lower mortality than the established topical hemostatic agent. In the current model, zone III REBOA had high rates of technical success and resulted in no adverse aortic injury. The technique of zone III REBOA should be further developed as an adjunct to manage noncompressible pelvic and junctional femoral hemorrhage.

Acknowledgments

We are grateful for the expertise of Dr. Bijan Kheirabadi and the Damage Control Resuscitation Task Area at the US Army Institute of Surgical Research, whose advice and discussion assisted in the planning of the model used in this study.

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