



# Zones matter: Hemodynamic effects of zone 1 vs zone 3 resuscitative endovascular balloon occlusion of the aorta placement in trauma patients

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## ARTICLE INFO

### Article history:

Accepted 11 March 2019

### Keywords:

REBOA  
Aortic occlusion  
Resuscitation  
Hemorrhagic shock  
Endovascular therapy

## ABSTRACT

**Introduction:** Resuscitative endovascular balloon occlusion of the aorta (REBOA) has emerged as a therapy for hemorrhagic shock to limit ongoing bleeding and support proximal arterial pressures. Current REBOA algorithms recommend zone selection based on suspected anatomic location of injury rather than severity of shock. We examined the effects of Zone 1 versus Zone 3 REBOA in patients enrolled in the American Association for the Surgery of Trauma Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) Registry.

**Patients and methods:** The prospective observational AORTA Registry was queried from November 2013 to November 2017. Patients who received REBOA were included if their initial systolic blood pressure (SBP) was less than 90 mmHg upon arrival and they were not receiving cardiopulmonary resuscitation.

**Results:** There were 762 patients recorded in the AORTA database during the study period. Of these, 245 underwent REBOA and 99 patients met inclusion criteria. The initial balloon position was Zone 1 in 55 patients, Zone 3 in 36 patients, and unknown or Zone 2 in 8 patients. The change in proximal SBP was greater after REBOA in the Zone 1 group compared to the Zone 3 group ( $58 \pm 4$  mmHg vs  $41 \pm 4$  mmHg,  $P = 0.008$ ). The zone of occlusion was significantly associated with the change in proximal SBP in a linear regression analysis which included initial SBP, Glasgow Coma Scale score, and Injury Severity Score (Coefficient 26.82, 95% Confidence Interval 8.11–45.54,  $P = 0.006$ ).

**Conclusions:** In the hypotensive trauma patient, initial Zone 1 REBOA provides maximal hemodynamic support. Algorithms recommending initial Zone 3 placement for hypotensive trauma patients should be reconsidered.

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## Introduction

Exsanguination is the leading cause of early preventable deaths after traumatic injury, including over 80% of deaths that occur in the operating room following major trauma [1,2]. Furthermore, hemorrhagic shock is an important driver of subsequent organ dysfunction and poor outcomes in trauma patients that survive their initial resuscitation [3,4]. Non-compressible torso hemorrhage (NCTH) is an especially lethal and difficult to treat pattern of injury in both military and civilian trauma populations [5,6].

Resuscitative endovascular balloon occlusion of the aorta (REBOA) has been developed as a therapy for hemorrhagic shock due to NCTH to limit ongoing bleeding and support proximal arterial pressures [7–9]. The implementation of REBOA in trauma centers has grown in conjunction with improvements in endovascular equipment and the development of REBOA training courses [10,11]. REBOA use has also expanded for hemorrhage control to other etiologies, such as gynecologic emergencies [12].

The current paradigm of REBOA placement recommends two possible zones in the aorta for balloon inflation [8]. Recently published military and civilian guidelines recommend zone selection based on the anatomic location of injuries [13,14]. Zone 1 placement, in the descending thoracic aorta between the left subclavian artery and the celiac axis, is recommended for patients with abdominal injuries. Zone 3 placement, in the infrarenal abdominal aorta, is recommended for patients with hemorrhage

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due to pelvic injuries. Algorithms recommend obtaining a focused abdominal assessment for trauma (FAST) and a pelvic radiograph to guide zone selection in the hypotensive trauma patient [14,15].

It makes intuitive sense to select the zone of aortic occlusion based on injury location to limit hemorrhage distal to the balloon. However, this may not optimally augment proximal blood pressures to support perfusion of the heart, lungs, and brain in the setting of hemorrhagic shock. Recent translational large animal data suggest that Zone 3 placement does not provide a substantial increase in proximal blood pressure, and multiple authors now suggest immediate Zone 1 placement for patients at risk for hemodynamic collapse [16]. To date, there are no human studies evaluating the differences in hemodynamic support at different REBOA inflation zones. We sought to examine the effects of Zone 1 versus Zone 3 REBOA on proximal hemodynamics in patients enrolled in the American Association for the Surgery of Trauma (AAST) Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) Registry. We hypothesized that Zone 1 REBOA compared to Zone 3 REBOA would lead to a greater increase in systolic blood pressure (SBP) in hemodynamically unstable trauma patients.

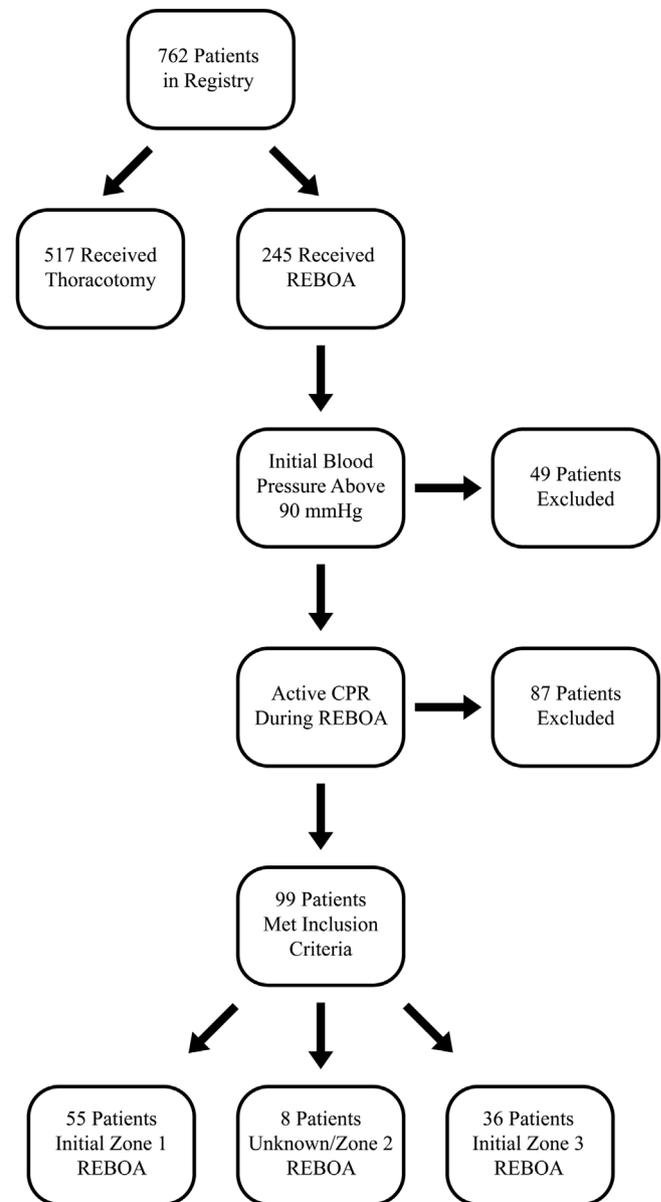
### Patients and methods

The AAST Multicenter Trials Committee approved the creation of the prospective observational AORTA Registry. All individual centers also received approval from local institutional review boards, which included a waiver of patient consent for data acquisition. The AORTA Registry, which includes patients from 29 different institutions, was queried from November 2013 to 2017. Patients were included for analysis if they received REBOA, their initial SBP was less than or equal to 90 mmHg at the time of initial evaluation, and they were not receiving cardiopulmonary resuscitation (CPR) at the time of balloon placement. Patients with an initial balloon placement in Zone 2 or in an unknown location were excluded.

To compare the frequency of interventions in each group, composite variables were defined for pelvic intervention, splenic intervention, and hepatic intervention. Pelvic intervention was defined as the placement of a pelvic binder, pelvic external fixation, pelvic embolization, or pelvic packing. Splenic intervention was defined as splenic embolization or splenectomy. Hepatic intervention was defined as hepatic packing, hepatic embolization, or hepatic resection. The primary outcome was the change in blood pressure after REBOA. Variables were compared between groups using a Student's *t*-test for continuous variables and a Chi square test for categorical variables. A linear regression analysis for the primary outcome was performed including initial SBP, Glasgow Coma Scale (GCS) score, and Injury Severity Score (ISS) as possible confounders. Results are presented as mean  $\pm$  the standard error of the mean. *P* values less than 0.05 were considered significant. All statistical analysis was performed using commercially available statistics software (Stata 14.2, StataCorp LLC, College Station, TX).

### Results

There were 762 patients recorded in the AORTA database during the study period. Of these, 245 underwent REBOA and 99 patients met inclusion criteria. The initial balloon position was Zone 1 in 55 patients, Zone 3 in 36 patients, and unknown or Zone 2 in 8 patients (Fig. 1). In the Zone 1 group, 36 patients died, and 13 patients died in the Zone 3 group. The proportions of patients receiving other interventions for different anatomic injuries differed by group (Fig. 2). More patients in the Zone 1 group compared to the Zone 3 group underwent splenic intervention (25% vs 3%,  $P=0.004$ ) and hepatic intervention



**Fig. 1.** Cohort derivation of hypotensive trauma patients from the Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) Registry. REBOA, resuscitative endovascular balloon occlusion of the aorta; CPR, cardiopulmonary resuscitation.

(40% vs 3%,  $P<0.001$ ). A smaller proportion of patients in the Zone 1 group had a pelvic intervention compared to patients in the Zone 3 group (20% vs 56%,  $P<0.001$ ).

Patient characteristics are shown in Table 1. The initial SBP was lower in the group that received Zone 1 occlusion compared to Zone 3 occlusion ( $59 \pm 2$  mmHg vs  $70 \pm 2$  mmHg,  $P=0.002$ ). The admission GCS score was lower in the Zone 1 group ( $6.1 \pm 0.7$  vs  $9.7 \pm 0.9$ ,  $P=0.001$ ), and there was no difference in ISS between groups ( $36.6 \pm 2.4$  vs  $37.3 \pm 2.9$ ,  $P=0.85$ ).

As shown in Fig. 3, the change in proximal blood pressure was greater after REBOA in the Zone 1 group compared to the Zone 3 group ( $58 \pm 4$  mmHg vs  $41 \pm 4$  mmHg,  $P=0.008$ ). There were no differences in post occlusion SBP ( $119 \pm 4$  vs  $111 \pm 4$ ,  $P=0.32$ ). Table 2 shows the results of the linear regression analysis which included initial SBP, GCS, and ISS. The zone of occlusion was significantly associated with the change in proximal blood

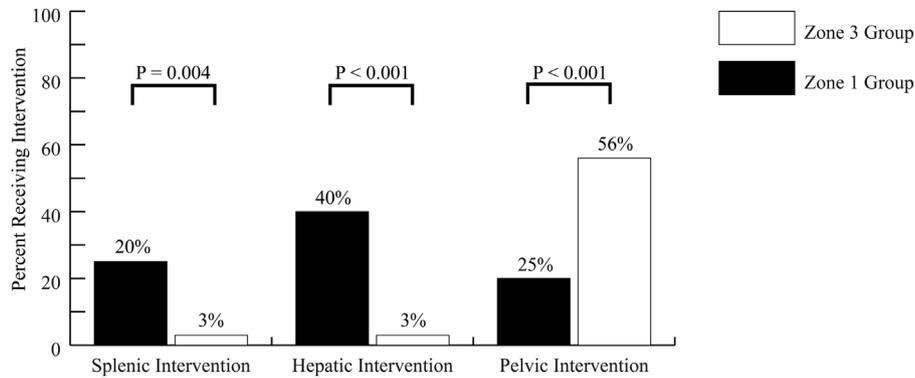


Fig. 2. Proportions of patients in the Zone 1 and Zone 3 groups that received splenic, hepatic, and pelvic interventions.

Table 1

Characteristics of 91 Hypotensive Trauma Patients that Received Zone 1 or Zone 3 REBOA.

Characteristic	Received Zone 1 REBOA (n = 55)	Received Zone 3 REBOA (n = 36)	P Value
Initial SBP, mean $\pm$ SEM	59 $\pm$ 2 mmHg	70 $\pm$ 2 mmHg	0.002
GCS score, mean $\pm$ SEM	6.1 $\pm$ 0.7	9.7 $\pm$ 0.9	0.001
ISS, mean $\pm$ SEM	36.6 $\pm$ 2.4	37.3 $\pm$ 2.9	0.85

REBOA Resuscitative endovascular balloon occlusion of the aorta, SBP Systolic blood pressure, SEM Standard error of the mean, GCS Glasgow Coma Scale, ISS Injury Severity Score.

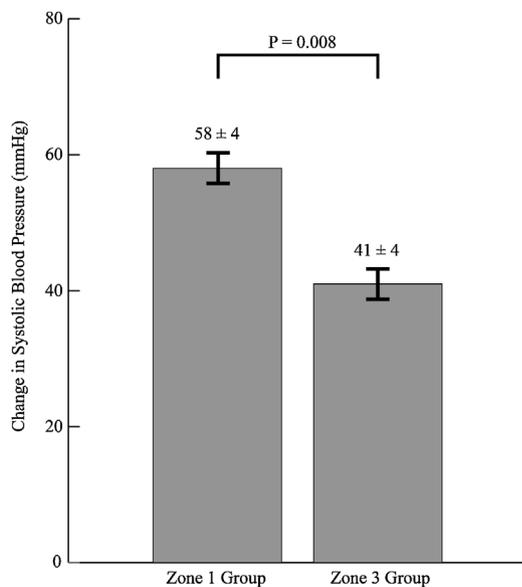


Fig. 3. The change in proximal blood pressure after resuscitative endovascular balloon occlusion of the aorta in Zone 1 compared to Zone 3.

Table 2

Linear Regression Analysis of the Change in Systolic Blood Pressure in 91 Hypotensive Trauma Patients that Received Zone 1 or Zone 3 REBOA.

Variable	Coefficient	95% Confidence Interval	P Value
Zone of Occlusion	26.82	8.11–45.54	0.006
Initial SBP	–0.42	–0.87–0.03	0.066
GCS score	1.71	0.15–3.27	0.032
ISS	–0.01	–0.57–0.55	0.965

REBOA Resuscitative endovascular balloon occlusion of the aorta, SBP Systolic blood pressure, GCS Glasgow Coma Scale, ISS Injury severity score.

pressure in this regression analysis (Coefficient 26.82, 95% Confidence Interval 8.11–45.54,  $P=0.006$ ).

## Discussion

As REBOA use expands in trauma patients and other patient populations experiencing hemorrhagic shock, it is important to establish evidence-based guidelines for its deployment and positioning. In our study of hemodynamically unstable trauma patients with an initial SBP less than or equal to 90 mmHg, Zone 1 REBOA led to a greater increase in SBP compared to Zone 3 REBOA. Furthermore, this larger increase in proximal blood pressure within the Zone 1 group occurred despite a lower initial SBP in the Zone 1 group. The association between change in proximal blood pressure and zone of occlusion remained significant in a linear regression model that included initial SBP, GCS score, and ISS.

In our cohort of hypotensive trauma patients receiving REBOA, 36% of patients received initial deployment of the balloon in Zone 3. These patients received fewer interventions for abdominal injuries and more interventions for pelvic injury. This suggests that contemporary use of REBOA is in line with current clinical practice guidelines and algorithms that recommend deployment of the balloon based on anatomic location of injury [14,15]. The rationale for this approach is to locate the balloon proximal to the source of hemorrhage, while minimizing ischemic burden. However, our results show that Zone 3 occlusion does not provide as much augmentation to the proximal arterial pressure.

Although additional data is limited, our study aligns with existing literature examining the hemodynamic effects of balloon location. One experiment in a porcine hemorrhagic shock model demonstrated that Zone 3 REBOA provided only minimal hemodynamic support when compared to Zone 1 REBOA [16]. Furthermore, the current REBOA paradigm considers balloon inflation in one of three large anatomic zones, and there may be different hemodynamic effects at distinct balloon locations even within each zone. While not in a model of hemorrhagic shock, Dogan et al demonstrated that different balloon locations within Zone 1 can change hemodynamic parameters during CPR for non-traumatic cardiac arrest [17]. This data suggests that there is likely importance beyond just which zone is chosen, but also where within the zone a balloon is placed.

The benefit of the increased proximal arterial pressure augmentation with Zone 1 REBOA does come with an additional ischemic burden compared to Zone 3 REBOA [16]. An absolute limit of Zone 1 occlusion time has not been established, but there is evidence of poorer outcomes with occlusion times longer than 60 min [18]. There are several strategies that can be employed in combination with initial Zone 1 placement in hypotensive trauma patients to mitigate the degree of distal ischemia. After initial stabilization, the balloon could be shifted to a Zone 3 position in patients with pelvic injuries and a negative FAST to prevent further pelvic hemorrhage while restoring flow to the abdominal viscera [19]. Other techniques, such as partial or intermittent occlusion, may be able to lessen the ischemic burden while maintaining the balloon position in Zone 1 [20].

There are several limitations to this study. This is an observational study within a relatively small total number of patients. Undoubtedly the reason for choosing each zone of occlusion is not only influenced by current practice guidelines, but also by institutional norms as well as provider preference. These subtle differences cannot be accounted for in the current dataset. Furthermore, this study is not able to compare the longer-term outcomes of aortic occlusion, such as morbidity and mortality, in these groups with fundamental baseline differences. These limitations notwithstanding, this is the first examination of the hemodynamic effects of initial REBOA location in humans. Future research should focus on gathering high quality evidence for the development of clear guidelines for REBOA, including optimal placement locations.

## Conclusions

Initial Zone 1 REBOA provides maximal hemodynamic support and the greatest chance for stabilization in the hypotensive trauma patient. Guidelines and algorithms recommending initial Zone 3 placement for hypotensive trauma patients should be reconsidered.

## Source of funding

This was an investigator-initiated study without funding.

## Conflicts of interest

Dr. Johnson receives grant funding from the Department of Defense, the Henry M. Jackson foundation, and the Military Health Research Foundation. Dr. Johnson is a co-founder of Certus Critical Care, Inc. All other authors have no conflicts of interest to report.

## Disclaimer

The views expressed in this material are those of the authors, and do not reflect the official policy or position of the U.S. Government, the Department of Defense, the Department of the Air Force, or the University of California, Davis.

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