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Intraoperative REBOA: an analysis of the American Association for the Surgery of Trauma AORTA registry

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ABSTRACT

Background Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a less-invasive technique for aortic occlusion (AO). Commonly performed in the emergency department (ED), the role of intraoperative placement is less defined. We hypothesized that operating room (OR) placement is associated with increased in-hospital mortality.

Methods The American Association for the Surgery of Trauma AORTA registry was used to identify patients undergoing REBOA. Injury characteristics and outcomes data were compared between OR and ED groups. The primary outcome was in-hospital mortality; secondary outcomes included total AO time, transfusion requirements, and acute kidney injury.

Results Location and timing of catheter insertion were available for 305 of 321 (95%) subjects. 58 patients underwent REBOA in the OR (19%). There were no differences with respect to sex, admission lactate, and Injury Severity Score. The OR group was younger (33 years vs. 41 years, p=0.01) and with more penetrating injuries (36% vs. 15%, p<0.001). There were significant differences with respect to admission physiology. Time from admission to AO was longer in the OR group (75 minutes vs. 23 minutes, p<0.001) as was time to definitive hemostasis (116 minutes vs. 79 minutes, p=0.01). Unadjusted mortality was lower in the OR group (36.2% vs. 68.8%, p<0.001). There were no differences in secondary outcomes. After controlling for covariates, there was no association between insertion location and in-hospital mortality (OR 1.8, 95% CI 0.30 to 11.50).

Discussion OR REBOA placement is common and generally employed in patients with more stable admission physiology. OR placement was not associated with increased in-hospital mortality despite longer times to AO and definite hemostasis when compared with catheters placed in the ED.

Level of evidence IV; therapeutic/care management.

BACKGROUND

Hemorrhage remains the most common cause of preventable death in trauma patients and the second most common cause of all trauma-related deaths.[1 2] In this population, non-compressible torso hemorrhage accounts for 60% to 70% of deaths[3 4] due to severe hemorrhage from major vessels or solid organs in the chest, abdomen, or pelvis.[4] Rapid hemorrhage control is essential in these situations,[5] as delayed control is associated with increased mortality.[6 7]

In select patients with non-compressible torso hemorrhage, resuscitative endovascular balloon occlusion of the aorta (REBOA) can be used as a bridge to definitive hemostasis.[8–12] This approach affords temporary occlusion of the thoracic or infrarenal aorta with a balloon catheter inserted through the common femoral artery.[13 14] As such, it represents a rapid, less-invasive alternative to open aortic occlusion (AO).

Because the median time to death from severe hemorrhage is approximately 1 hour,[15] there is now appropriate emphasis on shortening the time to hemostasis as much as possible.[5] Currently, the majority of REBOA catheters are placed either in the emergency department (ED) or the operating room (OR).[16] ED placement may afford more rapid time to temporary hemostasis or potentially delay definitive hemostasis if placed unnecessarily. Placement in the OR may delay temporary hemostasis, leading to increased mortality. As such, the benefits of ED REBOA insertion as compared with perioperative insertion in the OR have not been explored. We sought to characterize the use of intraoperative REBOA and hypothesized that insertion in the OR is associated with increased in-hospital mortality.

METHODS

The American Association for the Surgery of Trauma (AAST) AORTA registry prospectively identifies trauma patients undergoing open and endovascular AO at 29 centers. Using the AORTA registry, we performed a retrospective review of all patients who underwent endovascular occlusion of the aorta from January 2013 to December 2017. Collected variables included demographic information, mechanism of injury, blood transfusion requirements, admission physiology, time to successful AO, duration of occlusion, time to definitive hemorrhage control, and location of occlusion. Our primary endpoint was in-hospital mortality, and secondary outcomes included total AO time, transfusion requirements, and development of acute kidney injury.

A univariate analysis for non-parametric continuous variables was analyzed for skewness using the Shapiro-Wilk test of normality. Values <0.05 were considered skewed and were represented as medians and IQRs. Mann-Whitney U test was used

to compare medians between groups, and Student's t-test was used for normally distributed data. Categorical values were represented as n (%). A χ^2 analysis was performed to compare categorical values. Statistical significance was set at $p<0.05$.

To investigate the relationships between REBOA occlusion location (OR vs. ED) and in-hospital mortality, we first performed univariate regression between candidate variables and inpatient mortality. Each candidate variable with $p<0.2$ was then used in a multivariable regression model on the outcome of in-hospital mortality. To adhere to the principle of parsimony and avoid overfitting, we removed variables from the final multivariable model that did not contribute to model discrimination. To assess the adequacy of our sample size, we performed a post-hoc CI analysis with the minimal clinically important difference in mortality set at 10%.[17] Stata V.14.2 was used for all statistical analyses.

RESULTS

Endovascular AO was performed on 321 patients during the study period. Data on the location and timing of insertion were available for 305 (95%) patients. Fifty-eight (19%) patients underwent REBOA in the OR compared with 247 (81%) in the ED. Thirty-six (64%) catheters were placed in aortic zone I in the OR versus 164 (69%) placed in zone I in the ED ($p=0.60$). There were no differences between groups with respect to sex, admission lactate, and Injury Severity Score (ISS). However, patients who underwent REBOA in the OR were younger (33 years vs. 41 years, $p=0.01$) and were more likely to have a penetrating mechanism (36% vs. 15%, $p<0.001$). There were significant differences with respect to admission physiology; patients in the OR group were more likely to present with higher admission systolic blood pressure (SBP) (110 mm Hg vs. 80 mm Hg, $p<0.001$), Glasgow Coma Scale (GCS) score (7 vs. 3, $p<0.001$), and heart rate (HR) (114 vs. 101 beats per minute, $p=0.04$). Patients in the OR group were less likely to have cardiopulmonary resuscitation (CPR) in progress at admission (3.4% vs. 32.5%, $p<0.001$). Time from admission to AO was longer in the OR group (75 minutes vs. 23 minutes, $p<0.001$) as was time to definitive hemorrhage control (116 minutes vs. 79 minutes, $p=0.01$) (table 1).

Unadjusted in-hospital mortality was lower in the OR group (36.2% vs. 68.8%, $p<0.001$), but there were no differences in transfusion requirements or acute kidney injury. Total AO time was also similar between the OR and ED groups (33 minutes vs. 30 minutes, $p=0.61$). On univariate analysis, time to AO, admission SBP, GCS score, HR, ISS, age, lactate, CPR at admission, and location of REBOA insertion were all associated with the outcome of in-hospital mortality (table 2) and were included in a multivariate logistic regression model.

After controlling for these covariates, there was no independent association between insertion location and in-hospital mortality (OR 1.8, 95% CI 0.30 to 11.50) (table 3).

When time to definitive hemorrhage control was added to the model, the number of observations decreased by 30% (106 to 74). In this smaller model, there was again no association between REBOA insertion location (ED vs. OR) and in-hospital mortality, and time to definitive hemorrhage control was not associated with in-hospital mortality when controlling for the other covariates (online supplementary file 1).

CI analysis demonstrated that a larger sample size would not have identified any clinically significant increase in mortality with OR placement (online supplementary file 2).

Table 1 Characteristics of patients undergoing OR vs. ED REBOA placement

	Total (n=305)	OR REBOA (n=58)	ED REBOA (n=247)	P value
Age	39 (26–57)	32.5 (22–51)	40.5 (27–58)	0.01
Sex				0.92
Male	233 (76.4)	44 (75.8)	189 (76.5)	
Female	72 (23.6)	14 (24.2)	58 (23.5)	
Mechanism				<0.001
Penetrating	59 (19.3)	21 (36.3)	38 (15.4)	
Blunt	243 (79.6)	37 (63.7)	206 (83.4)	
ISS		34 (25–42)	34 (25–45)	0.38
Admission SBP	82 (49–114)	110 (80–130)	80 (0–111)	<0.001
Admission HR	106 (69–130)	114 (92–132)	101 (52–129)	0.04
Admission GCS score	3 (3–13)	7 (3–15)	3 (3–9)	<0.001
Admission lactate	8.2 (5–11.8)	6.5 (3.9–10.8)	8.2 (5.2–12.1)	0.05
Prehospital CPR	89 (29.1)	2 (3.4)	87 (35.2)	<0.001
Time from admission to AO (min)	25 (15–46)	75 (36–110)	23 (14–27)	<0.001
Time to definitive hemorrhage control	91 (53–165)	116 (78–172)	79 (48–155)	0.01
Occlusion time (min)	32 (12.5–66)	33 (11–67)	30 (15–63)	0.61
pRBC (units)	12 (6–25)	16 (8–28)	12 (5–22)	0.06
Acute kidney injury	57 (18.7)	10 (17.2)	47 (19.0)	0.75
Mortality	191 (62.6)	21 (36.2)	170 (68.8)	<0.001

Data for non-parametric continuous variables expressed as median (IQR); categorical values expressed as n (%).
AO, aortic occlusion;CPR, cardiopulmonary resuscitation; ED, emergency department; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score;OR, operating room; pRBC, packed red blood cells; REBOA, resuscitative endovascular balloon occlusion of the aorta; SBP, systolic blood pressure.

DISCUSSION

In this analysis of the AORTA registry, we examined the use of intraoperative REBOA and characterized the relationship between REBOA placement location and mortality. We found that REBOA placement in the OR was not associated with increased in-hospital mortality in similarly injured patients. Interestingly, the total AO time was similar between the ED and OR groups despite longer time to definitive hemorrhage control in the OR group, and there was no difference in acute kidney injury as a marker of end-organ malperfusion.

Our study is the first to specifically characterize the use of OR REBOA and compare outcomes between ER and OR REBOA placement. Almost 20% of REBOA catheters in this analysis of

Table 2 Univariate analysis on the outcome of in-hospital mortality

	OR	95% CI	P value
Admission time to successful AO	0.98	0.981 to 0.996	0.002
Admission GCS score	0.78	0.743 to 0.834	<0.001
Admission HR	0.98	0.984 to 0.995	<0.001
Admission SBP	0.98	0.984 to 0.995	<0.001
ISS	1.02	1.006 to 1.045	0.009
Age	1.02	1.004 to 1.033	0.013
Admission lactate	1.1	1.034 to 1.175	0.003
CPR	9.3	4.064 to 21.189	<0.001
Location of AO (operating room)	0.53	0.393 to 0.737	<0.001

AO, aortic occlusion; CPR, cardiopulmonary resuscitation; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score; SBP, systolic blood pressure.

Table 3 Multivariate logistic regression analysis on the outcome of in-hospital mortality

	OR	95% CI	P value
Admission time to successful AO	1.00	0.981 to 1.021	0.921
Admission GCS score	0.80	0.720 to 0.900	<0.001
Admission HR	1.01	0.996 to 1.028	0.158
Admission SBP	0.99	0.980 to 1.012	0.627
ISS	1.05	1.006 to 1.090	0.025
Age	1.06	1.021 to 1.101	0.002
Admission lactate	1.08	0.978 to 1.208	0.123
CPR	10.16	1.440 to 71.745	0.02
Location of AO (operating room)	1.8	0.295 to 11.498	0.513

Number of observations: 106.
AO, aortic occlusion; CPR, cardiopulmonary resuscitation; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score; SBP, systolic blood pressure.

the registry were placed in the OR, compared with 26% of catheters in a 2016 study using the same registry.[16] Similar to this analysis, using the Aortic Balloon Occlusion Trauma Registry, which identifies REBOA patients from 13 hospitals and six countries across the world, Sadeghi *et al*[18] found that 16% of catheters were placed in the OR and an additional 16% were placed in a hybrid-type setting.

REBOA use outside of the ED for non-trauma indications has been described.[19–22] Studies that have evaluated the use of REBOA in non-trauma and combined trauma/non-trauma settings have noted a higher OR placement rate.[9 23] In one study with a total of 11 patients undergoing REBOA placement, most commonly for ruptured visceral aneurysms and massive upper gastrointestinal bleeding, 82% of devices were placed in the OR.[23] The authors of that study found OR placement particularly helpful in patients with "hostile" abdomens.

The importance of rapid hemorrhage control has been well established in the trauma literature. Mortality in hypotensive trauma patients remains high and occurs early after presentation. Harvin *et al*[24] found that hypotensive trauma patients requiring emergent laparotomy (within 90 minutes of admission) had a 46% mortality; 65% of those deaths were related to hemorrhage. In another study looking at trauma deaths within 4 hours of admission, 50% of patients died within the first hour.[15] In our study, OR placement was associated with longer time to AO (75 minutes vs. 23 minutes), although location of placement and time to AO were not associated with increased in-hospital mortality after controlling for admission physiology and GCS score. This is in contrast to earlier studies that have shown an association between increased time to hemorrhage control and mortality. Meizoso *et al*[6] found that patients with hypotension with torso gunshot wounds, the majority of which were abdominal, had higher mortality if they arrived in the OR after 10 minutes; cumulative 50% mortality was at 16 minutes. Clarke *et al*[7] found that hypotensive trauma patients with abdominal injuries requiring laparotomy had a 1% increase in the probability of death for every 3 minutes spent in the ED. Prolonged prehospital transfer times have also been associated with increased mortality in patients with torso injuries.[25] Our results could differ from those above because patients in the OR group were not hypotensive on arrival, although we attempted to control for this in our regression analysis. It is apparent that REBOA may be used according to patient physiology regardless of location.

None of the aforementioned studies included patients who underwent REBOA, and the effects of early temporary control with balloon occlusion on outcomes prior to definitive operative intervention are less clear. Placement of REBOA catheters can take time, with one study showing a median time from procedure start to zone I occlusion of 474 seconds (7.9 minutes), compared with 317 seconds (5.3 minutes) for open AO.[26] Other studies have shown shorter open procedural times of <4 minutes.[27] Although the clinical significance of this time delay is unclear, any benefits of early temporary hemorrhage control with REBOA must be weighed against potential delays in definitive operative intervention especially if the REBOA procedure is challenging and/or unsuccessful. This may be particularly true of patients not truly in extremis.[28] One study has shown an association between longer times to the arterial access phase of REBOA placement and mortality.[29] Our results showed that time to definitive hemorrhage control was longer in patients who underwent OR placement, probably because these patients were stable in the ED. It can be assumed that catheter placement would not delay definitive control if placed during induction of anesthesia or even during the incision. Perhaps REBOA should be placed in the ED for "non-responders" but can be reserved for the OR in those with ongoing torso hemorrhage who initially respond to resuscitation measures.

Duration of AO may be another factor that differs between location of REBOA placement. Increased time of balloon occlusion has been associated with increased inflammatory mediators, lactate levels, renal dysfunction, and liver necrosis in animal models.[30 31] Saito *et al*[32] showed that the mean duration of AO was shorter in survivors after REBOA placement (21 minutes vs. 35 minutes), although there are many possible explanations for this finding. In our study, the total time of occlusion was similar in the ED and OR groups. This is a surprising finding, as one would expect longer occlusion times for balloons deployed in the ED. One possible explanation is that clinicians are too aggressive in placing catheters in the ED in patients who may not actually require the procedure or may be placing catheters prophylactically without initial inflation of the balloon. In general, it is recommended that zone I occlusion not be performed if time to operative intervention is likely to exceed 15 minutes.[33] We did not find a difference between groups with respect to acute kidney injury, a surrogate of end-organ malperfusion during AO.

We acknowledge the limitations of this study. Although the AAST AORTA registry prospectively captures patients undergoing REBOA placement, data are retrospectively entered into the database and suffer from inherent limitations regarding missing data and time accuracy. In addition, there are factors that influence the decision to perform REBOA and placement location that are not captured in the registry, such as rapid changes in clinical condition, exact indications for placement (ie, transient responder vs. non-responder), provider judgment and experience, initial physiology and injury pattern, and availability of ORs or interventional suites. Full capture of the physiologic response to resuscitation or further decompensation is beyond the scope of the database. Differences in the outcomes related to location of REBOA placement could suffer from selection or survival bias. We attempted to mitigate some of this bias by controlling for the effects of admission physiology and GCS score in our logistic regression model.

CONCLUSIONS

Placement of REBOA catheters in the OR is relatively common and does not appear to be associated with increased in-hospital mortality despite longer times to AO and definite hemostasis when compared with catheters placed in the ED. These findings could be related to the complex interplay between time to temporary versus

definitive hemorrhage control. Future studies are needed to further elucidate the timeframe in which REBOA is most effective.

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