Increased mortality with resuscitative endovascular balloon occlusion of the aorta only mitigated by strong unmeasured confounding: An expanded analysis using the National Trauma Data Bank

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BACKGROUND: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is being increasingly adopted to manage noncompressible torso hemorrhage, but a recent analysis of the 2015 to 2016 Trauma Quality Improvement Project (TQIP) data set showed that placement of REBOA was associated with higher rates of death, lower extremity amputation, and acute kidney injury (AKI). We expand this analysis by including the 2017 data set, quantifying the potential role of residual confounding, and distinguishing between traumatic and ischemic lower extremity amputation.

METHODS: This retrospective study used the 2015 to 2017 TQIP database and included patients older than 18 years, with signs of life on arrival, who had no aortic injury and were not transferred. Resuscitative endovascular balloon occlusions of the aorta placed after 2 hours were excluded. We adjusted for baseline variables using propensity scores with inverse probability of treatment weighting. A sensitivity analysis was then conducted to determine the strength of an unmeasured confounder (e.g., unmeasured shock severity/response to resuscitation) that could explain the effect on mortality. Finally, lower extremity injury patterns of patients undergoing REBOA were inspected to distinguish amputation indicated for traumatic injury from complications of REBOA placement.

RESULTS: Of 1,392,482 patients meeting the inclusion criteria, 187 underwent REBOA. After inverse probability of treatment weighting, all covariates were balanced. The risk difference for mortality was 0.21 (0.14–0.29) and for AKI was 0.041 (−0.007 to 0.089). For the mortality effect to be explained by an unmeasured confounder, it would need to be stronger than any observed in terms of its relationship with mortality and with REBOA placement. Eleven REBOA patients underwent lower extremity amputation; however, they all suffered severe traumatic injury to the lower extremity.

CONCLUSION: There is no evidence in the TQIP data set to suggest that REBOA causes amputation, and the evidence for its effect on AKI is considerably weaker than previously reported. The increased mortality effect of REBOA is confirmed and could only be nullified by a potent confounder. (*J Trauma Acute Care Surg.* 2021;91: 790–797. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Therapeutic/care management, level IV.

KEY WORDS: REBOA; noncompressible hemorrhage; outcomes; complications; sensitivity analysis.

Noncompressible torso hemorrhage is a leading cause of mortality in both civilian and military trauma.[1] Resuscitative endovascular balloon occlusion of the aorta (REBOA) has emerged as a temporizing measure to stop internal hemorrhage and maintain perfusion of vital organs until definitive control can be established in the operating room (OR). Temporary aortic occlusion with a balloon was originally reported during the Korean war[2] but did not garner widespread attention until recent improvements in endovascular technology and infrastructure.[3]

Resuscitative endovascular balloon occlusion of the aorta use has increased in recent years, but the quality of evidence supporting its use remains poor.[4] Cohort studies[5–8] demonstrated improved survival for REBOA relative to resuscitative thoracotomy (RT) but likely suffer from selection bias. While both RT and REBOA are options for noncompressible hemorrhage, patients undergoing RT are typically in cardiac arrest and, hence, have higher baseline risk than patients undergoing REBOA.[4]

When RT patients are excluded from the control group, these benefits are no longer observed. Joseph and colleagues[9] used the 2015 to 2016 National Trauma Database (NTDB) from the American College of Surgeons Trauma Quality Improvement Project (ACS-TQIP) to show that REBOA placement was associated with higher rates of death, lower extremity amputation, and acute kidney injury (AKI) than a matched control group. Unlike the previous cohort studies, Joseph et al.[9] excluded patients undergoing RT and instead relied on propensity score matching to identify a comparable control group. These results

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raised widespread concerns that the use of REBOA during this period may have had more harm than benefit.

The results of Joseph et al.[9] depend on the assumption that the propensity score matching produced a comparable control group. This is only possible if all confounders of the relationship between REBOA placement and outcomes are measured. Previous authors have noted several key confounders, which are not available in the NTDB, and raised concerns that the results could be driven by residual confounding.[10–12] Furthermore, it is unclear if the increased risk of lower extremity amputation was due to REBOA-induced ischemic injury or severe lower extremity traumatic injury requiring amputation unrelated to REBOA.

In this article, we expand upon the analysis of Joseph et al.[9] and address several of its limitations. First, we replicate the analysis in the 2015 to 2017 NTDB, thereby increasing the sample size with an additional year of data. Next, we assess the role of residual confounding by quantifying the strength of a potential confounder that could explain the mortality effect. We compare this potential confounder to the strength of measured covariates, allowing us to judge if it is plausible that such a variable exists. Finally, we investigate the reported effect of REBOA on amputation risk by distinguishing between traumatic and ischemic lower extremity injury. We hypothesized that the detrimental effect of REBOA would be sensitive to confounding, such that even a weak confounder could explain the effect.

TABLE 1. Number of REBOA Cases Meeting Inclusion Criteria for Each ICD Code

A.

ICD-9/10 Code	<1 h	1–2 h	2–3 h	>3 h	Unknown
02LW3DJ — Occlusion of thoracic aorta, descending with intraluminal device, temporary, percutaneous approach	0	1	0	2	0
04L03DJ — Occlusion of abdominal aorta with intraluminal device, temporary, percutaneous approach	1	2	0	0	1
04L03DZ — Occlusion of abdominal aorta with intraluminal device, percutaneous approach	52	124	14	38	24
04L03ZZ — Occlusion of abdominal aorta, percutaneous approach	2	2	2	1	1
04L04DZ — Occlusion of abdominal aorta with intraluminal device, percutaneous endoscopic approach	2	0	2	8	1
04L04ZZ — Occlusion of abdominal aorta, percutaneous endoscopic approach	0	1	0	4	0
39.78 — Endovascular implantation of branching or fenestrated graft(s) in aorta	0	0	1	3	0
Total	57	130	19	56	27

B.

ICD-10 Code	2015	2016	2017
02LW3DJ — Occlusion of thoracic aorta, descending with intraluminal device, temporary, percutaneous approach	0	0	1
04L03DJ — Occlusion of abdominal aorta with intraluminal device, temporary, percutaneous approach	0	0	3
04L03DZ — Occlusion of abdominal aorta with intraluminal device, percutaneous approach	3	24	149
04L03ZZ — Occlusion of abdominal aorta, percutaneous approach	0	1	3
04L04DZ — Occlusion of abdominal aorta with intraluminal device, percutaneous endoscopic approach	0	2	0
04L04ZZ — Occlusion of abdominal aorta, percutaneous endoscopic approach	1	0	0
Total	4	27	156

(A) by time of placement and (B) by year. Note that the REBOAs placed after 2 hours are excluded from the analysis and do not appear in B.

ICD, International Classification of Diseases; *ICD-9*, *International Classification of Diseases, Ninth Revision*; *ICD-10*, *International Classification of Diseases, Tenth Revision*.

PATIENTS AND METHODS

Study Design

We conducted a retrospective cohort study using the 2015 to 2017 NTDB, a database that collects data from trauma centers enrolled in ACS-TQIP. Data entry into the NTDB is conducted by specifically trained registrars at each trauma center. At present, more than 850 trauma centers participate in ACS-TQIP.

Patients who underwent REBOA placement were identified based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* code 39.78, and the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Procedure Coding System* codes were used: 02LW3DJ, 04L03DJ, 04L03DZ, 04L03ZZ, 04L04DZ, and 04L04Z (descriptions in Table 1).

The institutional review board at Yale University exempted this study from approval, as the data set is deidentified. This study is reported following the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[13]

Baseline Variables

Baseline variables included in the analysis were demographics, vitals (systolic blood pressure, heart rate, respiratory rate), Glasgow Coma Scale score, Injury Severity Scores (ISSs), organ-specific injury scores, and teaching status of hospital. The organ-specific injury scores were compiled from the Abbreviated Injury Scale (AIS) to provide a finer representation of a patient's injuries.

Inclusion and Exclusion Criteria

Patients were excluded if they were younger than 18 years, had no signs of life on arrival, were transferred from outside hospital, or had aortic injury. Patients with missing values in the baseline variables were excluded, and a complete case analysis was performed. Finally, patients who underwent REBOA were excluded if the procedure was not started within 2 hours after arrival. Characteristics of excluded patients are shown in Supplemental Table 1 (http://links.lww.com/TA/C7).

Missing Data Analysis

The primary analysis excluded patients with missing data in any baseline variable. We included a secondary analysis using the "missing-indicator" approach, which includes these patients. Specifically, for each baseline variable that had more than 10 missing samples in REBOA group, we added a dummy variable indicating whether it was missing. For categorical variables, this simply involved adding an extra "missing" level. For continuous variables, the value was imputed to be the mean among nonmissing

individuals, and an additional Boolean variable denoting that it was missing was also added.

Outcomes

Our primary outcome was mortality, which included death in the emergency department and as an inpatient. Thirty-day mortality was not available. Secondary outcomes were ischemic lower extremity amputation, AKI, compartment syndrome, myocardial infarction (MI), and unplanned return to the OR. Acute kidney injury, compartment syndrome, MI, and unplanned return to the OR directly correspond to individual data elements abstracted and defined by the NTDB. In contrast, lower extremity amputation could only be identified via procedure codes (Supplemental Table 2, http://links.lww.com/TA/C7). Given that amputations in REBOA patients may be indicated because of lower extremity trauma, as opposed to REBOA-induced ischemia, we excluded patients with amputations likely driven by direct extremity injury. These were defined as patients with lower extremity AIS score of 3 or greater, or those with AIS codes specific to traumatic amputation. We also excluded those patients who underwent amputation on the same day as REBOA placement, as it is unlikely that these amputations were due to REBOA-induced ischemia.

Statistical Analysis

Patients who underwent REBOA are often in extremis and represent some of the most critically ill patients in the NTDB. Hence, the severity of injury strongly confounds the relationship between REBOA and negative outcomes. To account for this confounding, we used propensity scores with inverse probability of treatment weighting.[14] First, we used logistic regression to model the probability of receiving REBOA using the baseline covariates listed previously. Overlap between propensity score distributions was inspected visually. The propensity score model (Supplemental Table 3, http://links.lww.com/TA/C7) was then used to balance covariates by inverse probability of treatment weighting. Specifically, the average treatment effect among the treated was obtained by reweighting the non-REBOA group so that the baseline variables matched those of REBOA group. In this setting, average treatment effect among the treated is the effect of REBOA among patients who received REBOA. In contrast, the average treatment effect would be the effect of REBOA on general trauma patients, where it would not be indicated in the vast majority of cases. Covariate balance was then assessed using standardized mean difference, with a standardized mean difference of <0.1 considered acceptable balance. Results were reported as risk differences (RDs), namely, the probability of an outcome in the REBOA group minus the probability in the non-REBOA group.

There are several potential confounders that are not measured in the NTDB. These include ongoing bleeding from an uncontrolled source (that may or may not be controlled by REBOA), degree of shock, and degree of direct tissue injury that leads to an inflammatory response further exacerbating the degree of shock. All of these variables are potential confounders because they affect the decision to attempt REBOA and also affect the outcome. The vital signs and injury variables do not capture the full, dynamic clinical picture, raising concerns that the treatment effect may be biased by residual confounding.

We conducted a sensitivity analysis to determine the required strength of an unmeasured confounder that could explain the effect of REBOA on mortality. Let A denote placement of REBOA, Y the outcome, X measured covariates, and U an unmeasured binary confounder. We use a result of VanderWeele and Arah[15] on the bias in the effect of A on Y attributable to U. Specifically, let δ denote the association of REBOA with the confounder,

$$\delta = P(U = 1|A = 1, X) - P(U = 1|A = 0, X),$$

which we assume to be constant over strata of X. Let γ denote the association of the outcome and confounder,

$$\gamma = E(Y|A, X, U = 1) - E(Y|A, X, U = 0),$$

which we assume to be constant over strata of A and X. The magnitude of bias due to U is then

$$\mathrm{d} = \delta\gamma.$$

We compute δ and γ for various measured covariates to give context as to the strength of a hypothetical unmeasured covariate that could explain the effect of REBOA on mortality.

The code used to produce the results in this article is available at https://github.com/linqiaozhi/TQIP-REBOA-Paper.git.

RESULTS

In the 2015 to 2017 NTDB, there were a total of 2,873,920 patients, including 499 patients who underwent REBOA. After applying the exclusion criteria, the analysis was conducted with a total of 1,392,482 patients, including 187 who underwent REBOA (Supplemental Fig. 1, http://links.lww.com/TA/C7). The number of patients meeting criteria who underwent REBOA in 2015 was 4, in 2016 was 27, and in 2017 was 156 (Table 1, A). Characteristics of excluded patients are in Supplemental Table 1 (http://links.lww.com/TA/C7). Of note, 102 patients who met inclusion criteria but underwent REBOA later than 2 hours after arrival were excluded (Table 1, B).

Patients who underwent REBOA presented with lower systolic blood pressure (mean [SD], 109 [35] mm Hg vs. 140 [27] mm Hg), greater overall burden of injury (mean [SD] ISS, 34 [15] vs. 9 [8]), and higher injury scores in every system and were more likely to present to a university center (81% vs. 40%) when compared with patients who did not undergo REBOA (Table 2). After inverse probability of treatment weighting, balance between the two groups was achieved for all variables, with absolute standardized mean differences below 0.1 (Fig. 1 and Table 2).

The unadjusted RD for death was 0.52 (95% CI, 0.45–0.59), and after propensity-score weighting, the RD decreased to 0.21 (95% CI, 0.14–0.29). In contrast, the adjusted RDs for deep venous thrombosis, pulmonary embolism, stroke, MI, compartment syndrome, unplanned return to the OR, and AKI did not have lower 95% CI limits that exceeded 0 (Table 3 and Supplemental Table 4 [http://links.lww.com/TA/C7]).

Missing Data Analysis

The following variables had more than 10 missing values in the REBOA group: race, systolic blood pressure, pulse, respiratory rate, Glasgow Coma Scale assessment qualifier 1, and respiratory assistance description. The final data set used for missing data

TABLE 2. Baseline Characteristics Before and After Inverse Probability of Treatment Weighting

	No REBOA, Unweighted (n = 1,392,295)	No REBOA, Weighted	REBOA (n = 187)
Age, y	51.9 (21.3)	41.9 (18.3)	42.2 (18.2)
Sex			
– Female	537,183 (38.6%)	59 (31.0%)	58 (31.0%)
– Male	855,112 (61.4%)	132 (69.0%)	129 (69.0%)
Race			
– Black or African American	227,260 (16.3%)	53 (27.8%)	51 (27.3%)
– Other race	158,771 (11.4%)	36 (18.8%)	35 (18.7%)
– White	1,006,264 (72.3%)	102 (53.4%)	101 (54.0%)
Teaching status			
– Community	575,318 (41.3%)	30 (15.8%)	30 (16.0%)
– Nonteaching	255,565 (18.4%)	5 (2.6%)	5 (2.7%)
– University	561,412 (40.3%)	156 (81.6%)	152 (81.3%)
Systolic blood pressure (mm Hg)	140.0 (27.2)	108.0 (39.7)	108.6 (35.5)
Pulse (beats/min)	88.2 (19.7)	110.0 (30.8)	109.6 (29.4)
Respiratory rate (breaths/min)	18.6 (4.4)	21.1 (9.8)	21.0 (8.2)
GCS	14.2 (2.5)	8.1 (5.3)	8.2 (5.3)
Head and neck	0.8 (1.4)	1.5 (1.8)	1.4 (1.8)
Face	0.2 (0.6)	0.4 (0.8)	0.4 (0.9)
Thorax	0.6 (1.2)	2.5 (1.7)	2.5 (1.6)
Abdomen	0.3 (0.9)	2.9 (1.7)	2.9 (1.7)
Extremities	1.1 (1.2)	2.5 (1.6)	2.4 (1.7)
External	0.6 (0.6)	1.0 (0.8)	1.0 (0.8)
Spleen			
– Grade V	2,967 (0.2%)	12 (6.3%)	12 (6.4%)
– Grade IV	4,104 (0.3%)	9 (4.7%)	9 (4.8%)
– Grade III	6,955 (0.5%)	11 (6.0%)	11 (5.9%)
– Grade I–II	14,213 (1.0%)	14 (7.1%)	13 (7.0%)
– Unspecified	4,408 (0.3%)	11 (5.6%)	10 (5.3%)
– No injury	1,359,648 (97.7%)	135 (70.4%)	132 (70.6%)
Kidney			
– Grade V	791 (0.1%)	4 (2.1%)	4 (2.1%)
– Grade IV	1,903 (0.1%)	8 (4.4%)	8 (4.3%)
– Grade III	3,529 (0.3%)	6 (3.2%)	6 (3.2%)
– Grade I–II	5,068 (0.4%)	5 (2.7%)	5 (2.7%)
– Unspecified	5,920 (0.4%)	15 (8.1%)	15 (8.0%)
– No injury	1,375,084 (98.8%)	152 (79.6%)	149 (79.7%)
Liver			
– Grade VI	71 (0.0%)	4 (1.9%)	3 (1.6%)
– Grade V	1,690 (0.1%)	14 (7.2%)	13 (7.0%)
– Grade IV	4,387 (0.3%)	17 (8.7%)	16 (8.6%)
– Grade III	6,804 (0.5%)	8 (4.3%)	8 (4.3%)
– Grade I–II	15,003 (1.1%)	22 (11.4%)	21 (11.2%)
– Unspecified	6,240 (0.4%)	13 (6.9%)	13 (7.0%)
– No injury	1,358,100 (97.5%)	114 (59.7%)	113 (60.4%)
Femur fracture			
– Injury	182,385 (13.1%)	37 (19.6%)	37 (19.8%)
– No injury	1,209,910 (86.9%)	154 (80.4%)	150 (80.2%)
Tibia fracture			
– Injury	110,788 (8.0%)	37 (19.4%)	36 (19.3%)
– No injury	1,281,507 (92.0%)	154 (80.6%)	151 (80.7%)
Pelvis fracture			
– Pelvic ring fracture, incomplete disruption of posterior arch	13,203 (0.9%)	26 (13.5%)	25 (13.4%)
– Pelvic ring fracture, complete disruption of posterior arch	3,216 (0.2%)	28 (14.8%)	26 (13.9%)

Continued next page

TABLE 2. *(Continued)*

	No REBOA, Unweighted (n = 1,392,295)	No REBOA, Weighted	REBOA (n = 187)
– Pelvic ring fracture, posterior arch intact	51,503 (3.7%)	24 (12.8%)	24 (12.8%)
– Pelvic ring fracture, not further specified	16,209 (1.2%)	9 (5.0%)	9 (4.8%)
– No injury	1,308,164 (94.0%)	103 (54.0%)	103 (55.1%)
Lower extremity vascular			
– Laceration, perforation, puncture major >20% volume loss	2,272 (0.2%)	9 (4.7%)	9 (4.8%)
– Laceration, perforation, puncture minor <20% volume loss	1,222 (0.1%)	2 (1.2%)	2 (1.1%)
– Intimal tear	564 (0.0%)	3 (1.6%)	3 (1.6%)
– NFS	3,605 (0.3%)	8 (4.4%)	8 (4.3%)
– No injury	1,384,632 (99.4%)	168 (88.2%)	165 (88.2%)
Iliac vessels			
– Laceration, perforation, puncture major >20% volume loss	819 (0.1%)	7 (3.8%)	7 (3.7%)
– Laceration, perforation, puncture minor <20% volume loss	347 (0.0%)	0 (0.0%)	0 (0.0%)
– Intimal tear, Laceration, perforation, puncture NFS	951 (0.1%)	12 (6.5%)	11 (5.9%)
– NFS	784 (0.1%)	7 (3.6%)	6 (3.2%)
– No injury	1,389,394 (99.8%)	165 (86.2%)	163 (87.2%)
Any vascular			
– Laceration, perforation, puncture major >20% volume loss	10,355 (0.7%)	38 (19.9%)	37 (19.8%)
– Laceration, perforation, puncture minor <20% volume loss	5,172 (0.4%)	7 (3.9%)	7 (3.7%)
– Laceration, perforation, puncture NFS	6,806 (0.5%)	20 (10.2%)	18 (9.6%)
– Intimal tear, no disruption	4,580 (0.3%)	10 (5.5%)	10 (5.3%)
– No injury	1,365,382 (98.1%)	116 (60.5%)	115 (61.5%)
ISS	8.9 (8.0)	34.1 (18.7)	33.6 (15.2)

Values are presented as mean (SD) unless otherwise specified.
GCS, Glasgow Coma Scale; NFS, not further specified.

analysis had 1,640,433 non-REBOA patients and 220 REBOA patients. As in the complete data analysis, balance between the two groups was achieved for all variables. The primary outcome of death was nearly identical to the complete case analysis, with an unadjusted RD of 0.52 (95% CI, 0.45–0.58), and after adjustment, the RD decreased to 0.19 (95% CI, 0.13–0.26). The secondary outcomes before and after adjustment were also similar (Supplemental Table 5 [http://links.lww.com/TA/C7] and Supplemental Table 6 [http://links.lww.com/TA/C7]).

Sensitivity Analysis

We controlled for measured confounders by propensity-score weighting, but the estimates may still be biased by residual confounding due to unmeasured covariates. We conducted a sensitivity analysis to determine the strength of a hypothetical confounder that could explain the reported effect of REBOA on mortality (Fig. 2). The variable would need to be more strongly related to REBOA placement and the outcome than all measured covariates.

Effect of REBOA on Amputations

Of the 187 included patients who underwent REBOA, 11 had a lower extremity amputation. Only two of these patients had AIS severity scores of less than 3. One of these was specifically coded as "Amputation [traumatic]," and the other underwent amputation on day 1 of injury. Each of these patients also suffered severe lower extremity injuries, as indicated by AIS codes.

DISCUSSION

In the absence of randomized trials,[16] the effects of REBOA on patient outcomes can only be determined using observational studies. We conducted a propensity score analysis to measure the treatment effect of REBOA in a large national trauma registry and found that REBOA was associated with a significantly increased risk of death. In a sensitivity analysis, we found this effect to be robust to even the strongest confounders. In contrast, there was no evidence of increased lower extremity amputation risk due to the REBOA-induced ischemia.

Our results further support the association of increased mortality with REBOA placement reported by Joseph et al.[9] Furthermore, we found this effect to be robust to strong residual confounding. To explain the mortality effect, a confounder would need to be more closely related to REBOA and mortality than hypotension, abdominal organ injury, and pelvic fracture or having an ISS of 25. We argue that the existence of an unmeasured confounder (or a set of unmeasured confounders) of such importance is unlikely. However, we note that a particularly important potential unmeasured confounder is occult shock. This would not be identified by presenting systolic blood pressure but would manifest later with decompensation and hypotension leading to REBOA placement. This study, among others, demonstrates the importance of occult shock, and we would recommend that this be collected in the NTDB by documenting the delayed development of overt shock.

A feared complication of REBOA is vascular injury of the lower extremity leading to ischemia and amputation,[17,18] particularly

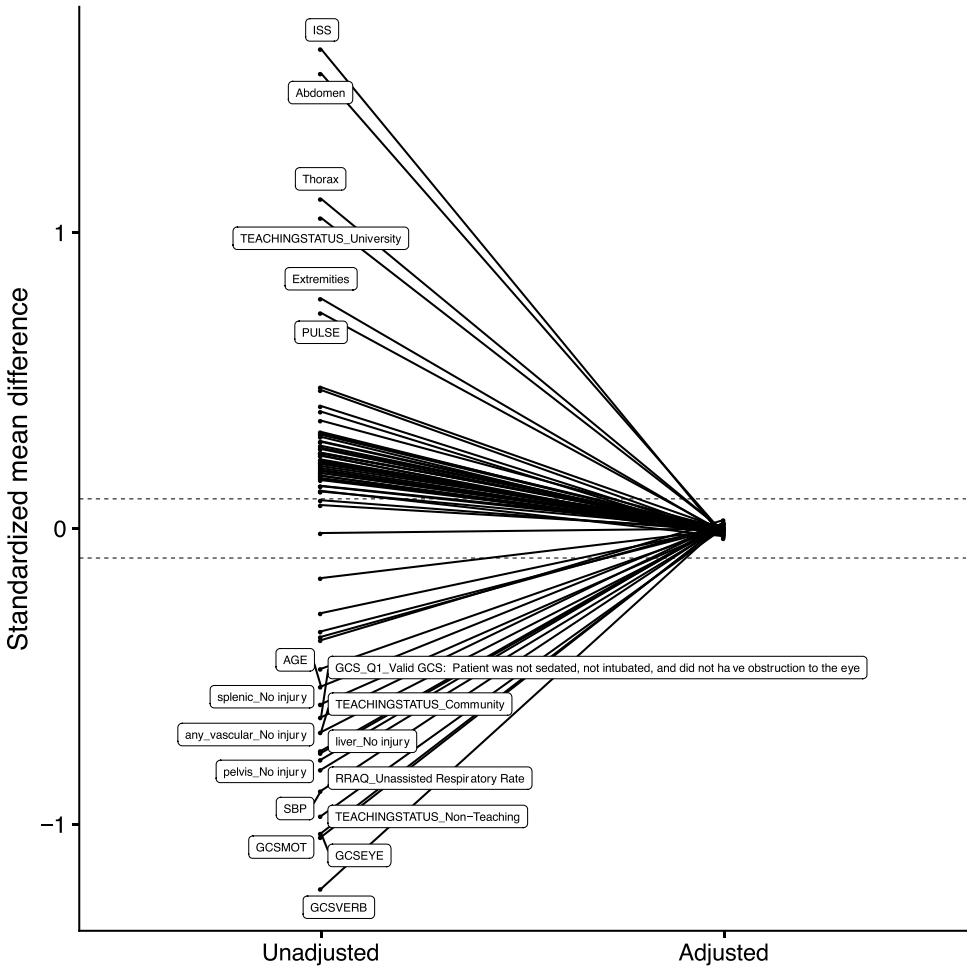

Figure 1. Covariate balance before and after weighting. Covariates with a positive SMD are larger in the REBOA group, and covariates with a negative SMD are smaller in the REBOA group. Covariates with SMD between at –0.1 and 0.1 (dotted lines) are considered balanced. The labels for covariates with SMD of >0.5 or SMD of <–0.5 are shown. Anatomically labeled data are organ-specific injury scores. SMD, standardized mean difference.

with large (10–14 Fr) femoral artery sheath sizes.[19] Joseph et al.[9] reported 5/140 lower extremity amputations in the REBOA group, which was significantly higher than the control group. In our study, we found that every REBOA patient who underwent lower extremity amputation had severe lower extremity trauma, was specifically coded as traumatic amputation, or underwent amputation on the first day of injury. It is likely that these amputations were at least partly driven by traumatic injury as opposed to vascular injury from REBOA placement. In particular, the rates of this complication among patients in the NTDB are likely substantially lower than those reported by Joseph et al.[9] Recently, Levin and colleagues[20] also published a study in which they reanalyzed the 2015 to 2017 NTDB and reached the same conclusion.

Resuscitative endovascular balloon occlusion of the aorta has been rapidly introduced as a treatment modality in severely injured patients at high risk for mortality. This combination of a new procedure and high-risk patients may lead to rapid acceptance of this technology by inexperienced surgeons. Although REBOA has been shown to be clinically useful in moderately large case series in comparison with RT, its safety profile must be shown to be superior to the standard of care before it becomes a widely used approach outside of high-volume centers. Our study with its larger sample size and evaluation of strength of confounder necessary to explain the apparent effect of REBOA continues to cast doubt on the efficacy of REBOA in widespread use.

TABLE 3. Number of Patients With Each Outcome in Non-REBOA (Weighted) and REBOA Groups

Outcome	Non-REBOA	REBOA	RD (95% CI)
Death	63 (0.33)	102 (0.55)	0.214 (0.140–0.287)
Deep vein thrombosis	7 (0.04)	11 (0.06)	0.022 (−0.012 to 0.056)
Pulmonary embolism	3 (0.02)	4 (0.02)	0.004 (−0.017 to 0.025)
Stroke	3 (0.02)	5 (0.03)	0.011 (−0.012 to 0.035)
MI	1 (0.00)	0 (0.00)	−0.005 (−0.006 to −0.003)
Compartment syndrome	2 (0.01)	4 (0.02)	0.011 (−0.010 to 0.032)
Unplanned return to OR	9 (0.05)	13 (0.07)	0.022 (−0.015 to 0.059)
AKI	13 (0.07)	19 (0.11)	0.041 (−0.007 to 0.089)

Proportions are shown in parentheses. See Supplemental Table 4 (http://links.lww.com/TA/C7) for unweighted estimates.

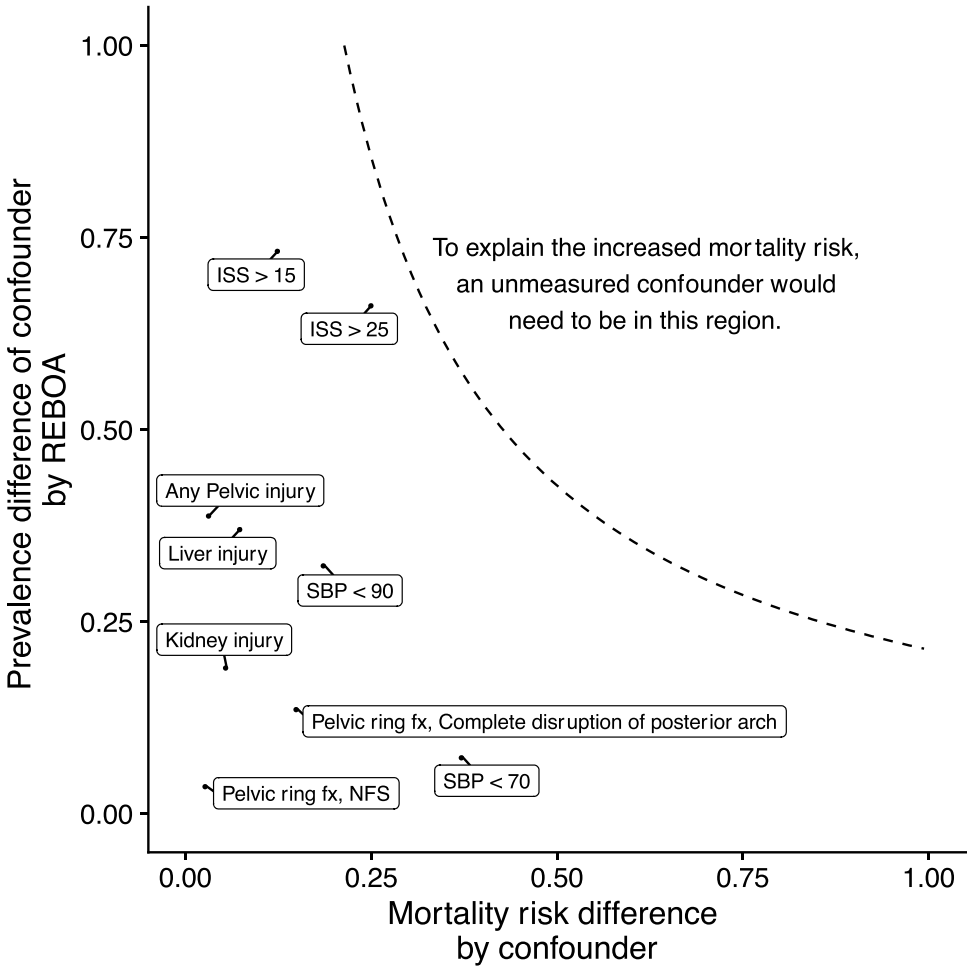

Figure 2. Strength of unmeasured confounders to explain observed effect size.

Our study is limited by its retrospective nature and the absence of key variables from the NTDB. The propensity score analysis can only balance measured variables, and hence, treatment effects can be arbitrarily biased by unmeasured confounders. To address this, we quantified the strength of an unmeasured confounder that could explain the reported mortality effect. However, we note that this sensitivity analysis assumes that the relationship of a putative confounder with both the treatment and outcome does not vary across strata of other covariates, which may not be true for many variables. Our study is also limited by the relatively small number of REBOA patients, about 20% of which were excluded due to missing values. The NTDB also does not report several variables that may explain the poor outcomes of patients undergoing REBOA, most importantly, occult shock, as described previously. Similarly, there is no information about the duration of aortic occlusion, duration of in-dwelling sheath, zone of occlusion, or pre-REBOA resuscitation efforts and response to resuscitation. Each of these variables could help identify subpopulations that may benefit from REBOA. Finally, we note that it is possible that some of the detrimental effects of REBOA are due to the minimal experience with this technology. Ongoing follow-up studies are necessary to determine if increased experience leads to improved outcomes. Unfortunately, because of the nature of the NTDB, this is impossible to assess.

CONCLUSION

Using the NTDB, we found that placement of REBOA was associated with increased mortality, even after adjusting for measured confounders using propensity scores. This effect was further supported by our sensitivity analysis, as any unmeasured confounder would need to be stronger than almost all measured confounders to explain REBOA's effect on mortality. Finally, we showed that previously reported amputations in REBOA patients were likely at least partly related to traumatic injury rather than a pure iatrogenic injury.

AUTHORSHIP

G.C.L. and K.M.S. conceptualized and designed the study. G.C.L. performed the statistical analysis in consultation with W.L. All authors contributed in the interpretation of results and drafting of the article.

DISCLOSURE

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