A core outcome set for resuscitative endovascular balloon occlusion of the aorta: A consensus based approach using a modified Delphi method

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AUTHORS/CONTRIBUTORS

Megan Brenner, Prytime Medical Inc, Honorarium, Board Member; Charles Fox, Prytime Medical Inc, Honorarium, Board Member; Ernest Moore, Haeomonetics/Instrumentation Laboratory/Stago/ThromboTherapeutics, Grant/Grant/Grant/Owner, PI/PI/PI/CoFounder; Laura Moore, Frontline Technologies, Honorarium, Consultant; Jonathan Morrison, Prytime Medical Inc., Honorarium, Consultant; D. Dante Yeh, UptoDate, Royalties, Author. The other authors have nothing to disclose.

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Jeffry Nahmias, MD, MHPE, FACS, Saskya Byerly, MD, Deborah Stein, MD, FACS, Elliott R. Haut, MD, PhD, FACS, Jason W. Smith, MD, PhD, FACS, Rondi Gelbard, MD, FACS, Markus Ziesmann, MD, FRCSC, Melissa Boltz, MD, FACS, Ben Zarzaur, MD, MPH, FACS, Walter L. Biffl, MD, Megan Brenner, MD, Joseph DuBose, MD, Charles Fox, MD, Joseph Galante, MD, FACS, Matthew Martin, MD, Ernest E. Moore, MD, Laura Moore, MD, Jonathan Morrison, MD, Tatsuya Norii, MD, FACEP, Thomas Scalea, MD, *and* **D. Dante Yeh, MD, MHPE, FACS***, Orange, California*

BACKGROUND:	The utilization of resuscitative endovascular balloon occlusion of the aorta (REBOA) in trauma has grown exponentially in recent years. However, inconsistency in reporting of outcome metrics related to this intervention has inhibited the development of evidence-based guidelines for REBOA application. This study sought to attain consensus on a core outcome set (COS) for REBOA.
METHODS:	A review of "landmark" REBOA articles was performed, and panelists (first and senior authors) were contacted for participation in a modified Delphi study. In round 1, panelists provided a list of potential core outcomes. In round 2, using a Likert scale (1 [not important] to 9 [very important]), panelists scored the importance of each potential outcome. Consensus for core outcomes was defined a priori as greater than 70% of scores receiving 7 to 9 and less than 15% of scores receiving 1 to 3. Feedback was provided after round 2, and a third round was performed to reevaluate variables not achieving consensus and allow a final "write-in" round by the experts.
RESULTS:	From 17 identified panelists, 12 participated. All panelists (12 of 12, 100%) participated in each subsequent round. Panelists initially identified 34 unique outcomes, with two outcomes later added upon write-in request after round 2. From 36 total potential outcomes, 20 achieved consensus as core outcomes, and this was endorsed by 100% of the participants.
CONCLUSION:	Panelists successfully achieved consensus on a COS for REBOA-related research. This REBOA-COS is recommended for all clinical trials related to REBOA and should help enable higher-quality study designs, valid aggregation of published data, and development of evidence-based practice management guidelines. (*J Trauma Acute Care Surg.* 2022;92: 144–151. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.)
LEVEL OF EVIDENCE:	Diagnostic test or criteria, level V.
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KEY WORDS:	REBOA; hemorrhage control; torso hemorrhage; resuscitative endovascular balloon occlusion of the aorta.

While balloon occlusion of the aorta was first described in 1954 in the context of open surgery during the Korean War,[1] the modern adoption of resuscitative endovascular balloon occlusion of the aorta (REBOA) for trauma has grown exponentially with advances in endovascular surgical technique and technology.[2,3] Beginning from early reports in the 1980s[4,5] to more widespread adoption because of the proliferation of courses[6,7] and increasing experience with the procedure,[8] the use of REBOA has expanded rapidly. Suggested indications for use include noncompressible torso hemorrhage,[9,10] pelvic fractures,[11] severe junctional hemorrhage, cardiac arrest,[12] as well as prehospital use.[13,14] However, some authors have suggested concern with this proliferation because of a lack of documented survival benefit and risk of complications associated with use of REBOA.[15–17]

Further complicating this picture is the inconsistency in the reporting of key data points related to REBOA, which was highlighted by the joint statement from the American College of Surgeons Committee on Trauma, the American College of Emergency Physicians, the National Association for Emergency Medical Services Physicians, and the National Association of Emergency Medical Technicians in 2019. This document stated that "Defining the optimal use of REBOA requires rigorous and complete data acquisition, including … clinical outcomes."[18] One method to address this concern is the development of a core outcome set (COS). A COS refers to the minimum set of

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From the Department of Surgery (J.N.), University of California, Irvine, Orange, California; Department of Surgery (S.B.), University of Tennessee Health Science Campus, Memphis, Tennessee; Department of Surgery (D.S.), Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, California; Division of Acute Care Surgery, Department of Surgery (E.R.H.), The Johns Hopkins University School of Medicine, Baltimore, Maryland; Hiram C. Polk Md Department of Surgery (J.W.S.), University of Louisville, Louisville, Kentucky; Division of Trauma and Acute Care Surgery, Department of Surgery (R.G.), University of Alabama at Birmingham, Boshell Building, Birmingham, Alabama; Department of Surgery (M.Z.), University of Manitoba, Winnipeg, Manitoba, Canada; Division of Trauma, Acute Care and Critical Care Surgery, Department of Surgery (Mel.B.), Penn State Hershey Medical Center, Hershey, Pennsylvania; Department of Surgery (B.Z.), University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; Department of Surgery (W.L.B.), Scripps Clinic Medical Group, La Jolla, California; Department of Surgery (Meg.B.), University of California Riverside School of Medicine, Riverside CA; R Adams Cowley Shock Trauma Center (J.D., C.F., J.M., T.S.), University of Maryland School of Medicine, Baltimore, Maryland; Department of Surgery (J.G.), University of California, Davis, Sacramento; Department of Surgery (M.M.), Scripps Mercy Hospital, San Diego, California; Ernest E Moore Shock Trauma Center at Denver Health (E.E.M.), University of Colorado Denver, Denver Colorado; Department of Surgery (L.M.), The University of Texas Health McGovern Medical School, Houston, Houston, Texas; Department of Emergency Medicine (T.N.), University of New Mexico Health Sciences Center, Albuquerque, New Mexico; Department of Traumatology and Acute Critical Medicine (T.N.), Osaka University Graduate School of Medicine, Osaka, Japan; and Department of Surgery (D.D.Y.), University of Miami Miller School of Medicine, Miami, Florida.

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Address for reprints: Jeffry Nahmias, MD, MHPE, FACS, Division of Trauma, Department of Surgery, University of California, Irvine, Suite 1600, 333 The City Blvd West, Orange, CA 92868-3298; email: jnahmias@hs.uci.edu.

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outcomes to be measured and reported in all clinical studies related to a condition.[19] The development of a COS thereby addresses what outcomes should be studied prior to how and when these outcomes should be measured. Standardized outcome reporting across studies ensures that meaningful endpoints are conveyed and allows health care providers to make more informed decisions about the use of an intervention. A proliferation of COS has already begun across medical fields,[20,21] including the development of best practices via the Core Outcome Measures in Effectiveness Trials (COMET) tool.[22] The Eastern Association for the Surgery of Trauma (EAST) has been a leader in clinical practice management guideline development for over two decades[23] and has realized the limitations caused by lack of standardized outcomes across published articles in trauma. Therefore, EAST created a task force to develop a COS for prospective studies regarding REBOA, as well as define variables that merit incorporation within national databases evaluating REBOA. The objectives of this study were to describe and analyze the process, statistical analysis, and final COS using a modified Delphi survey approach among a group of published REBOA experts.

METHODS

The COS in REBOA (COS-REBOA) study was developed following the COMET[22] tool and conducted in accordance with recommendations from the COS-Standards for Development and Reporting (COS-STAR).[24] The study was registered with the COMET database and deemed exempt according to institutional review board.

The development of the REBOA-COS began with a review of the published literature (from 1966 to present) regarding REBOA (M.Z. and Mel.B. performed this review) using search phrases including "REBOA," "Resuscitative Endovascular Balloon Occlusion of the Aorta," and "Balloon Aortic Occlusion." In addition, we reviewed all EAST Landmark articles, which were previously determined and already linked on the EAST landmark articles in trauma and acute care surgery website.[25] These articles were determined to be landmark studies after a professional medical librarian first performed a comprehensive search using the Web of Science Database, limited to only primary literature. Titles were then scanned, and studies unrelated to acute care surgery were eliminated. Next, the publications were reviewed in full, considering (1) number of citations, (2) number of citations per year for newer publications, (3) quality of scientific method, and (4) relevance to clinical practice. Additional select publications not meeting initial search criteria were also considered. For example, a newly published article may be considered a "landmark" if it was deemed to be high quality and likely to immediately impact clinical practice without having received an arbitrary number of citations (because of its recency). Finally, an article was designated "landmark" status by majority group consensus vote by the affiliated EAST committee. The list of "landmark" articles undergoes annual review by the affiliated EAST committee, and studies are added or deleted as deemed necessary.

This was followed by a modified Delphi survey study to achieve consensus (Fig. 1). The Delphi method is a type of consensus method used to define agreement among stakeholders when empirical data may not exist. Participants are first allowed to brainstorm ideas. Subsequent rounds then seek to develop consensus, selecting only outcomes that are deemed crucial by participants. Notably, between rounds, the participants are given individualized and anonymous feedback with an opportunity to revise their responses.

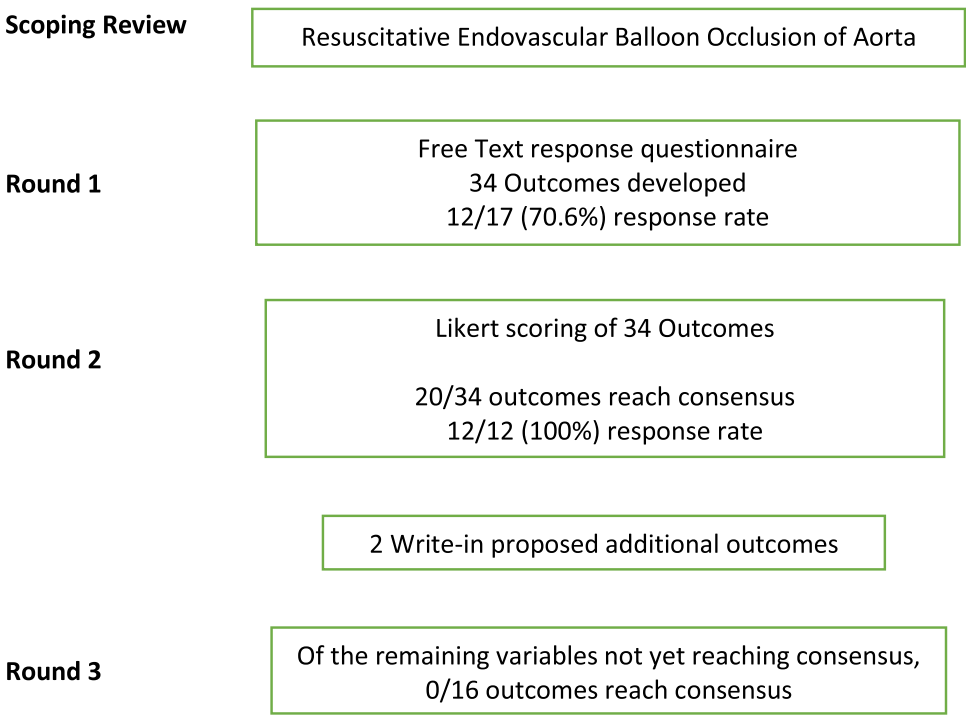

Figure 1. Core outcomes for REBOA study flow diagram.

To recruit Delphi participants, the task force first reviewed all first and last author investigators of REBOA-related articles deemed "landmark studies" by task force consensus including those posted on the EAST landmark articles website. The list was then reviewed and revised by the EAST COS task force to ensure that all participants are currently practicing trauma care providers with significant clinical expertise in addition to their research regarding REBOA. We attempted to invite patients (REBOA survivors) and queried Delphi participants to assist with this effort but could not obtain any community member participants who had undergone REBOA. Names and affiliations of the Delphi participants are provided as a supplemental online form (eTable 1, http://links.lww.com/TA/C159).

In round 1, REBOA experts were contacted individually and asked to list candidate COS variables with no limit to the number of suggested variables. These were then reviewed by the REBOA COS task force, with duplicates removed. In round 2, the nonduplicate COS identified in round 1 were sent to the experts with instructions to rank each variable using the Grading of Recommendations Assessment, Development and Evaluation scale of 1 to 9, with scores 1 to 3 signifying a lesser important variable, 4 to 6 important but not critical, and 7 to 9 a critically important variable.[26] In congruence with previous studies, consensus was defined a priori as greater than 70% of scores receiving 7 to 9 and less than 15% of scores receiving 1 to 3.[27,28] After round 2, individual experts were provided feedback regarding their answers compared with the entire group consensus via a histogram. Although each panelist knew how she/he scored each outcome, they could not discern how any other individual panelist scored each outcome nor were they specifically made aware of the other panelists' identities. The experts were provided an opportunity to write-in additional variables to be evaluated by the panel in the final round. In round 3, similar voting occurred for all remaining variables (variables not achieving consensus in round 2 plus write-in variables from the experts in between rounds 2 and 3). After round 3, only those outcomes that met the prespecified definition of consensus were considered core outcomes for future studies on REBOA.

All statistical tests were performed in the R version 4.0.2 environment.[29] Intraclass correlation estimates and their 95% confidence intervals(CIs) were calculated using R statistical package intraclass correlation Version 2.3.0[30] based on a mean-rating (k = 12), absolute-agreement, two-way mixed-effects model.

RESULTS

In total, 17 potential participants (content experts) were identified, of which 12 (71%) participated in the Delphi process. A 100% (12/12) participation was achieved in all subsequent rounds of the Delphi process.

Round 1

The Delphi process for Round 1 was conducted from December 11, 2020, until December 31, 2020. During this time, 12 participants responded with a total of 35 suggested REBOA COS (Fig. 2). One of these COS was removed by the REBOA COS task force as it was a duplicate entry for discharge disposition.

Round 2

The Delphi process for Round 2 was conducted from January 16, 2021, until January 31, 2021. All 12 participants responded (12 of 12, 100%) and 20 outcomes reached a consensus (Fig. 3). Upon informing the panel of participants, there were no objections to these consensus COS variables. Afterward, an email was sent to all participants soliciting additional potential COS variables. One participant proposed two additional variables for consideration (cause of death and organ donation). Intraclass correlation among the expert panel (two-way mixed effects model with the average of k = 12 raters) was 0.86 (95% CI, 0.79–0.91; $p < 0.001$). Thus, by accepted definitions of agreement the panelists had good to excellent agreement.

Round 3

The Delphi process for Round 3 was conducted from March 8th, 2021 until March 22nd, 2021. From the 16 Round 3 variables evaluated (14 previously not reaching consensus plus 2 new proposed variables, cause of death and organ donation), no variables achieved consensus after review by all participants (12/12, 100%). Intraclass correlation among the expert panel (two-way mixed effects model with the average of k = 12 raters) was 0.66 (95% CI, 0.42–0.84; $p < 0.001$). Although no new outcomes were accepted, this round had more variability in responses than the second round. Therefore, as we had already met prior goals for consensus, no further rounds were attempted.

DISCUSSION

The use of REBOA has gained popularity recently in patients with life-threatening hemorrhage below the diaphragm. However, its use remains somewhat controversial and results have been variable. This may be because of the fact that indications for REBOA have not been well established and institutional practices vary greatly. In addition, institutional volumes differ and those with higher volumes may have better outcomes.[31] In the American Association for the Surgery of Trauma Aorta registry, two institutions treated about 40% of the patients. Thus, having an agreed upon set of outcome measures would be highly advantageous to establish indications and efficacy.

This consensus study of content experts established a COS for REBOA, which includes 20 core outcomes (Fig. 2). This should serve as the minimum number of outcomes reported for future studies evaluating REBOA, with additional outcomes to be reported when appropriate depending on the research question. To the knowledge of these authors, this is the first COS developed for REBOA and assists with ongoing research in the constantly evolving areas of trauma and emergency surgical care.

As REBOA is designed to temporize life threatening hemorrhage, outcomes related to mortality were determined by content experts to be core outcomes. Consensus inclusion for various points of time regarding mortality (i.e., survival out of the Emergency Department, 6-hour and 12-hour; survival out of the operating room and intensive care unit) is likely related to concern that a significant effect related to hemorrhage control may only be demonstrable in an early period. This is supported by two extensive resuscitation studies, the Prospective Observational Multicenter Major Trauma Transfusion and Pragmatic Randomized Optimal Platelet and Plasma Ratios trials, that demonstrated a

median time to hemorrhagic death of 2.6 hours and 2.3 hours, respectively.[32,33] These study authors went on to convey the inclination of the US Food and Drug Administration to require early evaluations for mortality related to traumatic hemorrhage. Furthermore, the outcome of mortality is clearly objective and already commonly reported as the trauma mortality rate in a 2018 systematic review on REBOA was 63%.[34]

In contrast to the binary determination of death, variables related to the timing of REBOA placement include time to definitive hemorrhage control, door-to-balloon inflation time, early transfusion requirements, and time to achieve hemodynamic stability were also deemed core outcomes. Interestingly, some of these outcomes have been lacking in previous studies based on a recent meta-analysis.[34] In addition, some variables draw parallel to quality indicators within other fields of medicine, such as door-to-balloon and/or intervention, which is utilized by vascular surgery for ruptured abdominal aortic aneurysms[35] and cardiology for percutaneous coronary intervention.[36] Finally, given the varying rates of complications reported with use of REBOA, multiple COS complications were adopted (i.e., vascular complications, limb amputation on access side, limb ischemia requiring procedure to treat, and ruptured aorta).

In addition to the significant outcomes related to inpatient hospitalization, this study also determined core outcome variables related to post-discharge life, including 30-day and 6-month mortality, as well as neurologic outcomes at discharge, which

Proposed Core Outcomes
Cardiac arrest after ED arrival
6-hour mortality
24-hour mortality
Survival out of Emergency Department
Survival out of Operating Room
Survival out of Intensive Care Unit
30-day mortality
Long-term survival 6 months after discharge
Time to definitive hemorrhage control
Door-to-balloon inflation time
Return of spontaneous circulation (ROSC)
Transfusion requirement
Early transfusion requirements
Time to achieve hemodynamic stability (systolic blood pressure >110mmHg)
Re-operation
Glasgow coma scale (GCS)
GCS at 48hours
Glasgow Outcome Scale-Extended (GOSE)
Neurological outcomes at discharge (e.g. modified Rankin scale or cerebral performance category)
Ventilator days
Acute Respiratory Distress Syndrome (ARDS)
Acute Kidney Injury (AKI)
AKI requiring hemodialysis
Discharge disposition
Multi-system organ failure
Organ failure among survivors
Intensive care unit (ICU) length of stay (LOS)
Hospital discharge disposition
Overall infection rate
Device related complications
Vascular complications
Limb amputation on access side
Limb ischemia-requiring procedure to treat
Ruptured aorta
Minor complications (e.g. skin infection, pain at site)

Figure 2. Round 1 "write-in" proposed core outcomes by content experts.

	Proposed Core Outcomes
	Cardiac arrest after ED arrival
	6-hour mortality
	24-hour mortality
	Survival out of Emergency Department
	Survival out of Operating Room
	Survival out of Intensive Care Unit
	30-day mortality
	Long-term survival 6 months after discharge
	Time to definitive hemorrhage control
	Door-to-balloon inflation time
	Return of spontaneous circulation (ROSC)
	Transfusion requirement
	Early transfusion requirements
	Time to achieve hemodynamic stability (systolic blood pressure >110mmHg)
	Neurological outcomes at discharge (e.g. modified Rankin scale or cerebral performance category)
	Device related complications
	Vascular complications
	Limb amputation on access side
	Limb ischemia-requiring procedure to treat
	Ruptured aorta

Figure 3. Twenty variables achieving consensus after rounds 2 and 3.

would undoubtedly affect quality of life. Other related COS have included even more outcomes related to this aspect of recovery including physical function, return to work, and objective measurements of quality of life.[37,38] While this current study has developed a minimum list of outcomes that should be studied and thus are able to be compared across studies (e.g., meta-analysis), it is essential to convey that investigators should continue to explore other outcomes of REBOA research and expand or narrow the COS list based upon our evolving understanding of REBOA including its indications, efficacy, and associated complications. In particular, outcomes that are relevant in nontrauma patients or special populations (e.g., children, elderly patients and pregnant women) might need to be investigated in the future because studies have suggested that they might benefit from REBOA in some clinical circumstances.[39,40] As systematic reviews and meta-analyses are critical steps in the evidence-based guideline creation process,[41] standardizing the underlying data enhances the overall quality of evidence and hopefully allows future guidelines to make more substantial evidence-based recommendations.

Factors, such as the participant panel, number of survey rounds, feedback between rounds, and the ability of panelists to add their own views, must be considered according to Core Outcome Set-STAndards for Development.[24] While we attempted to follow best practices outlined via COMET and Delphi guidelines, it should be noted that there are several limitations to this study. One potential limitation was the relatively low number of content experts participating in the Delphi study. However, REBOA remains a highly specialized niche research topic, even within the field of trauma surgery. This low sample size may have prevented variables close to consensus from achieving consensus, such as cause of death, organ donation, and acute kidney injury requiring hemodialysis. However, non-COS status does not preclude them from being studied or reported in future studies. The decision for inclusion of experts is notably arbitrary, as research on a topic does not necessarily make someone a clinical expert. However, the investigators sought to incorporate surgeons who had published negative data on REBOA as well. Furthermore, the selection process for experts was based on a task force's decision thus introducing human bias to the decision. In addition, when designing this study, we aimed to incorporate community members who had undergone REBOA but were unable to accomplish this. Future efforts to develop COS throughout medicine may benefit from developing formalized community outreach programs via national organizations such as the Coalition for National Trauma Research to facilitate patient participation in this important effort. Furthermore, after a discussion among the organizing task force members it was decided to forgo industry participation, although a few other studies have engaged industry as a stakeholder.[19,42] Although we did not incorporate allied health care providers (e.g., nurses, physical therapists etc.), we hope to do this in the future with increased knowledge and experience regarding this process. Another limitation specifically related to this topic is that certain COS may be more applicable depending on the indication for placement of REBOA and location of REBOA deployment; however, all outcomes selected can occur in any trauma patient and thus may still be relevant. Most importantly, we have adhered to the transparency of reporting our process by following the COS-Standards for Reporting,[43] and utilizing the best content experts available.

Using a rigorous methodology and 12 content experts, we achieved consensus on 20 variables for a COS for REBOA. We believe this sets a foundation for future research to become more standardized and recommend implementation immediately for all trials, cohort analyses, meta-analyses, and systematic reviews of the current or next-generation REBOA technology.

AUTHORSHIP

J.N., S.B., Mel.B., and D.D.Y. conducted a literature search. J.N. performed the data collection. S.B. performed the data analysis. J.N., S.B., and D.D.Y. performed the writing. J.N., S.B., D.S., E.R.H., J.W.S., R.G., M.Z., Meg.B., B.Z., W.L.B., Meg.B., J.D., C.F., J.G., M.M., E.E.M., L.M., J.M., T.N., T.S., D.D.Y. participated in the study design, data interpretation, and critical revisions of the article.

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