A Research Protocol and Case Report of Emergency Department Endovascular Aortic Occlusion (REBOA) in Non-traumatic Cardiac Arrest

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Background: There are over 395,000 out-of-hospital cardiac arrests (OHCA) annually in the United States with an estimated 70–90% mortality rate and fewer than 10% surviving with a favorable neurologic outcome. Research in animal models and early human studies suggests that resuscitative endovascular balloon occlusion of the aorta (REBOA) may play a role in augmenting coronary perfusion during OHCA by reducing blood flow to the lower body and re-directing it towards the heart and the brain. We describe our initial case and research protocol to investigate the feasibility of REBOA in the emergency department for OHCA as an adjunct to advanced cardiac life support.
Methods: We plan to enroll 20 patients in a single-arm interventional device study utilizing an exception from informed consent over a 2-year period. The primary outcome is feasibility, with secondary outcomes assessing for hemodynamic changes pre- and post-aortic occlusion.
Results: Enrollment began in January 2020 and is ongoing. For the initial patient, an emergency physician (EP) obtained common femoral arterial access under chest compressions, followed by advancement of the REBOA catheter by an interventional radiologist. Immediately after aortic occlusion, investigators noted a substantial improvement in mean arterial pressure (37 mmHg to 50 mmHg) and end tidal carbon dioxide (33 mmHg to 50 mmHg), with transient but non-sustained return of spontaneous circulation.
Conclusion: This is the first research protocol and case report describing successful REBOA placement in the emergency department (ED) involving EPs for non-traumatic OHCA as an adjunct to advanced cardiac life support.

Keywords: *Resuscitative Endovascular Balloon Occlusion of the Aorta; REBOA; Resuscitation; Aortic Occlusion; Cardiac Arrest; Out-of-Hospital Cardiac Arrest; Non-traumatic Cardiac Arrest*

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INTRODUCTION

There are an estimated 395,000 out-of-hospital cardiac arrests (OHCAs) annually in the United States, with fewer than 10% surviving with a favorable neurologic outcome. Despite advances in resuscitative strategies over the past several decades, patient-centered outcomes have remained frustratingly poor [1].

Resuscitative endovascular balloon occlusion of the aorta (REBOA) involves the use of a balloon tipped catheter to occlude the aorta and prevent distal blood flow. REBOA was initially developed for the management of non-compressible intra-abdominal hemorrhage to temporize further blood loss and bridge the patient to definitive operative repair [2]. To perform REBOA, an introducer sheath is placed in the common femoral artery (CFA) and a balloon-tipped catheter is advanced through the sheath retrograde into the aorta. When the intra-aortic balloon is inflated, the thoracic aorta is occluded, preventing distal blood flow and increasing blood pressure in the aortic arch and coronary arteries [3]. Intra-vascular aortic procedures are typically performed by endovascular specialists; however, a recent report demonstrated that anesthesiologists could be trained to safely perform REBOA during OHCA [4]. In the United States, REBOA is typically performed by trauma surgeons and its use by emergency physicians (EPs) has been limited. In Europe, the majority of REBOA procedures are performed by non-surgical specialties (e.g. emergency medicine, critical care, anesthesiology) [5].

While REBOA has been employed primarily in traumatic bleeding, the increase in blood pressure in the aortic arch may be beneficial in patients suffering from OHCA to increase cardiac and cerebral perfusion. Cardiac output generated by chest compressions during OHCA is often inadequate to maintain sufficient coronary and cerebral perfusion pressure [6]. Aortic occlusion may compensate for this by reducing the effective circulating area of a patient's blood and redirecting flow towards the heart and the brain. Numerous pre-clinical studies demonstrate the effectiveness of REBOA during non-traumatic cardiac arrest [7,8]. Clinical research involving REBOA used as an adjunct to advanced cardiac life support (ACLS) in OHCA is limited and, to our knowledge, has not been reported in the *emergency medicine* literature [8,9]. Demonstration of feasibility by EPs and non-specialists is essential, as the majority of OHCAs present to smaller hospitals without in-house specialist coverage. A recent study of 10 patients undergoing REBOA for prolonged OHCA in the field demonstrated statistically significant improvements in end tidal carbon dioxide ($ETCO_2$) after aortic occlusion, with return of spontaneous circulation (ROSC) in six patients and one patient discharged with a favorable neurologic status. These results are promising, especially given the prolonged mean down-time prior to REBOA. We hope to build upon this study by assessing for real-time improvements in diastolic blood pressure (a surrogate for coronary perfusion pressure) pre- and post-aortic occlusion.

METHODS

In January 2020, we began the implementation of the first emergency department (ED)-based REBOA protocol involving EPs as part of single-arm early feasibility trial
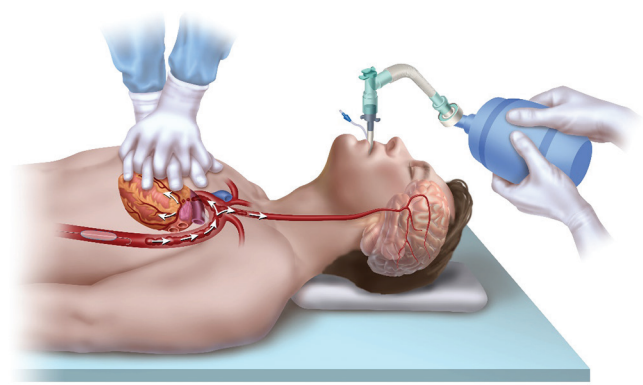

Figure 1 Thoracic aortic balloon occlusion as adjunct to ACLS. Thoracic aortic balloon occlusion during cardiac arrest with bag-valve mask ventilation and manual chest compressions demonstrating the re-direction of blood flow with aortic occlusion.

with and planned enrollment of 20 patients (ClinicalTrials.gov identifier: NCT03703453). Our goal is to demonstrate that REBOA for OHCA is feasible and that EPs can be successfully trained to perform this procedure during chest compressions (Figure 1). The primary outcome is feasibility, defined as successful intra-aortic balloon inflation in greater than 70% of cases, with secondary procedural, hemodynamic, and clinical outcomes (Figure 2). To be included, the patient must have had a witnessed cardiac arrest with bystander cardiopulmonary resuscitation (CPR) (Figure 3). Upon patient enrollment, the REBOA procedure will be performed as rapidly as possible, with a maximum total aortic occlusion time of 15 min (while ACLS is continued). If ROSC is obtained, the intra-aortic balloon will be deflated step-wise as rapidly as possible to avoid subjecting the recovering heart to increased afterload and to minimize lower body ischemic time.

Enrollment occurs during defined times when a research assistant and EP investigator are present. Eight EP investigators completed the cadaveric-based basic endovascular skills for trauma (BEST) course with additional OHCA-focused training in our simulation laboratory. ED nurses and technicians underwent REBOA training involving in-situ simulation as it is essential that all staff know their role, their expected location, and have an understanding of the procedure so they may better assist during REBOA. Figure 4 depicts our staff and room setup for a right-handed procedural physician. Once a patient is enrolled, the EP investigator (separate from the EP leading the resuscitation) prepares all necessary equipment on a sterile field (Figure 5). The EP investigator will then place a 7 Fr introducer sheath into the CFA under ultrasound guidance during chest compressions. CFA access is typically the most difficult and rate-limiting step of the REBOA procedure [5]. To improve the probability of procedural success and patient safety, the US Food and Drug Administration (FDA) has required that EP investigators enlist the assistance of interventional radiologists (IR) to
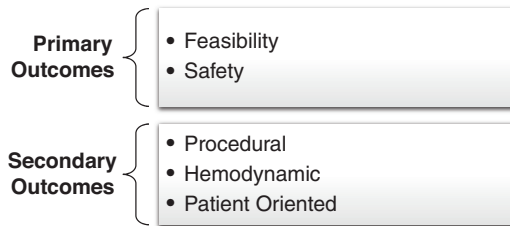
Primary Outcomes
- Feasibility
- Safety

Secondary Outcomes
- Procedural
- Hemodynamic
- Patient Oriented

Figure 2 Study primary and secondary outcomes. Primary outcomes are feasibility, defined by successful supra-celiac placement of the intra-aortic balloon in at least 70% of patients. Safety is measured as a composite score of five pre-determined adverse events. Secondary outcomes are procedural (e.g. time to balloon placement), will assess for hemodynamic changes before and after balloon inflation, and are patient oriented (e.g. proportion of patients discharged with a favorable neurologic outcome).
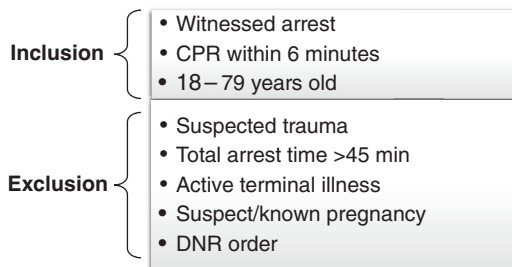
Inclusion
- Witnessed arrest
- CPR within 6 minutes
- 18 – 79 years old

Exclusion
- Suspected trauma
- Total arrest time >45 min
- Active terminal illness
- Suspect/known pregnancy
- DNR order

Figure 3 Patient inclusion and exclusion criteria. Inclusion and exclusion criteria of out-of-hospital cardiac arrest patients eligible for ED-initiated REBOA. DNR: Do not resuscitate.

Figure 4 Resuscitation room setup. Emergency department staff performing REBOA as an adjunct to ACLS in a non-traumatic cardiac arrest patient. (**A**) Primary proceduralist. (**B**) Procedural/research assistant. (**C**) Code team leader. (**D**) Nurse obtaining intra-osseous access. (**E**) Chest compressor. (**F**) Respiratory therapist. (**G**) medications nurse. (**H**) Documenting nurse.

insert and manipulate the actual REBOA catheter. For the initial patients in the trial, EPs will obtain CFA access with ultrasound guidance and the supporting IR will then advance the REBOA catheter and inflate the intra-aortic balloon. For the subsequent patients, as EPs gain experience, we plan to file a study protocol amendment with the FDA to permit EP advancement of the REBOA catheter with IR in a supporting role. Subjects will undergo aortic occlusion for no longer than a total of 15 min. This time period was decided on through expert opinion; 15 min is likely enough time for the intervention to induce a beneficial effect, while still well under the generally accepted maximum aortic occlusion time in an attempt to mitigate any ischemic damage. If ROSC is not obtained after 15 min of aortic occlusion, the resuscitation will cease due to perceived futility.

Ethical Approval and Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsink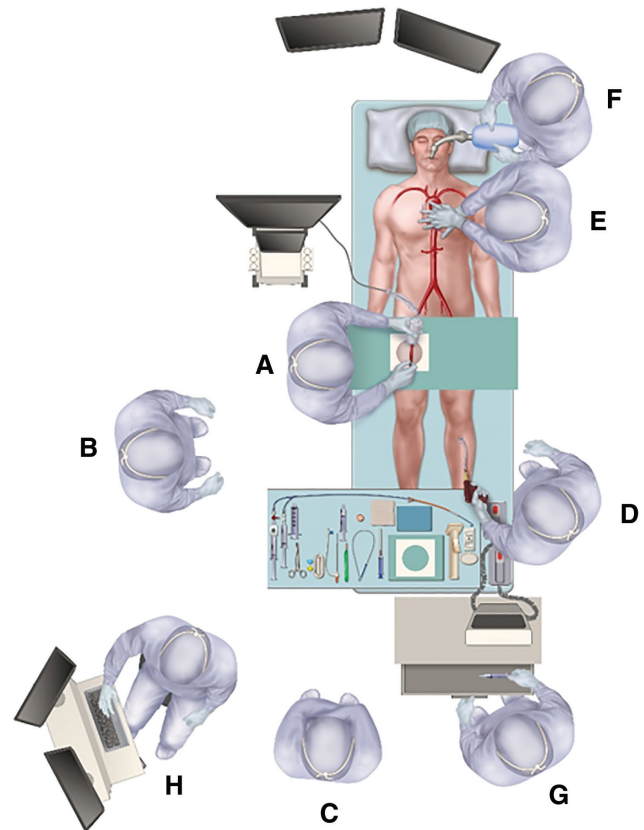i declaration and its later amendments or comparable ethical standards. The study was granted an investigational device exemption under the FDA and an exception from informed consent (EFIC).

RESULTS

A 77-year-old male had a witnessed OHCA with bystanders providing basic life support including chest compressions within several minutes of his collapse. He had a past medical history significant for congestive heart failure (baseline ejection fraction 40%), atrial fibrillation, hypertension, diabetes, and chronic renal disease (baseline creatinine 1.8 mg/dl).

When paramedics arrived, they found the patient in sinus bradycardia with a faintly palpable pulse. He was prepared for transport to the ED and subsequently suffered a ventricular fibrillation (VF) cardiac arrest. Paramedics began ACLS, attempted defibrillation unsuccessfully, and intubated the patient. Several minutes after his arrival to the ED, the patient had ROSC with sinus bradycardia. Then, 3 min after that, he suffered a repeat VF arrest and the decision was made to activate the ED-REBOA protocol.
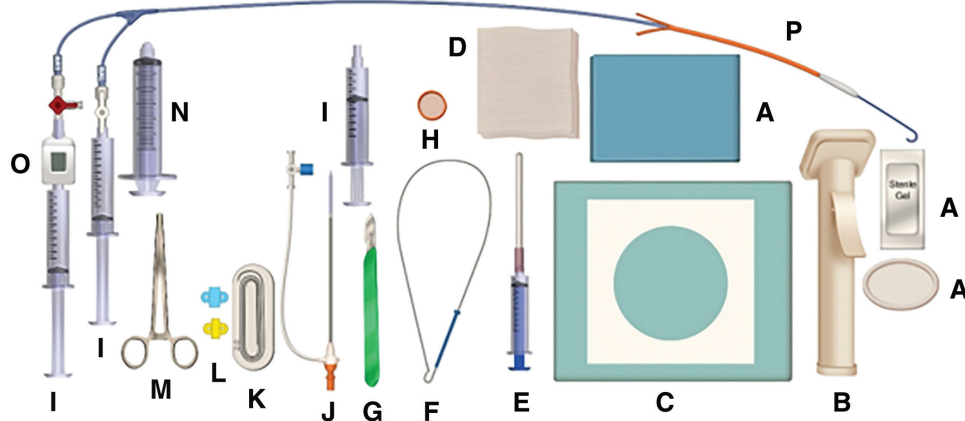
Figure 5 Essential equipment and setup for the REBOA procedure. Items are prepared in the order of their use, from right to left. (**A**) Sterile gel and probe cover and kit. (**B**) Antiseptic sponge. (**C**) Patient drape. (**D**) Gauze. (**E**) Cannulation needle and syringe. (**F**) Guide wire. (**G**) Scalpel. (**H**) Needle holder. (**I**) Sterile saline flushes. (**J**) 7 Fr sheath. (**K**) Sutures. (**L**) Catheter clamps. (**M**) Needle driver. (**N**) Empty syringe. (**O**) Centurion Compass® (Mirador Biomedical) pressure monitoring device. (**P**) ER-REBOA™ catheter.

A "REBOA alert" was sent to on-call EM and IR trial investigators. The patient was enrolled as he had multiple positive prognostic factors despite his comorbidities: his initial rhythm of ventricular fibrillation, ROSC in the ED just prior to enrollment, rapid bystander CPR, and an $ETCO_2$ of 35 mmHg on arrival. Per protocol, an exemption from informed consent was utilized.

Approximately 10 min after his arrival in the ED, an EP investigator began to obtain right CFA access using ultrasound guidance to place the 7 Fr introducer sheath in preparation for ER-REBOA™ (Prytime Medical Devices) catheter insertion. Sheath insertion was successful on the first needle puncture and required approximately 4 min to complete. Arterial placement was then confirmed post-procedure with bedside ultrasound.

IR subsequently advanced the REBOA catheter 45 cm from the insertion site into the thoracic aorta. Investigators did not encounter any difficulty when rapidly advancing the REBOA catheter. The EP performed a bedside ultrasound of the aorta which confirmed placement of the intra-aortic balloon superior to the celiac artery (Figure 5) and the balloon was subsequently inflated with 8 ml of saline. Inflation of the balloon occurred approximately 17 min after ED arrival, and 30 min after his initial arrest.

Significant improvements in the patient's hemodynamics were noted almost immediately after aortic occlusion. A total of 30 s after balloon inflation, the patient's mean arterial pressure (MAP) had increased from 37 mmHg to 50 mmHg and $ETCO_2$ had increased from 35 mmHg to 50 mmHg. ROSC with sinus bradycardia was obtained for approximately 60 s post-balloon inflation, but then devolved into ventricular fibrillation. Defibrillation with 200 J was attempted but on the subsequent pulse check the patient was once again in asystole. Investigators continued ACLS with aortic occlusion for 15 min in total per protocol but the patient never regained cardiac function and was declared deceased. The patient's MAP ranged from 50 to 60 mmHg and $ETCO_2$ from 50 to 57 mmHg for the entirety of the aortic occlusion period.

DISCUSSION

While the use of REBOA in the setting of trauma is becoming more common, we are not aware of any literature describing REBOA placement in the ED for OHCA involving EPs, although there are two similar reports from Europe involving critical care physicians [4,8]. This report provides evidence that the performance of REBOA by an EP lead team during OHCA is feasible and some encouraging hemodynamic data that it may be an effective adjunct to ACLS.

In the United States, when patients suffer trauma or an OHCA, the first physician they typically encounter is an EP. If REBOA eventually proves to be effective at improving perfusion to the heart and brain, its application soon after patient presentation will be crucial. In order for early application of REBOA to be possible in most cases, it is imperative that EPs are adept at utilizing REBOA as an adjunct to current standard of care, as the majority of US hospitals lack around-the-clock in-house intra-vascular specialist coverage.

This report provides early evidentiary support that EPs can build a REBOA program and perform the REBOA procedure for OHCA in conjunction with IR assistance. In this case, the EP was able to successfully perform the most difficult aspect of the procedure: accessing the CFA during chest compressions and achieving first pass success in under 5 min [10]. Correct CFA placement is crucial as unintentional placement in the femoral vein or distal to the CFA bifurcation in the femoral artery could cause sig-

nificant morbidity. While the EP did not advance the actual REBOA catheter due to protocol restrictions, it is unlikely that they would have had difficulty doing so, given the ease with which IR performed this step. We hope to confirm this suspicion in subsequent enrollments.

The physiologic hypothesis supporting the use of REBOA in OHCA is innovative and straight forward: by limiting blood flow to the lower body, one might maximize the perfusion of the brain and heart, in particular the coronary arteries, during OHCA. REBOA is unique in that it seeks to redistribute the cardiac output generated during chest compressions in a more effective manner and may improve cardiac function by improving coronary perfusion. We chose to occlude the aorta in Zone 1, above the level of the celiac artery, because it seemed more likely to provide the desired hemodynamic improvements than placement distally (e.g. Zone 3, distal to the renal arteries). A recent study in swine demonstrated improvements in coronary perfusion with aortic occlusion in Zone 1 compared with Zone 3, which did not improve coronary perfusion (measured through diastolic blood pressure) [11]. There are important ethical considerations when depriving most of the body of needed blood flow, as placement in Zone 1 will potentially cause more ischemic injury than Zone 3. It is our hope that by limiting aortic occlusion time to no more than 15 min, we may mitigate the risk of any resulting ischemic damage. However, patients enrolled in the trial have already undergone at least 15 min of standard ACLS, and evidence has demonstrated that by that point they are highly unlikely to survive with standard care alone [12].

This report provides evidence that EP-initiated REBOA in conjunction with IR assistance is feasible and may improve cardiac perfusion and chest compression quality, as evidenced by immediate improvements in the patient's MAP and $ETCO_2$, respectively. These improvements were maintained for the subsequent 15 min throughout the period of aortic occlusion, save for expected decreases in MAP when chest compressions were paused for pulse checks. Prior to aortic occlusion, the patient had been pulseless for approximately 20 min and then subsequently regained a pulse soon after aortic occlusion was initiated (although this was not sustained). While the patient ultimately died, the temporal association of the patient's hemodynamic improvements and ROSC with aortic occlusion suggests that REBOA may prove to be an effective adjunct to ACLS. It is possible that these hemodynamic improvements could lead to improved patient-centered outcomes, although a much larger controlled study would be required to provide any certainty regarding this hypothesis.

Our initial experience demonstrates that REBOA for OHCA appears to be feasible and associated with a positive hemodynamic effect. The EP-initiated application of REBOA in this case seemed to induce sustained increases in $ETCO_2$ and MAP, and a brief period of ROSC. These changes temporally correlated with aortic balloon inflation, suggesting a causal relationship. Furthermore, this was an important step in demonstrating the feasibility of an EP-initiated pathway for REBOA in OHCA. Significant preparation and staff training enabled an EP lead team to perform the procedure without undue difficulty. However, the involvement of two EPs and one IR makes it unlikely that smaller EDs would be able to enact this protocol as currently written. If future evidence supports the use of REBOA for OHCA, our goal would be to then investigate the feasibility of a single-physician protocol that could be utilized in smaller EDs. Given the positive hemodynamic response and this initial demonstration of feasibility, ED-initiated REBOA may prove to be an effective adjunct to ACLS. Due to the potential complications of REBOA and its promising but uncertain effectiveness, we believe that further research on a much larger scale is warranted before this technique should be widely applied for OHCA patients.

Ethics Statement

(1) All the authors mentioned in the manuscript have agreed to authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript.

(2) The authors declare that they have read and abided by the JEVTM statement of ethical standards including rules of informed consent and ethical committee approval as stated in the article.

Conflicts of Interest

The primary author, JD, would like to declare a potential conflict of interest. JD received funding in the form of a research grant from Prytime Inc., the manufacturer of the ER-REBOA™ catheter used in this trial. JD has no other financial relationship with the company and does not personally receive payments of any kind. Prytime Inc. has not viewed this manuscript and had no part in its preparation or the design of the trial.

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Author Contributions

AJ and CM should be considered joint senior authors. All authors have substantially contributed to the study and manuscript writing.

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