Feasibility study for implementation of resuscitative balloon occlusion of the aorta in peri-arrest, exsanguinating trauma at an adult level 1 Australian trauma centre

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Abstract

Objective: This prospective, observational, interventional study sought to determine if the introduction of resuscitative balloon occlusion of the aorta (REBOA) at an Australian adult major trauma centre would improve survival for major trauma patients.

Methods: Patients aged 18–60 years, transported directly from scene with exsanguinating, sub-diaphragmatic haemorrhage and hypovolaemic shock (systolic BP <70 mmHg or hypovolaemic cardiac arrest) were eligible for recruitment and followed up until hospital discharge (ACTRN 12618000550202).

Results: During the 14-month study period (17 January 2015 to 12 March 2016) 3032 patients were admitted directly from scene with a mortality of 97 (3.71%). Of these patients 3019 had trauma centre vital signs recorded in the data set (99.57%) and 1523 were between the ages of 18–60, including 143 patients with a shock index of >1.0 (4.74%). There were 13 (0.43%) patients with a systolic BP <70 mmHg and/or cardiorespiratory arrest on arrival. The mortality in this group was six out of 13 (46.15%). Of these 13 patients, there were two (0.07% of the total cohort) where REBOA was attempted. There were no eligible patients for whom REBOA was achieved. None of the six patients who died would have benefited from REBOA deployment.

Conclusions: Despite considerable training and resource allocation to ensure 24-h availability, the introduction of REBOA failed to effectively demonstrate any impact on patient outcome. Despite retrospective literature supporting the introduction of REBOA, in this 14-month prospective study there was no evidence of benefit. Further studies may define indications and subgroups of patients who may benefit.

Key words: haemorrhage, shock, trauma.
Background

Non-compressible torso haemorrhage is a leading cause of preventable trauma death.1–4 Although trauma systems have optimised access to surgery and interventional radiology for definitive haemorrhage control, a substantial proportion of deaths occur before this can be achieved.5

Resuscitative thoracotomy with aortic occlusion is a means of temporary haemorrhage control. This procedure is effective in patients with a thoracic source of haemorrhage that can be directly controlled but is invasive and has limited utility in those with either isolated or concomitant sub-diaphragmatic haemorrhage secondarily to blunt trauma.6

Temporary occlusion of the aorta with an endovascular balloon is a technique that is used to control haemorrhage in shocked patients with ruptured aortic aneurysms.7,8 This technique has also been described in other forms of non-compressible haemorrhage such as gastrointestinal bleeding9 and post-partum haemorrhage.10

Resuscitative endovascular balloon occlusion of the aorta (REBOA) as an adjunct for traumatic, haemorrhagic shock has recently been promoted.11 REBOA provides a means of temporary control in patients with severe non-compressible haemorrhage – as a potential bridge to definitive haemorrhage control and therefore survival.12 However, the procedure requires specific technical expertise as well as integration into current models of trauma reception and resuscitation – and there are conflicting reports about whether REBOA contributes to survival.13–19 There are also significant reported complications associated with REBOA insertion.20

This study involved the introduction and evaluation of balloon occlusion for aortic control of exsanguinating trauma related haemorrhage (The ACE Study) at an Australian adult major trauma centre, to determine whether REBOA would be a feasible and effective strategy to provide temporary circulatory support to trauma patients with critical, refractory, hypovolaemic shock or/and hypovolaemic cardiac arrest. The expectation was that REBOA deployment in this peri-arrest, exsanguinating population would allow transfer to an operating theatre for definitive haemorrhage control surgery.

The primary hypothesis was that the introduction of REBOA would result in improved survival (from hospital arrival until hospital discharge) of blunt or penetrating trauma patients aged 18–60 years with exsanguinating, sub-diaphragmatic haemorrhage as detailed in the hospital record.

The secondary outcome was to measure the incidence of successful REBOA deployment in the trauma centre within the first 4 h of hospital arrival as documented in the Alfred Trauma Registry and cross-checked against the hospital record. This was to determine if the training and deployment processes matched the clinical triggers.

Study rationale

The inclusive, integrated Victorian State Trauma System (VSTS) was established in 2000 and serves a population of 6.2 million.21 The Alfred Hospital and the Royal Melbourne Hospital are the two VSTS level 1 adult trauma centres. The VSTS mandates that critically injured patients are transported primarily to a major trauma centre if within defined transport times. The Alfred Trauma Registry currently records pre-hospital and hospital data on all major trauma patients – defined as those having a new Injury Severity Score greater than 12, or requiring urgent surgery, or ICU admission, or dying in hospital.

At the time of trial design, there were no clear indications for REBOA deployment. A systolic BP (SBP) <70 mmHg was the agreed consensus used at The Alfred as the decision point for consideration of resuscitative thoracotomy for the severely injured with thoraco-abdominal trauma not responding to external haemorrhage control following pleural decompression as well as an intravenous volume push of at least 2000 mL 0.9% NaCl.22,23 A study published in 2013 from Baltimore and Houston reported REBOA deployment in ‘end-stage’ shock, where the mean SBP at time of deployment was 59 mmHg. This appeared to support a SBP <70 mmHg as a decision trigger.24 Therefore, for the purposes of this study, this trigger was used to prompt consideration for REBOA deployment.

Methods

Baseline data from 2013 indicated there were 3526 trauma patients aged 18–60 years treated in The Alfred Emergency and Trauma Centre (E&TC), of whom 2438 (69.14%) were transported direct from scene. Of those transported directly from scene, 24 patients had a SBP <70 mmHg (including arrested patients) documented at the E&TC (0.98%). The at-discharge mortality of these patients was 8/24 (33%). At that time, the investigators were informed from initial British data that up to 50% of those who ultimately die from junctional haemorrhage suffer a cardiac arrest prior to or immediately after hospital arrival.25

It was argued at the time that between 7 and 15 patients per year may have benefited from REBOA, with the knowledge that this group would also include those with thoracic haemorrhage and lethal head injuries. The sample size required to test disparity in two survivor functions corresponding to a 50% reduction in the hazard of the experimental group (a hazard ratio of 0.5) from historical mortality rates (2013), using a two-sided 5% log-rank test with 80% power was 33 patients in the prospective arm. We aimed to enrol 36 patients to account for any loss to follow up. It was anticipated the study would be completed within 18 months of commencement.

The Alfred Ethics Committee approved the ACE study on 4 July 2014, allowing participant enrolment without consent using procedural authorisation. Provision of approval from The Alfred Innovations...
Committee was required before commencement of the study – along with the necessary staff training, protocols and equipment deployment.

Enrolment eligibility

The Trauma Team Leader was to consider REBOA deployment for patients if they met the following criteria:

- Blunt or penetrating trauma patient aged 18–60 years transported directly from scene with:
  - Potential exsanguinating sub-diaphragmatic haemorrhage,
  - Hypovolaemic shock with an SBP <70 mmHg or agonal state/pulseless cardiac arrest with electrical activity of <10 min and
  - Non/partial responder to volume resuscitation as determined by the Trauma Team Leader.

Key exclusion criteria were the presence of untreated causes of obstructive shock (tension pneumothorax and cardiac tamponade) (Fig. 1).

At the time this study was undertaken, an institutional precedent had been set by cardiology and intensive care specialists conducting the CHEER study using extra-corporeal membrane oxygenation (ECMO) for post-refractory cardiac arrest.26,27 This ECMO group provided a 24/7 service and were experts at sub-diaphragmatic vascular access - but were not usually involved in trauma resuscitation. After discussion with the Institutional Health and Research Ethics committee it was agreed that the already trained and available ECMO specialists would also perform REBOA. As well as their proven procedural expertise, it was considered that adding the REBOA technique using ECMO specialists not normally involved in trauma resuscitation would not diminish the standard trauma team reception and resuscitation configuration (Fig. 2). To ensure enough staff coverage, additional Anaesthesiology and Emergency Medicine consultants were trained in REBOA deployment using a torso vascular access mannequin by intensive care medicine ECMO specialists.

The Alfred E&TC has four fully equipped, identical, trauma resuscitation bays. Potential participants were to be identified on scene from the pre-hospital information provided by Ambulance Victoria paramedics. Pre-hospital patients were to be considered for REBOA Activation Criteria if the patient age was ≤60 years, a sub-diaphragmatic injury was suspected and an SBP of <100 mmHg had been recorded.

The ‘REBOA alert’ was incorporated into the standard trauma call-out notification. REBOA equipment boxes were stocked and located in the E&TC. The REBOA operator’s role was to insert a femoral arterial line which could then be upsized to a 12-F sheath through which REBOA could be performed if required using a COOK Coda balloon catheter.

Figure 1. Resuscitative balloon occlusion of the aorta in peri-arrest decision-making algorithm, The Alfred.

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Staff were trained in indications and underwent training on a specifically designed simulation mannequin. REBOA ‘Action Cards’ were available for the Trauma Team Leader, REBOA Operator and REBOA Assistant.

**Study design**

A non-randomised, prospective, observational, interventional cohort study of all major trauma patients transported directly from scene to The Alfred E&TC was then undertaken. The primary outcome variable was mortality at hospital discharge assessed against pre-intervention historical control data.

Presenting SBP, heart rate and related shock index were used as indicators of haemorrhagic shock.28,29 Variables related to performance of REBOA and trauma centre cardiopulmonary arrest were also gathered.

Data were collated using Microsoft Excel and analysed using **stata** version 13.1 (StataCorp LP, College Station, TX, USA). Proportions are expressed as a percentage. The \( \chi^2 \) test was used to assess categorical variables. Two-sided \( P \)-values of <0.05 were considered statistically significant.

The study commenced on 17 January 2015 and continued until 12 March 2016 (trial registration A CTRN12618000550202).

**Results**

During the 14-month study period 3032 patients were admitted direct from scene through The Alfred E&TC with an overall mortality of 97 (3.71%). Of these patients 3019 had trauma centre vital signs recorded in the data set (99.57%) and 143 patients had a shock index of \( \geq 1.0 \) (4.72%) – a marker considered indicative of haemorrhagic shock.28 Blunt trauma was the mechanism of injury for 95.5%. The pretrial population from 2013 that was used for the sample size calculation had a similar SBP <70 mmHg incidence and mortality to the trial period (\( P = 0.5 \)).

There were 13 (0.30%) patients transferred direct from scene, aged 18–60 years, with a SBP <70 mmHg and/or cardiorespiratory arrest that met criteria to be considered for REBOA deployment. There were three patients on whom REBOA was attempted. This included an 80-year-old patient with multisystem trauma, including neurotrauma, who underwent successful deployment despite losing cardiac output. The patient died in Intensive Care on day 2 secondary to severe neurotrauma. The age of the patient was unknown and at the time and was thought to be within the 18–60 years old enrolment criteria (Fig. 3).

The indicated REBOA procedure was abandoned during the resuscitation of two eligible patients who underwent immediate abdominal operative intervention for haemorrhage control. Both patients survived – despite one losing cardiac output during the attempted REBOA procedure and undergoing immediate laparotomy with control of a large retroperitoneal haemorrhage.

The second patient’s pelvic and perineal haemorrhages were controlled with operative control of lacerated pelvic vessels and packing. Of the 11 potential patients in whom REBOA was considered but not deployed, six died (Table 1). None of the six preceded to REBOA, as none had demonstrable sub-diaphragmatic haemorrhage.

The study was suspended 14 months after commencement after no eligible patients had been enrolled.

**Discussion**

There is controversy in the literature about the outcome effectiveness of
REBOA for traumatic shock, with enthusiastic proponents\textsuperscript{13,14,19,30,31} counterbalanced by cautious sceptics.\textsuperscript{32} Clear evidence supporting its introduction is lacking,\textsuperscript{16,20,33} with much of the literature derived from animal studies, retrospective data and meta or propensity analyses.\textsuperscript{13,17,33} In a recent US national matched analysis, Joseph \textit{et al.}\textsuperscript{.} reconfirmed the need to define the patient population for which REBOA has benefit.\textsuperscript{34} Lendrum \textit{et al.} have also recently articulated the need to define when deployment should occur.\textsuperscript{19}

Despite considerable training and resource allocation to ensure 24-h availability, there were only two eligible patients for whom REBOA was attempted during the 14-month study period. The procedure was terminated in both cases – and both patients survived following immediate operative intervention. There was one elderly, ineligible patient for whom REBOA was achieved and who subsequently died. However, there were no eligible patients for whom REBOA was achieved. None of the six patients who were eligible for REBOA consideration, but in whom it was not attempted and who died during the study period would have benefited from REBOA (Table 1).

This study was conducted within the VSTS setting, which is an inclusive, integrated system with sophisticated pre-hospital and hospital care.\textsuperscript{21} Ambulance Victoria paramedics have

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**TABLE 1. Enrolled patients who died without REBOA deployment**

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Gender</th>
<th>Mechanism</th>
<th>SBP on arrival</th>
<th>Intervention</th>
</tr>
</thead>
</table>
| 1   | 40  | M      | Blunt             | 0 (CPR in progress for 25 min) | Truncal trauma. No cardiac activity on FAST. 
Resuscitation ceased. |
| 2   | 25  | M      | Blunt             | 0 (CPR in progress for 24 min) | Truncal trauma. No cardiac output, massive right haemothorax. 
Resuscitation ceased. |
| 3   | 30  | M      | Blunt             | 0 (IPPV in progress – lost palpable pulse on arrival) | Truncal trauma. Immediate thoracotomy. Lacerated right ventricle repaired. 
Contused left ventricle. Unable to regain ROSC. Resuscitation ceased. |
| 4   | 25  | F      | Blunt             | 0 (CPR in progress for 20 min) | Truncal trauma. Immediate thoracotomy. Tension right haemothorax, lacerated right pulmonary artery. 
Unable to regain ROSC. Resuscitation ceased. |
| 5   | 37  | M      | Penetrating       | 0 (CPR in progress for 9 min) | Truncal trauma. Immediate thoracotomy. GSW wound left pulmonary hilum. 
Clamped. Unable to regain ROSC. Resuscitation ceased. |
| 6   | 55  | F      | Blunt             | 0 (lost palpable pulse on arrival) 
83 min transport time | Head and truncal trauma. Open skull fracture. Fixed pupils for 83 min. 
No thoraco-abdominal bleeding on FAST. 
Resuscitation ceased. |

CPR, closed chest cardiopulmonary resuscitation; FAST, focused assessment with sonography for trauma; IPPV, intermittent positive pressure ventilation; ROSC, return of spontaneous circulation; SBP, systolic blood pressure.
an established, audited and evidenced-based approach to the management of the seriously injured and there is a long-established pre-hospital notification system. Surgical staff are rapidly available if operative intervention is required, as evidenced by the operative control of bleeding in the first patient (for whom REBOA was abandoned).

The patient group considered most likely to benefit were those with pelvic fractures and shock. However, since the introduction of pelvic fracture guidelines, the widespread use of pelvic binders and pre-hospital transfusion of blood on Ambulance Victoria helicopters (but not road ambulances), few of these patients arrived shocked.35 The impact of sophisticated pre-hospital shock management for a predominantly blunt trauma cohort was demonstrated by the relatively low incidence, on hospital arrival, of haemodynamic instability among the severely injured, blunt trauma patients in this study. It is possible that the combination of advanced pre-hospital and in-hospital trauma systems has improved management of severely injured patients to a level where marginal benefits from newer interventions are difficult to demonstrate.

This study’s finding has limitations as it was conducted at a single centre – albeit with a relatively large trauma throughput. In retrospect, the numbers of preventable deaths estimated to have been reversed with REBOA was overestimated, even though the pre-trial population from 2013 that was used for the sample size calculation had similar incidence of shock and mortality to the trial period.

The ACE REBOA study was conducted using COOK Coda balloon catheters, which require a 12-F sheath for access. There is a large endovascular sheath that is technically difficult to insert in the context of profound vasocostriction and comes with significant risks of femoral puncture site morbidity. Since conducting the study newer REBOA catheters utilising a 7-F access sheath have appeared on the market that potentially make the procedure easier to perform and following removal, haemostasis at the common femoral arterial puncture site can be obtained with direct pressure.

There was also a variable skill level among the REBOA operators. This ranged from experienced ECMO proceduralists to those who had mannequin training only. However, this was not associated with failure to deploy or avoidable death (Table 1).

Nonetheless, in this study there were no patients identified who died and whose outcome would have been altered by easier or more proficient REBOA deployment.

The peak death rate after severe truncal trauma occurs at approximately 30 min post injury before the majority of exsanguinating trauma patients reach hospital to receive definitive haemostasis in the operating theatre or interventional radiology suite.36,37 This occurred in five of the six deaths in this study. It is also conceivable that the cohort of patients most likely to benefit from interventions such as REBOA are those who currently die prior to arrival at hospital. Studies involving pre-hospital care systems with appropriately trained physicians may answer this question.38

Our threshold of the indication of SBP <70 mmHg despite blood product resuscitation reflects a population of patients in an advanced adult major trauma service where traditional resuscitative measures have worse outcomes and innovative strategies may be indicated. REBOA has been previously suggested to be indicated in the setting of a diagnosis of exsanguinating pelvic haemorrhage included hypotension, specifically defined as ‘low volume or absent peripheral pulses’.39

Such thresholds are based on the concept of permissive hypotension, where BP targets in the intervention arms varied from SBP 50 mmHg to 70 mmHg and were associated with a pooled odds ratio of 0.70 (95% confidence interval 0.53–0.92) for survival benefit when compared to higher targets.40

However, a universal definition of accurate objective indications for REBOA in major trauma patients is challenging and dependent on location, services and resources available. A higher threshold (e.g. SBP <90 mmHg) may be considered in centres where there may be delays associated with access to definitive surgical care. This view has been supported by a Delphi panel consensus on REBOA and in centres adopting such a threshold, would result in more patients having the procedure. However, the panel also agreed that decisions should be individualised.41

Studies currently being performed in the UK42 and the USA18 may further define the indications and utility of REBOA for exsanguinating haemorrhage secondary to trauma.

Conclusions

The introduction of REBOA – for a predefined group of peri-arrest, shocked, predominantly blunt trauma patients – occurred with considerable education, resource allocation and 24-h availability of trained clinicians. However, in this high-volume trauma centre, there were no defined patients for whom REBOA was deployed during the study period and no defined patients who died for whom REBOA deployment may have contributed to survival. Despite literature supporting the introduction of REBOA, in this 14-month prospective study there was no evidence of mortality benefit. It is conceivable that patients most likely to benefit from REBOA are those who currently die, often pre-hospital, from exsanguinating sub-diaphragmatic/pelvic haemorrhage. Further studies may help define indications and subgroups of patients who may benefit.

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Competing interests

BM is a section editor for Emergency Medicine Australasia.
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