Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Resuscitative endovascular balloon occlusion of the aorta (REBOA) during cardiopulmonary resuscitation: A pilot study

Anja Levis[a,b], *Robert Greif*[a,c,d], *Wolf E. Hautz*[e], *Lutz E. Lehmann*[a], *Lukas Hunziker*[f], *Tobias Fehr*[g], *Matthias Haenggi*[b,*]

[a] *Department of Anaesthesiology and Pain Medicine, Bern University Hospital, Inselspital, University of Bern, Bern, Switzerland*
[b] *Department of Intensive Care Medicine, Bern University Hospital, Inselspital, University of Bern, Bern, Switzerland*
[c] *ERC Research NET, Niel, Belgium*
[d] *School of Medicine, Sigmund Freud University Vienna, Vienna, Austria*
[e] *Department of Emergency Medicine, Bern University Hospital, Inselspital, University of Bern, Bern, Switzerland*
[f] *Department of Cardiology, Bern University Hospital, Inselspital, University of Bern, Bern, Switzerland*
[g] *Bern Ambulance Services (Schutz & Rettung Bern), Bern, Switzerland*

Abstract

Aim: Resuscitative endovascular balloon occlusion of the aorta (REBOA) during cardiopulmonary resuscitation (CPR) increases coronary and cerebral perfusion pressure, which might improve neurologically intact survival after refractory cardiac arrest. We investigated the feasibility of REBOA during CPR in the emergency department.

Methods: Patients in refractory cardiac arrest not qualifying for extracorporeal CPR were included in this pilot study. An introducer sheath was placed by ultrasound-guided puncture of the femoral artery, and a REBOA catheter was advanced to the thoracic aorta in 15 patients undergoing CPR. Primary outcome was correct placement within 10 min of skin disinfection. Secondary outcomes included perfusion markers (mean central arterial blood pressure, end-tidal CO_2, non-invasively measured cerebral oxygenation) and procedural information (number and duration of attempts, complications, verification of correct position and occlusion).

Results: Successful catheter placement was achieved in 9 of the 15 patients (median 9 min 30 s). Median interval from dispatch to start of the procedure was 59 min. A small, albeit significant increase in non-invasively measured cerebral oxygenation was found, but none in blood pressure or end-tidal CO_2. However, two patients with pulseless electrical activity of more than 20 min achieved return of spontaneous circulation immediately after REBOA.

Conclusion: In this pilot trial, REBOA during CPR was successful in 60% of attempts. Long resuscitation times before start of the procedure might explain difficult insertion and missing effects. Nevertheless, insertion of REBOA in patients suffering from non-traumatic cardiac arrest is feasible and might increase coronary and cerebral perfusion pressures and perfusion.

Keywords: Out-of-hospital cardiac arrest, Resuscitation, CPR cardiopulmonary resuscitation, ALS life support care

* Corresponding author at: Department of Intensive Care Medicine, Bern University Hospital, Inselspital, Freiburgstrasse, CH 3010 Bern, Switzerland.
E-mail address: matthias.haenggi@insel.ch (M. Haenggi).

https://doi.org/10.1016/j.resuscitation.2020.08.118
Received 31 May 2020; Received in revised form 28 July 2020; Accepted 21 August 2020
Available online xxx

Introduction

Every year, 5–10 of every 10 000 citizens suffer from sudden out-of-hospital cardiac arrest (OHCA) with a survival rate of about 10%.[1–5] Since heart and brain depend on adequate perfusion, irreversible damage after cardiac arrest (CA) occurs within minutes.[6] Chest compressions are intended to restore perfusion to these vital organs but achieve only about 30% of normal coronary or cerebral perfusion.[7] During cardiopulmonary resuscitation (CPR), coronary perfusion pressure predicts return of spontaneous circulation (ROSC) and survival.[8] Cerebral perfusion pressure is crucial for a good neurological outcome.[6]

Therefore, improving coronary and cerebral perfusion pressure might increase survival with favourable outcome after CA. Occlusion of the descending aorta increased carotid and coronary artery blood flows and perfusion pressures in animal CA models,[9–14] which led to improved ROSC and better 48-h survival and neurological function.[12–16] In humans, occlusion of the descending aorta has mostly been performed together with open-chest CPR in the trauma population, with no clear evidence of superiority of the open-chest approach compared to standard CPR.[17]

Recently, balloon occlusion of the aorta in trauma (REBOA, resuscitative endovascular balloon occlusion of the aorta) has emerged as an alternative to surgical cross-clamping of the aorta in exsanguinating trauma patients,[18] and REBOA placement is feasible with ultrasound.[19,20] Reports of severely injured patients who arrested during or immediately before REBOA-catheter placement demonstrated improved blood pressure in the upper body.[21] Furthermore, retrospective comparisons of REBOA versus thoracotomy from trauma registries suggest that REBOA is usually faster and at least as effective as (if not superior to) thoracotomy and open- chest CPR for trauma patients in or near cardiac arrest.[22,23]

This pilot study aimed to investigate the feasibility of ultrasound-facilitated REBOA-catheter placement during CPR in the everyday setting of the emergency department of a university hospital.

Methods

The study was registered at ClinicalTrials.gov (NCT03664557). The Bern Cantonal Ethics Committee (Kantonale Ethikkommission Bern, Nr 2018-00741, 30/AUG/2018) approved this study and mandated a study-independent physician as a safeguard for each patient until a deferred informed consent could be obtained from survivors or next of kin. Deferred informed consent was waived by the ethics committee for non-survivors to avoid additional burden on relatives who had already suffered the loss of a loved one. An independent Data Safety and Monitoring Board reviewed the first 5 patients and reported results to the ethics committee after the 1st, 2nd and 5th patient.

We included patients suffering from refractory CA who failed ROSC after 10 min of high-quality advanced life support. Patients were excluded for any of the following reasons: qualifying for the local extracorporeal CPR (e-CPR) program, age <18 years, pregnancy, presence of upper body/torso trauma or known aortic aneurysm, both femoral arteries unable to accommodate a 7Fr introducer sheath, available written advanced directives excluding CPR, or study personnel/equipment being unavailable.

CA victims were transported by the local emergency medical service under continuous mechanical CPR to the university hospital. Inclusion took place in the emergency department after reassessment by the study-independent physician and the emergency team on duty. After study inclusion under continuous mechanical CPR, the senior intensivist on duty punctured the femoral artery with ultrasound guidance. Before a 25-cm-long 7F introducer (Radifocus Introducer II, Terumo Europe, Leuven, Belgium) was inserted, the emergency physician on duty verified correct arterial placement of the guidewire by abdominal ultrasound. The ultrasound showed either the guidewire in the abdominal aorta or the lack of guidewire in the inferior vena cava at the confluence with the hepatic veins. REBOA was aborted if the placement procedure took more than 20 min or if more than 3 unsuccessful puncture attempts or guidewire and sheath insertion attempts occurred.

After successful introducer placement, continuous invasive pressure monitoring started simultaneously at the tip of the catheter and at the side port of the introducer. The catheter (ER-REBOA; Prytime Medical, Boerne, TX, USA) was inserted and advanced into the thoracic aorta at the 4th intercostal space. The catheter's balloon was filled with NaCl 0.9% until pulsatility of the pressure trace distal to the occlusion at the side port of the introducer disappeared, or the maximal filling volume of 24 ml was reached. The study period ended 10 min after balloon inflation, at which point the emergency team re-evaluated the patient's situation and made a decision on further therapeutic options, including stopping resuscitative efforts.

Blood pressure at both the catheter tip and side port, heart rate and end-tidal CO_2 were recorded in the local anaesthesia information system (Philips Intellivue MP5, Philipps Healthcare Switzerland, and COPRA System GmbH, Berlin, Germany) every 1 min. Non-invasive measurement of cerebral oxygenation was performed bilaterally on the forehead (NONIN SenSmart® Model X-100 with internal storage, NONIN Europe, Tilburg, The Netherlands) and recorded before REBOA occlusion and 1, 5 and 10 min after.

Because of a lack of previous data, we chose a convenience sample of 15 patients. For this small data set we did not test for normality and used non-parametric tests. Median and interquartile range are the descriptive statistics. Repeated measurements were analysed with the Friedmann test (GraphPad Prism Version 8; GraphPad Software, San Diego, CA, USA). Data are presented as percentages or median and interquartile range. A P level of <0.05 is considered significant.

Results

Overall, successful catheter placement was achieved in 9 patients (60%; Tables 1 and 2). Median time to balloon inflation was 9 min 30 s (range 8 min 32 s–13 min). In 6 patients, inflation was achieved within 10 min. In the remaining 3 patients the procedure was prolonged. In one patient (patient 2; Tables 1 and 2) it took 18 min because the guidewire was initially placed in the vein twice, which was detected through sonographic visualization of the guidewire in the inferior vena cava. In another patient we were unable to advance the guidewire despite appropriate aspiration of blood and a second puncture was needed (14 min, patient 5, Tables 1 and 2). In an obese patient ultrasound visualization of the guidewire was unsuccessful and led to an insertion delay of 13 min (patient 3; Tables 1 and 2).

In 3 patients (patients 6, 8, 10; Tables 1 and 2), puncture attempts were abandoned after reaching the time limit or when more than 3 unsuccessful attempts were performed. In all three of these cases,

Table 1 – Details on REBOA insertion in the individual patients.

Patient	REBOA insertion	Time to inflation (min:s)	Ultrasound inferior vena cava	Ultrasound abdominal aorta	Blood pressure (mmHg) from sheath before inflation	Remarks
1	Success	8:32	Wire absent	Insufficient quality	83/21	–
2	Success, after 2× venous puncture	18:00	Wire 2× in inf. v. cava	Wire identified on 3rd attempt	80/25	2× venous puncture, identified by guidewire in inf. v. cava during ultrasound
3	Success	13:00	Insufficient quality, wire absent	Insufficient quality	33/5	Time to inflation prolonged because correct placement difficult to confirm by ultrasound (obesity), and diastolic blood pressure only 5 mmHg
4	Success	8:00	Wire absent	Not done	64/30	—
5	Success	14:00	Wire absent	Insufficient quality	Damped curve	Time to inflation prolonged because guidewire could not be advanced after 1st puncture, and difficult confirmation after 2nd puncture
6	Failure		n/a	n/a	n/a	Puncture failed 3×
7	Venous insertion (unnoticed)		Insufficient quality, wire absent	Insufficient quality	67/5	Guidewire could not be advanced after 1st puncture, and difficult confirmation after 2nd puncture. Although diastolic blood pressure was low, decision was made to move on
8	Failure		Wire absent	Wire absent	n/a	Guidewire could be advanced in the 2nd attempt only, but sheath could not be advanced. Abortion of attempt after 18 min
9	Success	10:00	Not documented	Not documented	Not measured	—
10	Failure		n/a	n/a	n/a	Puncture failed 3×
11	Success	6:05	Not documented	Wire identified	28/20	–
12	Success	9:30	Wire absent	Wire identified	Not measured	–
13	Arterial sheath directed caudally (unnoticed)		Wire absent	Wire absent	60/25	Difficult anatomical landmarks because of large scrotal hernia. Although wires not visible in aorta, high diastolic blood pressure made intraarterial position likely. X-ray confirmed caudal position
14	Venous insertion (unnoticed)		Wire absent	Wire absent	38/0	Ultrasound equivocal: wire absent in both vessels. Decision to advance despite low diastolic pressure. X-ray confirmed venous position
15	Success	9:00	Wire absent	Not done	Not measured	–

Note. REBOA: resuscitative endovascular balloon occlusion of the aorta.

Table 2 – Details of cardiac arrest circumstances.

Patient	Success	Interval dispatch time to start of procedure (min)	Witnessed cardiac arrest	First documented rhythm	Rhythm before start of procedure	Interval collapse to start of CPR (min)	Bystander CPR	ROSC
1	Yes	81	Yes	Shockable (AED)	PEA	0	Yes	No
2	Yes	60	Yes	VF	PEA	0	Yes	No
3	Yes	88	Yes	VF	PEA	<1	Yes	No
4	Yes	41	Yes	VF	Asystole	0	Yes	No
5	Yes	32	Yes	Asystole	PEA	1	Yes	No
6	No	No sooner than 44	No	VF	PEA	n/a	No	No
7	No (vein)	85	Yes	PEA	PEA	5	Yes	No
8	No	107	Yes	VF	PEA	5	Yes	No
9	Yes	26	Yes		PEA	0	EMS	Yes
10	No	No sooner than 52	No	VF	Asystole	n/a	No	No
11	Yes	58	Yes	VF	Asystole	<1	Yes	No
12	Yes	59	Yes	VT	PEA	7	Yes	No
13	No (sheath directed caudally)	30	Yes	VT	VT	7	Yes	No
14	No (vein)	128	Yes	VF	PEA	10	Yes	No
15	Yes	40	Yes	PEA	PEA	14	No	Yes

Note. ROSC: return of spontaneous circulation; AED: automatic external defibrillator; VF: ventricular fibrillation; VT: ventricular tachycardia (pulseless); PEA: pulseless electrical activity; EMS: emergency medical service.

CPR was discontinued because more than 60 min of CPR time had elapsed.

In one patient (patient 13; Tables 1 and 2) with a large scrotal hernia, arterial puncture could be achieved but the sheath and REBOA catheter were directed caudally, which was noticed only after an attempt to inflate the balloon. Obesity and difficult anatomy made ultrasound challenging, and diastolic blood pressure correctly indicated intraarterial position.

In 2 patients, the REBOA catheter was erroneously placed venously (patients 7, 14; Tables 1 and 2). In both cases, ultrasound could not confirm the guidewire within the aorta but it could not be detected in the vena cava either, yet the diastolic pressure below 10 mmHg at the side port of the sheath pointed toward a venous position. Since one previous patient (patient 3) with successful insertion also had very low diastolic pressure, uncertainty during the attempt persisted. The procedure was continued, resulting in venous misplacement of the catheter, which was confirmed only later by chest radiograph.

In 2 patients with a relatively short duration of CPR, ROSC was achieved immediately after the REBOA balloon was inflated. Unfortunately, both patients died, one after deflation of the balloon and the other after withdrawal of life sustaining therapy because of hypoxic-ischemic encephalopathy. In one patient, the attempt to ensure complete occlusion of the aorta by guiding the filling volume on the basis of the pressure trace obtained from the sheath led to overinflation and balloon rupture.

Regarding the secondary outcomes, a small, albeit significant increase could only be detected for cerebral oxygenation with near-infrared spectroscopy (NIRS). End-tidal CO_2 and blood pressure remained unchanged (Table 3).

Discussion

This pilot study shows that REBOA during CPR is not easy to accomplish but is feasible, as REBOA-catheter placement was possible in 9 of 15 patients, and 2 patients temporarily achieved ROSC. Although a 60% success rate seems low, we report, for the first time, clinical application of REBOA under ongoing CPR in patients with prolonged advanced life support.

Arterial puncture and ultrasound-confirmed correct catheter placement during resuscitation efforts are challenging. Ultrasound examinations are difficult as ongoing CPR moves the chest and abdomen, and ultrasound image quality is poor due to gastric and intestinal air from prior bag-mask ventilation. This often leads to unreliable confirmation of the correct guidewire position. In 1 of 3

Table 3 – Secondary outcomes: changes in cerebral oxygenation measured by NIRS, MAP proximal to the occlusion and end-tidal CO_2.

Outcome	Before occlusion	After occlusion	1 min	5 min	10 min	
NIRS (%)	41 (21–58)	41 (24–62)	41 (33–63)	41 (34–68)	42 (31–68)	$P<0.001$
MAP (mmHg)	39 (22–55)	44 (19–76)	45 (21–81)	43 (21–60)	37 (17–67)	$P=0.08$
End-tidal CO_2 (mmHg)	22 (12–33)	20 (12–33)	19 (13–27)	17 (9–32)	14 (11–27)	$P=0.17$

Note. All measurements are median and interquartile range (1–3). NIRS: near-infrared spectroscopy; MAP: mean arterial blood pressure; end-tidal CO_2: end-tidal carbon dioxide concentration.

patients with venous puncture (patient 2; Tables 1 and 2), ultrasound confirmed venous guidewire position, thereby preventing inadvertent balloon inflation in the vena cava and allowing for another puncture attempt. In the 2 other patients (patients 7, 14) with unnoticed venous misplacement, ultrasound was equivocal. The diastolic blood pressure below 10 mmHg obtained from the sheath before catheter insertion was suggestive of venous position when compared to the findings in other patients with correct arterial placement, who in most cases showed a diastolic blood pressure over 20 mmHg. However, low blood pressure during CPR does not reliably exclude correct arterial position, as seen in patient 3 (Tables 1 and 2).

Apart from confirmation of arterial position, palpation at the contralateral artery or pressure monitoring at the introducer side port is used to confirm complete aortic occlusion by the loss of pulsatile pressure readings upon balloon inflation in the trauma setting.[24] With ongoing CPR this does not prevent overinflating the balloon: in one patient, the REBOA-catheter balloon was inflated stepwise according to the manufacturer's instructions with a 24-ml balloon-filling volume (resulting in a diameter of 32 mm) but the balloon ruptured during intra-aortal inflation. Later we discovered on a previously performed, 2-year-old abdominal computerized tomography (CT) scan an aortic diameter of 20 mm. After discussion with the manufacturer, the Data Safety and Monitoring Board, and the Cantonal Ethics Committee, it was agreed not to fill the balloon upon cessation of pulsatile pressure trace obtained from the femoral artery. We agreed to a protocol amendment limiting the balloon-filling volume to below the official maximum (12 ml in women, 20 ml in men, corresponding to a 25- and 30-mm balloon diameter).

In one case the femoral artery was punctured correctly, but the guidewire was unintentionally directed caudally, resulting in incorrect femoral artery REBOA-catheter placement. The puncture was technically difficult because of a large scrotal hernia, which may have contributed to the misplacement. CPR was continued for 10 min with the catheter left in place. Two minutes after balloon inflation, mean arterial blood pressure dropped from 47 mmHg to 11 mmHg without pulsatility. Five minutes after occlusion no blood pressure was measurable. NIRS-detected cerebral oxygenation and end-tidal CO_2 remained unchanged. After another 10 min of advanced life support, the resuscitation team withdrew further CPR attempts as 59 min had passed since a second CA after previous temporary ROSC, with no reversible causes and no ventricular activity in transthoracic echocardiography found. Radiologic control showed the catheter in the right leg.

Interestingly, Brede et al.,[25] recently showed correct and reliable out-of-hospital arterial placement of such catheters in groin vessels verified by sonography. Severe vasoconstriction due to high cumulative doses of adrenaline and local haemostasis at the site of insertion due to prolonged reduced blood flow may both explain why earlier insertion as conducted by Brede et al. is more often successful than later attempts. The feasibility of this out-of-hospital approach needs to be confirmed in a larger study. Both, the study by Brede and colleagues and our findings suggest that to generate evidence about the effect of such a possibly lifesaving intervention, the REBOA catheter should be used only in the setting of a randomised controlled trial. Since early interventions seem to have higher success rates and, at least theoretically, better outcomes, a future study might investigate REBOA catheter placement by a dedicated pre-hospital emergency team following a strict study protocol.

Coronary blood flow and coronary perfusion pressure (of at least 15 mmHg[8]) drive myocardial oxygen supply and are strong predictors of ROSC and survival to hospital discharge.[8,26] During CPR, coronary perfusion pressure results from the difference between right atrial pressure and aortal pressure during decompression. Increased coronary and cerebral perfusion pressure and flows in animal models have translated into improved rates of ROSC, 48-h survival and neurological function.[12–16] Occlusion of the descending aorta in CA animal models showed increases in coronary and carotid artery blood flow, resulting in higher perfusion pressures.[9,16] It has been demonstrated in severely injured patients who arrested during trauma resuscitation that in addition to temporary haemostasis distal to aortic occlusion, the REBOA procedure improved upper body blood pressure.[21]

This was reflected in the 2 patients with refractory CA and ROSC immediately after REBOA. In both cases, traditional advanced life support had failed to achieve sustained ROSC, and occlusion of the aorta took place 37 and 49 min after the initial onset of arrest, a duration of CPR usually associated with very poor chances of ROSC.[27,28]

One patient (patient 15; Tables 1 and 2) with initial pulseless electrical activity (PEA) had intermittent ventricular fibrillation and defibrillation during transport. After 27 min of CPR, the REBOA procedure was started. ROSC followed immediately after balloon inflation and NIRS-detected cerebral oxygenation increased from no measurable value to 72% right/74% left over the following 10 min. The effect remained stable for the time the balloon remained inflated. Transesophageal echocardiography and CT scanning revealed a type A aortic dissection confined to the ascending aorta. The patient remained haemodynamically stable (blood pressure 139/102 mmHg) without inotropic support even under stepwise balloon deflation. Unfortunately, a brain CT scan showed early and extensive hypoxic-ischemic brain injury. Aortic surgery was postponed to allow neurological evaluation, but the patient died 2 days later after life support was withdrawn because of the extensive brain injury.

The other patient (patient 9; Tables 1 and 2) arrested with PEA 13 min after hospital admission because of severe dyspnoea. Multiple

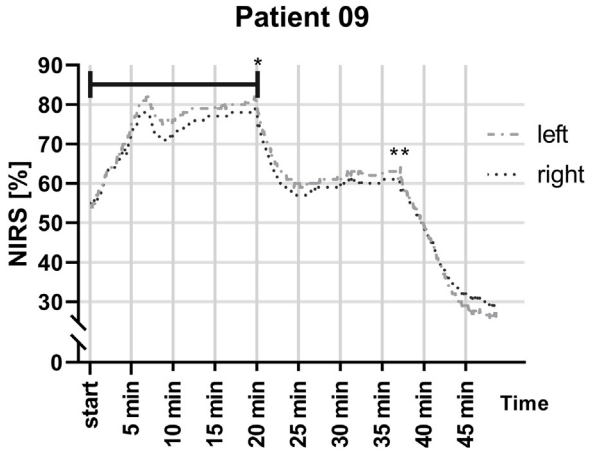

Fig. 1 – Near infrared spectroscopy (NIRS) of patient 9: during resuscitative endovascular balloon occlusion of the aorta, there was an increase in cerebral oxygenation from 53% to 80% and return of spontaneous circulation. Deflation (*) caused a decrease in cerebral oxygenation, and after the decision to withdraw further treatment because of futility (**), the patient deteriorated and died.

comorbidities excluded her from e-CPR. REBOA balloon occlusion occurred another 23 min later, followed by immediate ROSC with marked increase in NIRS-detected cerebral oxygenation from 53% to 80% (Fig. 1). After ruling out reversible CA causes, further resuscitative measures were abandoned and the REBOA balloon deflated. After deflation of the REBOA balloon, a decrease in blood pressure and cerebral oxygenation occurred immediately, followed by re-arrest 17 min later. Even though further therapy was withdrawn in both patients due to lack of therapeutic options, the occurrence of ROSC in these patients supports the pathophysiological concept and findings in animal models regarding REBOA in CA.

Several factors might have been contributed to the major limitation of this study: the high rate of incorrect catheter placement. First, our local approach to OHCA includes EMS personnel judge whether they can transport the patient in time for e-CPR to begin within 45 min. Therefore, this study included only patients not qualifying for e-CPR who had received prolonged advanced life support. CPR and skin disinfection for the REBOA manoeuvre took about 59 min (41 −88 min). In cases where REBOA was performed early, higher sheath and catheter placement success rates were achieved. The very long duration of CPR before the procedure started (due to the study design) might have contributed to challenging REBOA placements. This could be one explanation of the high success rate of early out-of-hospital REBOA placement at the scene.[25] The long duration from CA to aortal balloon occlusion may also explain the minimal observed effect on blood pressure proximal to the occlusion. After more than 1 h of CPR, the increased acidosis and vasoplegia might have impeded any detectable effects on blood pressure and end-tidal CO_2. The significant effect on NIRS-detected cerebral oxygenation is most probably not clinically relevant in this setting.

Second, the critical care physician on call performed the REBOA-catheter placement in this pilot study, as they are responsible for the hospitals' e-CPR interventions. Therefore, vascular access experience during CPR was given. The specific handling of the REBOA-balloon-catheter was taught at the start of the study, but we should have offered more brush-up sessions over the course of the study period.

Third, an important factor influencing success is the clinical environment and resuscitation team composition. At the Bern University Hospital, e-CPR vascular cannulation is performed in the hospital's coronary catheter suite or in the intensive care unit, not in the emergency department. Performing an ultrasound-guided femoral artery puncture during CPR in a busy emergency room is challenging and puts special burdens on communication, procedural skills and handling of equipment compared to the usual familiar environment.

Team composition during the study was different from in the standard e-CPR approach. The sole study intervention was restricted to a small group of investigators, but the clinical resuscitation teams were composed of the available on-call personnel on duty for the emergency room and were not always the same people.

Summarizing our experience and in contrast to published evidence in the trauma literature,[24] in this pilot study, neither sonography nor distal invasive blood pressure monitoring alone was reliable in excluding misplacement of the REBOA catheter. Abdominal ultrasound can confirm position in the abdominal aorta or vena cava in case of successful wire visualization, but acquisition of those images can be difficult under CPR. When ultrasound is inconclusive, we suggest adding blood pressure monitoring at the sheath, where a diastolic blood pressure below 10 mmHg is suggestive of venous malposition.

Also unlike in a trauma setting, balloon filling based on palpation or measurement of distal pulses carries the risk of balloon (rather than aortic) rupture due to overinflation. Intrathoracic and intra-abdominal pressure changes generated by CPR are possibly transmitted to the femoral artery, without necessarily indicating blood flow. To our knowledge, no data exist describing the direct correlation of palpable femoral pulse and actual blood flow during CPR.

In conclusion, this pilot study showed that REBOA during refractory CA under ongoing CPR is feasible, and REBOA-catheter placement was successful in 60% of study patients. In 2 patients ROSC occurred. An early REBOA procedure might increase success rates. Therefore, structured repeated training over time for the intervention team is crucial. Larger outcome studies need to define the proper timing of the REBOA procedure in CA patients and its effects on survival and the long-term neurological outcome.

Authors' contributions

AL conceived the study, developed the protocol, managed the trial and drafted the manuscript; MH conceived the study, oversaw development of the protocol and was responsible for the overall conduct of the trial. All authors contributed to protocol development. WH, TF, LH and LL were responsible for implementation of the study within their departments. AL, RG and MH drafted the manuscript and all co-authors reviewed and edited the final manuscript before submission.

Funding

This trial was funded by the Bangerter-Rhyner Stiftung für medizinische Forschung, Switzerland, awarded to Anja Levis; and the Stiftung zur Förderung der Forschung in Anästhesie und Intensivmedizin, Switzerland, awarded to Anja Levis.

Prytime Medical Inc., Bourne, TX, USA, the manufacturer of the ER-ROBOA catheter, provided a discount of 20% off the listed European price of the catheter.

Departmental funds of the Departments of Anaesthesiology, Intensive Care Medicine and Emergency Medicine of the Inselspital Bern and the Bern Ambulance Service (Schutz und Rettung Bern) funded the authors during the study. The funding agencies, the manufacturer and the respective employers had no role in planning, executing, analysing or writhing of this study.

Conflict of interest statement

RG is European Resuscitation Council Director of Education and Training as well as Chair of the International Liaison Committee on Resuscitation Task Force on Education, Implementation and Team.

All other authors do not have any conflict of interest in the context of this study.

WEH has received research funding from Mundipharma Research, UK and Roche Diagnostics, Germany and was paid for consultancy services by the AO Foundation, Zurich.

The Department of Intensive Care Medicine, University Hospital Bern, has, or has had in the past, research contracts with Orion Corporation, Abbott Nutrition International, B. Braun Medical AG, CSEM SA, Edwards Lifesciences Services GmbH, Kenta Biotech Ltd, Maquet Critical Care AB, Omnicare Clinical Research AG and

research and development/consulting contracts with Edwards Lifesciences SA, Maquet Critical 3Care AB and Nestlé. The money was paid into a departmental fund; no author received personal financial gain.

The Department of Intensive Care Medicine has received unrestricted educational grants from the following organizations for organizing a quarterly postgraduate educational symposium, the Berner Forum for Intensive Care (until 2015): Fresenius Kabi, GSK, MSD, Lilly, Baxter, Astellas, AstraZeneca, B | Braun, CSL Behring, Maquet, Novartis, Covidien, Nycomed, Pierre Fabre Pharma AG (formerly known as RobaPharm), Pfizer, Orion Pharma, Bard Medica S.A., Abbott AG and Anandic Medical Systems.

The Department of Intensive Care Medicine has received unrestricted educational grants from the following organizations for organizing bi-annual postgraduate courses in the fields of critical care ultrasound, management of ECMO and mechanical ventilation: Pierre Fabre Pharma AG (formerly known as RobaPharm), Pfizer AG, Bard Medica S.A., Abbott AG, Anandic Medical Systems, PanGas AG Healthcare, Orion Pharma, Bracco, Edwards Lifesciences AG, Hamilton Medical AG, Fresenius Kabi (Switzerland) AG, Getinge Group Maquet AG, Dräger Schweiz AG, Teleflex Medical GmbH.

Acknowledgements

The authors would like to acknowledge the nurses and physicians of the Emergency Department, the Department of Anaesthesiology, and the Department of Intensive Care Medicine, the staff of the Departments of Radiology and Cardiology of the University Hospital Bern, and the EMS providers who contributed to this study as well as other individuals who made this study possible. We would specifically like to thank the following people for their contributions to the project:

Data Safety and Monitoring Board:

PD. Dr. med. Martin Dünser, Kepler Universitätsklinikum Linz, Universitätsklinik für Anästhesiologie und Operative Intensivmedizin, Linz, Austria.

Dr. Andreas Schneider, University of Cologne, Klinik für Anästhesiologie und Operative Intensivmedizin, Kliniken Maria Hilf GmbH, Mönchengladbach, Germany.

Prof. Dr. med. Osmund Bertel, HerzGefässZentrum Zürich, Klinik im Park, Zürich, Switzerland.

Language editing: Anita Todd, Bloomington, Indiana, USA.

REFERENCES

1. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: systematic review of 67 prospective studies. Resuscitation 2010;81:1479–87.
2. Nichol G, Thomas E, Callaway CW, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA 2008;300:1423–31.
3. Jabre P, Penaloza A, Pinero D, et al. Effect of bag-mask ventilation vs endotracheal intubation during cardiopulmonary resuscitation on neurological outcome after out-of-hospital cardiorespiratory arrest: a randomized clinical trial. JAMA 2018;319:779–87.
4. Kiguchi T, Okubo M, Nishiyama C, et al. Out-of-hospital cardiac arrest across the world: first report from the International Liaison Committee on Resuscitation (ILCOR). Resuscitation 2020;152:39–49.
5. Grasner JT, Wnent J, Herlitz J, et al. Survival after out-of-hospital cardiac arrest in Europe – results of the EuReCa TWO study. Resuscitation 2020;148:218–26.
6. Harris AW, Kudenchuk PJ. Cardiopulmonary resuscitation: the science behind the hands. Heart 2018;104:1056–61.
7. Voorhees WD, Babbs CF, Tacker Jr. WA. Regional blood flow during cardiopulmonary resuscitation in dogs. Crit Care Med 1980;8:134–6.
8. Paradis NA, Martin GB, Rivers EP, et al. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. JAMA 1990;263:1106–13.
9. Sesma J, Labandeira J, Sara MJ, Espila JL, Arteche A, Saez MJ. Effect of intra-aortic occlusion balloon in external thoracic compressions during CPR in pigs. Am J Emer Med 2002;20:453–62.
10. Nozari A, Rubertsson S, Wiklund L. Improved cerebral blood supply and oxygenation by aortic balloon occlusion combined with intra-aortic vasopressin administration during experimental cardiopulmonary resuscitation. Acta Anaesthesiol Scand 2000;44:1209–19.
11. Gedeborg R, Rubertsson S, Wiklund L. Improved haemodynamics and restoration of spontaneous circulation with constant aortic occlusion during experimental cardiopulmonary resuscitation. Resuscitation 1999;40:171–80.
12. Rubertsson S, Bircher NG, Alexander H. Effects of intra-aortic balloon occlusion on hemodynamics during, and survival after cardiopulmonary resuscitation in dogs. Crit Care Med 1997;25:1003–9.
13. Spence PA, Lust RM, Chitwood Jr. WR, Iida H, Sun YS, Austin III EH. Transfemoral balloon aortic occlusion during open cardiopulmonary resuscitation improves myocardial and cerebral blood flow. J Surg Res 1990;49:217–21.
14. Dogan EM, Horer TM, Edstrom M, et al. Resuscitative endovascular balloon occlusion of the aorta in zone I versus zone III in a porcine model of non-traumatic cardiac arrest and cardiopulmonary resuscitation: a randomized study. Resuscitation 2020;151:150–6.
15. Liu X. Cerebral resuscitation in experimental studies. Focus on reperfusion injury and free radical scavengers. Uppsala Uppsala; 2002.
16. Tiba MH, McCracken BM, Cummings BC, et al. Use of resuscitative balloon occlusion of the aorta in a swine model of prolonged cardiac arrest. Resuscitation 2019;140:106–12.
17. Wang M, Lu X, Gong P, Zhong Y, Gong D, Song Y. Open-chest cardiopulmonary resuscitation versus closed-chest cardiopulmonary resuscitation in patients with cardiac arrest: a systematic review and meta-analysis. Scand J Traum Resus Emer Med 2019;27:116.
18. Morrison JJ, Galgon RE, Jansen JO, Cannon JW, Rasmussen TE, Eliason JL. A systematic review of the use of resuscitative endovascular balloon occlusion of the aorta in the management of hemorrhagic shock. J Traum Acute Care Surg 2016;80:324–34.
19. Sadek S, Lockey DJ, Lendrum RA, Perkins Z, Price J, Davies GE. Resuscitative endovascular balloon occlusion of the aorta (REBOA) in the pre-hospital setting: an additional resuscitation option for uncontrolled catastrophic haemorrhage. Resuscitation 2016;107:135–8.
20. Lendrum R, Perkins Z, Chana M, et al. Pre-hospital Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for exsanguinating pelvic haemorrhage. Resuscitation 2019;135:6–13.
21. Brenner M, Teeter W, Hoehn M, et al. Use of resuscitative endovascular balloon occlusion of the aorta for proximal aortic control in patients with severe hemorrhage and arrest. JAMA Surg 2018;153:130–5.
22. Brenner M, Inaba K, Aiolfi A, et al. Resuscitative endovascular balloon occlusion of the aorta and resuscitative thoracotomy in select patients with hemorrhagic shock: early results from the American Association for the Surgery of Trauma's Aortic Occlusion in Resuscitation for Trauma and Acute Care Surgery Registry. J Am Coll Surg 2018;226:730–40.
23. Moore LJ, Brenner M, Kozar RA, et al. Implementation of resuscitative endovascular balloon occlusion of the aorta as an alternative to resuscitative thoracotomy for noncompressible truncal hemorrhage. J Traum Acute Care Surg 2015;79:523–30 discussion 30–2.

24. Ogura T, Lefor AK, Nakamura M, Fujizuka K, Shiroto K, Nakano M. Ultrasound-guided resuscitative endovascular balloon occlusion of the aorta in the resuscitation area. J Emer Med 2017;52:715–22.
25. Brede JR, Lafrenz T, Klepstad P, et al. Feasibility of pre-hospital resuscitative endovascular balloon occlusion of the aorta in non-traumatic out-of-hospital cardiac arrest. J Am Heart Assoc 2019;8: e014394.
26. Andreka P, Frenneaux MP. Haemodynamics of cardiac arrest and resuscitation. Curr Opin Crit Care 2006;12:198–203.
27. Funada A, Goto Y, Tada H, et al. Duration of cardiopulmonary resuscitation in patients without prehospital return of spontaneous circulation after out-of-hospital cardiac arrest: results from a severity stratification analysis. Resuscitation 2018;124:69–75.
28. Reynolds JC, Frisch A, Rittenberger JC, Callaway CW. Duration of resuscitation efforts and functional outcome after out-of-hospital cardiac arrest: when should we change to novel therapies? Circulation 2013;128:2488–94.