# Questions and answers

Frequent questions regarding REBOA in general and in pre-hospital cardiac arrest in specific.

### What is REBOA?

REBOA stands for Resuscitative Endovascular Balloon Occlusion of the Aorta. It is inserted through an introducer sheath in the femoral artery, placed blindly or under ultrasound guidance, and advanced retrogradely up the aorta. The positioning of the balloon can be done fluoroscopy-free. When the balloon is inflated, it prevents blood flow distally, partially or complete, and augments blood flow to organs proximal to the balloon. At present, REBOA is used in-hospital in the setting of non-compressible hemorrhage below the diaphragm, in Norway particular post-partum [1]. It is also used prehospital in London (London HEMS) on the same indication [2], although it should be mentioned that the evidence for use in trauma is conflicting and low grade [3-5].

### What is the REBOARREST Trial?

The REBOARREST Trial is a multicenter randomized controlled study on patients with non-traumatic out-of-hospital cardiac arrest. The inclusion criteria are age 18 to 80 years, less than 10 minutes from debut of arrest to start of basic or advanced cardiac life support and commenced ACLS is established and can be continued. Patients will be randomized 1:1 to balloon occlusion of the aorta during CPR or control with standard care. Primary endpoint is rate of ROSC. For more details, such as full list of exclusion criteria and secondary endpoints, please see the protocol.

### What is the scientific basis for applying REBOA in non-traumatic cardiac arrest?

For a person in cardiac arrest, there are two main issues. The first is to achieve return of spontaneous circulation (ROSC). The second is to optimize cerebral perfusion as the main cause of death in those who are admitted to hospital, is anoxic brain injury, and the main sequela of survivors is neurological disability [6]. As the following will outline, REBOA may address both these issues.

The pivotal principle of today’s Advanced Cardiac Life Support (ACLS), besides termination of malignant arrythmia by defibrillation, is to increase coronary perfusion pressure. This in turn leads to increased coronary blood flow and is associated with increased rates of ROSC [7]. External chest compressions generate a systemic arterial pressure and some perfusion of the whole body. The objective of using epinephrine is to increase peripheral vasoconstriction in order to increase coronary perfusion pressure and thus increase coronary blood flow. This comes at the cost of lower perfusion of the rest of the body.

Several animal studies (mostly pigs and dogs), show consistently and convincingly that occlusion of the aorta during cardiopulmonary resuscitation (CPR) lead to increase in mean arterial pressure, coronary perfusion pressure and coronary blood flow [8], [9]. More importantly, studies show increased rates of ROSC and survival [10], [11], [12]. An important second effect of occlusion of the descending aorta, is that cerebral perfusion pressure and cerebral blood flow increase [8], [9], [13], [14]. It is now suggested that REBOA in cardiac arrest is tested in clinical trials [15, 16].

The first clinical study worldwide on REBOA in non-traumatic cardiac arrest was the prehospital feasibility study performed in Trondheim, Norway. The study included 10 patients, 1 survivor with good neurological outcome, balloon inflation time mean 45 min after arrest, and 60 % ROSC [17]. Before this pilot trial, the use of aortic occlusion in cardiac arrest is documented in 4 articles with 5 cases [18], [19], [20], [21]. The first article describes two patients who arrested while on IABP (Intra Aortic Balloon Pump), constant inflation achieved increase in coronary perfusion pressure, but no ROSC. The three other patients achieved ROSC shortly after balloon inflation.

### Will this procedure draw attention away from ACLS and lower the quality?

Obviously, performing an invasive procedure will draw attention from the physician and the assistant. But according to protocol, inclusion criteria is “commenced ACLS is established and can be continued”. If ACLS cannot be performed as per national guidelines, the procedure should be aborted (Protocol 2020). Thus, if only the Air Ambulance team is on scene, REBOA cannot be performed. During the training period, the importance of ACLS of high standards will be emphasized. The pilot trial demonstrated that prehospital REBOA procedure during resuscitation is feasible and did not negatively influence the quality of the ACLS [17]. The quality of ACLS in the present trial will be analyzed after study period.

### What about the ischemic lower body?

Ischemia in organs distal to occlusion is of great concern every time REBOA is applied. London HEMS uses 60 min as a cut off for balloon deflation for patients exsanguinating (Sadek, lecture EUPHOREA 2020). In a registry study of Japan Trauma Data Bank no one survived zone 1 occlusion for more than 45 minutes, but this was in the setting of traumatic hemorrhage. In cardiac arrest the whole body is in severe ischemia. The best way to resolve this, is by achieving return of spontaneous circulation. REBOA will direct more of the blood flow to heart and brain - at the cost of the lower body. We don’t know if this will turn out with survivors having more ischemic injuries.

Of note, the study population have an estimated rate of ROSC of 18% according to a needs assessment study, and expectedly even more dismal numbers of survival [22].

### What are the complications to the use of REBOA?

The greatest limitation to the use of REBOA is lower body ischemia caused by aortic occlusion as outlined above. Complications of REBOA insertion, as with other endovascular devices, are vessel injury (dissection, rupture, and perforation, both in the femoral artery and the aorta), thrombosis, embolization, including air, and peripheral ischemia leading to amputation [23]. More complications have been noted for the larger 12-14 French system, but complications are also observed with the 7 French systems [24]. In a retrospective study from Norway, of 36 patients, six patients experienced complications. Five had local thrombus formation, in all a short 11 cm introducer was used. One person had a tear of the aorta but recovered without any permanent sequelae. This have led to the use of smaller size balloons [1]. In another review, iatrogenic injury was below 5 % [25].

Performing prehospital REBOA might be in a challenging environment. Training will therefore follow a systematic training program published previously [26], and every physician and paramedic will have to be certified to join the study (Protocol 2020). In the REBOARREST Trial ultrasound is mandatory and only 7 French systems with 20 cm introducers will be used.

Adverse events are monitored and will be followed up closely throughout the study.

### If REBOA-group achieves ROSC more often, will this lead to more patients with poor neurologic survival?

There exists no exact time limit for when CPR should be aborted because of anoxic brain injury. Further, there are no absolute prognostic factors, but factors related to the circumstance around the cardiac arrest, such as bystander CPR, may aid in this question. Some suffer a devastating neurologic injury after a few minutes, and some can survive without disability after more than an hour of CPR. In the CHEER-trial from Australia, although only 26 patients, they reported 54% survival with full neurological recovery (CPC 1) after median time of CPR of 56 (IQR 40-85) minutes (time from cardiac arrest to ECMO (Extracorporal Membrane Oxygenation -heart lung machine)([27].

### Why not ECMO instead of REBOA?

The ECMO circuit is more advanced technology and today ECMO requires a specialized team. This is costly and not easily transferred to a prehospital setting. However, centers in London and Paris try to do this in an urban setting.

### Are the resources used for the REBOA procedure worth the price?

This is a highly relevant question and need to be addressed if the present study shows a positive effect. The answer depends on many factors, among them how many extra persons will survive with good neurologic outcome (NNT), equipment costs, training costs etc. We have come to the conclusion that the evidence and experience with REBOA so far supports performing this trial.

### Technical aspects of REBOA

#### What is zone 1 aortic occlusion?

According to Stannard, aorta is divided into 3 zones. Zone 1 is between the left subclavian artery and the celiac trunk, zone 2 between the celiac trunk and the lowest renal artery, and zone 3 is below the lowest renal artery until the aortic bifurcation [28].

#### How long time is necessary to perform the procedure?

In the feasibility study, to date the only prehospital case series, procedure time (time from decision to balloon inflation) was 11,7 minutes (range 8-16).

#### When/how to deflate the balloon?

In the REBOARREST Trial, balloon deflation is to be done slowly over 30 seconds as soon as ROSC is confirmed.

#### Can the ambulance crew perform REBOA?

In the REBOARREST Trial, all physicians are confident in the Seldinger technique, and have passed an educational program. Ambulance crew should not perform REBOA.

#### Are there benefits of REBOA after admission to hospital?

The REBOA introducer sheath can be used for invasive procedures such as PCI, IABP and ECMO.

#### How do you train for this procedure?

The training is a structured educational program, described in a previously published article [26]. It consists of 4 phases: a theoretical part, basic skills training, 1 day at the interventional radiology department with insertion of equipment on patients under guidance and supervision of skilled interventional radiologists, and lastly high-fidelity simulation.

## References

1. Stensaeth, K.H., et al., *Fluoroscopy-free Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for controlling life threatening postpartum hemorrhage.* PloS One, 2017. **12**(3): p. e0174520.

2. Sadek, S., et al., *Resuscitative endovascular balloon occlusion of the aorta (REBOA) in the pre-hospital setting: An additional resuscitation option for uncontrolled catastrophic haemorrhage.* Resuscitation, 2016. **107**(Supplement C): p. 135-138.

3. Inoue, J., et al., *Resuscitative endovascular balloon occlusion of the aorta might be dangerous in patients with severe torso trauma: A propensity score analysis.* J Trauma Acute Care Surg, 2016. **80**(4): p. 559-66; discussion 566-7.

4. Irahara, T., et al., *Retrospective study of the effectiveness of Intra-Aortic Balloon Occlusion (IABO) for traumatic haemorrhagic shock.* World journal of emergency surgery : WJES, 2015. **10**(1): p. 1-1.

5. Doucet, J. and R. Coimbra, *REBOA: is it ready for prime time?* J Vasc Bras, 2017. **16**(1): p. 1-3.

6. Dragancea, I., et al., *The influence of induced hypothermia and delayed prognostication on the mode of death after cardiac arrest.* Resuscitation, 2013. **84**(3): p. 337-342.

7. Paradis, N.A., *Coronary Perfusion Pressure and the Return of Spontaneous Circulation in Human Cardiopulmonary Resuscitation.* JAMA: The Journal of the American Medical Association, 1990. **263**(8): p. 1106.

8. Spence, P.A., et al., *Transfemoral balloon aortic occlusion during open cardiopulmonary resuscitation improves myocardial and cerebral blood flow.* Journal of Surgical Research, 1990. **49**(3): p. 217-221.

9. Sesma, J., et al., *Effect of Intra-aortic occlusion balloon in external thoracic compressions during CPR in pigs.* The American Journal of Emergency Medicine, 2002. **20**(5): p. 453-462.

10. Tang, W., et al., *Augmented efficacy of external CPR by intermittent occlusion of the ascending aorta.* Circulation, 1993. **88**(4 Pt 1): p. 1916-21.

11. Rubertsson, S., N.G. Bircher, and H. Alexander, *Effects of intra-aortic balloon occlusion on hemodynamics during, and survival after cardiopulmonary resuscitation in dogs.* Crit Care Med, 1997. **25**(6): p. 1003-9.

12. Gedeborg, R., S. Rubertsson, and L. Wiklund, *Improved haemodynamics and restoration of spontaneous circulation with constant aortic occlusion during experimental cardiopulmonary resuscitation.* Resuscitation, 1999. **40**(3): p. 171-180.

13. Gedeborg, R., et al., *Cerebral ischaemia in experimental cardiopulmonary resuscitation — comparison of epinephrine and aortic occlusion.* Resuscitation, 2001. **50**(3): p. 319-329.

14. Nozari, A., et al., *Maximisation of cerebral blood flow during experimental cardiopulmonary resuscitation does not ameliorate post-resuscitation hypoperfusion.* Resuscitation, 1999. **40**(1): p. 27-35.

15. Daley, J., et al., *The role of resuscitative endovascular balloon occlusion of the aorta (REBOA) as an adjunct to ACLS in non-traumatic cardiac arrest.* The American Journal of Emergency Medicine, 2017. **35**(5): p. 731-736.

16. Nowadly, C.D., et al., *The use of resuscitative endovascular balloon occlusion of the aorta (REBOA) for non-traumatic cardiac arrest: A review.* Journal of the American College of Emergency Physicians Open, 2020. **n/a**(n/a).

17. Brede Jostein, R., et al., *Feasibility of Pre‐Hospital Resuscitative Endovascular Balloon Occlusion of the Aorta in Non‐Traumatic Out‐of‐Hospital Cardiac Arrest.* Journal of the American Heart Association, 2019. **8**(22): p. e014394.

18. Deakin, C.D. and D.J. Barron, *Haemodynamic effects of descending aortic occlusion during cardiopulmonary resuscitation.* Resuscitation, 1996. **33**(1): p. 49-52.

19. Aslanger, E., et al., *Intraaortic balloon occlusion during refractory cardiac arrest. A case report.* Resuscitation, 2009. **80**(2): p. 281-283.

20. McGreevy, D., et al., *Endovascular resuscitation with aortic balloon occlusion in non-trauma cases: First use of ER-REBOA in Europe.* Journal of Endovascular Resuscitation and Trauma Management, 2017. **1**(1): p. 42.

21. Coniglio, C., et al., *Resuscitative Endovascular Balloon Occlusion of the Aorta for Refractory Out-of-Hospital Non-Traumatic Cardiac Arrest - A Case Report.* Prehospital and Disaster Medicine, 2019. **34**(5): p. 566-568.

22. Brede, J.R., J. Kramer-Johansen, and M. Rehn, *A needs assessment of resuscitative endovascular balloon occlusion of the aorta (REBOA) in non-traumatic out-of-hospital cardiac arrest in Norway.* BMC Emergency Medicine, 2020. **20**(1): p. 28.

23. Ribeiro Junior, M.A.F., et al., *The complications associated with Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA).* World J Emerg Surg, 2018. **13**: p. 20.

24. Osborn, L.A., et al., *Resuscitative endovascular balloon occlusion of the aorta: current evidence.* Open Access Emergency Medicine : OAEM, 2019. **11**: p. 29-38.

25. Borger van der Burg, B.L.S., et al., *A systematic review and meta-analysis of the use of resuscitative endovascular balloon occlusion of the aorta in the management of major exsanguination.* Eur J Trauma Emerg Surg, 2018. **44**(4): p. 535-550.

26. Brede, J.R., et al., *Resuscitative endovascular balloon occlusion of the aorta (REBOA) in non-traumatic out-of-hospital cardiac arrest: evaluation of an educational programme.* BMJ Open, 2019. **9**(5): p. e027980.

27. Stub, D., et al., *Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial).* Resuscitation, 2015. **86**: p. 88-94.

28. Stannard, A., J.L. Eliason, and T.E. Rasmussen, *Resuscitative endovascular balloon occlusion of the aorta (REBOA) as an adjunct for hemorrhagic shock.* The Journal of Trauma, 2011. **71**(6): p. 1869-1872.