# 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.

### **Miscellaneous**

### Will REBOA create supranormal blood pressures?

We have no data to support such claim. Jang et al (Resuscitation 2022) presented 15 patients where blood pressure was measured proximal to the balloon and no supranormal measurements were found. They found a significant increase in the coronary perfusion pressure.

### Can we measure blood pressure on all REBOA catheters?

We can measure blood pressures on the REBOA catheter produced by Prytime. In REBOARREST, this catheter is used only at the Italian study site at Bologna. The catheter produced by REBOA Medical are used in all other study sites and we cannot measure blood pressure in this catheter. The reason is that the catheter is CE/FDA approved with the guidewire in place, so we are not allowed to remove the guidewire – hence, there is no available lumen to measure pressure.

### Why must the guidewire stay in the catheter?

This is due to the CE/FDA approval, we are not allowed to remove the wire. Further, the REBOA Medical catheter do not have a soft pigtail tip, so if the guidewire is removed, the tip may injure the aorta.

### Why do we use different catheter types at different study sites?

We use a different catheter type in Italy (Prytime), due to that the ethical approval in Italy only allows for use of the Prytime catheter.

### Will we perform autopsy on patients?

This is a highly relevant question. The legislation regarding autopsy, for scientific or forensic reasons, are different from nation to nation. In this study, we welcome any autopsy that may be performed and have facilitated in the database for any information, if autopsy should be performed. The indication for autopsy will not be made by the prehospital clinicians, due to the severity of the incident, a need for proper handling of next-of-kin and the ethical issues of the use of an emergency unit to transport a non-survivor. This agrees with the ethical approval in Norway.

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