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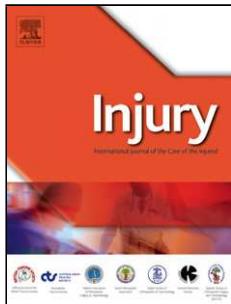
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Author: Jose Andres MD

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Resuscitative endovascular balloon occlusion of the aorta (REBOA): what have we learned?

Jose Andres MD¹, Julian Scott MD, FRCS FRCSEd FEBVS,² Peter V Giannoudis MD, FACS, FRCS^{3,4}

¹Orthopedic Surgery Department. Hotpital Universitari Vall d'Hebron. Barcelona, Spain.

² Academic Department of Vascular Surgery, LGI, Leeds, UK

³ Academic Department of Trauma and Orthopaedics, Floor A, Clarendon Wing, LGI, University of Leeds, Leeds, UK

⁴ NIHR Leeds Biomedical Research Unit, Chapel Allerton Hospital, Leeds, UK

Corresponding Author Address:

Professor Peter V Giannoudis MB, BSc, MD, FACS, FRCS (Glasg), FRCS(Eng)

Academic Department Trauma & Orthopaedic Surgery

School of Medicine

University of Leeds

Leeds, UK

Email: p.giannoudis@leeds.ac.uk

Tel: +44-113-3922750

Fax: +44-13-3923290

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Introduction.

Pelvic ring, thoracic and abdominal injuries are often seen in young adults with polytrauma presenting in a state of shock being at an increased risk of morbidity and mortality (1-6).

Hemorrhage is the main cause of preventable death in both military and civilian trauma patients, thus affecting a young and otherwise healthy population (7-12). This fact remains unchanging despite heterogeneity of the samples reported in terms of trauma event, injury pattern and care resources available. Most of these patients perish by Non-Compressible Torso Hemorrhage (NCTH) (13). The definition and management of this picture is constantly evolving. Many techniques have been developed in an effort to deal with the high mortality encountered; Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) being one of the most promising practices. Arisen from the field of great vessels surgery, this procedure has developed into an efficient tool in hemorrhage control and resuscitation. It offers a less invasive approach for the salvage of the most severely injured in comparison to resuscitative thoracotomy (RT), which may explain the increased uptake of this technique in many emergency departments (14,15).

Physiological effects of the aortic occlusion: proximal and distal concerns.

Numerous clinical and preclinical studies support the utility of REBOA in restoring hemodynamics in the context of hemorrhagic shock (15-22). Nonetheless, physiological tolerance to aortic occlusion is related to the metabolic and vascular impact in the areas proximal and distal to the balloon. Those effects have been described in animal models.

Ischemia of the tissues distal to the occlusion triggers the elevation in cytokines concentration. After balloon deflation, its distribution throughout the circulatory system may thrust the Systemic Inflammatory Response Syndrome (SIRS), leading to increased resuscitation requirements and progression to Acute Respiratory Distress Syndrome (ARDS) (23). Hypoxia activates the anaerobic metabolism of the cells, thus increasing lactate levels and contributing to the lethal triad of hypothermia, acidosis and coagulopathy (17,14,25). This tendency has, however, shown to be less severe in REBOA than in RT in a swine model (18). Histologic evidence of visceral lesion due to hypoperfusion has been inconsistently reported and its functional impact is actually unknown

(17,22,25,26). It does seem to be a relationship between spinal cord ischemia and neurological dysfunction in REBOA, being more probable and severe with proximal occlusion (21). The magnitude of all the aforementioned effects is proportional to the time of occlusion.

Experimental research has demonstrated an increase in arterial pressure above the baseline in the areas proximal to the balloon (22,26). It could be mediated by the restriction of arterial tree and the effect of circulating catecholamines and has a potential of harm to myocardial perfusion and respiratory function, besides a raised intracranial pressure. This last issue is of particular importance, since many candidates for REBOA sustain a brain injury (9–11). Thus, redistribution of the excess of output in the areas proximal to the balloon while some degree of distal perfusion is maintained is of paramount importance. The inherent limitations of animal trials highlight the need for further clinical investigations to assess these concerns. Several methods have been developed to mitigate these effects including intermittent balloon deflation (27); Others, being still laboratory focused consist of partial occlusion of the aorta (22) and establishment of an arterial shunt from above to below the balloon (28).

Outcomes, features and keys for success.

Survival rates of trauma patients undergoing REBOA from available studies (USA, Japan and Europe) range from 13% to 67% (14–16,18,20,27,29–34). Unfortunately, there are huge discrepancies in methodology, inclusion criteria and interventions. Recently, a multicenter REBOA registry has been created (15) and in time may produce interesting data which may clarify the role of this technique in modern resuscitation and, even, its advantage over RT.

The main predictors of mortality in REBOA are the severity of injury and the duration of occlusion (16,20,31,34), which are not independent of each other. Patients in poor conditions are likely to present higher resuscitation requirements, being occluded earlier. Greater complexity of lesions entails longer treatments, delaying the release of occlusion. Additionally, the dramatic improvement

of hemodynamics may bring about a false sense of security that sets back decision-making and leads to unnecessary further examinations. Several authors have raised concerns about safety of REBOA (32,33), showing an increased mortality with the use of this tool. Maybe the poor prognosis that they found is the product of a non-ideal scenario. In these works the times of occlusion were long, probably due to singularities of infrastructure and staff. Thus, the impact of ischemia was severe. This demonstrates that the use of REBOA should always be coordinated with other resuscitative efforts, focusing the resources on the rapid achievement of definitive hemostasis.

There is good evidence from animal models that prolonged aortic occlusion of greater than 60 minutes will have a substantial systemic effect on cord perfusion and a poor outcome (17,21,23,25) Further work is, however, required to translate these finding into the clinical setting, but it appears that 40 minutes maybe an appropriate cut off time

Systemic complications have been reported and include multisystem organ failure, acute kidney injury and ARDS (15,31). However, it is impossible to assess the contribution of REBOA and or trauma to the development of these complications. REBOA is directly associated with femoral artery injury (with or without ischemia and amputation), embolism, device malposition (catheter exiting through an aortic lesion or placed in a non-desired position) and cord lesion; these globally ranging from 2% to 13% (15,30,31).

Clinical guidelines highlight the primary role of RT for patients with severe chest trauma (35). In this scenario, the advantages of RT include; (1) evacuation of cardiac tamponade, (2) clamping of thoracic great vessels hemorrhage, (3) control of heart and hilum injuries and (4) direct cardiac massage. Current guidelines comprise the use of REBOA. In the future, a better knowledge and experience of use could expand its indications, even on cases in which a thoracotomy is indicated nowadays. A recent publication on autopsies revealed only 32% of subjects met clinical criteria for REBOA, instead of 54% that could benefit based on anatomical findings (36).

Available data disagree in asserting superiority of REBOA over RT in terms of survival (14,15). However, the studies agree that REBOA controls better the hemorrhage. There's a risk of bias related to the use of balloon in less critical patients. The lesser aggressivity of this technique pushes doctors to its early application, even prophylactically in patients that may fall into shock (30). Besides, release of occlusion is more progressive in REBOA, thus avoiding shock relapse. Even in this case, deflation should be preceded by intensification of resuscitation medical maneuvers.

Three different zones for occlusion have been described in REBOA (37). Zone I occlusion (from the left subclavian artery to the celiac trunk) is recommended for abdominal hemorrhage and zone III (distal to the lowest renal artery) for pelvic hemorrhage, like in unstable pelvic ring fractures (35). Zone II is a visceral territory that should be avoided. In comparison to RT, REBOA allows for more selective circulatory exclusion, theoretically decreasing the chance of systemic compromise. Most of REBOA procedures reported occluded the aorta in zone I (14,15). To date, the occlusion of one zone or either the other has not been comparatively studied.

Deployment of the catheter can be carried out via an percutaneous arterial or open approach and placement undertake blindly or by image-guided techniques. Morphometric studies have proven the association of external corporal measurements, and other parameters, with the depth of insertion needed to deploy the balloon at the target site (32,33) This supports the feasibility of an accurate deploy of the balloon by the only means of physical exam. Most studies do not use any imaging (16,18,20,31,34) and as such does not require either a vascular surgeon or interventional radiologist. There are, however reports of malposition (16,34) and bilateral femoral pulse abolition must be assessed in order to ensure total aortic occlusion (16).

The future: who and where?

As the use of REBOA gains popularity, there is an increasing need for high fidelity training models and teaching programs. One of the main advantages of this technique is that it can be acquired in a reasonable time frame and without significant endovascular surgical (40,41). There is however a need for further innovation particularly in respect of (1) deployment without imaging, (2) small flexible delivery systems, (3) wifi haemodynamic data and (4) stable aortic position (19,26).

Most of deaths in trauma patients take place in the prehospital setting (7–10). They are usually related to hemorrhage and could be preventable, which raises the question of deploying REBOA in the pre hospital setting (42,43). Recently, the world's first prehospital REBOA was successfully performed by the London Air Ambulance crew (44). The patient sustained an exsanguinating hemorrhage due to pelvic ring fracture. REBOA III was safely inserted on the ground with the aid of ultrasonography. After achieving temporary hemostasis, the patient was transferred to hospital and finally survived the injuries (38). This case exemplifies the wide range of scenarios in which REBOA could have a role in resuscitation.

Summary

REBOA is a promising procedure that can save lives. It has temporary effects on hemostasis and hemodynamics, possessing the capacity to bridge the gap between shock and definitive care. The key for success is to achieve definitive hemostasis as soon as possible, for which focused resources are needed. Its great versatility and easy application makes REBOA accessible to many professionals and in different clinical scenarios. It is, however, a technique in its infancy and further clinical experience, better devices and formalized training/high fidelity models are required to assess its true role in modern resuscitation. Nonetheless based on the currently available information the following recommendations can be made:

- Use of the most technical free techniques, according to individual training and resources available.

- Early insertion and inflation of the device in patients falling into shock, even on the prehospital setting.
- Prophylactic insertion in borderline patients could be beneficial, permitting rapid inflation of the balloon when necessary.
- Use of zone III REBOA in pelvic bleeding. Check bilateral femoral pulse abolition.
- Minimize occlusion times to less than 40 minutes, putting aside unnecessary examinations and achieving definitive hemostasis as soon as possible (proper staff and infrastructure needed).
- Hemodynamic parameters should be monitored in areas proximal to occlusion.
- Intensification of other resuscitative options (volume replacement, vasoactive agents) before balloon deflation.

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