

The use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) in Civilian Trauma in an Israeli Level 1 Trauma Center

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ABSTRACT **Background:** Massive, non-compressible bleeding is a leading cause of preventable trauma mortality. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) is a minimally invasive procedure in which a balloon catheter is maneuvered into the aorta to temporarily occlude large vessels and enable stabilization of the exsanguinating patient.

Objectives: To present experiences in assimilating REBOA at a single level 1 trauma center in Israel, to evaluate the technical aspects of the procedure, and to describe patient characteristics and outcomes.

Methods: This retrospective cohort study comprised civilians admitted with hemorrhagic shock to our trauma department who were treated with REBOA between November 2017 and July 2021. Descriptive statistics of the patients, characteristics of the injuries and patient outcomes are presented.

Results: The study included 22 patients (median age 30.1 years, 21 male). The mean systolic blood pressure (SBP) before REBOA inflation was 59.6 ± 11.4 mmHg, and the mean SBP measured after the procedure was 115.2 ± 26.3 mmHg. In 20 patients (91%), the SBP was normalized (> 90 mmHg) shortly after inflation of the balloon, and they survived the treatment in the trauma department; 15 (75%) survived the first 30 days.

Conclusions: REBOA is an effective method for the initial resuscitation and hemorrhage control of patients with massive, non-compressible bleeding and is relatively easy to assimilate in a hospital. The achievement of immediate normalization of SBP enables medical personnel to correct physiological parameters and obtain accurate imaging before proceeding to the operating theater.

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KEY WORDS: hemorrhage, massive bleeding, Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), shock, trauma

BOA was first used more than 50 years ago for injured soldiers during the Korean War [2] and is considered today as a potential alternative for aortic cross-clamping via resuscitative thoracotomy [3]. In a minimally invasive procedure, a balloon catheter is inserted into the femoral artery, where it is maneuvered into the aorta to temporarily occlude large vessel blood flow distal to the diaphragm. This procedure enables stabilization of the exsanguinating patient by restoring cerebral and myocardial perfusion. The main accepted indications for the use of REBOA include blunt or penetrating traumatic life-threatening hemorrhage below the diaphragm in patients in hemorrhagic shock who are unresponsive to resuscitation efforts and cardiac arrest caused by injury due to hemorrhage below the diaphragm. In the former scenario, the accepted time frame for the use of REBOA is the same as for resuscitative thoracotomy [3]. For intra-abdominal and for pelvic bleedings, recent studies have shown that REBOA is not inferior to pre-peritoneal packing and is obviously less invasive [4]. REBOA has recently been reported as an effective technique in obstetric emergencies such as placenta accrete, uterine atony, and hemorrhagic ovarian cyst [5].

Technically, the aorta is divided into three separate zones for the purposes of REBOA. Zone 1 extends from the origin of the left subclavian artery to the celiac artery, zone 2 continues from the celiac artery to the renal artery, and zone 3 extends from the lowest renal artery to the aortic bifurcation. The balloon catheter may be inflated at zone 1 for the control of intra-abdominal or retroperitoneal hemorrhage or for those with traumatic arrest; and at zone 3 for patients with severe pelvic, junctional, or proximal lower extremity hemorrhage.

The use of REBOA may cause morbidity, as occlusion of the aorta may result in tissue ischemia and lead to organ dysfunction such as kidney or spinal cord injury [6]. Thus, the total time of the inflated balloon in the aorta is a crucial parameter. In addition, complications related to femoral access, such as arterial disruption, dissection, pseudoaneurysms, hematoma, and extremity ischemia [7] have been reported. In addition, there are reports of aortoiliac injuries including intimal tear, dissection, and thrombosis. Some authorities have suggested that the use of

Massive, non-compressible bleeding constitutes a leading cause of preventable trauma mortality [1]. During the last two decades, Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has become widely available as a quick and practical tool for primary urgent control of this condition. RE-

catheters with smaller diameters may be associated with a lower rate of overall complications [8].

The primary aim of the current analysis was to present our experience with REBOA at a single tertiary care level 1 trauma center and to evaluate the technical aspects of the procedure, patient characteristics, and outcomes following REBOA use.

PATIENTS AND METHODS

STUDY POPULATION AND DATA COLLECTION

This retrospective cohort study included all patients who were admitted to a level 1 trauma center at Soroka, a tertiary care university medical facility and treated in the trauma department with REBOA between November 2017 and July 2021. Soroka University Medical Center is the only regional hospital in southern Israel (estimated population of 1,000,000).

The data regarding any trauma patient who arrives at the medical center and is treated with REBOA are entered into an international database (Abotraum registry). This database was designed to capture data for all trauma patients in hemorrhagic shock for which the management includes REBOA placement and thus enabled retrospective collection of data during hospitalization.

TREATMENT PROTOCOL AND TECHNICAL DETAILS

Prior to initiating use of the device, we developed a protocol that was presented to all the relevant medical teams. The protocol includes the rationale of using the REBOA technique, an explanation regarding the division of the aorta into three zones, a step-by-step description of the procedure including insertion and removal of the sheath and the balloon catheter, and a detailed description of the equipment included in EndoVascular Trauma Management (EVTM) kits. EVTMs are used in the endovascular and combined open-endo methods approach for hemodynamic instability in trauma and non-trauma patients. The protocol includes indications and contraindications to the use of REBOA. The trauma team leader should consider using REBOA in trauma patients who are in profound non-compressible hemorrhagic shock (systolic blood pressure < 80 mmHg) in whom the major source of bleeding is below the diaphragm and when the shock is determined as non-responsive to initial standard resuscitation. The procedure should also be considered as an adjunct to standard management in patients with profound neurogenic shock.

Contraindications to REBOA include no signs of life, similar to the contraindication to performing resuscitative thoracotomy; the source of major bleeding above the diaphragm (especially the heart and great thoracic vessels); groin abnormality such as previous vascular surgery or a huge inguinal hernia; and known severe vascular disease.

Technically, for balloon insertion, we used Cordis® (Cordis,

USA) introducer sheath. The sheath is 11 cm long. The initial diameter we used was 7 French gauge (FG), but later 8 FG was preferred. The guiding wire is 0.035 inch. The balloon in use was Rescue Balloon Occlusion Catheter (Tokai Medical Products, Japan). The catheter was 80 cm long with a diameter 7 FG. Balloon volume was 40 ml.

STATISTICAL ANALYSIS

Descriptive statistics are presented using summary tables. Continuous variables include mean and standard deviations. Due to a relatively small number of patients in our cohort, most variables were presented as categorical variables and described with numbers and percentages.

The variable Glasgow Coma Scale (GCS) score on-site was divided into four categories: 3, 4–8, 9–12, and 13–15. GCS scores are presented as the number of patients and percentages in each group. We used the Injury Severity Score to assess trauma severity. This measure has been shown to correlate with mortality, morbidity, and hospitalization time after trauma [9]. Systolic blood pressure (SBP) on arrival to the trauma department was divided into five categories: non-measurable (as for an inability to measure the SBP due to severe hemorrhagic shock), < 50 mmHg, 50–80 mmHg, 80–100 mmHg, and > 100 mmHg. The variable heart rate, expressed in beats per minute (bpm), was divided into two categories: > 120 bpm and within the range of 100–119 bpm. The measures were presented as numbers and percentages for each category. Attempts of REBOA insertion by the performing physician were presented either as *one*, if there was immediate success on first attempt, or as *more than one* attempt. The variable *total time of aortic balloon occlusion inflated (min)* was divided into two categories according to differences in anatomical parameters of the inflated balloon. The first refers to zone 1 (extending from the origin of the left subclavian artery to the celiac artery). The second refers to zone 3 (extending from the lowest renal artery to the aortic bifurcation). The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the institutional review board of Soroka Medical Center (protocol number 0299-20-SOR) on August 2020. No informed patient consent was required.

RESULTS

We analyzed data of 22 civilian trauma patients who were treated by REBOA due to blunt or penetrating injuries. All the patients had life-threatening hemorrhagic shock and were unresponsive to resuscitation efforts.

PATIENT POPULATION AND CHARACTERISTICS OF INJURY

Table 1 summarizes the demographic characteristics of the study population, characteristics of the injuries, and clinical status upon arrival to the trauma department. All but one patient

Table 1. Demographics and injury characteristics (n=22)

Characteristic		Value
Age in years, mean ± SD		30.1 ± 12.7
Male sex, n (%)		21 (95)
Type of injury, n (%)		
	Blunt	17 (77)
	Penetrating	5 (23)
GCS score on site, n (%) (n=20)		
	GCS = 3	6 (30)
	GCS= 4–8	2 (10)
	GCS= 9–12	3 (15)
	GCS= 13–15	9 (45)
Arrived during night shift (23:00–06:00), n (%)		
	Yes	4 (18)
	No	18 (82)
Injury score, median (IQR)		32.5 (16–41)
SBP on arrival to the trauma department, mmHg, n (%)		
	Non-measurable	8 (36)
	< 50	1 (4.5)
	50–80	10 (45.4)
	80–100	2 (9.0)
	> 100	1 (4.5)
SBP on arrival to the trauma department, mmHg, mean ± SD		59.6 ± 11.4
Heart rate on arrival to the trauma department (bpm), n (%)		
	> 120	18 (82)
	100–119	4 (18)
Eye pupil response on arrival to the trauma department, n (%)		
	Yes	15 (68)
	No	7 (32)
Enlarged eye pupils on arrival to the trauma department, n (%)		
	Yes	5 (23)
	No	17 (77)
Mechanisms of injury and main bleeding sources, n (%)		
Blunt trauma, n=11 (50%)	Renal vessels	1
	Pelvic fractures	3
	Peripancreatic vessels	1
	Spleen	3
	Liver	3
Penetrating trauma, n=11 (50%)		

bpm = beats per minute, GCS = Glasgow Coma Scale, ISS = injury severity score, IQR = interquartile range, SBP = systolic blood pressure

was male; 17 (77%) experienced blunt trauma, and only three (14%) had SBP > 80 mmHg on arrival to the trauma department. The mean SBP before REBOA insertion was 59.6 \pm 11.4 mmHg. None of the patients had undergone cardiopulmonary resuscitation (CPR) on scene or during trauma department treatment, regardless of their hemodynamic status.

PROCEDURE CHARACTERISTICS

Table 2 summarizes the technical characteristics of REBOA insertion. Twelve (55%) of the sheath insertion procedures were performed by general surgeons. Sixteen (73%) were performed blindly, that is, non-ultrasound guided. The first attempt success rate was 68% (15/22). The most common site for REBOA localization was zone 1 (13 patients, 59%). The balloon was localized in a specific zone by anatomical landmarks. None of the devices were found to be migrated in the aorta during treatment nor were any ruptured after the insertion. The REBOA balloon inflation time exceeded 60 minutes with only three patients (14%).

Short- and long-term outcomes

Table 3 summarizes patient outcomes after REBOA insertion. In 20 patients (91%), SBP was normalized (> 90 mmHg) shortly after inflation of the balloon. The mean first SBP measured after the procedure was 115.2 \pm 26.3 mmHg. All 20 patients survived the initial treatment in the trauma department and were transferred alive to the next station (usually the operating theater). Fifteen (75%) survived the first 30 days of hospitalization. For these 15 patients, the median duration of hospitalization in the intensive care unit was 20 days (interquartile range [IQR] 9.5–43); and the duration of mechanical ventilation was 16.5 days (IQR 2.5–37.5).

Figure 1 presents the complications observed after insertion of REBOA. Three patients had significant complications: two had extremity ischemia and one had new onset renal failure that was related to the procedure rather than the shock.

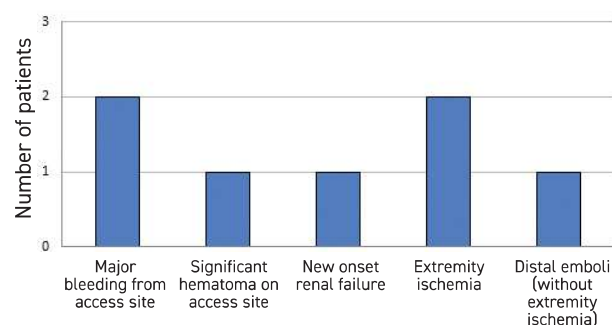
Figure 1. Procedure complications

Table 2. Procedure characteristics (N=22)

Characteristic	Number of patients (%)
REBOA insertion attempts	
One	15 (68)
More than one	7 (32)
Side of femoral artery access	
Left	12 (55)
Right	10 (45)
Femoral artery identification technique	
Blind	16 (73)
Ultrasound	6 (27)
Physician specialty Performing physician (REBOA insertion)	
General trauma surgeon	12 (55)
Anesthetist	2 (9)
Anesthetist and general trauma surgeon	2 (9)
Vascular surgeon	4 (18)
ER physician and general trauma surgeon	2 (9)
Primary localization of the balloon	
Supraceliac (zone 1)	13 (59)
Infrarenal (zone 3)	9 (41)
Partial inflation of the balloon	
Yes	11 (50)
No	11 (50)
Total time of balloon inflation (min), zone 1, n=13	
15–20	3 (23)
20–30	3 (23)
30–40	4 (31)
40–50	1 (8)
50–60	1 (8)
> 60	1 (8)
Total time of balloon inflation in minutes; zone 3, n=9	
20–30	3 (38)
30–40	2 (25)
50–60	2 (25)
> 60	2 (25)
Site to which patient was transferred from the trauma department	
Computed tomography	8 (36)
Operation room	14 (64)

The data are presented as n (%)

REBOA = Resuscitative Endovascular Balloon Occlusion of the Aorta

DISCUSSION

Our retrospective cohort study presents nearly 4 years of experience of REBOA use in civilian trauma in an Israeli level 1 trauma center. To the best of our knowledge, this is the largest series published of patients in Israel.

This study demonstrated effectiveness of the REBOA technique in achieving hemodynamic improvement, a high survival rate, and a small number of significant complications. The use of REBOA enabled achievement of immediate hemodynamic stabilization in more than 90% of the injured patients (SBP > 100 mmHg). As a result, for eight (36%) patients, complete total body CT imaging was possible and safe to perform before transportation to the operating room. The ability to achieve high quality imaging before moving to the next station, which is almost always the operating room, is a great advantage, and illustrates the superiority of REBOA over the aortic cross clamp. Twenty (91%) patients who were hemodynamically stabilized after the insertion of the balloon exited the trauma department alive, of whom 15 (75%) survived the first 30 days. None of the patients experienced substantial damage to limbs during insertion of the balloon. All the injured who survived the first day also survived the first 30 days after the injury.

The 24-hour mortality rate of 23% in our study is similar to rate of 26.4% reported for 420 patients with civilian trauma who were treated with REBOA in the United States [10]. Notably, a higher proportion of our patients died in the trauma department, 9% vs. 2.9%. However, comparing the mortality rates might be somewhat misleading, as the missing data regarding mortality of two patients may have significantly affected the result. For example, if only one patient was added to the survivors of our cohort, the mortality rate would have reached 4.6%, compared to 2.9% in the nationwide U.S. analysis.

The mean values of SBP in our cohort were 59.6 and 115.2 mmHg, before and after REBOA, compare with 71 and 107 mmHg, respectively, reported in a small study of 25 patients in Japan [11]; and 60 and 110 mmHg, respectively, reported for a multicenter study of 142 patients in Japan [12]. Only four patients (2.8%) in the latter study had significant limb region complications: one had a massive hematoma, one thromboembolism, and two had leg ischemia that required fasciotomy followed by amputation.

With the intention of assimilating the REBOA technique at their hospital, a team of trauma surgeons were trained in the endovascular resuscitation and trauma management department in Örebro, Sweden. They learned the procedure and practiced it on animal models. Subsequently, the team taught the procedure to a wider circle of physicians in the hospital until many physicians were able to provide a 24/7 response within the hospital. In addition, to achieve optimal learning, after every use of REBOA, a detailed performance review was conducted, and conclusions disseminated among the relevant teams. It is important

Table 3. Short-term outcomes (n=22)

Stabilization after REBOA insertion (SBP > 90 mmHg), n (%)	
Yes	20 (91)
Improved but not stable\ transient improvement	2 (9)
SBP after REBOA insertion (mmHg), mean \pm SD	
115.2 \pm 26	
Survived trauma department resuscitation, n (%)	
Yes	20 (91)
No	2 (9)
Survival, 24 hours, n (%)	
Yes	15 (68)
No	5 (23)
Missing data*	2 (9)
Survived the first 30 days of hospitalization, n (%)	
Yes	15 (68)
No	5 (23)
Missing data*	2 (9)

REBOA = Resuscitative Endovascular Balloon Occlusion of the Aorta, SBP = systolic blood pressure

*Missing data: Survival data for two patients could not be located due to technical issues

to emphasize that the training of such a circle of physicians is not sufficient, as optimally, multidisciplinary teams should be involved. Such teams should include general surgeons, vascular surgeons, invasive radiologists, emergency medicine physicians, anesthesiologists, intensive care physicians, and highly trained nursing staff.

We think that REBOA is an excellent bridging technique that saves valuable time, while investing in preparations to optimize subsequent steps in patient care. In addition to enabling informative CT scans, the technique gives time for transfusion of blood products, normalization of the coagulation mechanism, external warming, preparation of specific surgical equipment, preparation for vascular ablation, and calling specialized staff to the hospital. In most of our injured patients (n=13, (59%)), the balloon was inflated in zone 1; and in most of these (n=11, 85%), the occlusion time was up to 50 minutes. In the multicenter registry study conducted in Japan, results of the total average duration of occlusion for the 142 patients was 50 minutes (25–93), and in the 24-hour survival group (n=81), the duration was 34 minutes (13–62).

Notably, some guidelines allow 20–30 minutes and up to 60 minutes for occlusion time for zone 1, and even longer occlusion times for zone 3 [12]. In this context, the major complication of prolonged inflation of the balloon in zone 1 is ischemia to the kidneys or to the spine. This situation did not occur in any of our patients. The insertion of the sheath itself into the femoral

artery can be performed by one of the following methods: ultrasound-guided, cut-down procedure, or blindly. For the majority (72%) of our patients, the insertion was performed blindly by a trauma or vascular surgeon, anesthesiologist, or emergency medicine physician. However, the insertion of the balloon itself and its localization and inflation in the aortic cavity were performed uniquely by a trauma surgeon. We think that training and encouraging the relevant physicians to perform ultrasound-guided insertion procedures may lead to higher success rates and fewer complications. Due to the extreme conditions of the wounded, and to save time, in our trauma center the location of the balloon is performed through anatomical evaluation and rough measurement and not by fluoroscopy. While the balloon is inflated, two methods are possible for maintaining distal perfusion. For one, after confirming hemodynamic stabilization, physicians partially deflate the balloon in small steps, to keep the SBP > 90 mm Hg. This partially deflated inflated balloon is known as Partial REBOA, or P-REBOA. In the second method, the intermittent REBOA or I-REBOA, the balloon is inflated and deflated every few minutes to allow some transient perfusion to the organs. The method we use in our center for patients with a suitable hemodynamic condition is partial REBOA. This procedure allows for low but continuous distal perfusion. Regardless of the method, during complete deflation of the balloon, after gaining control of the bleeding, deflation should be conducted slowly to prevent ischemic re-perfusion syndrome. Considering its effectiveness, the REBOA technique has been implemented for regular use in our medical center. Four kits are currently available for use at key points in the hospital: the trauma department, the operating room, the delivery room, and the intensive care unit. The tendency in our medical center is to insert a sheath into a femoral artery for any bleeding patient in severe hemorrhagic shock from traumatic and non-traumatic causes even if there is no immediate intention to use REBOA.

Our study has some limitations. First, this is a relatively small single-center study in which all the REBOA procedures were performed by a small group of trauma surgeons. All of the staff were trained for this specific procedure using the same methods and by the same mentors. Second, due to the retrospective design and the use of the international database (Abotraumaregistry), some data, including details regarding blood products, were missing and impossible to track. Such data could have enhanced understanding of patient acuity.

CONCLUSIONS

REBOA is an effective method for the initial stabilization of patients with massive, non-compressible bleeding. The SBP level achieved in our center after REBOA insertion was similar to that achieved in studies from other countries. The achievement of immediate stabilization gives the medical staff time and to correct physiological parameters by completion of resuscitation and to achieve accurate imaging. From our experience, the use

of REBOA is relatively easy to learn, with low rates of insertion failure and complications. This quick and effective method to control severe non-compressible bleeding was smoothly assimilated at our medical center.

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Beauty is the purgation of superfluities.

Michelangelo Buonarroti (1475–1564), sculptor, painter, architect, and poet

If we had paid no more attention to our plants than we have to our children, we would now be living in a jungle of weeds.

Luther Burbank (1849–1926), American botanist, horticulturist, and pioneer in agricultural science

Capsule

Preclinical models for prediction of immunotherapy outcomes and immune evasion mechanisms in genetically heterogeneous multiple myeloma

The historical lack of preclinical models reflecting the genetic heterogeneity of multiple myeloma (MM) hampers the advance of therapeutic discoveries. To circumvent this limitation, Larrayoz and colleagues screened mice engineered to carry eight MM lesions (NF- κ B, KRAS, MYC, TP53, BCL2, cyclin D1, MMSET/NSD2, and c-MAF) combinatorially activated in B lymphocytes following T cell-driven immunization. Fifteen genetically diverse models developed bone marrow (BM) tumors fulfilling MM pathogenesis. Integrative analyses of approximately 500 mice and approximately 1,000 patients revealed a common MAPK–MYC genetic pathway that accelerated time to progression from precursor states across genetically heterogeneous MM. MYC-dependent time to progression conditioned immune evasion mechanisms that remodeled the BM microenvironment differently. Rapid MYC-driven progressors exhibited a high number of activated/exhausted CD8⁺ T cells with reduced immunosuppressive

regulatory T (Treg) cells, while late MYC acquisition in slow progressors was associated with lower CD8⁺ T cell infiltration and more abundant Treg cells. Single-cell transcriptomics and functional assays defined a high ratio of CD8⁺ T cells vs. Treg cells as a predictor of response to immune checkpoint blockade (ICB). In clinical series, high CD8⁺ T/Treg cell ratios underlie early progression in untreated smoldering MM, and correlated with early relapse in newly diagnosed patients with MM under Len/Dex therapy. In ICB-refractory MM models, increasing CD8⁺ T cell cytotoxicity or depleting Treg cells reversed immunotherapy resistance and yielded prolonged MM control. These experimental models enable the correlation of MM genetic and immunological traits with preclinical therapy responses, which may inform the next-generation immunotherapy trials.

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