A Contemporary Report on U.S. Military Guidelines for the use of Whole Blood and Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)

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**Declaration of Interest:**

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Background

Noncompressible hemorrhage is the leading cause of preventable death on the battlefield\textsuperscript{1} and new approaches to manage this scenario are a priority for the military trauma research program and the DoD Joint Trauma System (JTS). It is estimated that for every 100 potentially survivable battlefield deaths, 8 are from respiratory compromise, and 92 are from bleeding, mostly in the torso. Research and adoption of Tactical Combat Casualty Care (TCCC) have resulted in use of effective tourniquets, hemostatic dressings, thoracic decompression devices, and airway access tools leading to unprecedented “golden hour” survival.

Unfortunately, golden hour care is not good enough as casualties in shock still have an exponential increase in mortality unless they receive blood within the first 30-40 minutes after injury.\textsuperscript{2} (Figure 1) In its pursuit to reduce mortality, the JTS has adopted whole blood and resuscitative endovascular balloon occlusion of the aorta (REBOA) as part of its clinical practice guidelines (CPG). While both require study and refinement, whole blood and REBOA have the potential to improve our approach to torso bleeding and shock and the military has updated its guidelines in these areas based on new clinical information and research findings.

The 2019 guidelines come at a time in which the military is planning for very different casualty scenarios. Future casualty care may occur amidst anti-access/areal denial environments in which rapid MEDEVAC through usual echelons is not possible\textsuperscript{3}. In these situations, medics will be faced with extending TCCC for prolonged periods. Out of this forward-looking stance, the JTS and its Committee on TCCC have also developed new Advanced Resuscitative Care (ARC) guidelines\textsuperscript{4}. This report reviews the rationale and content of these CPGs, and provides a contemporary account of their use. This report also provides a summary of training programs being implemented to prepare medics and providers to implement the guidelines.
Evolution of the REBOA Guidelines

Recognizing the significance of hemorrhagic deaths from torso hemorrhage, and prompted by positive pre-clinical animal data and subject matter expertise, the JTS created the first clinical practice guideline (CPG) for REBOA in 2014. This was based on older REBOA technology, namely balloon occlusion catheters (i.e. CODA, Cook Medical) that required larger arterial sheaths (12 Fr or larger), fluoroscopy and placement over long endovascular wires. Clinical data at that time consisted of single-center reports that compared REBOA to aortic clamping via thoracotomy or laparotomy.

In 2016 and 2017, a new 7 Fr compatible REBOA device (ER-REBOA™, Prytime Medical Devices) received CE Mark for use in Europe and was approved by the Food and Drug Administration (FDA) for use in the U.S. Soon thereafter the indications for the catheter were expanded to specify management of bleeding and shock, and its instructions for use were modified to remove the requirement for x-ray guidance. Although other makeshift devices can be used, the U.S. military has adopted the ER-REBOA™ as the device of choice for this procedure. An updated 2017 CPG reflects this change and led to adoption of a REBOA capability by combat hospitals and austere surgical teams.

Military and civilian use of REBOA is evolving rapidly and guidelines are now informed by approximately 5000 ER-REBOA™ uses worldwide. Although data from controlled studies is lacking, retrospective analyses and real-world experience point to an advantage with early attainment of femoral artery access and performance of REBOA in the pre-arrest state (i.e. proactive versus reactive use). The 7 Fr system is not without risk, but its lower profile facilitates arterial access, pressure monitoring, and quicker placement of the balloon. In some cases, this approach may preempt cardiovascular decompensation from shock and the onset of a terminal
arrhythmia (i.e. exsanguination shock). Experience also points to the importance of REBOA as part of a prepared (pre-trained), multi-disciplinary approach to resuscitation.

**Advanced Resuscitative Care (ARC) Guidelines**

In October 2018 under the auspices of the JTS, the Committee on Tactical Combat Casualty Care (CoTCCC) released CPG updates addressing challenges associated with early prehospital resuscitation. The term PFC (Prolonged Field Care) is used by the military to conceptualize, plan, and train for scenarios in which initial lifesaving maneuvers are not followed by immediate MEDEVAC. The term Advanced Resuscitative Care (ARC) was selected to describe a team-based, prehospital resuscitation approach in which physician-led resuscitation teams positioned close to the point of injury implement life-saving interventions using advanced techniques. In such settings, resuscitation teams in austere locations have the capability to mitigate risk and “extend the golden hour” in order to allow additional time to reach surgical care.

A more specific aim of the ARC guidelines is to enable resuscitation teams positioned near the point of injury to better manage torso hemorrhage and shock, recognizing that the current approach based on readily available MEDEVAC to surgical hemostasis does not work in many situations. Specifically, ARC more fully accounts for the fact that preventable death from bleeding occurs soon after injury, and that many combat missions require flexibility outside the ideal 60-minute MEDEVAC time frame. Clinical data and real-world evidence show that the mortality of patients with torso bleeding and shock is time-dependent and increases incrementally with each 15-minute interval after injury. In these scenarios minutes matter, and development and implementation of new capabilities as part of ARC guidelines represent the greatest opportunity to save lives in this early period after injury.
Pragmatic Implementation of New Approaches: ARC emphasizes a team-bases approach to battlefield resuscitation using the two main strategies of whole blood resuscitation and REBOA. While neither approach has prospective, controlled data demonstrating an outcome benefit with its use, the military has implemented them based on data from preclinical research studies, registry-based study and empiric observations of effectiveness. Importantly, the JTS recommends that whole blood and REBOA only be implemented as part of a practice guideline or standard operating procedure (SOP) within a system that has mature data collection and performance improvement processes.

The military has been praised for this approach to implementing new products into its guidelines, one the National Academy of Medicine refers to as *focused empiricism*, or “an approach to process improvement under circumstances in which: (1) high-quality data are not available to inform practice changes, (2) there is urgency to improve outcomes because of high mortality rates, and (3) some data collection is possible.” A key principle is using the best data available in combination with experience to develop guidelines that, through an iterative process, are refined until better data can be generated to further inform practice. While pursuit of high-level data should not be discouraged, it is this more pragmatic and efficient approach that has allowed for military and civilian trauma care advances over the years.

Low Titer Group O Whole Blood (LTOWB): A full account of the Armed Service Blood Program (ASBP) recommendations is beyond the scope of this report, but FDA-compliant, cold-stored LTOWB is now named by the Joint Trauma System and Defense Committee on Trauma (DCOT) as the resuscitation fluid of choice. LTOWB has been used by the military for more than 60 years, but it has only been recently reappraised and re-implemented. The use of group O low-titer donors eliminates steps in the transfusion process, and reduces the possibility of
incorrectly misinterpreting group-specific donors; a scenario which can lead to a hemolytic transfusion reaction.

Although FDA-compliant LTOWB may be available, fresh whole LTOWB is increasingly being utilized. The ASBP has gradually expanded the supply of cold-stored LTOWB shipped from the United States to the combat theaters, however the demand for this product continues to exceed the supply. Warm fresh LTOWB can be drawn from pre-screened donors at the point of injury, and this process is routinely used by advanced special operations medics. However, battlefield donation and administration at the point of injury is challenging, and involves an additional warfighter as the donor. Currently, priority for the limited supply and distribution of cold-stored, FDA compliant, LTOWB is for pre-hospital teams closest to the point of injury; special operations combat medics, MEDEVAC teams, and austere resuscitation and surgical teams have top priority. An additional process to procure LTOWB within theater was developed by the 75th Ranger Regiment and the ASBP (with Central Command (CENTCOM) approval) to allow pre-drawing of units of LTOWB from appropriately pre-screened personnel in support or “non-mission essential” roles before initiating a kinetic tactical objective. Per the CENTCOM standard operating procedure (SOP), the Blood Support Detachment will draw and label the units, perform point-of-care transfusion transmitted disease screening, and give the stored units to the team’s medics (image 1).

Progressive and leadership-driven LTOWB efforts like the Ranger O LOw Titer (ROLO) program, address point-of-injury warm fresh WB donation by testing the antibody titer levels of identified group O donors, identifying those with an IgM anti-A/B of <1:256 as “low titer”. Medics and infantryman also undergo training in whole blood collection and transfusion. Since
August 2015, every Ranger task force has deployed with a functioning ROLO program, and the capability has expanded to include other special operations teams. However, nearly all of the blood transfused by combat medics to date has been cold-stored LTOWB carried into combat by medics utilizing advanced cold-storage containers designed to store 1 or 2 units of blood for up to 72 hours. Based on successful military use, an increasing number of civilian trauma systems are also adopting cold-stored LTOWB as a resuscitation fluid of choice for patients meeting certain injury and hemodynamic criteria, including the Southwest Texas Regional Advisory Council for Trauma (STRAC) in San Antonio (image 2, 3).

**Resuscitative Endovascular Balloon Occlusion of the Aorta:** The updated guidelines for REBOA support performance of the procedure by trained physician providers as part of a resuscitation team. Per the REBOA CPG, aortic balloon occlusion is implemented by a surgical team with the capability for direct control of abdominal hemorrhage. ARC introduces the concept of intermittent aortic occlusion during ongoing resuscitation by a non-surgical advanced resuscitation team, potentially allowing more time to reach surgical capability while reducing the ischemic insult of aortic occlusion. Neither the JTS nor the ARC guidelines support performance of REBOA by lone, non-physician providers. The algorithm in the JTS guidelines parallels many civilian centers, and incorporates extended focused assessment with sonography for trauma (eFAST) and x-ray to exclude pericardial and thoracic bleeding, and confirm hemoperitoneum before placement and inflation of the REBOA balloon. While these steps are appropriate and routinely possible in hospitals with imaging and subspecialty expertise, the ARC guidelines also provide guidance for implementation of Zone 1 REBOA in more austere settings.

When imaging is not available or not feasible, JTS and ARC guidelines recommend REBOA for patients in whom the injury pattern and hemodynamics suggest abdominal or pelvic
bleeding and refractory shock; specifically, those with a systolic blood pressure (SBP) of less than 90 mmHg that has not responded to a unit of whole blood. Patients in this scenario have a high risk of death from hemorrhage if aortic occlusion is not performed. To emphasize a multi-faceted approach, the guidelines indicate that REBOA capability must be deployed in conjunction with the capability to transfuse whole blood, and to simplify the SOP and account for patients with a false negative eFAST, the ARC guidelines recommend only Zone I placement and inflation of the REBOA balloon.

Arterial access, monitoring lines and sheaths: The importance of attaining proper ultrasound-guided common femoral arterial access as the first step to invasive monitoring and REBOA cannot be overemphasized. This initial maneuver has even been shown to be the rate-limiting step to aortic occlusion at large volume centers that use REBOA routinely. Military experience in austere environments supports early ultrasound-guided placement of either an 18g angiocatheter or a 4 or 5 Fr micro-puncture kit and catheter into the femoral artery as an arterial pressure monitoring line in high-risk patients. Both of these catheter sizes are large enough to accommodate the 0.035” wire that will be necessary to place a 7 Fr sheath for REBOA, should it be needed. Military providers anecdotally point out that early femoral artery access is easier while the patient has a blood pressure (i.e. before the patient arrests), and that these smaller catheters can be removed with minimal complication if REBOA is not performed.

Management of an arterial monitoring line or access sheath in austere environments is less well defined and largely at the discretion of the resuscitation team. In most cases, arterial sheaths placed in austere environments should remain in place until the patient is fully resuscitated, coagulopathy resolved, and arrived at a location where the sheath can be removed under close observation and complications addressed. For casualties treated with REBOA who
are transferred outside of the US military trauma system, the sheath should be removed prior to transport with possible consideration of open arterial repair. When the sheath is removed, the environment must allow for a provider to apply direct manual pressure for hemostasis, and assessment of the groin, leg, and foot (with Doppler if available) to ensure good perfusion. If there are concerns for access site bleeding or thrombosis, the femoral artery should be explored and repaired through an open incision at the earliest opportunity.

 REBOA During Inter-Facility Transfer: A new or emerging capability is having critical care transport teams perform REBOA through a previously placed or existing femoral artery sheath during patient transport. Although this scenario is largely untested, it is conceivably useful in the event a patient should loses pulses after an initial damage control surgery or resuscitation. Today’s guidelines recommend against leaving a REBOA catheter in place (inflated or deflated) during transport, except for unusual circumstances and when a qualified provider accompanies and monitors the patient. However, there may be scenarios in which the femoral artery sheath can be left in place to facilitate rapid REBOA, in transit or at the next echelon of care, should it be required. Communication across the continuum of care is especially important for cases in which femoral access, with or without REBOA, has been performed.

 Thresholds of Time for Aortic Occlusion: Zone I REBOA is limited by balloon inflation time and recommendations state a desired complete aortic occlusion of 30 minutes or less, with a 60-minute maximum. ARC guidelines limit recommendations to Zone 1 occlusion for austere environments where provider experience and patient assessment may be limited, whereas the broader JTS recommendations accommodate zone 3 occlusion when abdominal ultrasound can be performed to rule out hemoperitoneum. In scenarios of Zone 3 REBOA, full occlusion should
be as brief as possible with a maximum of 4-6 hours. It is generally agreed that 30 minutes of full Zone 1 or 3 REBOA is safe and limits reperfusion injury that can precipitate decompensation.

**Concept of Partial REBOA:** A 30-60-minute time limit for Zone 1 aortic occlusion does not allow enough time to transport a casualty to the next role of care, even with the shortest transport times. As such, and based on animal data and clinical observations, ARC guidelines describe the notion of intermittent REBOA, an approach which may mitigate distal ischemia and extend the period during which this adjunct may be used. ARC guidelines recommend complete Zone I REBOA for 15 minutes (in combination with whole blood and other resuscitation maneuvers) followed by gradual balloon deflation over 30 seconds with assessment of the hemodynamic response. If SBP remains above 80, then the balloon may remain deflated while resuscitation and assessment of hemodynamics continue. If the SBP decreases below 80 mmHg while the balloon is deflated, then it should be reinflated for either a 30-minute period, or for 10 minute periods of inflation interspersed by 3 minute periods of deflation. A full account of all maneuvers is beyond the scope of this report, but the ARC guidelines provide detailed and practical steps that may be undertaken to extend the window in which REBOA can be used to support afterload and reduce bleeding.

**Training for Updated Guidelines**

No specific training protocol or platform is supported in the JTS REBOA guideline. For ARC, TCCC, and prolonged field care, proficiency in Advanced Trauma Life Support (ATLS) is foundational. It is critical that any team expected to use LTOWB or REBOA should have a strong foundation of clinical critical care skills and receive team training with a combination of didactics and high-fidelity simulation (mannequin based or wet lab based). The American College of Surgeons Basic Endovascular Skills for Trauma (BEST) course, which has a
dedicated military module, is one option for REBOA training taught at civilian sites across the U.S. Multiple “just in time” courses are also available using variations of didactic and hands on simulation experiences; many of which have been used effectively by the military in deployed locations around the world (image 4, 5). These courses are suitable for critical care physicians who have baseline skills for common femoral artery (CFA) access, arterial line management, and damage control resuscitation. Other courses under development (e.g. Resuscitation Adjuncts: Prehospital Transfusion & REBOA (RAPToR) course, Houston TX) may be of benefit for those who require more comprehensive initial training for REBOA. The RAPToR course is designed to incorporate the concepts of team dynamics, blood-based resuscitation and REBOA in line with ARC principles. Regardless of the training course, there is no substitute for planning, team exposure to the technique, and clinical exposure to REBOA before implementation.

Experiences with LTOWB and REBOA in the Austere Environment

Though REBOA has been used at higher levels of care in Afghanistan and Iraq, the majority of experience has been from 6-8 person teams consisting of a medic, an emergency physician, a nurse, an anesthesia provider, and a surgeon with one operating table. The first series of patients in whom REBOA was used in this environment included 4 who presented with severe injury and hemorrhagic shock. In all cases, use of the ER-REBOA catheter as a pre- or perioperative resuscitation adjunct resulted in successful restoration of blood pressure, completion of the damage control laparotomy, and patient survival to the next level of care.

A subsequent series of 20 war-injured patients in whom ER-REBOA was used in combination with fresh whole blood reported similar results, highlighting the effectiveness of this approach in the management of hemoperitoneum and shock in an environment with limited blood and intraoperative resources. These reports have also emphasized the importance of hand-
held ultrasound to enable safe and effective vascular access and performance of the eFAST. Although experience to date lacks outcomes information on patients in whom REBOA and/or LTOWB has been used because these patients received follow-up care at host nation facilities, the authors of these reports emphasize the early safe and efficacious use of the approach, and an empirical value that supports continued use with data collection and outcomes assessment.

The use of REBOA may also serve to extend the window of survival for a select number of patients in the immediate triage category during a multiple or casualty scenario. For example, as the sole surgeon on the team performs a laparotomy, an emergency physician may use REBOA to stabilize a different patient until blood can be collected from the walking blood bank and the initial operation completed. REBOA may also allow for more judicious use of a limited blood supply in a resource-limited setting. Establishing proximal aortic control with REBOA prior to opening the abdomen for hemoperitoneum may facilitate surgical hemostasis and minimize blood loss, especially in cases in which the surgeon is operating alone, with poor lighting or without adequate suction.

As military teams become more experienced with ARC, registry data on its use will allow the practice to be honed and guide its future application. Lessons from austere teams will help develop guidelines for the optimal timing and methods for femoral arterial access. Experience using the ARC guideline will also provide information on the training and experience level of different providers able to perform interventions such as arterial access, sheath placement, positioning and inflation of the REBOA balloon, and management of the femoral artery access site after these maneuvers have been performed.

**Conclusion**
In a requirements-driven approach to improving survival from torso bleeding and shock in the acute phase after injury, the Joint Trauma System and its Committee on Tactical Combat Casualty Care have published new guidelines on the use of LTOWB and REBOA. The military recognizes these adjuncts as having the potential to positively affect an injury scenario for which the mortality has remained excessively high for decades. The military trauma system supports the implementation of damage control resuscitation, LTOWB, REBOA and ARC using individual and team-based training, mature clinical data collection, and rigorous performance improvement. As it has done with cutting edge strategies for casualty care in the past, the Joint Trauma System will monitor the performance of care under these new guidelines and make real-time adjustments as indicated.
References:


Figure Legends:

Figure 1. Timeline of early and late mortality in recent military conflict. Adapted from Shackelford, et al. JTS 2016. Courtesy of COL Andre Cap.

Image 1. The first five units of LTOWB drawn from members of the 75th Ranger Regiment at Craig Joint Theater Hospital, Bagram Airfield, AFG in March 2016. Photo courtesy of Maj Andrew D. Fisher.

Image 2. Auto transfusion training with the Marines. Photo courtesy of LCDR Russel Wier.

Image 3. Service member training with fresh whole blood. Picture courtesy of Maj. Andrew D. Fisher

Image 4. Team training in REBOA (cadaveric model) in a simulated tactical environment, including common femoral artery cut-down training. Photo courtesy of LTC Ted T. Redman.

Image 5. REBOA use in the austere environment. Photo courtesy of Maj Justin D Manley.
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Number of KIA and DOW Deaths by Time Increment (AFG)
N=457

KIA  DOW
Must start resuscitation pre-hospital.
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