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Remote Damage Control Resuscitation in Austere Environments

Ronald Chang, MD^{1,2}, Brian J. Eastridge, MD³, and John B. Holcomb, MD^{1,2}

¹Center for Translational Injury Research, University of Texas Health Science Center, Houston, TX

²Department of Surgery, University of Texas Health Science Center, Houston, TX

³Department of Surgery, University of Texas Health Science Center, San Antonio, TX

Abstract

Hemorrhage is the leading cause of preventable military and civilian trauma death. Damage control resuscitation (DCR) with concomitant mechanical hemorrhage control has become the preferred in-hospital treatment of hemorrhagic shock. In particular, plasma-based resuscitation with decreased volumes of crystalloids and artificial colloids as part of DCR has improved outcomes in the military and civilian sectors. However, translation of these principles and techniques to the prehospital, remote, and austere environments, known as remote damage control resuscitation or RDCR, is challenging given the resource limitations in these settings. Rapid administration of tranexamic acid and reconstituted freeze-dried (lyophilized) plasma as early as the point of injury are feasible and likely beneficial, but comparative studies in the literature are lacking. Whole blood is likely the best fluid therapy for traumatic hemorrhagic shock, but logistical hurdles need to be addressed. Rapid control of external hemorrhage with hemostatic dressings and extremity tourniquets are proven therapies, but control of non-compressible hemorrhage (i.e. torso hemorrhage) remains a significant challenge.

Keywords

remote damage control resuscitation; hemorrhage; hemorrhagic shock

Introduction

Exsanguination occurs rapidly^{1,2,3} and is the leading cause of potentially preventable civilian^{4,5} and combat^{6,7} trauma deaths. Optimization of prehospital hemorrhage control and resuscitation are therefore critical,^{8,9} especially when transport to a facility capable of definitive hemorrhage control is delayed. “Remote” or “forward” has been proposed to

Corresponding author / reprint requests: Ronald Chang, MD, 6410 Fannin St., Suite 1100, Houston, TX 77030, t: 713-500-6247, f: 713-500-0683, ronald.chang@uth.tmc.edu.

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define the prehospital phase of resuscitation, and “austere” or “far-forward” as “the environment where professional health care providers normally do not operate, and basic equipment and capabilities necessary for resuscitation are often not available.”¹⁰ The translation of hospital-based damage control resuscitation (DCR) techniques to remote and austere settings forms the crux of remote damage control resuscitation (RDCR).¹¹ RDCR is applicable in a wide range of settings: rural, frontier/wilderness, ships at sea, and mass casualty incidents. Given the inherent logistical and resource limitations in these settings, however, translation of DCR to RDCR is challenging.

Damage control resuscitation (DCR)

Definition

DCR with concomitant efforts to achieve definitive hemorrhage control is the preferred in-hospital treatment of traumatic hemorrhagic shock. Core principles of DCR include minimization of crystalloid, hemostatic (balanced) resuscitation, and permissive hypotension. Overall, the goal of DCR is to quickly perform maneuvers that promote hemostasis while minimizing (iatrogenic) insults which would exacerbate bleeding.

Implementation of DCR in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF)

Prior to the advent of DCR, clinicians infused large volumes of crystalloid, artificial colloid, and red blood cells (RBCs) for resuscitation of hemorrhagic shock.^{12,13} However, this changed after a retrospective study of 246 massively transfused patients treated at a combat support hospital in Iraq found that increasing plasma:RBC ratio was associated with increased survival (odds ratio [OR] 8.6, 95% confidence interval [CI] 2.1–35.2), especially reduced exsanguination.¹⁴ Based on these data, a subsequent Joint Trauma System (JTS) clinical practice guideline (CPG) recommended 1:1 plasma:RBC for any patient at risk for massive transfusion, which was soon revised to 1:1:1 plasma:platelets:RBC. A study of OIF/OEF resuscitation practice between 2003–2012 found increasing survival over time despite increasing injury severity, which correlated with decreased crystalloid and artificial colloid use and increased plasma:RBC and platelet:RBC ratios.¹⁵

Lessons Learned: Evidence-based benefits of DCR in military and civilian sectors

In the civilian sector, the Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMTT) study found that plasma:RBC and platelet:RBC varied significantly over time during active resuscitation of bleeding trauma patients and that increased plasma:RBC and platelet:RBC were associated with decreased 6-hour mortality when risk of exsanguination was highest.¹ After 6 hours, however, product ratios no longer correlated with mortality as competing risks (e.g. traumatic brain injury [TBI]) became more important. The multicenter Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) Trial randomized 680 bleeding civilian trauma patients to resuscitation with 1:1:1 versus 1:1:2 plasma:platelets:RBCs.² Although 24-hour and 30-day mortality were not different, the 1:1:1 group had significantly decreased risk of exsanguination (9% vs 15%) and increased hemostasis (86% vs 78%). A recent systematic review and meta-analysis which analyzed 5,292 patients across 15 studies found that mortality was significantly reduced for patients

who received a high (approaching 1:1) versus low (1:2) plasma:RBC ratio (31% vs 38%).¹⁶ The mechanism behind this benefit is unclear but likely involves plasma-mediated endothelial repair^{17,18} in addition to replacement of volume and clotting factors. The same systematic review also found that mortality was reduced for 1,607 patients across 4 studies who received a high versus low platelet:RBC ratio (28% vs 43%).¹⁶ Overall, this supports a 1:1:1 ratio of plasma:platelets:RBCs for resuscitation of hemorrhagic shock. Increasing volumes of crystalloid, on the other hand, are associated inflammation (e.g. acute respiratory distress syndrome),¹⁹ edema (e.g. abdominal compartment syndrome),²⁰ and mortality.²¹

Remote damage control resuscitation (RDCR)

Definition

Hospital-based DCR practices and mechanical hemorrhage control techniques translated into the prehospital, remote, and austere settings are the central tenets of RDCR. However, the resource limitations and logistical restraints inherent in these settings preclude direct application of all DCR principles.

Translation of DCR components to RDCR

Permissive hypotension—In an animal model of uncontrolled hemorrhage, fluid resuscitation induced reproducible rebleeding (“popping the clot”) when the mean arterial pressure was increased above 64 ± 2 mmHg.²² Several clinical studies have shown either improved outcome²³ or no difference^{24,25} in civilian patients randomized to hypotensive versus normotensive resuscitation. However, these studies were performed in urban environments where prehospital transport times are relatively short. In remote and austere environments, permissive hypotension will undoubtedly lead to some accumulation of oxygen debt. The question of how low and how long hypotension may be allowed to persist remains unresolved but is likely contingent upon a number of factors including baseline health status and injury acuity. Real-time monitoring modalities are limited in the prehospital setting, which has been identified as a critical technological gap.²⁶ Closing this critical knowledge gap would enable resuscitation to be titrated to reduce both risk of rebleeding and optimize tissue perfusion. Although no such technology currently exists, advanced in computer-generated decision support tools utilizing continuous vital sign measures, tissue oxygen saturation monitoring,²⁷ and serial lactate measurements²⁸ have all demonstrated promising early results.

Balanced (hemostatic) resuscitation—Plasma is used as the primary volume expander in DCR. Storage conditions and therefore immediate availability of plasma products differ with implications for RDCR.²⁹ Fresh frozen plasma (FFP) and thawed plasma (TP) are ill-suited for RDCR; liquid plasma (LP) has fewer constraints, enabling wider use (Table 1). Freeze-dried (lyophilized) plasma (FDP) has been “rediscovered” as a more suitable plasma product for RDCR. FDP was used extensively during World War II, but production was stopped in the United States due to heightened risk of disease transmission.³⁰ Currently, FDP is manufactured by updated processes in France,³¹ Germany,³² and South Africa.³³ The French product has been in continuous production since WWII, albeit in small quantities. Advantages of FDP include its long shelf life (up to 2 years), room temperature storage,

rapid reconstitution within minutes, and relative stability at temperature extremes.^{30,31,32} The French and South African products are produced from pooled plasma. The advantages of pooling include uniform factor concentrations and universal ABO compatibility,³² while transmissible disease risk is minimized by pathogen inactivation.^{30,32} Currently, no FDP product is approved for general use in the US, although one product has completed phase I trials (LyP, HemCon Medical Technologies, Portland, OR). Additionally, there is limited use of French FDP by some U.S. Special Operations Forces under a FDA Investigational New Drug protocol.

Platelets are an important part of hemostatic resuscitation, but logistical constraints (constant agitation at room temperature and 5-day shelf life) make platelets essentially unavailable in remote and austere settings.^{34,35} Cold storage of platelets, which appears to preserve hemostatic function better than room temperature storage without the need for agitation, appears viable.³⁶ Another hemostatic resuscitation option when platelets are unavailable is whole blood, including fresh whole blood (FWB) obtained as needed from the “walking blood bank.” FWB has greater hematocrit, clotting factor activity, platelet count, and fibrinogen content compared to component therapy³⁷ (Table 2). Being fresh, the well-described “storage lesion” of aged RBCs³⁸ and platelets³⁹ is avoided. Transfusion of one bag of FWB in lieu of 3–4 bags of components is logistically simpler (reducing risk of administrative error) and reduces donor exposure (lowering the risk of disease transmission). The Committee on Tactical Combat Casualty Care (CoTCCC) now recommends whole blood as the preferred fluid for resuscitation of casualties in hemorrhagic shock.⁴⁰ During the Vietnam War, low anti-A/B (titer less than 1:256) type O whole blood was transfused universally with an acceptably low incidence of major hemolytic transfusion reactions (1 per 9,600 units transfused),⁴¹ and this strategy appears viable for modern use.⁴² Pathogen inactivation⁴³ is one promising solution of negating the potentially increased transmissible disease risk of FWB.⁴⁴ Additionally, pathogen inactivation by riboflavin/ultraviolet light followed by cold storage at 21 days was found to minimally affect the hemostatic potential of whole blood.⁴⁵ The Mayo Clinic, which provides prehospital whole blood transfusions by helicopter, has published their experience in establishing a universal whole blood donor group.⁴⁶

Tranexamic acid—Tranexamic acid (TXA) inhibits tissue plasminogen activator and fibrinolysis (clot breakdown), potentially making it an important DCR adjunct. The multinational CRASH-2 study randomized over 20,000 trauma patients at risk for hemorrhage to TXA versus placebo and found that TXA reduced all-cause mortality (14.5 vs 16%), and exsanguination-associated mortality (4.9% vs 5.7%).⁴⁷ An exploratory post-hoc analysis identified a time-dependent effect: exsanguination risk was most reduced when TXA was given within 1 hour of injury (5.3% vs 7.7%) with a lesser effect when given between 1–3 hours (4.8% vs 6.1%) and increased risk of exsanguination when given after 3 hours (4.4% vs 3.1%).⁴⁸ The retrospective MATTERS study also found that TXA was independently associated with improved survival (OR 7.2, 95% CI 3.0–17.3) in 231 massively transfused (≥ 10 RBC units in 24 hours) combat casualties.⁴⁹ The American College of Surgeons Committee on Trauma,⁵⁰ European Task Force for Advanced Bleeding Care in Trauma,⁵¹ and UK National Institute for Health and Care Excellence⁵² all

recommend administering TXA for hospitalized trauma patients as soon as possible if within 3 hours of injury. Of note, trauma is not an FDA-approved indication for TXA and is considered off-label use.

Evidence-based benefits of RDCR in military and civilian sectors

Given the time-course of hemorrhage, initiating balanced resuscitation as soon as possible is paramount. Making ready-to-transfuse universal-donor plasma and RBCs available on civilian prehospital transport was associated with less deranged patient physiology on admission and decreased 6-hour mortality in the most critically-ill patients.⁵³ In the military sector, decreased mortality was observed after implementation of several prehospital interventions including blood product transfusions and faster transport time.⁵⁴ Several groups have published their experiences with FDP, although these are currently limited to non-comparative observational studies.^{55,56,57} Nevertheless, compelling common themes include its observed clinical efficacy, ease of reconstitution and administration, rapid availability, and no adverse events. The Israeli Defense Force (IDF) have reported successful administration of FDP (and TXA) at the point of injury,⁵⁶ similar to how FDP was used in World War II. Two studies have found that FWB was associated with improved survival compared to resuscitation with plasma and RBCs (platelets not available) in combat casualties treated at a combat field hospital³⁴ by forward surgical teams.³⁵ In the civilian sector, pilot trials have reported successful use of crossmatched modified whole blood (leukoreduced, platelets removed)⁵⁸ and uncrossmatched cold-stored whole blood (leukoreduced, containing platelets)⁵⁹ in the initial resuscitation of civilian trauma patients. Norwegian Naval Special Operations has published their simplified protocol for whole blood “buddy” transfusions in the field,⁶⁰ and a similar protocol for US forces has been proposed.⁶¹

The optimal use of TXA after trauma remains controversial. While some advocate for its empiric use in all trauma patients within 3 hours of injury,⁶² others argue that an anti-fibrinolytic should be reserved for patients who demonstrate hyperfibrinolysis on coagulation testing,⁶³ although there are no prehospital assays for hyperfibrinolysis currently available. In the elective surgical setting, TXA reduces blood loss without increased risk of venous thromboembolism (VTE).⁶⁴ The TXA-related VTE risk in trauma is less clear, however. CRASH-2 reported no difference in VTE risk between the TXA and placebo groups, although the overall VTE incidence was unusually low (1.7% vs 2.0%),⁴⁷ and the adequacy of patient follow-up has been questioned.⁶⁵ The MATTERs study reported that patients who received TXA had higher VTE incidence on univariate analysis, but TXA was not an independent predictor of VTE on multivariable regression.⁴⁹ Nevertheless, the likely clinical efficacy and probable low risk suggest that prehospital administration of TXA (ideally at the point of injury) is justifiable.⁶³ Prehospital TXA is given by several military and civilian aeromedical transport services, and the IDF administers TXA (and FDP) at the point of injury, so far with no apparent increase in adverse events.⁶⁶ A recent matched-cohorts study found that prehospital TXA was associated with reduced 24-hour mortality (5.8% vs 12.4%) in 516 patients transported by the German Air Rescue Service without increased VTE incidence.⁶⁷

Mechanical hemorrhage control

Broadly speaking, hemorrhage can be classified as compressible (controllable with external pressure) or non-compressible (torso hemorrhage). A review of 4,596 combat casualties in Afghanistan and Iraq from 2001–2011 found that 24% of prehospital battlefield deaths were potentially survivable and primarily linked to uncontrolled hemorrhage.⁶ Source of lethal hemorrhage was 67% truncal (non-compressible), 19% junctional, and 14% extremity. One of the greatest successes in modern combat casualty care is the widespread adoption of tourniquets which has substantially reduced exsanguination from extremity hemorrhage. However, the prehospital management of non-compressible hemorrhage still presents a major challenge.

Hemostatic dressings

For millennia, plain gauze was used to pack wounds and tamponade bleeding. Modern products are impregnated with hemostatic agents for additional efficacy. Current TCCC guidelines recommend kaolin-impregnated QuikClot Combat Gauze (Z-Medica LLC, Wallingford, CT) as first-line therapy for external hemorrhage not amenable to tourniquet application.⁶⁸ Combat Gauze should be applied with at least 3 minutes of direct pressure. Two chitosan-impregnated gauzes, Celox (Medtrade Products Ltd., Crewe, UK) and ChitoGauze (HemCon Medical Technologies), were found to be equally efficacious as Combat Gauze in large animal models of hemorrhage and are recommended as second-line therapy if Combat Gauze is unavailable. All three products are FDA-approved.

Extremity tourniquet

Tourniquet use was discouraged up until the late 1990s because of the prevailing sentiment that tourniquet application resulted in limb ischemia and possible limb loss. Improvised tourniquets were successfully used in Somalia in 1993, and a report analyzing causes of combat death in Iraq and Afghanistan from 2003–2006 found that extremity hemorrhage accounted for 7.8% of all combat deaths (similar to the Vietnam era⁶⁹) but *one third* of potentially preventable combat deaths.⁷⁰ Subsequently, several commercially available tourniquets were evaluated with selection of the FDA-approved Combat Application Tourniquet (C-A-T, North American Rescue LLC, Greer, SC) and Special Operations Forces Tactical Tourniquets (SOFTT, Tactical Medical Solutions, Anderson, South Carolina), for deployment. Widespread adoption by the US military was evident by 2007.⁷¹ Tourniquets were consistently demonstrated to save lives, especially when applied early (before onset of shock).^{72,73} One of the landmark achievements of this initiative has been the reduction of death from extremity hemorrhage from 23.3 per year prior to 2006 to 3.5 per year after 2007.⁶

Given the effectiveness of tourniquets in controlling extremity hemorrhage, the 2015 Hartford Consensus emphasized the need for civilian preparedness in responding to mass casualty incidents, a major component of which is rapid hemorrhage control with the appropriate use of tourniquets and hemostatic dressings by professional first responders.⁷⁴ Emerging data suggest that tourniquet application reduces blood loss and shock⁷⁵ with a low risk of ischemic limb loss in civilian trauma patients.^{76,77,78} In a single-center retrospective

review of 326 tourniquets placed on 306 patients for extremity injuries, delayed tourniquet placement (in the trauma center) was associated with an increased likelihood of exsanguination (OR 8.5, 95% CI 1.1 – 68.9) compared to prehospital tourniquet placement.⁷⁷ However, in the austere environment where definitive hemorrhage control is delayed, prolonged tourniquet application could result in detrimental limb ischemia. A study using porcine models found that neuromuscular recovery was well-preserved when tourniquet application was < 3 hours but significantly diminished at 6 hours.⁷⁹ Current TCCC guidelines recommend reassessing every 2 hours and to convert the tourniquet to a hemostatic or compression dressing if the following criteria are met: 1) patient is not in shock, 2) limb was not amputated, and 3) it is possible to monitor the wound closely for bleeding.⁸⁰ Periodic loosening of the tourniquet to reperfuse the limb results in increased blood loss without any benefit (possibly worsening the ischemia-reperfusion injury)⁸¹ and should be avoided. Because of the risk of reperfusion syndrome, removal of a tourniquet which has been applied for > 6 hours should be done only when close monitoring and laboratory capability are available.⁸⁰

Junctional tourniquet

The extremity tourniquet is ineffective at controlling hemorrhage from “junctional” regions, such as the axillae and groins, since it cannot be applied proximal to the region of injury. The CoTCCC recommends three FDA-approved junctional tourniquet devices for bleeding control in these regions (Table 3).⁸² These devices differ somewhat in which body regions they can be used, but were equally effective at eliminating distal blood flow to the lower extremities in healthy volunteers.⁸³ In a porcine model of groin hemorrhage, 2-hour inguinal application of the Combat Ready Clamp (CRoC) to control common femoral artery inflow resulted in mild and reversible ischemic injury, but 2-hour umbilical application for aortic inflow control resulted in extensive lumbar muscle necrosis and severe disability.⁸⁴

Abdominal aortic & junctional tourniquet (AAJT)

The AAJT is FDA-approved for occlusion of the aortic bifurcation at the umbilicus and axillary artery at the delto-pectoral groove.⁸⁵ It would effectively control bleeding distal to its application (e.g. pelvic hemorrhage) but will exacerbate any proximal bleeding and should not be used in patients with known or suspected proximal injuries. A single-center retrospective study of 402 patients who required emergent trauma laparotomy for intraabdominal hemorrhage control found that only 9% had isolated hemorrhage originating distal to the aortic bifurcation and would have potentially benefitted from the AAJT.⁸⁶ To our knowledge, there is no evidence of improved outcomes from comparative studies of junctional tourniquets or the AAJT in the literature.

Non-absorbable, expandable, injectable hemostatic sponge (XStat)

XStat (RevMedx, Wilsonville, OR) is a novel device consisting of approximately 92 discoid chitosan-coated sponges loaded into a syringe. When injected into a wound cavity, the sponges expand from 4.5 mm disks to 40 mm tubes after coming into contact with blood, tamponading bleeding.⁸⁷ Sponges have radiopaque markers to facilitate retrieval. XStat is FDA-approved for junctional wounds in the axillae and groins not amenable to tourniquet application. It is particularly suited for penetrating injuries where the bleeding vessel is in a

deep, narrow wound tract. In porcine models of subclavian vessel transection, X-Stat took significantly less time to apply, did not require continuous external compression after application, and significantly reduced blood loss compared to QuikClot Combat Gauze.^{87,88} Current TCCC guidelines recommend XStat as a second-line therapy (in the same category as Celox and ChitoGauze) to external hemorrhage not amenable to extremity tourniquet application when Combat Gauze is not available.⁸⁹ To our knowledge, there are no comparative studies of XStat and junctional tourniquets and no clinical studies of XStat in patients.

Resuscitative endovascular balloon occlusion of the aorta (REBOA)

The new FDA-approved ER-REBOA device (Prytime Medical, San Antonio, TX) can be introduced through a 7-French sheath by percutaneous access to the common femoral artery without the aid of a guidewire.⁹⁰ Balloon inflation in the supraceliac aorta (Zone 1) functions similarly to an aortic cross-clamp placed during resuscitative thoracotomy and should be limited to 45–60 minutes to prevent necrosis of all intra-abdominal contents. Alternatively, the balloon can be inflated in the infrarenal abdominal aorta (Zone 3) to control pelvic bleeding for longer periods of time. REBOA should not be used for patients with thoracic bleeding since balloon inflation will increase blood loss.

Currently, REBOA use in Level 1 trauma centers is safe⁹¹ and may offer improved survival over resuscitative thoracotomy.⁹² However, the prehospital use of REBOA in its current design raises important safety concerns and is controversial secondary to the requisite prolonged inflation time. The arterial cannulation procedure is beyond the scope of many prehospital providers, and prolonged Zone 1 aortic balloon occlusion will inevitably induce irreversible ischemia of abdominal contents. Zone 3 occlusion in select patients⁹³ will likely be better tolerated; however, the difficulty of this approach (and of AAJT use) is identifying the patient with *isolated* pelvic bleeding in the prehospital setting. Encouraging animal studies of partial Zone 1 occlusion allowing some distal flow prolongs the exsanguination process,⁹⁴ but human data are lacking.

Intra-abdominal self-expanding foam

Intra-abdominal self-expanding foam (ResQ Foam, Arsenal Medical, Boston, MA – not FDA approved) is one of the first products which shows promise in prehospital control of non-compressible abdominal hemorrhage. Polyol and isocyanate solutions are delivered into the peritoneal cavity through a small anterior abdominal incision. When combined in situ, they polymerize into a self-expanding poly(urea)urethane polymer, tamponading intra-abdominal bleeding.⁹⁵ The foam is removed en bloc at the time of laparotomy. In porcine models, it was left in situ for 3 hours before explantation and was highly successful in rescuing animals from lethal hemorrhagic shock following Grade V hepatoportal venous injury⁹⁶ and iliac artery injury.⁹⁷ Focal bowel injuries caused by foam expansion were repaired during laparotomy. In a long-term survival study, 90% of animals survived to the end-point of 28 or 90 days without clinically significant complications.⁹⁸ At the time of this writing, no clinical use of this product has been reported, although studies in trauma patients are under discussion with the FDA.

Implications for RDCR in civilian austere sectors

Prehospital providers and lay persons are being trained in the control of external hemorrhage with hemostatic gauzes and extremity tourniquets under the Hartford Consensus Stop the Bleed Program.⁷⁴ However, there is little comparative evidence to guide the use of junctional tourniquets, the AAJT, XStat, or prehospital REBOA for civilian RDCR. Currently, the best resuscitation fluid reliably available in austere settings is FDP. However, there is still a minimum of several years before an FDP product will be FDA-approved for general use in the US. Some American prehospital providers in austere settings currently have access to blood products, but others may be faced with a difficult choice for bleeding patients: crystalloid, artificial colloid, or no fluid at all? Unfortunately, we do not believe there is enough evidence to make a recommendation in this situation. Finally, TXA is likely safe to be administered in the field, although confirmatory studies are needed. Our evidence-based recommendations for RDCR are summarized in Table 4.

Conclusions

Several gaps in knowledge and technology preclude optimal RDCR implementation and require further study (Table 5). Although the prehospital treatment of hemorrhagic shock remains a major challenge, this is an area where even small incremental improvements will improve outcomes of injured patients.

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Table 1

Characteristics of plasma products.

| | | Freeze-dried plasmas (FDP) | | | | |
|-----------------------|--|----------------------------|--------------------|---|--|---|
| Product | Fresh frozen plasma (FFP) | Thawed plasma (TP) | Liquid plasma (LP) | French lyophilized plasma (FLYP) (French Red Cross) | LyoPlas n-w (German Red Cross) | Bioplasma FDP (National Biomedical Institute, Pinetown, South Africa) |
| Source | Single donor | Single donor | Single donor | “Mini-pools” (10 donors), mixed ABO type | Single donor | Pooled, mixed ABO type |
| Pathogen inactivation | Screening only | Screening only | Screening only | Amotosalen ultraviolet light (UVA) method | Screening only (includes 4- month quarantine period) | Solvent-detergent method |
| Storage | -18°C | 1-6°C | 1-6°C | Room temperature | 2-25°C | <25°C |
| Shelf Life | 1 year | 5 days | Up to 40 days | 2 years | 15 months | Not specified |
| Notes | Can be relabeled and stored as TP after thawing. | | | ABO-universal. | | ABO-universal. |

Table 2

Calculated parameters of fresh whole blood (450 ml donor blood with 63 ml anticoagulant) compared to component therapy with 1 packed red blood cells unit (hematocrit of 55% in 335 mL), 1 fresh frozen plasma unit (80% coagulation factor activity, 250 mL), and 1 platelet unit (5.5×10^{10} platelets in 50 mL).

| | Fresh whole blood | 1:1:1 component therapy |
|----------------------------------|--|--------------------------------|
| Dilution factor | 12% | 35% |
| Hematocrit | 33–43% | 29% |
| Clotting factor activity | 86% | 65% |
| Platelets | $130\text{--}350 \times 10^9/\text{L}$ | $88 \times 10^9/\text{L}$ |
| Fibrinogen content | 675–1800 mg | 400–500 mg |
| Bags of product (donor exposure) | 1 | 3–4 |

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Table 3

Comparison of junctional tourniquets.

| | Combat Ready Clamp (CRoC, Combat Medical Systems LLC) | Junctional Emergency Treatment Tool (JETT, North American Rescue LLC) | SAM Junctional Tourniquet (SJT, SAM Medical Products) |
|-------------------------------------|--|--|--|
| Mechanism | Mechanical | Mechanical | Pneumatic |
| FDA-approved regions of application | Delto-pectoral groove Groin (unilateral) Neck (as a "last resort" for significant carotid artery bleeding) Umbilicus (as a "last resort" for significant bilateral bleeding or unilateral bleeding not controllable by another method) | Groins * | Delto-pectoral groove Groins * |
| Vessel occluded | Axillary artery Common femoral artery Carotid artery Aortic bifurcation | Common femoral artery | Axillary artery Common femoral artery |
| Notes | Unilateral use | Bilateral use (for groins) Literature supports use as pelvic stabilizer. ⁹⁹ | Bilateral use (for groins) FDA-approved as pelvic stabilizer |

* device allows for concurrent bilateral occlusion of bleeding from both groins

Table 4

Recommendations for RDCR

| |
|---|
| <ul style="list-style-type: none">• Rapidly identify patient with significant hemorrhage.• As soon as possible (ideally at point of injury): obtain mechanical hemorrhage control with hemostatic gauzes and/or extremity tourniquet, and commence resuscitation with reconstituted FDP and administer TXA (if available).• Transition to (in order of preference): whole blood, 1:1:1 plasma:RBCs:platelets, 1:1 plasma:RBCs.• Reassess limb tourniquet every 2 hours and convert to a hemostatic or pressure dressing if able.• Minimize use of crystalloids and artificial colloids.• Do not administer TXA >3 hours after injury.• For patients without TBI and minimal expected prehospital transport time, permissive hypotension is safe. However, there is insufficient data for a recommendation for patients with TBI or expected transport delay. |
|---|

FDP, freeze dried plasma; FDA, Food and Drug Administration; RBCs, red blood cells; TXA, tranexamic acid; TBI, traumatic brain injury.

Table 5

Topics needing further investigation in prehospital hemorrhage control.

| |
|--|
| <ul style="list-style-type: none">• Improved monitoring capability of oxygen debt accumulation.• Improved control of non-compressible hemorrhage.• Role for prehospital REBOA.• Role of permissive hypotension with prolonged prehospital time.• Prehospital resuscitation endpoints and goals.• Shelf life of cold-stored platelets and cold-stored whole blood.• Technology to minimize transmissible disease risk of whole blood transfusion.• Methods to store whole blood at ambient temperature.• Optimal balance between permissive hypotension and TBI after polytrauma. |
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