ORIGINAL ARTICLE

Remote damage control resuscitation and the Solstrand Conference: defining the need, the language, and a way forward

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Damage control resuscitation (DCR) is emerging as a standard practice in civilian and military trauma care. Primary objectives include resolution of immediate life threats followed by optimization of physiological status in the perioperative period. To accomplish this, DCR employs a unique hypotensive–hemostatic resuscitation strategy that avoids traditional crystalloid intravenous fluids in favor of early blood component use in ratios mimicking whole blood.

The presence of uncontrolled major hemorrhage (UMH) coupled with a delay in access to hemostatic surgical intervention remains a primary contributor to preventable death in both combat and in many domestic settings, including rural areas and disaster sites. As a result, civilian and military emergency care leaders throughout the world have sought a means to project DCR principles forward of the traditional trauma resuscitation bay, into such remote environments as disaster scenes, rural health facilities, and the contemporary battlefield. After reflecting on experiences from past conflicts, defining current capability gaps, and examining available and potential solutions, a strategy for "remote damage control resuscitation" (RDCR) has been proposed.

In order for RDCR to progress from concept to clinical strategy, it will be necessary to define existing gaps in knowledge and clinical capability; develop a lexicon so that investigators and operators may understand each other; establish coherent research and development agendas; and execute comprehensive investigations designed to predict, diagnose, and mitigate the consequences of hemorrhagic shock and acute traumatic coagulopathy before they become irreversible.

This article seeks to introduce the concept of RDCR; to reinforce the importance of identifying and optimally managing UMH and the resulting shock state as part of a comprehensive approach to out-of-hospital stabilization and en route care; and to propose investigational strategies to enable the development and broad implementation of RDCR principles.

INTRODUCTION

To the victim of trauma, time is the enemy.[1] While the advent of out-of-hospital emergency care has extended the "Golden Hour," longer time intervals between injury and resuscitative surgical intervention remain primary contributors to the modern epidemic of trauma mortality.[2,3] Yet, despite sizeable outlays in financial and intellectual resources into research, relatively little is known about the sequence of pathophysiologic events that commence with hemorrhage, then progress if unchecked toward coagulopathy, hemorrhagic shock, exsanguination, and death in the temporal period before trauma center arrival.[4,5]

Despite revolutionary advances in combat casualty care over the past century, the contemporary battlefield remains highly lethal and geographically remote.[6,7] Advances in armor, battlefield trauma system development, first responder care, forward resuscitative surgery,
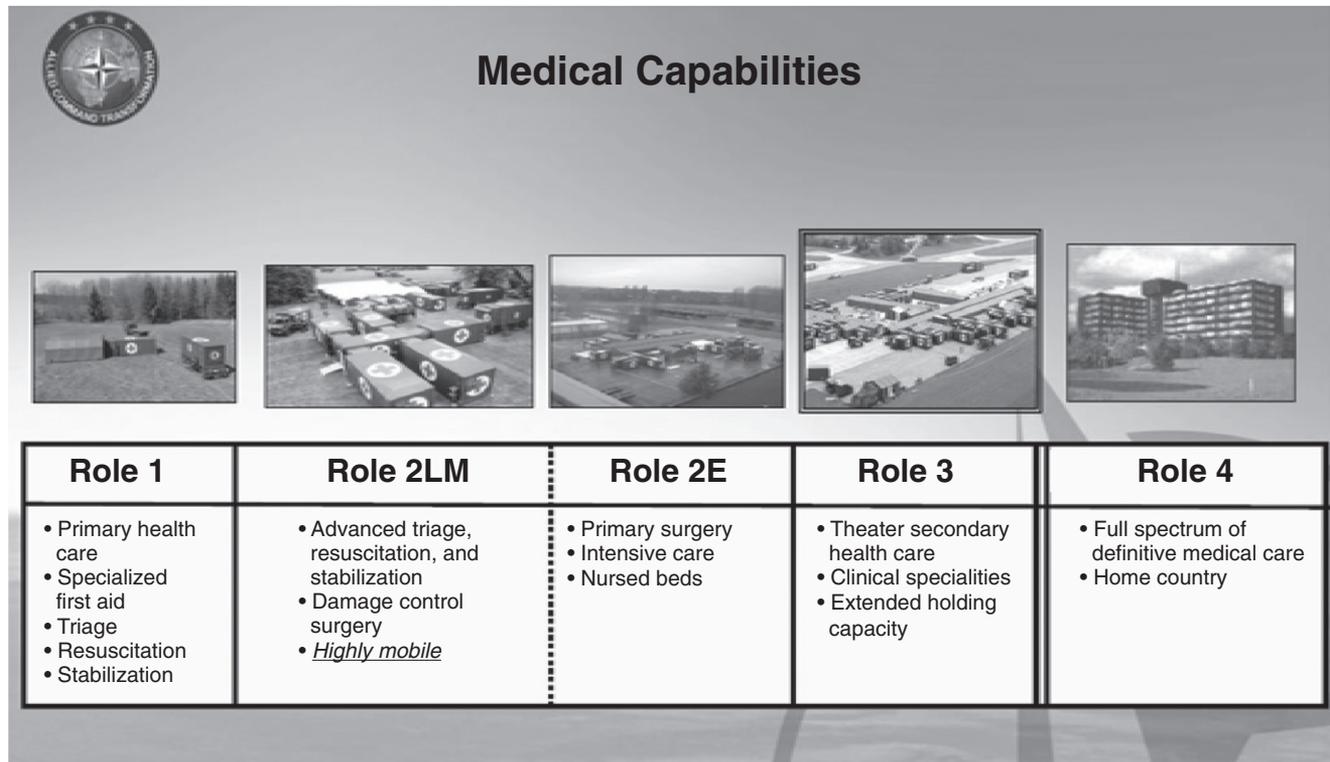
Fig. 1. A depiction of the North Atlantic Treaty Organization's (NATO) defined roles of health service support in the deployed environment.[12]

and strategic critical care transport have contributed substantially to improvements in casualty survival; however, further gains after hospital arrival are likely to be incremental at best.[8] In contrast, the out-of-hospital and pre-surgical phases of combat casualty care (referred to as North Atlantic Treaty Organization [NATO] Role-I) represent our greatest opportunity to further reduce the rate of potentially survivable combat deaths, as well as to minimize residual morbidity in survivors (see Fig. 1).[8-11] A remarkably similar scenario exists in domestic trauma systems, particularly in rural or other locales, characterized by time and distance factors that result in protracted time intervals between injury and arrival at a full-service trauma center.[13,14]

THE PROBLEM: POTENTIALLY SURVIVABLE COMBAT DEATH

Modern armed conflicts, which more frequently involve asymmetric strategies and violent nonstate actors, have expanded in geospatial terms, lethality, and complexity.[15] In many respects, the contemporary battlespace resembles the worldwide scope and the devastating pattern of explosive injuries last experienced in the Second World War. In contrast, wounding mechanisms and causes of death remain similar to more recent conflicts.[14-19] At least three phenomena contribute: 1) the pace of advances in war fighting technology; 2) adaptive and elusive adversaries; and 3) limited success in assimilating lessons from past conflicts and emerging civil-sector innovations in prehospital care, through effective knowledge translation strategies.[20-23]

Today, the primary causes of potentially survivable combat death include two broad categories: 1) under-performance of Life-Saving Interventions (LSI) when required; and 2) the combination of uncontrolled major hemorrhage (UMH) and delayed evacuation to surgical intervention.[6,24] Both circumstances possess subtle nuances worth noting, and perhaps redefining.

First, not all victims of trauma require that an LSI be performed; however, if an LSI is required but not performed correctly and in a timely manner, there is an association with increased mortality.[24] For our purposes, we have chosen to define LSI in a manner adapted from the recently published National Association of Emergency Medical Services Physicians/US Centers for Disease Control and Prevention's SALT Triage Method, namely: 1) control of major hemorrhage; 2) establishment of a patent airway and optimization of ventilation; 3) decompression of intrathoracic tension; and (4) administration of appropriate chemical or biologic antidotes, if applicable.[25,26]

Second, it is important to note that UMH is not limited exclusively to "non-compressible hemorrhage," but may also encompass compressible or junctional

sources of bleeding either overlooked or undertreated before the onset of acute traumatic coagulopathy and hemorrhagic shock. Also, despite optimal LSI performance, it is plausible to consider that clinical, tactical, or other confounding circumstances might thwart optimal hemostatic control. In a broader sense, trauma might not even be involved: gastrointestinal hemorrhage, placental abruption, and hematopoietic disorders come to mind as examples of nontraumatic sources of major hemorrhage, often uncontrollable in the out-of-hospital setting. Thus, we would define any of the aforementioned conditions, whether alone or in combination, as UMH.

OUT-OF-HOSPITAL COMBAT CASUALTY CARE: SALVAGING THE SALVAGABLE

Mounting evidence confirms the linkage between the successful performance of LSI earlier in the time sequence of casualty care and improved combat survival. Gerhardt and colleagues reported a 35% decrease in overall combat mortality associated with emergency medicine practitioners, a permissive-hypotensive resuscitation strategy, and an Emergency Medical Services (EMS) model for combat medic direction, in conventional combat units in an urban warfare setting.[8] Kotwal and colleagues reported a 44% decrease in potentially salvageable causes of death in the 75th Ranger Regiment, attributed to universal tactical combat casualty care training and Command oversight.[10] Most recently, Mabry and colleagues' analysis of Army Medical Evacuation (MEDEVAC) records of a paramedic-level Army National Guard air ambulance unit in Afghanistan found a 47% decrement in 48-hour mortality after wounding, attributed to advanced scope-of-practice tactical en route care.[11]

UMH

Significant progress has been realized in preventing death from compressible hemorrhage.[27,28] The use of improved tourniquets, hemostatic dressings, new junctional compression devices, and "hasty" tourniquets for severe bleeding in otherwise intact extremities is credited with significant reductions in combat mortality.[29,30] Despite these innovations, and the broad availability of improved body armor, roughly 15% of contemporary battle casualties suffer torso trauma, often resulting from blast overpressure and fragment penetration through unprotected anatomical portals.[6] These wounds may compromise cardiothoracic structures, and may also involve noncompressible intracavitary or visceral injuries requiring surgical hemostasis. Thus, presuming that the other required LSI have been performed, UMH from noncompressible sources becomes the leading cause of potentially survivable combat death.[24] Furthermore, as NATO Role-1 combat medical personnel acquire

advanced competencies and systematic medical direction, there is evidence suggesting that the relative rate of death from noncompressible UMH may actually rise, as mortality is shifted away from otherwise preventable causes (R.T. Gerhardt, Tactical Study of Care Originating in the Prehospital Environment (TACSCOPE), unpublished data, 2012).

The current mainstream options for treatment of UMH are severely limited[31] Rapid access to surgery remains the primary objective. Available data reveal an excess of 75% of combat fatalities occurring before arrival at a medical treatment facility.[6] Thus, our best opportunity to continue the trend toward improvement in combat casualty survival is through assurance of appropriate LSI performance and the search for beneficial interventions to temporize UMH before arrival at surgical intervention.[31]

DAMAGE CONTROL RESUSCITATION (DCR)

For the majority of casualties in the contemporary operational environment, standard resuscitation practice including the judicious use of crystalloid infusions are not likely to be harmful, and may be preferable for nonhemorrhagic volume depletion.[32] In contrast, modern combat casualties often sustain poly-trauma and significant burns.[33] Many manifest UMH, and when coupled with the aforementioned delays in evacuation, ultimately experience profound shock and the "Lethal Triad": coagulopathy, acidosis, and hypothermia.[32-34] To mitigate this downward spiral, DCR and damage control surgery (DCS) principles were adapted to the contemporary battlefield to sustain adequate oxygenation and coagulation until surgical intervention could be provided.[35]

DCR employs a two-pronged hypotensive and hemostatic resuscitation strategy. Permissive-hypotensive resuscitation is conducted by limiting intravascular volume replacement to the minimum required to perfuse vital organs without stimulating bleeding by increased blood pressure or hemodilution. This translates practically to a target mean arterial pressure of 50 mmHg, a systolic blood pressure over 80 mmHg, or return of a palpable peripheral pulse.[36,37] Hemostatic resuscitation employs red blood cells (RBCs), fresh frozen plasma, and platelets transfused in a ratio approximating 1:1:1, mimicking whole blood.[38,39]

Additional objectives of DCR include mitigation of hypothermia and acidosis before DCS, and use of "fresher" RBCs: the selective use of the most recently collected units as a strategy for minimizing the "storage lesion" with the objectives of maximizing tissue oxygen delivery while mitigating adverse immune, coagulation, and inflammatory responses.[40,41] Although still considered controversial by some, studies of DCR report an associa-

tion with improved survival from 16 to 40% over standard care in both combat and civilian settings.[35,42,43]

In addition to the aforementioned practice of blood component transfusion in the 1:1:1 ratio, contemporary combat medical facilities have adopted the practice of contingency blood collection from prescreened healthy volunteers, followed immediately by transfusion of type-specific fresh whole blood to unstable UMH patients: a process we label as "Contingency Blood Collection and Transfusion" (CBC/T). While employed to date primarily in circumstances of blood component shortage, CBC/T has been associated with outcomes comparable to 1:1:1 component therapy and is now a core element of military DCR.[39]

HISTORY REPEATS ITSELF AGAIN: WHOLE BLOOD AND FREEZE-DRIED PLASMA

The ultimate objective of DCR is the timely delivery of a living patient to a surgical facility, where hemostasis and physiological stabilization can take place.[31] The severely injured patient with UMH is likely to experience massive blood loss normally incompatible with survival beyond a brief period, an absent hemostatic intervention, or an as-yet undefined strategy to stave off coagulopathy and hemorrhagic shock while en route to the operating table.[44] If the patient or casualty is to survive in such a situation, an out-of-hospital resuscitation strategy including blood component transfusion becomes a practical necessity.[45] In theory, modern blood banks working in concert with sophisticated clinical laboratories can provide carefully calibrated component-based therapeutic bundles for transfusion, based upon laboratory investigations of a patient's physiologic status and immunophenotypic profile.[46] This idealized approach, however, is impractical in the face of the exsanguinating patient, even in a modern trauma center. This may explain in part the trend toward adoption of "massive transfusion" protocols employing RBCs, plasma, and platelets administered in ratios mimicking whole blood.[38] In any case, the use of all of the blood components normally employed in a hospital-based massive transfusion protocol is not feasible in the contemporary out-of-hospital setting, where potential transfusion decisions are made under difficult circumstances, with limited clinical and laboratory data, and with a severely constrained supply chain.

Fortunately, past becomes prologue once again, and a review of combat casualty resuscitation from prior conflicts offers valuable perspective and evidentiary support that can guide current RDCR development.

At the beginning of the Second World War, it was thought that severely wounded casualties could be adequately resuscitated with plasma in anticipation of evacuation and eventual surgical management.[47] The impossibility of keeping plasma frozen before use in combat settings stimulated a frenzied development program that yielded a freeze-dried universal plasma product, of which over 10 million units were ultimately produced during the war.[47] Although normal saline solution and albumin were also employed frequently, reconstituted freeze-dried plasma was the resuscitation fluid of choice for far-forward casualty care throughout the war. This approach, though practical, was found to be inadequate to the task of preventing or reversing shock physiology.[47] The experiences of British and US Forces during the North Africa Campaign in 1943 showed that whole blood, with its oxygen-carrying as well as hemostatic capacities, was critical to successful resuscitation.[47] Ironically, the same conclusion had been reached in the First World War, where universal donor whole blood (type O, low isohemagglutinin titer) was delivered to far-forward British and American positions in order to maximize the odds of survival for the most severely injured.[48] Nevertheless, these hard lessons were rapidly re-assimilated, and assurance of the availability of whole blood, as well as plasma, at the Anzio beachhead in January 1944 was a major factor in Allied operational planning.[47] From that point until the end of the Vietnam era, whole blood and plasma were the main pillars of trauma resuscitation in the US military, although freeze-dried plasma was abandoned during the Korean conflict due to the high rates of transmission of viral hepatitis.[45,49]

US Forces in the Second World War established what could be termed "Field Blood Banks," where fresh whole blood was collected from immediately available donors and either used on site immediately, or packaged and delivered as far forward as possible for resuscitation near point of wounding (foreshadowing current strategies for "Buddy Transfusion" or CBC/T as defined here). Units actively engaged in combat used freeze-dried plasma and any available whole blood until casualties could be evacuated to surgical facilities.[50] This approach was replicated successfully in Korea.[49] In Vietnam, universal donor whole blood was the primary resuscitation agent until apheresis-derived fresh frozen AB plasma was introduced in 1968.[51] Eventually type-specific whole blood was introduced, but universal donor whole blood was the only blood product used in forward, prehospital settings.

In contrast, the conflicts in Iraq and Afghanistan have seen US and Coalition Forces employ whole blood, particularly when other platelet-containing products were unavailable, but rarely in the prehospital setting where reliance on crystalloid- and colloid-based resuscitation has dominated practice.[50]

REMOTE DCR (RDCR)

While the DCR paradigm is state of the art, it remains predicated upon access to a facility with hemostatic surgical capability and a blood bank. In the contemporary operational environment, neither the supply of surgical

assets nor blood bank services are sufficient for placement in close proximity to every combatant population at risk. Likewise, in rural or other dispersed, regionalized domestic trauma systems, employment of both DCR and DCS strategies will likely be delayed until arrival at a trauma center, if the patient survives. Thus, in order to realize greater benefits in survival and functional recovery, DCR will have to be adapted and projected closer to the point of injury or wounding.[31]

Recent reports from both the battlefield and domestic settings have catalyzed increasing interest in the earlier initiation of DCR in the course of trauma patient care. In prior experience, blood transfusion forward of combat surgical facilities was implemented successfully and reported by Israeli and British Forces during tactical evacuation, and by US Navy emergency physicians operating with Shock Trauma Platoons in support of the US Marine Corps, using credentialed practitioners.[52-54] In these instances, and in addition to providing blood products when appropriate, emergency medical teams place advanced airways, initiate rudimentary mechanical ventilation, decompress intrathoracic tension, administer advanced pharmaceuticals, and even perform the occasional emergency resuscitative thoracotomy. The United Kingdom has also reported the successful prehospital use of tranexamic acid (TXA), RBCs, and thawed plasma by their Medical Emergency Response Teams.[55] The Israeli Defense Force has deployed TXA and Fibrinogen Concentrate on their military and civilian search and rescue platforms.[56] Most recently, we have received compelling anecdotal reports of successful employment of both prescreened RBC and thawed plasma transfusion by US Army MEDEVAC units, and of the successful out-of-hospital use of CBC/T at a NATO Role-I forward aid station in combat.[12,57]

On the domestic front, civilian hospital-based air medical transport teams in Rochester, Minnesota, and Houston, Texas, have adopted plasma for trauma scene-response calls.[58,59] Civilian emergency air medical transport units in London and throughout Norway have likewise employed RBCs, plasma, and are implementing TXA protocols, adding further credence to the practice of forward projection of DCR, and of effective military-to-domestic translation.[60,61]

In essence, these military and civilian trauma systems are performing DCR in a remote setting, with promising results.

Reinforced by these developments, yet challenged by a limited pool of equivalent medical personnel, we seek to adapt RDCR for use by paramedical combat personnel, and their domestic EMS counterparts participating in regional trauma systems or disaster response efforts under EMS medical direction.[31] The ultimate goal is to deliver an optimized preoperative patient to the trauma surgeon, maximizing survival and preserving organ function.

TABLE 1. Proposed RDCR research agenda

1. Can we define then identify who needs RDCR before they deteriorate?
2. Would RDCR improve or preserve optimal physiological status before arrival at a surgical facility?
3. Does RDCR actually improve survival?
4. Which products, devices, and interventions for RDCR will provide an optimal risk–benefit ratio?
5. How can whole blood, components, and hemostatic drugs be safely incorporated into RDCR?
6. How do we define the Medical Equipment Set and the logistics to support it?
7. What scope-of-practice do we need for RDCR providers, or should it use a tiered approach?
8. How can we assure medical direction or decision support when needed?
9. How will RDCR interventions be documented and communicated to higher roles of care?
10. What regulatory constraints are there?
11. How to most efficiently implement RDCR principles with blood bank personnel that address logistic and supply chain concerns?
12. How will the evolution of RDCR practices be monitored? How will outcomes be tracked?

To accomplish this successfully, we must define and identify the UMH target population before onset of coagulopathy and shock, a task which currently is obvious in many cases, but obscured until the point of decompensation in others.[62] Optimal scope-of-practice for RDCR practitioners must also be defined, and may well take the form of a spectrum of care with commensurate indications and interventions. Appropriate medical devices and consumables complementary to this proposed RDCR spectrum await conception, development, and evaluation before implementation. It is quite likely that emerging agents such as TXA, fibrinogen, and prothrombin complex concentrates, freeze-dried plasma, and even CBC/T among others, will each play some role within a comprehensive RDCR formulary. Field-deployable thromboelastometry, volume-based physiological monitors capable of "learning" a patient's hemodynamic status and predicting clinical trajectory, modern donor testing, and emerging pathogen reduction technologies will enable these innovations but will require further study and development. Perhaps most challenging will be formulating an effective model for medical direction and regulation of out-of-hospital blood product use by combat medical personnel or their civil-sector counterparts in locales where the predominant model does not routinely employ critical care physicians as part of medical aircrews.

Table 1 depicts an end-user–focused proposal for an RDCR research agenda. While neither validated nor consensus-developed as of this writing, it represents a viable "first strike" for scientists, clinical investigators, and end users to consider as we collectively seek to establish and advance the science and practice of RDCR, with the ultimate goal of improving survival for future victims of hemorrhage, both on the battlefield and at home.

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