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Damage control: The modern paradigm

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It is more than 20 years since the term 'Damage control' was introduced to describe an emerging surgical strategy of abbreviated laparotomy for exsanguinating trauma patients. This strategy of temporisation and prioritisation of physiological recovery over completeness of anatomical repair was associated with improved survival in a subset of patients with combined major vascular and multiple visceral injuries. The ensuing years saw the rapid adoption of these principles as standard of care for massively injured and physiologically exhausted patients. Resuscitation of severely injured patients has changed significantly in the last decade with the emergence of a new resuscitation paradigm termed 'damage control resuscitation'. Originating in combat support hospitals, damage control resuscitation emphasises the primacy of haemorrhage control while directly targeting the 'lethal triad' of coagulopathy, acidosis, and hypothermia. Integral to damage control resuscitation is the appropriate application of damage control surgery and together they constitute the modern damage control paradigm. This review aims to discuss the modern application of damage control resuscitation and damage control surgery and to review the evidence supporting its constituent components, as well as considering deficiencies in current knowledge and areas for future research.

Keywords
Damage control, resuscitation, trauma

Introduction

Haemorrhage accounts for 30–40% of overall trauma deaths and is the commonest cause of preventable mortality in trauma patients.[1,2] Preventing death from trauma haemorrhage, however, poses a number of challenges. Exsanguination is the commonest cause of death in those found without vital signs by emergency medical services,[3] indicating the rapidity with which bleeding trauma patients may deteriorate to a state of profound shock or cardiac arrest. Haemorrhage is also the leading cause of death in the first hour after arrival in hospital and is responsible for more than 80% of deaths in the operating theatre,[4,5] indicating the difficulty in reversing this decline. Furthermore, management of trauma haemorrhage requires a more complex approach than simply 'turning off the tap' and 'refilling the bucket'. Major trauma haemorrhage induces a 'genomic storm', with substantially altered expression of many thousands of genes, activation of inflammation, and coagulation as well as microvascular dysfunction which may lead to multi-organ failure and death.[6,7]

Resuscitation of these severely injured patients has changed significantly in the last decade with the emergence of a new paradigm termed 'damage control resuscitation' (DCR). DCR emphasises the primacy of haemorrhage control while directly targeting the 'lethal triad' of coagulopathy, acidosis, and hypothermia and minimising iatrogenic harm from unrestrained fluid resuscitation. Integral to the success of DCR is the early definitive control of haemorrhage. This serves to prevent exsanguination, but also to limit the harmful downstream consequences of inflammation and resuscitation.[7]

The majority of haemorrhagic deaths are due to bleeding at non-compressible sites.[8] These injuries require surgical or radiological intervention to control haemorrhage. In the most severely injured and shocked patients, however, adverse physiology may preclude definitive surgical repair of all injuries in one sitting. The futility of attempting complete surgical repair in

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the face of extreme physiological derangement has long been recognised. More than 30 years ago, Stone et al.[9] described a strategy of 'truncated laparotomy' for severely injured patients with physiological exhaustion in whom clinically evident coagulopathy had developed and a decade later, Rotondo et al.[10] popularised the term 'damage control'. Damage control surgery is a strategy of temporisation, prioritising physiological recovery over completeness of anatomical repair, and its use has been associated with dramatically increased survival in a subset of severely injured patients.[9–11]

We aim to discuss the rationale for applying DCR and damage control surgery following major trauma and to review the available evidence supporting its use.

DCR: Origins of a modern resuscitation paradigm

Modern resuscitation of trauma haemorrhage incorporates a new paradigm referred to as Damage Control Resuscitation (DCR). Its origins are in the military's experience of management of major haemorrhage over the course of the last decade of conflicts in Afghanistan and Iraq. While the concept of damage control surgery was well established at the outset of these conflicts and the 'lethal triad' was well characterised, DCR was a novel development.

The efficacy of conventional resuscitation strategies had been questioned for many years amid concerns regarding the detrimental effects of crystalloid resuscitation. These include: haemodilution and dilution of clotting factors, exacerbation of hypothermia, worsening of acidosis and increasing intra-vascular pressure with resultant disruption of clot, and promotion of bleeding, as well as specific immunologic effects leading to organ failure.[12,13]

The association between coagulopathy and injury is not new. Simmons et al.[14] described coagulation abnormalities in U.S soldiers during the Vietnam conflict and recognised they were related to the severity of wounding. Subsequently, however, conventional wisdom suggested coagulopathy was attributable to: dilution, massive transfusion, hypothermia, and acidosis. Brohi et al.[15] described an endogenous coagulopathy in a large proportion of severely injured civilian trauma patients, which was detectable on arrival in hospital and was not attributed to large volume crystalloid resuscitation. The recognition of this 'acute traumatic coagulopathy' and its association with poor outcome promoted interest in resuscitation strategies that directly target coagulopathy and promote haemostasis. Furthermore, observational data from combat support hospitals emerged demonstrating a strong association between survival and more aggressive use of blood products in bleeding military casualties.[16]

The concentration of large numbers of severely injured casualties in well-resourced combat support hospitals over the last decade provided an opportunity to develop and study alternative resuscitation strategies, in which crystalloid usage was minimised in favour of early use of blood products, with apparently good effect.[17] It was in this setting that DCR emerged. In 2007, Holcomb et al.[17] described DCR as: '*a proactive early treatment strategy that addresses the lethal triad on admission to a combat hospital*'[17] DCR aimed, not only to keep casualties warm and prevent acidosis, but also to directly and pre-emptively target coagulopathy from the outset. In UK military circles, Hodgetts et al.[18] chose a broader definition, which incorporated the pre-hospital management and the primacy of haemorrhage control in exsanguinating haemorrhage. They defined DCR as: *'a systematic approach to major trauma combining the <C>ABC paradigm with a series of clinical techniques from point of wounding to definitive treatment in order to minimise blood loss, maximise tissue oxygenation and optimise outcome'*.

These techniques have been further refined and broadly adopted into civilian trauma care, such that they are reflected in evidence-based guidelines for management of civilian trauma.[19]

The major constituent elements of DCR are:

- <C>ABC resuscitation (see below).
- Permissive hypotension.
- Limitation of crystalloid with early use of blood products.
- Early use of tranexamic acid (TXA).
- Early and appropriate use of damage control surgery.

There is emerging evidence supporting the use of DCR. Observational studies of patients undergoing damage control laparotomy have demonstrated an association with improved survival and fewer complications for patients resuscitated using DCR principles when compared with historic controls.[20–22] In addition, there is emerging evidence that employing DCR might result in more favourable peri-operative physiology, lessening the need for damage control surgery.[23–25] The evidence supporting individual constituent components of DCR is reviewed below.

Primacy of haemorrhage control in 'catastrophic' haemorrhage (<C> ABC)

Hodgetts et al.[26] published the <C> ABC paradigm for military trauma in 2006. This new paradigm reflected the need to effect haemorrhage control as the first intervention (i.e. prior to 'airway') in the subset of military trauma patients presenting with 'catastrophic' external haemorrhage.

Earlier analysis of combat injury profiles had shown that up to 10% of U.S. battlefield deaths in Vietnam were due to extremity bleeding. These represented more than half of all preventable combat deaths and were potentially amenable to local control.[27] By contrast, only approximately 1% of all combat deaths were due to airway obstruction, justifying the prioritisation of massive haemorrhage control over airway manoeuvres.

The nature of military trauma (high-energy ballistic/blast injuries) dictates that a far greater proportion of casualties will be at risk of catastrophic limb haemorrhage than their civilian counterparts. Nonetheless, the <C> ABC is applicable for all trauma victims. When catastrophic external haemorrhage is present, regardless of mechanism or environment, control of external haemorrhage is now established as the first priority.[19]

In addition to redefining priorities of treatment, the recent conflicts provided an impetus to develop new approaches to control external haemorrhage. To this end, a range of novel haemostatic agents emerged in the last decade (e.g. Quickclot®, HemCon®). These developments have also been adopted by the civilian sector and the Joint Royal Colleges Ambulance Liaison Committee (JRCALC) has approved use of haemostatic dressings by UK ambulance services. Furthermore, there has been a re-emergence of tourniquet use for catastrophic limb bleeding. The routine issue of combat application tourniquets (CAT) to troops and the emphasis on training and appropriate use of these has resulted in a body of evidence supporting their efficacy.[28] In the civilian setting, tourniquet use is recommended to stop life-threatening bleeding from open extremity injuries in the pre-surgical setting[29] and a number of UK ambulance services now issue tourniquets to frontline vehicles.

In patients with suspected blunt pelvic trauma, early pre-hospital control of concealed haemorrhage by use of a pelvic binder is also advocated.[30] There is very limited clinical research in this field and no good quality evidence that the use of pelvic binders reduces mortality or bleeding in unstable pelvic fractures.[31] However, a number of case series and reports suggest an improvement in haemodynamic parameters and a reduction in blood transfusion after application of a pelvic binder and a recent consensus statement of the faculty of pre-hospital care in the U.K. has recommended their use.[30]

Permissive hypotension

Permissive hypotension, also known as 'hypotensive resuscitation' is a strategy whereby fluid resuscitation is deferred or restricted until such time as control of haemorrhage is achieved while accepting a limited period of sub-optimal end-organ perfusion.[32] The concerns regarding large volume crystalloid resuscitation are well founded and there are abundant pre-clinical data favouring hypotensive resuscitation in uncontrolled haemorrhage.[33] However, there is currently only limited trial evidence in humans to support this approach.

The largest trial, conducted in a single centre in Houston, Texas by Bickell and colleagues in 1994, recruited 598 non-head-injured hypotensive patients (SBP <90 mmHg) with penetrating torso trauma into 'delayed' (until arrival in the operating room) or 'immediate' resuscitation groups. They demonstrated an 8% absolute reduction in mortality ($p = 0.04$) and a trend towards reduced complications in the 'delayed' resuscitation group ($p = 0.08$).[34]

There were a number of methodological weaknesses in this trial, including absence of allocation concealment (patients were not randomised, but instead were allocated to alternate treatment arms on alternate days) and significant crossover between the groups (8% of patients allocated to the 'delayed' resuscitation arm were inadvertent administered fluid). Patients with a revised trauma score of 0 were excluded from analysis, as were those with 'minor injuries' not requiring surgical exploration. In total, 44% of all hypotensive patients with penetrating torso injuries included in the trial were subsequently excluded from analysis, limiting the validity of the trial. It is also worth noting that pre-hospital transport times were very brief, limiting applicability in other settings.

Two further trials in patients with blunt trauma, or a mixture of blunt and penetrating trauma, failed to show benefit with a permissive hypotension strategy.[35,36] Significant methodological flaws thwarted interpretation of the results in both trials. A Cochrane review, incorporating these trials *'found no evidence from randomised controlled trials to support early or larger volume of intravenous fluid administration in uncontrolled haemorrhage'* and commented that: '*there is continuing uncertainty about the best fluid administration strategy in bleeding trauma patients'*.[37]

There is currently a paucity of trial evidence supporting permissive hypotension. In particular, the depth and duration of hypotension that may be tolerated is not known and its role in sub-groups such as those with traumatic brain injury has not been defined. Furthermore, there are pre-clinical data suggesting harm from prolonged hypotensive resuscitation in a blast injury model.[38] Despite these concerns, permissive hypotension is considered a cornerstone of DCR and has been incorporated into resuscitation guidelines worldwide.[29] While there is no human trial evidence of harm from this strategy, it is not currently recommended in patients with concomitant or isolated head injury, in view of concerns

regarding the significant deleterious effects of hypotension in this population.[29]

Limitation of crystalloid and early use of blood products

The rationale for limiting crystalloid use has been outlined above. It is an often quoted tenet of fluid resuscitation that fluid losses should be replaced 'like for like'. It is logical, therefore, to conclude that massively bleeding patients should receive volume replacement with blood. By contrast, transfusion of blood to those without significant haemorrhage would unnecessarily expose them to the risks of transfusion. This is clearly not desirable; however, rapidly distinguishing between these groups is not straightforward.[39] Scoring systems have been developed in both civilian and military settings to facilitate this clinical decision.[39,40] The 'Assessment of Blood Consumption score' (ABC score) is one such strategy. This uses four dichotomous, non-weighted parameters that are available early in the course of trauma assessment (Table 1) and can correctly classify patients with reasonably accuracy (area under receiver-operating characteristic curve > 0.83)[41] and acceptable 'over-triage' rates.[7]

The early experience of transfusion for major haemorrhage was with fresh whole blood; however, after World War II, the fractionation of whole blood into its components became widely accepted. The transition to 'component therapy' provided logistic and safety advantages but occurred with very few supporting clinical trials[42] and none in the setting of trauma haemorrhage.[43] In the modern era, transfusion of whole blood in trauma has largely been confined to military settings. There is observational data demonstrating an association with improved outcomes in military trauma when compared with component therapy.[44,45] A small pilot randomised trial of modified whole blood *versus* component therapy in civilian practice showed no significant differences in the primary end-point of transfusion volumes at 24 h.[43] A larger randomised study assessing the effect on mortality is proposed.[42]

Outside of the research setting, however, current civilian transfusion practice for trauma haemorrhage is synonymous with component therapy. Therefore, as well as using blood early in the resuscitation of major haemorrhage, attention must be given to the ratio of blood components used. Borgman et al.[16] first described the association between higher ratio of fresh frozen plasma (FFP) to packed red cells (PRCs) and survival in 2007. In a retrospective review of 246 combat casualties requiring massive transfusion they compared three groups according to the ratio of FFP to PRCs transfused. The authors demonstrated a 46% reduction in absolute mortality ($p < 0.001$) for those treated with the highest FFP:PRC ratio (median ratio = 1:1.4) when compared with those treated with the lowest ratio (median ratio = 1:8). Subsequent to this, several large retrospective reviews, including civilian trauma registries, replicated these findings.[46–51] However, given that there is usually a significant time lag between transfusion of PRCs and the availability of FFP, all these retrospective studies of transfusion ratios are potentially invalidated by the effect of survival bias (i.e. cannot differentiate whether patients survived because they received high-ratio transfusions or whether they receive high-ratio transfusions because they were still alive to receive FFP). Snyder et al.[52] examined the confounding effect of survival bias on retrospectively reviewed transfusion data and concluded that no benefit was demonstrable when survival bias was accounted for and that prospective trial data were necessary to demonstrate the true effect.

The prospective, observational, multi-centre, major trauma transfusion study (PROMMTT), published in 2013, examined the in-hospital mortality of 1245 trauma patients receiving transfusion within 6 h of admission. This study gave a number of insights into the time course of trauma haemorrhage as well as contemporary transfusion practice in the 10 participating U.S. Level 1 trauma centres; 60% of all haemorrhagic deaths occurred within 3 h and 81% within 6 h of admission. Most patients received a FFP:PRC ratio of 1:2 or higher by 3 h and a platelet:PRC ratio of 1:2 or higher by 6 h, indicating the intention to adopt DCR principles in these centres. However, 10% of patients did not receive FFP and 28% did not receive platelets within the first 3 h (peak time interval for haemorrhagic

Table 1. Assessment of blood consumption (ABC) score.

Component	Score	
Penetrating mechanism of injury	Yes = 1	No = 0
Systolic BP in emergency department ≤90 mmHg	Yes = 1	No = 0
Heart rate in emergency department ≥120 bpm	Yes = 1	No = 0
Focused abdominal sonography in trauma (FAST) scan	Positive = 1	Negative = 0

Note: Possible range of scores: 0–4. Total score ≥2 is predictive of need for massive transfusion.[40,41]

death) and patients did not receive a constant ratio during the period of active resuscitation. The most significant finding of this study was that early infusion of higher plasma and platelet ratios was associated with decreased mortality within 6 h of admission (i.e. within the timeframe in which it is anticipated that haemorrhagic death might be influenced).[53]

The first randomised clinical trial comparing transfusion ratios, the PROPPR trial, was published earlier this year. This pragmatic multi-centre trial randomised 680 severely injured patients that were predicted to require massive transfusion to receive plasma, platelets, and packed red blood cells in a 1:1:1 ratio compared with a 1:1:2 ratio. It is worth noting that there were differences, not only in the ratios, but also in the order in which products were administered. In the 1:1:1 arm, platelets were transfused first, followed by alternating units of PRCs and plasma. By contrast, those in the 1:1:2 arm first received platelets after six PRCs and three units of FFP had been transfused.

There were no significant differences in mortality at 24 h or at 30 days; however, more patients in the 1:1:1 group achieved haemostasis and fewer experienced death due to exsanguination by 24 h. There were no differences between the groups in terms of complications.[54]

Given the physiological rationale for high ratio resuscitation (i.e. to help effect haemostasis in bleeding patients), the short timeframe in which haemorrhagic deaths occur (median 2.6 hours following admission in PROMMTT and 2.3 h in PROPPR) and the anticipated diminution of any treatment effect at longer follow-up intervals (due to competing risks from non-haemorrhagic death), successful achievement of haemostasis can be considered a valid end-point. To this end, PROPPR might provide justification for on-going 1:1:1 ratio resuscitation in bleeding trauma patients. The significance of the 'platelet first' transfusion protocol in the 1:1:1 arm of this trial is not known but might limit the validity of generalising the results to contemporary transfusion practice.

When considering transfusion ratios, it is worth noting that transfusion of PRCs, FFP, and platelets in a ratio of 1:1:1, which is often termed 'reconstituted whole blood', does not replicate whole blood. Rather, it produces a relatively anaemic, thrombocytopaenic, and coagulopathic solution[42] with a haematocrit <30%, platelet count of approximately 80×10^9/l and with coagulation factors diluted to approximately 60% of their usual concentration.[55] Fibrinogen concentrations are particularly depressed.[56] Although in vitro functional testing of this 'reconstituted whole blood' has demonstrated relatively normal thromboelastometric parameters,[56] functional effects in vivo are not known.

This raises further questions in relation to optimal composition of component therapy. Pre-defined protocolised delivery of blood products in the form of 'massive transfusion protocols' has been widely adopted worldwide[53] and their use has been associated with a reduction in multi-organ failure, infectious complications, and mortality when compared with historical transfusion practices.[20,57]. However, an alternative strategy is that of individualised 'goal-directed coagulopathy management'.[58] This strategy employs near-patient visco-elastic testing with thromboelastograpy (TEG®) or thromboelastometry (ROTEM®) to guide blood product usage. A potential advantage of near-patient visco-elastic testing is its additional value in predicting massive transfusion requirement.[59] Furthermore, advocates of goal-directed coagulation management favour use of purified coagulation factor concentrates over FFP.[58] These can be administered in an individualised manner to target specific deficiencies and have a number of advantages over FFP: they can be stored for immediate use, do not require cross-matching, and carry minimal risk of infection or transfusion-related acute lung injury.[60] There is, however, currently inadequate evidence to assess the efficacy of this strategy and there are no clinical trials comparing targeted versus empirical transfusion.[61]

TXA

TXA is the only intervention in bleeding trauma patients for which there is good quality randomised control trial evidence of mortality benefit. The CRASH 2 trial randomised 20,211 patients in 40 countries who were bleeding or considered 'at risk of bleeding' within 8 h following trauma to receive TXA or placebo. The trial demonstrated a highly significant 1.5% reduction in absolute mortality (relative risk of death 0.91, relative risk of death due to bleeding 0.85) with no excess of vascular occlusive events.[62] Post hoc analysis of prospectively defined sub-groups by the trial collaborators revealed a considerable influence of time to administration of TXA on outcome. Maximal benefit was derived when TXA was administered within 1 h of injury and there was evidence of potential harm when administered ≥3 h post injury.[63] The mechanisms by which TXA exhibits effects following trauma may not be limited to inhibition of fibrinolysis and may also include modulation of plasmin-mediated inflammation and neurotoxicity.[64]

Recombinant factor VIIa

Recombinant factor VIIa (rFVIIa) (NovoSeven®) is activated recombinant factor VII, a drug developed and licensed for the treatment of patients with haemophilia A and B with antibodies against factor VIII and factor IX. Though heavily utilised 'off label' in the

formative years of application of DCR, its use is no longer recommended and the history of its widespread adoption into trauma care without adequate supporting evidence is a cautionary tale.

The first description of rFVIIa use in trauma was a case report published in the Lancet in 1999 of a severely injured Israeli soldier with apparent resolution of coagulopathy and bleeding following repeated administration.[65] Despite a dearth of evidence to support its use in trauma, the next decade saw an explosion in its unlicensed use, such that by 2008, rFVIIa was incorporated into the massive transfusion protocols of three quarters of U.S. Level 1 trauma centres[66] and was administered to 22% of massively transfused U.S. civilian trauma patients as well as one quarter of all U.S combat casualties in Iraq.[67] The manufacturers saw a 140-fold increase in sales of the drug and by 2008, 97% of rFVIIa use in the United States was 'off-label', predominantly in trauma patients.[68]

Neither of the two randomised control trials of rVIIa in trauma found a mortality benefit for the drug, though a reduction in transfusion requirement was observed following severe blunt trauma.[69,70]. The latter of the two trials, the CONTROL trial, aimed to recruit 1502 patients but was abandoned on the grounds of futility after enrolling just over one third of the planned cohort. Meta-analysis of RCTs of rFVIIa use off-label raised significant safety concerns concerning arterial thrombotic events[71] and a Cochrane review of off-label use in 2012 recommended that use be restricted to clinical trials.[72] There has been considerable controversy regarding the rFVIIa use in trauma, not least legal proceedings against Novo Nordisk by the U.S Justice Department and its subsequent payment of $25 million to resolve its civil liability arising from illegal promotion of off-label use. The debate surrounding the use of rFVIIa in trauma is undoubtedly complex and emotive[68]; however, it is difficult to justify its on-going routine use in non-haemophiliacs.

Damage control surgery

Integral to the success of DCR is the rapid control of haemorrhage. While DCR may offer several advantages over historical strategies, there is robust evidence that it fails to correct either hypoperfusion or coagulopathy in the absence of mechanical control of haemorrhage.[73] To this end, early and appropriate application of damage control surgery is a cornerstone of the modern DCR paradigm.

DCS is a surgical strategy for managing a subset of the most severely injured patients, in whom immediate steps to restore physiology are required to save life and in whom lengthy attempts to restore anatomical integrity are likely to fail. DCS therefore limits the goals of the initial operation to control of haemorrhage and limitation of contamination. Originally synonymous with 'abbreviated laparotomy' following abdominal trauma, damage control surgery principles have also successfully been applied following: thoracic trauma,[74–77] penetrating neck trauma,[78] and peripheral vascular injuries.[79]. In addition, damage control principles have been adopted in non-traumatic abdominal emergencies in order to reduce mortality compared with primary definitive surgery.[80,81]

Origins of DCS

DCS arose from the observation that massively injured patients lack the physiological reserve to survive complex and prolonged definitive or reconstructive surgery.[82] The earliest application of this principle could be considered in terms of medieval battlefield amputations[25] but the first description of intra-abdominal packing, a cornerstone of modern damage control laparotomy, can be credited to Joseph Pringle. In his seminal paper, 'Notes on the arrest of hepatic haemorrhage due to trauma,' published in 1908, he described the technique of peri-hepatic packing.[82] Halsted later refined this, suggesting placement of rubber sheets between the packs and liver to protect the liver parenchyma.[83] However, in the ensuing decades, packing was regarded as poor surgical care[84] and the technique was all but forgotten in the middle part of the last century.[85]

Lucas and Ledgerwood[86] described the management of 637 patients treated for liver injuries in Detroit. Just three of these patients underwent packing and subsequent re-operation but all three survived. Calne et al.[87] described four cases in whom primary packing was employed at a district general hospital prior to transfer of patients to Addenbrooke's hospital in Cambridge for subsequent management. All four survived and the authors clearly described the rationale behind damage control surgery, stating:

> The management of liver trauma should be to do the minimum that is necessary to staunch bleeding by suture, arterial ligation . . . . . or simply by packing. This allows the patient's haemodynamic state to be restored to normal before further surgery is attempted.[87]

Nonetheless, it is usually Stone et al.[9] that are credited with 'inventing' damage control surgery. They described a technique of 'truncated laparotomy' for patients with clinically evident coagulopathy and retrospectively reviewed its efficacy in 1983. Rotondo[10] subsequently popularised the term *'damage control'*. The term has its origins in American naval literature, referring to the ability of a ship to absorb damage while

maintaining mission integrity and highlights the primacy of function over form.[88]

Early evidence supporting DCS

Stone et al. retrospectively reviewed the management of 31 trauma patients (80% with penetrating injuries) that developed clinically evident coagulopathy during laparotomy. They described the survival of 11 of 17 patients (65%) in whom laparotomy was terminated as soon as possible after onset of coagulopathy. They employed a technique in which only major vascular injuries were formally repaired with ligation of resected bowel ends without 'ostomies' and purse-string closure of G.I. and bladder perforations. The abdomen was packed and closure was carried out 'under considerable tension'. This contrasts with current practice of laparostomy. Packs were left in situ and definitive repair was delayed for 15–69 h (average 27), during which time patients were managed on intensive care unit (ICU) and coagulopathy was addressed. Survival in this group was favourable when compared with survival of 1 of 14 (7%) historical controls, attending the same institution in the preceding three-year period, in which definitive surgery was attempted.[9]

Rotondo retrospectively reviewed the management of 46 patients undergoing laparotomy for exsanguinating penetrating injuries (requiring urgent transfusion of > 10 units PRCs); 22 patients underwent definitive laparotomy while a further 24 patients underwent a damage control procedure over the course of a three-and-a-half year period. There were no statistically significant differences between the groups in terms of baseline characteristics, including physiology, and there was no difference in survival. The authors did, however, identify a subset of 22 maximally injured patients (major vascular injury with two or more visceral injuries) in which survival was markedly improved in the damage control group (10 of 13 versus one of nine, $p < 0.02$).[10]

Establishment and evolution of DCS

There are no prospective trials of DCS and the nature of the cohort for whom DCS is advocated (subset of trauma patient that are exsanguinating due to massive injuries) might preclude these. Supporting evidence is available only from observational studies; however, the principles were widely accepted and it rapidly became established as standard of care for severely injured patients.[89] A review of the cumulative literature just five years after Rotondo's seminal paper described more than a thousand patients that were managed in this manner and reported a survival and major morbidity rates of 50% and 40%, respectively.[11] A single centre, prospective study with long-term follow up has demonstrated survival in excess of 71% following damage control laparotomy, with 81% of survivors returning to work and resuming normal activities.[90]

Rotondo et al.[10] originally detailed a three-phase approach. However, Johnson and Schwab[91] subsequently described a fourth (pre-operative) phase, which they termed 'damage control ground zero'. In addition, definitive abdominal closure is considered separately from the 'definitive care' phase of injury management.[92] Thus, the modern damage control sequence can be considered in five phases[79,92,93] as outlined below.

Damage control ground zero (DC0)

This pre-operative phase emphasises injury-pattern recognition and early selection of candidates likely to benefit from damage control surgery. Truncated scene times, direct transport to regional trauma centres, DCR, judicious use of imaging to localise sites of bleeding, and expedient transport to the operating theatre are the key elements.

Damage control part 1 (DC I)

This consists of immediate exploratory surgery with rapid control of 'mechanical haemorrhage' and visceral contamination before physiological exhaustion ensues.[93] Cell salvage should be in place to maximise autologous blood capture and return. A recent Cochrane review identified only a single randomised trial of cell salvage in the setting of trauma.[94] In this small trial ($n = 44$) of patients with penetrating trauma requiring laparotomy, almost 80% had sustained bowel injuries and no increase in infection rates or mortality was observed following cell salvage.[95] While this trial might well have been underpowered, on the basis of currently available data, enteric contamination does not appear to preclude cell salvage.

Rapid haemorrhage control may be achieved by: ligation, packing, vascular shunts,[96] stapling devices, or balloon catheter tamponade.[97] Adjunctive use of intra-cavity haemostatic agents may also have a role.[98] Temporary wound closure is the norm. Adjunctive angioembolisation should be considered following DC I, and may have particular use following high-grade liver injury[99] and when a non-expanding retroperitoneal haematoma has been identified.[100]

Damage control part 2 (DC II)

This is the ICU resuscitative phase where re-warming and restoration of physiology are achieved. Persistent elevation of lactate suggests under-resuscitation and/or

on-going bleeding and is predictive of infectious complications and mortality[101,102] However, targeting lactate as an end-point for resuscitation has not been demonstrated to improve survival.[103] On-going transfusion of blood products may be targeted according to thromboelastography or conventional laboratory indices. Once bleeding has been controlled and indices of coagulation and haematocrit have normalised, patients may still have significant on-going fluid requirements that do not need to be met with further use of blood products. However, limitation of fluid resuscitation may reduce bowel oedema and subsequent adverse effects, including abdominal compartment syndrome.[79] When considering choice of fluid: there is no evidence to support the superiority of any crystalloid or colloid over another in trauma patients.[7] Failure to achieve physiological recovery may indicate on-going haemorrhage and should prompt consideration of return to theatre or angioembolisation. A detailed examination and review of available imaging is also performed during this phase to identify injuries. Consideration may be given to transfer for additional imaging. This should only occur where imaging might significantly alter management and the benefits are judged to outweigh the risks of transfer.

Damage control part 3 (DC III)

This occurs once physiology has normalised and consists of re-exploration in theatre to perform definitive repair of all injuries. The timing of DC III is dependent on the individual patient's physiology. An association has been demonstrated between a short interval from DCI to DC III, and success of primary fascial closure[104] but the goal should be to resuscitate the patient to within normal physiologic parameters prior to undertaking DCIII. Where possible, definitive procedures should be performed prior to pack removal, as re-bleeding following pack removal may prevent completion of the intended operation.[79] Thorough intra-operative evaluation is required as the incidence of missed injuries is high.[105] DC III may require several separate visits to theatre to complete.

Damage control part 4 (DC IV)

Once all of the repairs are completed, formal abdominal closure without tension is the challenging final step in the planned reoperation sequence. If gentle adduction allows the fascial edges to approximate, a standard fascial closure should be possible. However, persistent oedema within the retroperitoneum, bowel wall, and abdominal wall may render primary closure impossible. Should peak airway pressure rise by greater than 10 cm H_20 during temporary fascial approximation, it is suggested the fascia be left open[106] and the temporary abdominal closure device be replaced. In this setting, aggressive diuresis is implemented, as tolerated, with the aim of reducing bowel and body wall oedema in a bid to facilitate early definitive closure. If fascial closure is not achieved after seven days, the surgeon faces a number of alternatives to cover the abdominal defect, but will likely leave the patient with a large ventral hernia.[107] This may be repaired at a later date.

Indications for damage control surgery

Appropriate patient selection for damage control surgery is critical. Attempts to undertake primary definitive surgery in patients with physiological exhaustion will inevitably lead to poor outcome or unplanned abbreviation of the procedure. By contrast, excessively liberal use of DCS may deny patients with adequate physiological reserve the benefits of early definitive surgery and expose them to unnecessary additional procedures with attendant risks. These risks include higher rates of intra-abdominal infection, fistula formation, and abdominal wall herniae,[90,108,109] as well as significant resource implications for theatres and ICU.

Rotondo and Zonies[89] described 'conditions, complications, and critical factors' to guide patient selection (Table 2) but no single 'physiological threshold' has been defined.

These indications were defined in the era of conventional fluid resuscitation. It has been suggested that DCR, by direct targeting of the lethal triad, might obviate the need for damage control surgery[25] allowing definitive surgery to be completed at the primary

Table 2. Conditions, complications, and critical factors guiding selection for damage control surgery.

Conditions
• High-energy blunt torso trauma
• Multiple torso penetrations
• Hemodynamic instability
• Presenting coagulopathy and/or hypothermia
Complexes
• Major abdominal vascular injury with multiple visceral injuries
• Multifocal or multi-cavitary exsanguination with concomitant visceral injuries
• Multi-regional injury with competing priorities
Critical factors
• Severe metabolic acidosis (pH < 7.30)
• Hypothermia (temperature <35°C)
• Resuscitation and operative time >90 min
• Coagulopathy as evidenced by development of non-mechanical bleeding
• Massive transfusion (>10 units packed red blood cells)

Reproduced from Rotondo and Zonies.[89]

operation and there is some evidence to support this evolution.[23,24] In this context, traditional 'indications' might not hold true in the current era.

Non-surgical haemorrhage control

Foley catheter balloon tamponade is an established resuscitative technique for temporary haemorrhage control, most notably following penetrating neck injuries and 'junctional' trauma[97,110,111] and may buy time to allow transport, initiation of resuscitation, and establishment of vascular control.

Transcatheter arterial embolisation is a minimally invasive procedure with an established role for the management of selected traumatic injuries,[112] including haemodynamically unstable patients with pelvic fractures.[113] Deployment of endovascular stent grafts is an alternative to surgery, especially for the aorta and its major branches.[114] Stenting of major veins for haemorrhage control is also feasible.[115] Combined angiographic and surgical approaches, ideally in the setting of dedicated 'hybrid' suites, could provide advantages for exsanguinating patients with multiple injuries and especially for management of major vascular, high-grade liver, or pelvic bleeding.[7]

Finally, resuscitative endovascular balloon occlusion of the aorta (REBOA) has been proposed as a novel strategy for emergent haemorrhage control in exsanguinating trauma. Evidence supporting REBOA is limited to pre-clinical trials and a handful of observational studies. The largest of these reported REBOA use in 452 of 45,153 patients registered in the Japan Trauma Data Bank over eight years up to 2011. REBOA use was associated with mortality of 75%, probably indicating it being used as a 'last ditch' effort.[116] In 2014, London's air ambulance reported the first successful use of REBOA in the pre-hospital setting. Although attractive as a means of rapid reduction of haemorrhage, it is clear from limited published case series that significant complications may ensue[117] and current data would support judicious rather than liberal application of the technique.[118] The American Association for the Surgery of Trauma (AAST) are supporting a prospective observational study (Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery – AORTA trial) to further inform its use.

Conclusion

The last decade has seen the advent of a new resuscitative paradigm termed DCR. This strategy compliments the established principles of damage control surgery. There is, however, limited evidence to support these approaches and much of our current practice is based on weak observational evidence. As our knowledge of the pathophysiology of massive haemorrhage increases and technology advances, it is hoped that rational treatment protocols will continue to be refined. To this end, we should aim to perform high-quality randomised controlled trials and co-ordinate research efforts. A number of priority areas require to be addressed and these include:

- The role of permissive hypertension in trauma patients, including head injuries.
- Which patients benefit from DCR and what are the optimal strategies to use?
- Which blood products should be used and in which manner?
- What is the role of near-patient testing such as thromboelastometry in guiding therapy?
- Which patients benefit from DCS in the era of DCR?
- What role is there for novel therapies, including radical new treatments such as REBOA?

CRASH-2 and PROPPR have demonstrated that large, high quality, and multi-centre trials are feasible in the setting of trauma haemorrhage and that efficacy of current interventions, in terms of hard end-points, can be assessed.

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