

Review Article

Fluid therapy in trauma resuscitation : A review of changing practices.

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Abstract

Background: Haemorrhage is the leading preventable cause of post trauma death. Acute trauma resuscitation has evolved over the last decade. The ATLS guidance used since 2012 is being updated in 2018.

Objectives : To search relevant representative literature over 6 years between 2012 and 2018 to gain an insight into changing concepts, practices and recent advances in acute trauma fluid resuscitation and provide a structured review of the topic.

Search methods: A relevant MEDLINE search was undertaken to obtain a list of 1512 articles from which 107 were utilised to prepare this review.

Selection criteria: 1. Inclusion: Articles from human medicine relevant to fluid resuscitation in trauma published in English between January 2012 and January 2018. **2. Exclusion:** Articles restricted to Brain, spinal trauma or cardiovascular trauma, post traumatic arrest patients, animal or human laboratory model studies and articles on septic, postoperative, obstetric patients and single case studies were excluded.

Results: This review categorises the topic into various parts to explain the evolving understanding of fluid resuscitation, trauma induced coagulopathy and endotheliopathy of trauma. The strategies for acute fluid management like damage-controlled resuscitation, balanced and haemostatic resuscitation and massive transfusion protocol are explained. A detailed discussion is carried out regarding crystalloid, colloid and blood transfusion. Special consideration is given to specific age groups, combat casualties and prehospital trauma care.

Conclusions: Fluid resuscitation in trauma is a complex and rapidly evolving subject. Massive transfusion protocols and principles of damage control are significant for patient outcome. Standard guidance like ATLS is relevant and important for training professionals to deliver systematic, high quality of trauma care. There is scope for local improvisation based on resources and need for more high-quality trials and frequent systematic reviews.

Introduction

More than 5 million people die annually as a result of trauma, which accounts for nine percent of global mortality¹.

Death due to injury occurs in three periodical peaks. The first peak within seconds to minutes of a catastrophic injury like severe brain or high spinal injury and is rarely salvageable. The second peak within minutes to several hours post trauma and is usually associated with severe blood loss. The third peak occurs days after injury and is attributed to sepsis and multi organ dysfunction. In this trimodal distribution², the second peak is where the golden hour of trauma care is advocated as a means of rapid assessment and resuscitation by several structured guidelines of which the Advanced trauma life support (ATLS) developed by the American College of Surgeons is widely accepted.

Haemorrhage is the leading preventable cause of post trauma death³. Identification of the source of bleed, controlling

ongoing blood loss and restoring the lost volume are the three major components of management.

The understanding of the pathophysiological mechanisms and implementation of strategies to counteract traumatic haemorrhage has undergone a significant change in the last decade. The data from recent combat casualties have led to trials testing its recommendations on civilian population. There is marked variability in population profile, baseline health, demographic characteristics and resource availability in many of the trials and research methods concerning early resuscitation in trauma care and hence there are conflicting results and inferences.

The vast literature over the years have led to rapidly changing recommendations in trauma care. The ATLS guidance currently used since 2012 is being revised in 2018⁴. Because of the complexity and multifaceted nature of trauma care along with widespread differences in infrastructure across the globe it is apparent that standard of care, local implementation and applicability of international recommendations are not uniform.

The current article tries to present the established fluid resuscitation practices in acute post major trauma care and also attempts to provide an overview of changing concepts based on a review of representative literature over the last six years.

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Objectives:

1. To review the representative literature relevant to acute fluid resuscitation in trauma over the last six years and correlate the changing research trends in this field with the updated recommendations mainly based on ATLS guidelines between 2012 and 2018.
2. To provide a synopsis of current understanding and established practices of acute fluid resuscitation in trauma and contrasting them with recent updates, their relevance and barriers in local implementation.

Methods:

A MEDLINE search was carried out with the following search term

(traum* OR bleed* OR injur* OR hemorrhag*)AND(fluid* OR resuscit* OR crystalloid* OR colloid* OR blood)

This search was filtered with the term

[DT 2012-2018] [Abstracts] [Document type Case Reports OR Classical Article OR Clinical Study OR Clinical Trial OR Comparative Study OR Controlled Clinical Trial OR English Abstract OR Guideline OR Journal Article OR Meta-analysis OR Multicenter Study OR Observational Study OR Practice Guideline OR Pragmatic Clinical Trial OR Randomized Controlled Trial] [Languages English] [Humans]

The resulting 1512 articles were manually sorted based on their titles or abstracts wherever necessary with the following criteria:

Inclusion criteria:

1. Articles related to human medicine relevant to fluid resuscitation in trauma published in English between 2012 and 2018 (till 28 Jan 2018).

Exclusion criteria:

1. Articles specifically on brain and spinal cord trauma OR specifically on cardiac surgery or cardio vascular trauma.
2. Articles were population comprised only of post trauma cardiac arrest patients.
3. Studies on simulated trauma models either animal or human volunteers
4. Non human studies.
5. Articles on sepsis, post operative, obstetric OR non traumatic bleed.

The search was filtered to obtain 291 articles that were considered relevant for this topic. Their analysis revealed that a further 103 articles needed to be discarded based on the inclusion or exclusion criteria or were animal or laboratory models or were single case studies.

Results:

Finally, the abstracts and available full texts along with included references wherever necessary of the 107 (Figure 1) selected articles were utilised to prepare the current review article.

Discussion:

1. Principles of fluid resuscitation and changing practices

Improved survival from trauma associated with a trend for more blood products and less crystalloids during resuscitation have been explained by newer concepts⁵.

1.a. Trauma Induced Coagulopathy (TIC)

Coagulopathy has been taught as a late consequence of injury resuscitation⁶. The current understanding is that severe traumatic injury causes an endogenous coagulopathy⁷ secondary to oxygen debt and classic resuscitation strategies based on crystalloid or colloid⁷. This creates a rationale for procoagulant resuscitation⁶.

1.b. Endotheliopathy of Trauma⁸

Recent advances in understanding inflammatory modulation and end organ failure in trauma have important clinical implications. This includes imbalanced proinflammatory and anti-inflammatory responses, acute coagulopathy of trauma, and endovascular glycocalyx degradation with microcirculatory compromise⁹. These abnormalities are all interlinked and concomitant, not sequential and their resolution is an active process. Plasma based resuscitation is said to repair this endotheliopathy⁸.

1.c. Global Increased Permeability Syndrome (GIPS)¹⁰

The initial insult of trauma is followed by 'ischaemia reperfusion injury' and postinjury oedema. This phenomenon is considered a resultant of high volume fluid resuscitation. It can cause complications such as secondary intra-abdominal hypertension, abdominal compartment syndrome, cardiac dysfunction etc. The proponents of colloids, hypertonic saline or hyper oncotic albumin solutions to restore intravascular volume with less administered fluid have used this to debate against isotonic crystalloids.

1.d. Coagulopathy without the lethal triad¹¹

The lethal triad of coagulopathy, hypothermia and acidosis has been classically recognised to have fatal outcomes in severe trauma. Haemodilution has been regarded as an important factor for coagulopathy. As explained above coagulopathy is being recognised in the absence of these other factors. Coagulopathic patients have been found to have more severe injury (based on injury severity score, ISS), more base deficit, raised lactate levels, lower admission temperature, lower pH and higher prehospital crystalloid volume. They also have more need for blood product transfusion, mechanical ventilation and higher rates of nosocomial infections, multiorgan failure and mortality. This knowledge warrants more biochemically targeted strategies for trauma management.

2. Evolving management strategies

Many strategies have been put forth for acute trauma management. They are not well defined and studies have been carried with local pathways that vary.

2.a. Hemostatic resuscitation

The understanding of trauma induced coagulopathy¹² and dilutional coagulopathy has given rise to the concept of hemostatic resuscitation which involves early coagulation therapy combined with permissive hypotension. Minimising crystalloid volumes has shown to reduce mortality and morbidity¹³. These strategies still do not overcome hypoperfusion and acute coagulopathy.

2.b. Damage Control Resuscitation (DCR)^{14,15}

Utilizes the concepts of haemostatic resuscitation and permissive hypotension till bleeding is controlled. It includes a goal directed correction of coagulopathy and crystalloids being increasingly replaced by plasma. Damage control surgery¹⁶ with a priority for haemorrhage and contamination control is undertaken before patient is stabilised for definitive surgery.

2.c. Balanced resuscitation

This is the strategy preferred for fluid resuscitation in DCR in order to minimize the impact of trauma-induced coagulopathy¹⁷. The key principles are to limit crystalloid use and transfuse blood products early in ratios similar to whole blood. Organ perfusion and risk of bleeding are balanced usually by employing permissive hypotension.

2.d. Massive transfusion protocol (MTP)

Conventional transfusion triggers like haemoglobin levels are not appropriate for post trauma emergencies¹⁸. Early transfusion triggers based on vital signs, blood gas results, injury patterns and anticipated major bleeding are appropriate. Delays in blood transfusion as short as 10 minutes have been found to be associated with increased odds of death¹⁹. A protocolised approach and activation of early transfusion reduces delay and improves mortality and reduces complications of aggressive crystalloid resuscitation¹⁷.

2.e. MTP/ Major Haemorrhage protocols guided by Thromboelastometry

Both early hyper and hypocoagulability in severely injured patients are associated with increased mortality²⁰. Standard doses of blood components may not consistently correct trauma-induced coagulopathy during haemorrhage. Studies with goal directed usage of different products like FFP, cryoprecipitate and platelet therapy with a high total fibrinogen load have been shown to provide consistent improvement in coagulation. This can be achieved by incorporating dynamic point of care thromboelastometry²² tests like TEG and ROTEM into MTP. This modification to MTP has shown reduction in mortality²³ related to trauma haemorrhage and also reduces wastage of blood products²⁴.

2.f. Permissive hypotension and perfusion

Permissive hypotension^{25,26} and DCR are strongly advocated for better patient outcomes until definitive haemostasis is obtained, after which focus should change to targeted resuscitation using traditional global endpoints of resuscitation to enhance global and regional perfusion.

Even in the acute state permissive hypotension may not be suitable for traumatic brain injury, pregnant patients, children and elderly patients especially with chronic hypertension.

2.g. Fluid volume

There is no clear evidence from randomised controlled trials for or against early or larger volume of intravenous fluid administration in uncontrolled haemorrhage²⁷. Although many trials have shown higher mortality²⁸ with initial liberal fluid resuscitation there is a higher possibility of selection bias and clinical heterogeneity in these trials. A balance between preventing shock and risk of bleed is an individualised clinical judgement.

3. Type of fluid

3.a. Isotonic and balanced Crystalloids

Crystalloids are the conventional first fluids to be infused in trauma. Hartman's solution/ Ringer's Lactate (RL) have been advocated over Normal saline (NS) which can cause hyperchloremic acidosis. Balanced solutions like RL or Plasmalyte A have shown better acid base status compared to NS at 24 hours²⁹. There is no clear evidence that clinical outcomes differ between commonly used crystalloids. Lactated solutions with D isomer have been associated with worse mortality and need for ventilation compared to L-Lactate³⁰.

Crystalloid resuscitation has been associated with ARDS³¹, abdominal compartment syndrome, cerebral oedema, and anasarca causing substantial increase in morbidity, length of hospital stays and need for intensive care³² especially in blunt injury³³. Although many of the study groups also had a higher Injury severity³⁴ which could have been a confounder. Crystalloids have been implicated in iatrogenic worsening of the lethal triad³⁵ due to marked acidosis. RL is associated with elevated lactate levels and NS worsens the base deficit.

3.b. Hypertonic saline

3% and 7.5% hypertonic saline have been found useful in traumatic hypovolemic shock by rapid restoration of mean arterial pressure and improved cardiac function and lesser rates of renal failure, coagulopathy and pulmonary oedema with about 50% lower required volume compared to RL³⁶. 7.5% saline has higher rates of complications like arrhythmia and hypernatremia compared with 3% saline.

Hypertonic resuscitation fluids with or without dextran have shown mortality benefits, inhibition of post traumatic inflammation and reduced multi organ dysfunction syndrome in animal models but there is no evidence of mortality benefit over isotonic crystalloids in human trauma patients^{37,38}.

Prehospital studies indicate that hypertonic solutions especially with dextran worsen hypercoagulability and hyperfibrinolysis after haemorrhagic shock causing imbalance in procoagulant-anticoagulant and profibrinolytic-antifibrinolytic activities³⁹.

3.c. Colloids

Colloids have been associated with increased mortality in critically ill septic patients but there is no clear evidence in trauma⁴⁰ for colloid related mortality in general except for pentastarch. Studies on blunt trauma have found Hydroxyethyl starch to be an independent risk factor for death⁴¹. Colloids are associated with acute kidney injury requiring renal replacement therapy (RRT) and the development of SIRS and sepsis in multiply injured patients⁴².

4. Blood transfusion

4.a. Transfusion practices

Advances in blood banking in 1970s caused blood components to abruptly replace⁴³ availability of whole blood (WB) without any studies in haemostatic potential on trauma patients. Introduction of MTP, studies favouring WB and the uncertainty regarding the ideal blood component ratio are all debatable issues⁴⁴. The need for appropriate and timely transfusion strategies has favoured involvement of transfusion medicine specialists in decision making and designing local pathways⁴⁵. Moreover, advanced practices like viscoelastic diagnostics, coagulation factor concentrate-based therapy and washed cell salvage may reduce the number of allogeneic blood transfusions.

4.b. Ratio of blood components

The PROPPR RCT found that early administration of RBC: Plasma: Platelets in 1:1:1 ratio compared with a 2:1:1 ratio did not result in significant differences in mortality at 24 hours or at 30 days⁴⁶. However, more patients in the 1:1:1 group achieved haemostasis and fewer experienced death due to exsanguination by 24 hours. Other studies^{47,48,49} have found a greater survival benefit from high ratios but have also found an association with higher rates of multiple-organ failure. There is reasonable debate regarding the validity of studies advocating 1:1:1 ratio including inconsistencies in adhering to a definition of massive transfusion. There is evidence to suggest that haemostasis is not possible above or below a range between 3:1 and 1:1 RBCs to plasma⁵⁰. It should also be noted that additional fluids for added anticoagulation, pitfalls in thromboelastometry affected by haematocrit, platelet levels and plasma levels need to be considered. A survivorship bias in favour of a higher FFP :RBC ratio is suggested⁵¹, since patients who died early never had the chance to receive sufficient FFP to match the number of RBC units transfused. Hence there may not be a golden 'one size fits all' ratio for haemostatic transfusion. Probably the biggest advantage in having a massive transfusion 'trauma pack'⁵² ratio based on local agreements is to reduce transfusion delays.

4.c. Plasma

Trauma patients resuscitated with plasma have shown better coagulation profile on thromboelastometry at 6 hours compared to isotonic saline who were also more acidaemic⁵³.

Prehospital studies have found NS to exacerbate tPA-mediated fibrinolysis which is associated with high mortality⁵⁴, whereas plasma attenuates fibrinolysis through preservation of plasma proteins.

Aggressive FFP transfusion as part of MTP in those patients who do not develop acute traumatic coagulopathy do not show improved outcomes⁵⁵. FFP transfusion carries inherent risks with substantial costs. There is a need to better define the population most likely to benefit.

4.d. Platelets

Trauma results in decreased count and function of platelets within hours leading to poor outcomes⁵⁶, this is worsened by blood transfusion including platelet transfusion which is possibly an effect due to donor plasma.

4.e. Whole blood (WB)

Fresh whole blood drawn from an uninjured companion or stored in advance is the ideal battlefield fluid⁵⁷ that can provide volume, coagulation factors, plasma, and oxygenation capacity. It is a practical choice in resource-limited setting with limited blood banking where apheresis platelets are not available⁵⁸. The US army data suggests it provides an improved or equal survival compare to blood component transfusion⁵⁹. Two units of uncrossmatched low anti A and anti B titre group O WB can be safely transfused^{60,61}. It can be leukoreduced with platelet sparing filters and stored at 4°C to retain platelet function for 15 days. Stored WB maintains haemostatic properties up to 21 days⁶² compared to reconstituted components that go through biochemical, biomechanical, and immunological changes⁶³ during long storage and form a larger transfusion volume but are also significantly anaemic, thrombocytopenic and coagulopathic^{64,65}. Modern storage of components is possible for several years⁶⁶. Although studies link prolonged storage to worse morbidity and mortality⁶⁷, larger systematic reviews have been inconclusive of this association⁶⁸. Multiple combat and civilian studies have shown a mortality benefit with WB^{69,70} and advocate it to be the first choice in MTP.

5. Recommendations in specific situations

5.a. Paediatric trauma

There is insufficient data⁷¹ on transfusion protocols for paediatric trauma patients. There is no evidence^{72,73} of better outcomes with high plasma: platelet: RBC ratios in children. The physiological response to hypovolemic shock is different in children compared to adults and permissive hypotension may not be appropriate. Unlike adults high volume crystalloid resuscitation for blunt injuries in children is not associated⁷⁴ with ARDS, abdominal compartment syndrome or multi organ failure although they have an increased hospital stay and need for mechanical ventilation. Early blood transfusion has a non-causal association with death and late transfusion is associated with increased morbidity in children⁷⁵. Adult data should not be generalizable to children.

5.b. Elderly

Older age, blood transfusion, pre-hospital GCS, acute traumatic coagulopathy and higher systolic blood pressure on presentation are associated with higher post trauma mortality⁷⁶. Early aggressive resuscitation especially along specific geriatric guidelines seem to improve outcomes

including survival to discharge in the elderly. Permissive hypotension has been discouraged⁷⁷ in the elderly due to increased cardiovascular risk profile and higher incidence of pre injury hypertension, although it may be beneficial to patients presenting hypotensive. The elderly patients are more likely to receive blood products due to altered coagulopathic response to trauma worsened by anticoagulant and antiplatelet medication use⁷⁸.

5.c. Combat recommendations

Although recent wars have produced valuable evidence in acute trauma resuscitation it should be realised that the severity and mechanism of injury, available medical facilities and premorbid health of combat casualties may not be similar to civilian population and this warrants civilian RCTs to test military recommendations. The Tactical Combat Casualty Care: TCCC Guidelines⁷⁹ recommends Whole blood or blood constituents as the most preferred options for resuscitation followed by Dried plasma (DP). If none of these are available Hextend (Hetastarch) is a less desirable option. Blood constituents in 1:1:1 DCR ratio is preferred to 1:1 DCR. Hypotensive resuscitation is emphasised to assist with body's haemostatic response and reduce complications of over resuscitation. A multidisciplinary approach to trauma in combat hospitals are associated with reduced mortality⁸⁰.

5.d. Prehospital care

Good quality and early prehospital phase of trauma care can give the greatest benefit in survival⁸¹. The PROMMTT study⁸² found that prehospital fluid therapy without increasing systolic blood pressure was associated with decrease in hospital mortality. Other studies conclude that excessive prehospital fluid replacement more than 1.5 L causes increased mortality in solid abdominal organ injury⁸³ and more than 1L is associated with increased need for in hospital blood transfusion⁸⁴. It is feasible for initiating prehospital transfusion and the rates of pRBC wastage have been found similar to that of emergency departments⁸⁵. Prehospital Plasma first transfusion with FDP (fresh dried plasma) is preferred⁸⁶ to provide coagulation factors and volume although it has shown to extend DCR by 24 hours and is not associated with a survival benefit but possibly reduces trauma induced coagulopathy⁸⁷. Pre trauma centre RBC transfusion can increase the probability of 24-hour survival⁸⁸, decrease the risk of shock, and lower the 24-hour RBC requirement.

Table 1

Parameter	class 1	class 2 Mild	class 3 Moderate	class 4 Severe
Blood loss	< 15%	15 - 30%	31 - 40%	>40%
Heart rate	Normal	Normal / ↑	↑	↑ / ↑↑
Blood Pressure	Normal	Normal	Normal / ↓	↓
Pulse Pressure	Normal	↓	↓	↓
Respiratory rate	Normal	Normal	Normal / ↑	↑
Urine output	Normal	Normal	↓	↓↓
GCS	Normal	Normal	↓	↓
Base deficit mEq/L	0 to -2	-2 to -6	-6 to -10	-10 or less
need for blood products	Monitor	Possible	Yes	Massive Transfusion

Table 1: sign symptoms of haemorrhage by class

6. Other parameters

6.a. Calcium

Initial resuscitation of severely injured patients can lead to hypocalcaemia or hypercalcemia both are associated with poor outcomes⁸⁹. Citrate in blood products can chelate calcium/ causing hypocalcaemia. Low ionised calcium levels are associated with hypotension, increased mortality and poor clot formation⁹⁰.

6.b. Base deficit and lactate

Initial blood lactate⁹¹, early lactate clearance and base deficit have been shown to be important prognostic biomarkers in trauma⁹². Base deficit⁴ has been incorporated as a quantitative measure to class haemorrhage (Table 1)⁴.

7. Thromboelastometry (Figure 2)¹⁰¹ and Procoagulants

7.a. Thromboelastogram (TEG) and Rotational Thromboelastometry (ROTEM)

Incorporating TEG and ROTEM as point of care dynamic rapid assessment of coagulation status to monitor and modify massive transfusion protocols guide in targeted use of blood products⁹³. They provide data about clot strength to establish if bleeding is due to coagulopathy and also quantify fibrinolysis to guide the use of anti-fibrinolytics like fibrinogen concentrate and cryoprecipitate⁹⁴. They can be used to diagnose platelet dysfunction and hypercoagulability and potentially prevent inappropriate transfusions of haemostatic blood products to non-coagulopathic patients.

7.b. Tranexemic acid (TXA)

The CRASH-2 trial⁹⁵ concluded that administration of TXA within 3 hours in bleeding trauma patients is a safe and highly cost effective method to reduce the risk of death. Although this trial had knowledge and evidence gaps⁹⁶ and the use of TXA has potential risk of thromboembolism but its implementation into trauma resuscitation has been recommended by many studies including MATTERs trial⁹⁷ with highest benefit in patients requiring massive transfusion

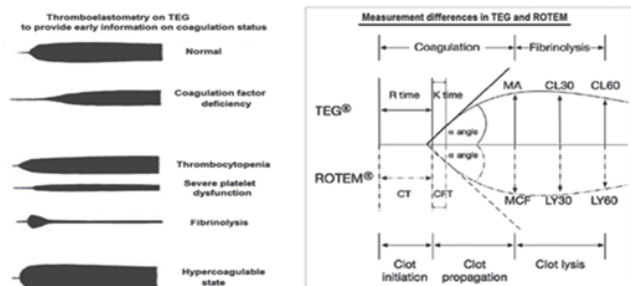


Figure 2 Thromboelastometry

8. Limitations and Future recommendation

8.a. The current article is a topic review based on a single directory search i.e. MEDLINE. Nevertheless, a systematic approach has been taken which could potentially be utilised for future systematic review on this topic utilising other relevant medical search directories and lay searches.

8.b. This topic is highly heterogeneous and complicated. Narrower search based on area and population of practice is encouraged eg. Geriatric trauma in low socioeconomic areas.

8.c. The understanding of acute fluid resuscitation in trauma is constantly evolving, newer techniques and improving technology are changing the clinical pathways. Statistically significant findings in this area are not clinically significant in many instances. There is a great need and scope for RCTs and regular systematic reviews.

9. Conclusions

The representative literature in this review gives an insight into recent areas of research within acute trauma resuscitation. These have been doubtful areas of clinical practice and the new evidences have influenced changes in guidelines and better patient outcomes.

9.a. Massive transfusion

One of the important reasons for inconsistent literature regarding trauma resuscitation is the variable definition of massive transfusion. The ATLS⁴ defines massive transfusion as more than 10 units of pRBC transfusion in 24 hours or 4 units in one hour.

9.b. ATLS recommendations⁴

The new recommendations include judicious administration of crystalloids to a maximum of 1litre (20mL/kg for child less than 40 kg) and encouraged use of blood and blood products at the earliest. Aggressive fluid resuscitation cannot substitute control of bleeding and is an important cause for increased mortality and morbidity. There is greater emphasis on massive transfusion protocol as a means of efficient delivery of goal directed fluid therapy. The focus of treatment is to prevent coagulopathy and provide a better chance of survival by reducing its risk factors. Tranexamic acid is an important recommendation as part of early resuscitation. Base excess has been incorporated into the class of haemorrhage table.

9.c. Local factors

Trauma is a global disease across the socio-economic spectrum⁹⁸. Coagulopathy and uncontrolled bleeding remain leading causes of death in trauma⁹⁹. Although transfusion of blood products reduces mortality in high risk patients it increases mortality in those at low risk¹². There is an increasing volume of scientific knowledge to underpin trauma resuscitation yet there is a significant inconsistency and some conflicting evidences. This suggests that there is scope for further high-quality research as well as to realize that a 'one size fits all' approach is not suitable¹⁰⁰. Local modifications based on patient population, available resources and expertise is essential. Successful resuscitation from major haemorrhage depends upon a variety of factors distilled into a trauma team with effective leadership, excellent technical and non-technical team skills as well as the early initiation of DCR⁹⁸.

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