Does a Controlled Fluid Resuscitation Strategy Decrease Mortality in Trauma Patients?

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Haemorrhage remains the biggest killer of major trauma patients



Wang et al, Critical Care Medicine. 2014

Bleeding and damage control surgery

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Curr Opin Anesthesiol 2016, 29:229–233

Purpose of review

Bleeding is still a major cause of death in trauma patients. Damage control surgery is a strategy that aims to control bleeding and avoid secondary contamination of the cavity. This article checks the principles and indications of damage control surgery, bleeding management, and the role of the anesthesiologist in

trauma context. The efficient treatment of severe trauma and exsanguinated patients includes a surgical approach to the patient performed as quickly as possible. Volemic resuscitation, hemostatic transfusion, prevention and/or treatment of coagulopathy, hypothermia, and acidosis are strategies that reduce bleeding, as well as permissive hypotension.

Specialized literature shows us that the adoption of all of these principles along with reduced surgical time has led to a broader concept called damage control resuscitation.

Summary

Damage control resuscitation is a treatment strategy in which the recovery of physiological variables is initially prioritized over anatomical variables and can be required in severe trauma patients.

Keywords

bleeding, damage control resuscitation, damage control surgery

Hemorrhagic shock is responsible for **30–40% of deaths from trauma**, and it is **believed** to be the most common cause of potentially **preventable deaths**.

The cause of death of approximately 50% of patients, who die within the first 24 h after trauma, is **bleeding**.

The mortality of coagulopathic pts is 3–4 times higher than pts without coagulopathy





Caused by tissue injury, hypoxia, hypoperfusion, platelet and coagulation protease dysfunction.

Fluid administered both in vitro and in vivo is an iatrogenic cause of traumatic coagulopathy

Bolliger D, Brit J Anaesth 2009;

Pathophysiology of Acute traumatic coagulopathy

Restoration of the physiological balance





Cohen MJ, J Trauma Acute Care Surg 2013

DCR is current best practice for bleeding trauma patients

Haemodilution causes

Prolongation of PT

Reduction FVII

Abnormal fibrin polymerisation

Fibrinogen dysfunction

Poor clot stability

Shaz BH, J Trauma 2011. Fenger-Eriksen C, J Thromb Haem 2009 More than 40% of trauma patients develop a coagulopathy after >2 L of crystalloid,

The more fluid replacement

Rising to >70% after >4 L • The more coagulopaty

Maegele M. Injury 2007;



Historical trends in resuscitation strategies

Era	Resuscitation approaches and other related issues	Outcomes
WWI WWII/Korean War	None Albumin, plasma, and blood use	Early death Better early survival but organ failure resulting in late deaths (especially acute renal failure)
Vietnam War	Crystalloids and banked blood use. Improved rapid evacuation methods	Better early survival. Organ failure resulting in late deaths still a problem, with less acute renal failure and more ARDS
1970s-early 1980s	Goal-directed aggressive resuscitation, use of pulmonary artery catheters, and oxygen delivery cathetions to deliver "supra-normal" resultation	Further improvement in early survival, increased MOF, and late deaths
Mid 1980s-1990s	Rapid field triage, maturation of civilian trauma systems, introduction of "damage contro surgery," improved ICU care	Improved early survival in severely injured. More MOF but better survival in MOF patients due to improved ICU care
Afghanistan and Iraq wars	Dramatic improvement in triage and long distance transfers. Excellent in-transit ICU care. "Damage Control Resuscitation," permissive hypotension, limited use of crystalloids, early use of blood products, higher ratio of FFP and platelets, and fresh whole blood use. In field use of recombinant factor VII. Development and use of advanced hemostatic dressings. Significant improvements in injury prevention with better body armor, and protective gear. Adoption of battlefield strategies by civilian trauma centers	Lowest KIA rate in any major conflict. Decreased incidence of ARDS, MOF, and coagulopathy. Significant improvement in early and late survival and long-term outcomes compared to historical controls.

ARDS, acute respiratory distress syndrome; MOF, multiple organ failure; ICU, intensive care unit; FFP, fresh frozen plasma; KIA, killed in action.

The New England Journal of Medicine

One of the first RCT

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IMMEDIATE VERSUS DELAYED FLUID RESUSCITATION FOR HYPOTENSIVE PATIENTS

Results. Among the 289 patients who received delayed fluid resuscitation, 203 (70 percent) survived and were discharged from the hospital, as compared with 193 of the 309 patients (62 percent) who received immediate fluid resuscitation (P = 0.04). The mean estimated intra-

 This strategy reported an 8% reduction in absolute mortality in for patients receiving delayed fluid resuscitation and experiencing a lower SBP preoperatively.

Immediate versus Delayed Fluid Resuscitation for Hypotensive Patients with Penetrating Torso Injuries

VARIABLE	IMMEDIATE Resuscitation (N = 309)	$\begin{array}{l} \text{Delayed} \\ \text{Resuscitation} \\ (\text{N} = 289) \end{array}$	P VALUE
Systolic blood pressure (mm Hg)	79±46	72±43	0.02
Hemoglobin (g/dl)	11.2±2.6	12.9±2.2	< 0.001
Platelet count (×10 ⁻³ /mm ³)	274±84	297±88	0.004
Prothrombin time (sec)	14.1±16	11.4 ± 1.8	<0.001
Partial-thromboplastin time (sec)	31.8±19.3	27.5±12	0.007

VARIABLE	IMMEDIATE Resuscitation	DELAYED RESUSCITATION	P VALUE
Survival to discharge — no. of patients/total patients (%)	193/309 (62)*	203/289 (70)†	0.04
Estimated intraoperative blood loss ml [‡]	3127±4937	2555 ± 3546	0.11
Length of hospital stay — days§	14±24	11±19	0.006

• Other RCTs, however, have not reported significant mortality benefits either from delaying fluid therapy or from targeting a lower SBP

Dutton RP, J Trauma 2002;

The concept of permissive hypotension represents a double-edged sword

Prolonged duration of shock may further aggravate the extent of postinjury coagulopathy

> Hypotensive resuscitation may aggravate the incidence of secondary insults in patients with severe head injuries

Prolonged Permissive Hypotensive Resuscitation Is Associated With Poor Outcome in Primary Blast Injury With Controlled Hemorrhage Article in Annals of surgery 251(6):1131-9.2010

 But other models provide conflicting results; a study in pigs with blast injuries reported a poorer outcome (survival time) with permissive hypotension compared to normotensive resuscitation.

Ideal Permissive Hypotension to Resuscitate Uncontrolled Hemorrhagic Shock and the Tolerance Time in Rats

Anesthesiology, 2011

Tao Li, Ph.D.,* Yu Zhu, M.S.,† Yi Hu, Ph.D.,‡ Lijie Li, B.A.,† Youfang Diao, M.S.,† Jing Tang, M.S.,† Liangming Liu, M.D., Ph.D.§

ABSTRACT

mmHg t loss (39% animal si

Used different levels of MAP to achieve volemic resuscitation (40, 50, 60, 70, 80, Backgro and 100 mmHg). sion for u resuscitat Approximately 80–100 mmHg exhibited more bleeding, mortality, and organ sure (MA dysfunction than those subjected to permissive hypotension (50 and 60mmHg). sion have Methods 40 mmHg showed less bleeding but **increased organ dysfunction and mortality**. time for rhagic shock rats, the effects of different target MAPs (40, 50, sure of 50-60 mmHg was applied during a maximum pe-60, 70, 80 and 100 mmHg) and 60- 90- and 120-min riod of 90 min permissiv Caution for patiens have head trauma: orrhagic Lower pressure levels can cause a reduction in cerebral perfusion pressure, and **Results:** had incre hence, contribute to the introduction or deterioration of secondary brain injury. ume), de vival (8 of 10 and 6 of 10) and vital organ function. kidney) and mitochondrial function, and decreased animal survival 1 A target MAP of 50–60 mmHg conferred most survival benefit MAP grd spectively drial fun Ninety minutes of permissive hypotension was the tolerance limit. survival

Hypotensive Resuscitation Strategy Reduces Transfusion Requirements and Severe Postoperative Coagulopathy in Trauma Patients With Hemorrhagic Shock: Preliminary Results of a Randomized Controlled Trial

C. Anne Morrison, MD, MPH, Matthew M. Carrick, MD, Michael A. Norman, MD, Bradford G. Scott, MD, Francis J. Welsh, MD, Peter Tsai, MD, Kathleen R. Liscum, MD, Matthew J. Wall, Jr., MD,

Data from an RCT (man), with 90 pts, in which target MAP of 50 mmHg (LMAP) and 65 mmHg (HMAP) were compared.

The LMAP group -Received significantly fewer blood products, -Need smaller volumes of fluids intra-operatively, -Were less likely to develop post-operative coagulopathy and Had a significantly lower all cause early mortality rate (p = 0.03).

Morrison CA, J Trauma 2011;

Doran CM, Trauma Acute Care Surg 2012; 72: 835e43.

Targeted resuscitation improves coagulation and outcome

Target MAP?

BACKGROUND: Acute trauma coagulopathy in seriously injured casualties may be initiated by tissue hypoperfusion. A targeted (or novel hybrid [NHI) resuscitation strategy was developed to overcome noor tissue oxygen delivery associated with prolonged.

However, extended hypotension increases tissue hypoperfusion and adds to ATC.

 1.87 ± 0.15 times presurgery, groups 2 and 4) compared with NH (1.44 \pm 0.09 and 1.36 \pm 0.06, groups 1 and 3, p = 0.001). Blast versus sham had no significant effect on prothrombin time (p = 0.56). Peak levels of interleukin 6 were significantly lower in NH groups. Arterial base excess was significantly lower with hypotension ($-18.4 \text{ mmol/L} \pm 2.7 \text{ mmol/L}$ and $-12.1 \text{ mmol/L} \pm 3.2 \text{ mmol/L}$) versus NH ($-3.7 \text{ mmol/L} \pm 2.8 \text{ mmol/L}$ and $-1.8 \text{ mmol/L} \pm 1.8 \text{ mmol/L}$, p = 0.0001). Hematocrit was not significantly different between groups (p = 0.16).

CONCLUSION: Targeted resuscitation (NH) attenuates the development of acute trauma coagulopathy and systemic inflammation with improved tissue perfusion and reduced metabolic acidosis in a model of complex injury. This emphasizes the challenge of choosing a resuscitation strategy for trauma patients where the needs of tissue perfusion must be balanced against the risk of rebleeding during resuscitation. (*J Trauma*. 2012;72: 835–843. Copyright © 2012 by Lippincott Williams & Wilkins)
 KEY WORDS:

• Animal models of uncontrolled haemorrhagic shock with trauma have demonstrated benefit using targeted lower mean arterial pressures

(MAP) of 60-70 mmHg whilst bleeding is ongoing.

• Human data have added further weight to this approach and suggested both shorter bleeding times and improved mortality.

The comparision of MAP of 40 mm Hg, as opposed to 80 mm Hg Results: LMAP

Increased/better

- -Splanchnic perfusion and
- Tissue oxygenation
 Improved survival

Decreased/less

- Blood loss,
- -Apoptotic cell death and
- -Tissue injury,
 - -Acidemia,
- -Hemodilution
- -Tthrombocytopenia,
- -Coagulopathy,

Lu YQ, J Trauma 2007;

Owens TM,. <i>J Trauma 1995</i> Bickell WH, <i>Surgery 1991;</i> Kowalenko T <i>J Trauma 1992</i>	Several animal studies (1980-1990) have shown a reduced risk of death using a lower-than-normal blood pressure as a guide to fluid resuscitation in a strategy referred to as hypotensive resuscitation
Mapstone J <i>, J Trauma 2003</i>	Fluid resuscitation strategies in animal models revealed a consistent improvement in mortality with employment of hypotensive resuscitation
Geeraedts LM Jr, Injury 2009	Furthermore, aggressive resuscitation might also result in dilutional coagulopathy, which may worsen bleeding
Ley EJ, Clond MA, Srour MK, et al. J Trauma 2011	Crystalloid infusion of 1.5 litres or more in trauma patients was an independent risk factor for mortality

Many studies between 190-2011 show the benefit of hypotensive resuscitation

Who uses what?



These are typically given in an empirical manner initially, according to local policy.

Other considerations Hypertonic saline

- Clinical studies however do not provide compelling evidence to support the use of HTS either for TBI or for haemorrhagic shock.
- Many RCTs have not demonstrated mortality benefit





Critical Care Medicine,2014

Liberal Versus Restricted Fluid Resuscitation Strategies in Trauma Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies*

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Meta-Analyses guidelines of RCT and the Meta-analysis Of Observational Studies in Epidemiology guidelines were used for this study The terms for hypotensive resuscitation, small/limited/restricted volume resuscitation, and delayed resuscitation; trauma, hemorrhagic shock, hypovolemic shock, and shock were searched

RESULTS

- 11 studies, including four RCTs, and seven observational studies were identified.
- Available studies from 1990 to 2012 were selected.
 - Bickell WH. N Engl J Med 1994.
 - Turner J, Health Technol Assess 2000.
 - Dutton RP, J Trauma 2002,
 - Morrison CA, *J Trauma* 2011.
 - Kaweski SM, J Trauma 1990.
 - Sampalis JS, J Trauma 1997.
 - Dula DJ,. Prehosp Emerg Care 2002.
 - Talving P. Prehosp Disaster Med 2005.
 - Ley EJ, J Trauma 2011;
 - Huβmann B, J Emerg Trauma Shock 2011.
 - Duke MD, J Trauma Acute Care Surg 2012

• **RCTs. For the four RCTs, there was no significant difference in** overall mortality between liberal and restricted fluid resuscitation strategies (RR,

1.18; 95% CI, 0.98–1.41; I2, 0%).



Forest plot for randomized controlled trials. Comparison of the effects of liberal versus restricted fluid resuscitation on overall mortality, expressed as risk ratio (RR) and 95% CI.

After excluding the trail which included a drastically different study population and a high protocol violation rate, the summary estimates showed that the liberal fluid resuscitation strategy was associated with significantly higher overall mortality (RR, 1.25; 95% CI, 1.01–1.55; *I2*, *0%*)



Comparison of the effects of liberal versus restricted fluid resuscitation on overall mortality, expressed as RR and 95% Cl.

 Twenty-four-hour mortality was not significantly different between two strategies (RR, 1.29; 95% CI, 0.58–2.88; *I2, 0%; two studies*).



Observational Studies

• The summary estimate showed that **liberal fluid resuscitation was associated with significantly higher mortality** in patients with trauma-related hemorrhage conditions (OR, 1.14; 95% CI, 1.01–1.28; *I2*, 21.4%)

DISCUSSION

	The liberal fluid resuscitation strategy	Restricted fluid resuscitation strategy
RCTs	associated with higher mortality (RR, 1.25; 95% cl, 1.01–1.55; 12, 0%)	Lower mortality
Obsv studies	associated with higher mortality (or, 1.14; 95% cl, 1.01–1.28; 12, 21.4%).	Lower mortality

Wang et al. Crit Care Med, 2014

- RCTs suggest that a restricted fluid strategy might be useful in trauma patients with penetrating injury but without TBI.
- The observational studies, the use of restricted fluid resuscitation strategies could be expanded to include those with blunt injury or TBI.
- Further confirmation in prospective RCTs is needed.



There has been limited, but evolving evidence for the role of permissive hypotension in trauma resuscitation



Tissue oxygen delivery and clearance of metabolic waste must, however, be maintained at a level compatible with life

Haemostatic resuscitation and transfusion strategies

 One of the central tenets of haemostatic resuscitation is the early use of 'balanced transfusion'; aiming to deliver red blood cells (RBC) and fresh frozen plasma (FFP) in a ratio approaching 1 unit of RBC to 1 unit of FFP with the aim of attenuating coagulopathy.

Why an incorporating equivalent ratios?



So incorporating equivalent ratios at an early stage appears vital

Borgman MA. J Trauma 2007	High ratios of FFP:RBC reduce death rate by 46%
Zehtabchi S, Acad Emerg Med 2009	No absolute agreement as to which specific FFP:RBC ratio (i.e. 1:1, 2:3, etc.) improves mortality
Duchesne JC, J Trauma 2008	Advocated the aggressive transfusion strategy of preemptive plasma substitution at a 1:1 ratio
Kashuk JL, Trauma 2008	Advocating the 1:1 concept have significant shortcomings (retrospective)
Scalea TM, Ann Surg 2008	Prospective but not controlled showed no benefit of a standardized 1:1 transfusion protocol
N. Curry, / Injury, Int. J. Care Injured 2012	The survival threshold appeared to be in the range of 1:2 to 1:3 FFP:RBC, and data did not support the use of a routine 1:1 transfusion
Gunter OL J Trauma 2008	Demonstrated that a 1:5 (plt:RBC) transfusion strategy for coagulopathic pts with massive transfusions was associated with increased survival.
Holcomb JB,J Am Med Assoc 2015; 313: 471e82	High Plt:FFP:PRBC ratios confer a survival advantage, But whether that is at 1:1:1 or 1:1:2 is not clear despite recent investigation.

Inaba K, J Am Coll Surg 2010	FFP has been reported of little benefit in patients receiving fewer than 10 units of RBC, with higher incidence of ARDS and no improvement to survival
Inaba KJ. Am Coll Surg 2010;	Supported the idea of higher than standard doses of platelets and fibrinogen in massively transfused trauma patients
Phan HH, Vox Sang 2010;	No high quality evidence to confirm that platelets:RBC should be given at a 1:1 ratio
Magnotti LJ, J Trauma 2011	increased of FFP has no benefit on mortality
de Biasi AR, Transfusion 2011	High number of RBC administration (instead of FFP:RBC ratio=1:1) was significantly associated with worse mortality in the first 2 h of resuscitation, and was a more sensitive marker of mortality
Spinella PC, J Trauma 2009;	Fresh whole blood (FWB) is argued by many to be the optimum transfusion product for patients in need of MT
West MA, J Trauma 2006	A target Hb level of 7–10 g/dl may be recommended as a safe transfusion strategy in polytrauma

mostatic effect was observed in the . prothrombin time (p = 0.006), 56% d .047), and 38% increase in maximum clot firn sion with ≥ 1 :1 ratio did not confer any addition There was a marked variability in response to FFP, and he deteriorated in some patients exposed to 1:1 ratios. The b plasma were confined to patients with coagulopathy.

Conclusions: Interim results from this prospective study suggest that FFP: PRBC ratios of \geq 1:1 do not confer any additional advantage over ratios of 1:2 to 3:4. Hemostatic benefits of plasma therapy are limited to patients with coagulopathy.

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Coordination and management of multicenter clinical studies in trauma: Experience from the PRospective Observational Multicenter Major Trauma

Results: <mark>Between July 2009 and October 2010, PROMMTT screened 12,561 trauma admissions and enrolled</mark> 1245 patients who received one or more blood transfusions within 6 h of Emergency Department (ED) dmission. A total of 297 massive transfusions were observed over the course of the study at a combined rate of 5.0 massive transfusion patients/week.



• Mortality, ICU admission, length of stay, need for emergent surgery were outcomes.

Acute transfusion practice during trauma resuscitation: Who, when, where and why?

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Aim: to describe the patterns, indications and timing of ET at level 1 trauma centre. Methods: A 12-month prospective study was performed on all trauma admissions requiring ET. Demographics, mechanism, injury severity (ISS) were collected. Timing, location, volume, the clinician initiating first unit of transfusion, reason for transfusion was recorded, with corresponding blood gas results and physiological parameters. Mortanty, reo and ission, length of stay, need for emergent surgery were outcordes.

Results: From 965 trauma admissions 91 (9%) required ET (76% male, median age: 38 (10–88, IQR: 22–59), blunt mechanism: 87%, ISS: 25 (4–66, IOR: 16–34), 43% (39/91) had massive transfusion protocol (MTP) activation. ET was initiated in ED (52%), OR (38%) or ICU (10%). MTP transfusions were started at a median of 0.5 h (0.5–4, IQR: 0.5–1.5), whilst non-MTP transfusions were initiated at a median 3 h (0.5–23, IQR: 2-9). The first unit of ET was initiated by trauma surgeon (35%), anaesthetist (30%), ED (19%), ICU (13%) and general surgeon (3%). Transfusions triggers at the first unit of transfusion were 'expected or ongoing bleeding' 29%, dropping haemoglobin 26%, haemorrhagic shock 24%, hypotension 10%, tachycardia 8%. Median systolic blood pressure was 90 (45–125, IQR: 80–100), heart rate was 100 (53–

2.7, IQR: –7.2 to 2.4) mmol/l at the time of transfusion. Emergency surgery was required in 86% (78/91 ICU admission rate was 69% (63/91). Mortality was 14%. Low volume transfusion (1–2 units) was mor likely to lead to overtransfusion (Hb > 110 g/l).



Damage control resuscitation





Haemostatic

resuscitation



Hypotensive or Novel hybrid resuscitation



Massive transfusion

• 2011, Ann Surg

Avoid crystalloid resuscitation

Aim for permissive hypotension whenever possible

Prevent coagulopathy through early use o blood products

Aggressively break the vicious cycle of acidosis, coagulopathy, and hypothermia

DAMAGE CONTROL RESUSCITATION IS ASSOCIATED WITH A REDUCTION IN RESUSCITATION VOLUMES AND IMPROVEMENT IN SURVIVAL IN 390 DAMAGE CONTROL LAPAROTOMY PATIENTS

2011, Ann Surg

RESULTS—390 patients underwent DCL. Of these, 282 were pre-DCR and 108 were DCR. Groups were similar in demographics, injury severity, admission vitals and laboratory values. DCR patients received less crystalloids (median 14 L vs. 5 L), RBC (13 U vs. 7 U), plasma (11 U vs. 8 U) and platelets (6 U vs. 0 U) in 24-hr; all p<0.05. DCR patients had less evidence of the lethal triad upon ICU arrival (80% vs. 46%, p<0.001). 24-hour and 30-day survival were higher with DCR (88% vs. 97%, p=0.006 and 76% vs. 86%, p=0.03). Multivariate analysis controlling

🖶 MT (% patients)

--- ISS

🛨 Median 24hr PRBC



Transfusion triggers

Definition of haemorrhagic shock

Low BE

Expected and ongoing bleeding

Coagulopathy and hypovolaemia

Low Hb with severe traumatic brain injur,

Persistent hypotension and tachycardia despite fluid replacement

Dropping Hb (Hb drop to below 80 g/l or below 100 g/l and 30 g/l drop within 2 ${\rm h}$

Use of Hemoglobin-based oxygen carriers (HBOC) for hemorrhagic shock compare with normal saline.



Resuscitative strategies in traumatic hemorrhagic shock



Conclusions



In appropriate patients limiting the rate and volume of fluid resuscitation is becoming the new norm and standard practice



Drugs are being aggressively investigated



Permissive hypotension is the new buzz word

PERMISSIVE HYPOTENSION ORE ORGAN PERFUSION AND OXY WITH DEFINITIVE RESULT The concept of "damage control resuscitation" with early use of blood components in appropriate pts became cornerstone

Provide physiological balance, rather than anatomic repair damage

patients who are actively bleeding should have their losses initially restored with fluids to replace the extracellular space.

This approach should, however, be conducted according to criteria

Yes, a Controlled Fluid Resuscitation Strategy can Decrease Mortality in Trauma Patients





outcome for these patients.

Damage control surgery
Prevention and treatment of hypothermia
Prevention and correction of acidosis
Prevention and treatment of coagulopathy
Hemostatic transfusion
Permissive hypotension

KEY POINTS

- DCR can be required in severe trauma victims.
- Hypothermia, coagulopathy, and acidosis should be aggressively treated.

Strategies such as permissive hypotension can be used to decrease the loss of blood.
Hemostatic therapy may also contribute to a better