Polytrauma patient

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OBJECTIVES
Introduction
Definition of polytrauma
Response to major injury
Polytrauma patients selection who might benefit from the damage control surgery

Initial Assessment: Advanced Trauma Life Support (ATLS 10-ed.) Protocol

Damage Control Resuscitation Once Bleeding Has Been Stopped

Conclusions

References

Introduction. Severe trauma is a major global public health issue. Globally, injuries contribute to around 10% of total deaths and 15% of disability-adjusted life-years, resulting in the annual worldwide death of more than 5.8 million people, a number that is predicted to increase to >8 million by 2020. According to the World Health Organization (WHO), road traffic accidents, suicides and homicides are the three leading causes of injury and violence-related deaths, with a greater share of hospitalizations, deaths, disabilities and socioeconomic losses in young and middle-age populations. Massive bleeding following injury remains the main cause of potentially preventable death with better control of bleeding. Within the largest European trauma registry, true polytrauma (ISS> 17 with at least two AIS 3+ injuries) using abbreviated injury scale criteria occurs, in only 12% (2008-2013) of cases but causes up to one third of all deaths in patients reaching hospital alive, mainly in adults <65 years. Uncontrolled hemorrhage is reported to be responsible for 40% of trauma deaths Most of the deaths occur due to poor decision and inappropriate interventions. Damage control resuscitation (DCR) is a strategic approach to the trauma patient who presents in extremis.

Defining polytrauma. Polytrauma can be defined as significant injury in at least two out of the following six body regions :

Head, neck and cervical spine

Face

Chest and thoracic spine

Abdomen and lumbar spine

Limbs and bony pelvis

External(skin)

Note: Significant injury=abbreviated injury score of ≥ 3out of 6

Evidence – based definition of polytrauma: Polytrauma can be defined as patients with an Abbreviated Injury Scale (AIS) score great than 2 points and at least one of the following covariables :

Hipotension (systolic blood pressure < 90 mmHg);

Level of consciousness (Glasgow Coma Scale score < 8 points);

Acidosis (base excess ≥ 6,0);

Coagulopathy (international normalized ratio 1.4/ partial thromboplastin time ≥ 40 s);

Age > 70 years.

Injury severity score (ISS) ISS is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an AIS and is allocated to one of six body regions (Head, Face, Chest, Abdomen, Extremities (including Pelvis), External). Only the highest AIS score in each body region is used .

The 3 most severely injured body regions have their score squared and added together to produce the ISS score. An example of the ISS calculation is shown in table1.

Table 1 Calculation of the injury severity score (ISS)

Region	Injury Description	AIS	Square Top Three
Head,neck and cervical spine	Cerebral contusion	3	9
Face	No injury	0	
Chest and thoracic spine	Flail Chest	4	16
Abdomen and lumbar spine	Minor Contusion of Liver	2	
	Complex Rupture of Spleen	5	25
Limbs and bony pelvis	Fractured femur	3	
External(skin)	No injury	0	
Injury Severity Score			50

Note: The ISS score takes values from 0 to 75.If an injury is assigned an AIS of 6 (usurvivable injury), the ISS score is automatically assigned to 75, AIS – Abbreviated Injury Scale.

Abbreviated injury scale (AIS) AIS is an anatomical scoring system first introduced in 1969.Injuries are ranked on a scale of 1 to 6 with 1 being minor,5 severe, and 6 a nonsurvivable injury (Table 2).

Table 2. Abbreviated Injury Scale(AIS)

Injury	AIS Score
1	Minor
2	Moderate
3	Serious
4	Severe
5	Critical
6	Unsurvivable

Note: AIS -abbreviated injury scale.

Response to major injury The systemic inflammatory response syndrome (SIRS) after injury occurs as a result of a complex set of interactions which result in a substantial host immune cell response and activation of both the complement and coagulation cascades. SIRS is defined as

two or more of the following: (Table 3). This SIRS response occurs within minutes of injury as a result of tissue hypoperfusion and tissue injury.

Table 3. Systemic inflammatory response syndrome (SIRS) criteria

Two or more of the following
Heart rate >90 bpm
WBC < 4000/mm^3 or >12000/mm^3 or >10% immature PMNs
Respiratory rate>20/mm with $PaCO_2$<32 mmHg
Core temperature < 36^{0}C or > 38^{0}C

Note: SIRS - systemic inflammatory response syndrome,

PMN-polymorphonuclear leukocytes.

Tissue ischemia-reperfusion after hemorrhage or tissue damage from trauma can elicit a sterile inflammatory response caused by release of damage-associated molecular patterns (DAMPs). This injury results in activation of the innate immune system, coagulation pathway, and complement cascade leading to a systemic inflammatory response (SIRS) and host tissue injury. The exaggerated host response to the severe injury can lead to significant tissue injury, end organ dysfunction, and ultimately multiple organ failure (MOF). MOF is defined as progressive, potentially reversible dysfunction of two or more organ systems including the lung, liver, gastrointestinal tract, renal, and hematologic systems [68]. Post-injury MOF is the most significant cause of late deaths in trauma patients [41].

A sustained inflammatory response to injury has been correlated with increased morbidity and mortality in trauma patients.

Physiological response to injury include:

Inflammatory immune response

Innate immune response

Adaptive immune response

Systemic Inflammatory Response Syndrome (SIRS)

Compensatory Anti-inflammatory Response Syndrome (CARS)

Multiple Organ Dysfunction Syndrome (MODS)

Lethal Triad. The term "lethal triad" was used to describe the physiologic derangement observed in these patients and refers to the triad of the deteriorating status of acute coagulopathy, hypothermia, and acidosis of exsanguinating trauma patients (Fig. 1).
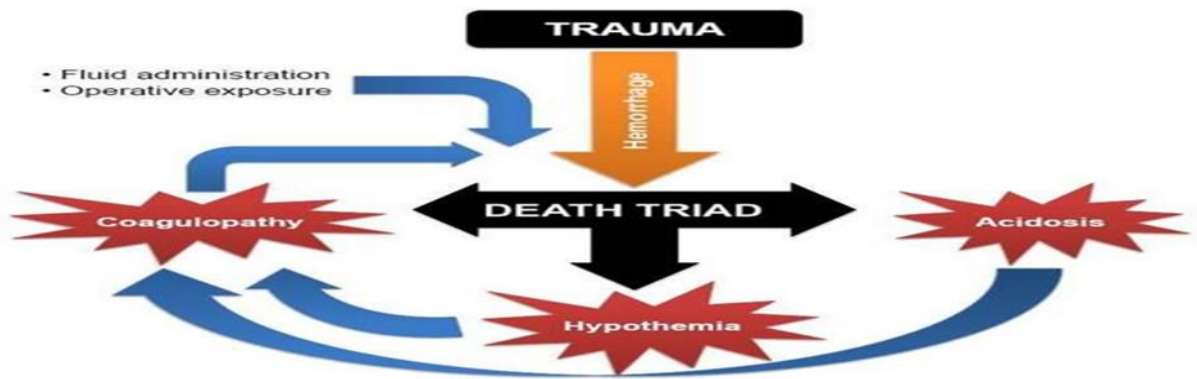
Fig.1 Lethal Triad

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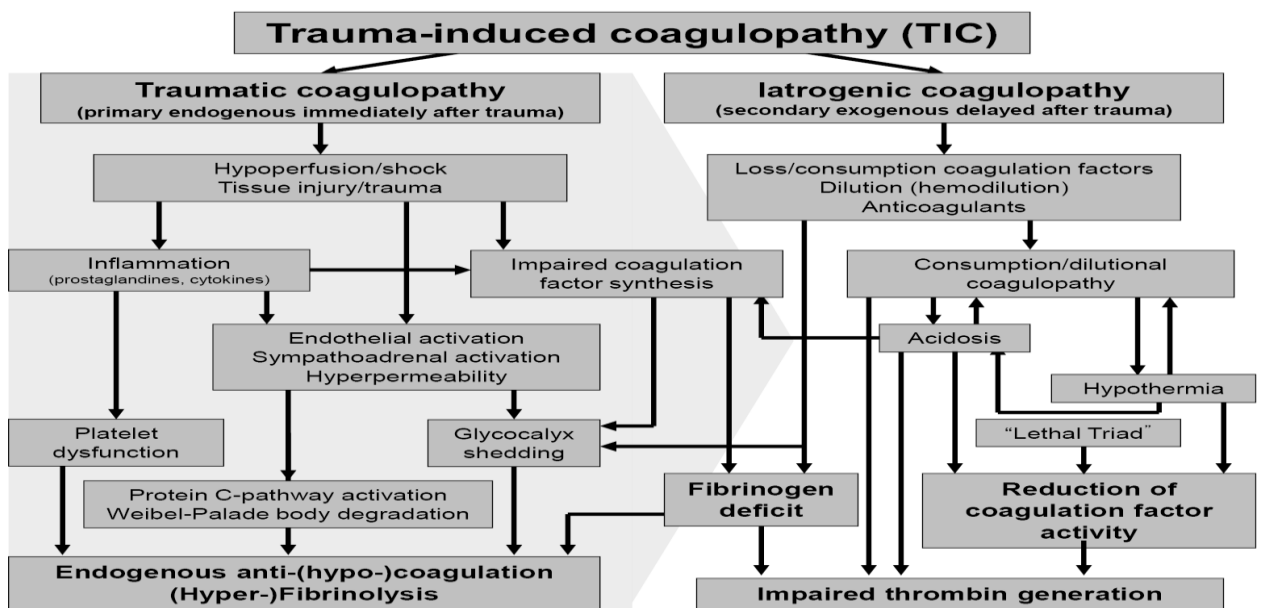
Fig.2. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. J Trauma. 2003;54 (6):112 7–30.

Polytrauma patients selection who might benefit from the damage control surgery

The aim of damage control surgery is to stop hemorrhage and minimize contamination. Hemorrhage is controlled by ligation, temporary clamping, shunting or packing . Contamination due to hollow viscus injury is minimized by closure or resection without anastomosis .Then abdomen is temporarily closed to prevent intra-abdominal hypertension. Planned reoperation to restore anatomy is performed after achieving normal physiology. Not all trauma patients require

damage control measures. Certain conditions and complexes of injuries assessed both preoperatively and intraoperatively require damage control.

At its core, damage control surgery attempts to identify those patients incapable of undergoing a definitive surgery due to loss of physiologic reserve and exchange an improvement in survival for increased morbidity. In general, there are two treatment strategies for fracture care in multiple-trauma patients. The aforementioned concept of "damage control orthopedics" (DCO) is characterized by temporary external fracture fixation in the primary phase with secondary conversion to definitive osteosynthesis after stabilization of the patient's physiological and immunological status in the intensive care unit.

In the majority of studies, it is accepted that stable patients benefit from the ETC concept, whereas unstable patients and patients „in extremes might benefit from DCO. In this study, borderline patients were shown to have a significantly higher incidence of acute lung injury (ALI) after ETC treatment compared to fracture stabilization according to the DCO concept. For the identification of these patients, the severity of thoracic trauma and physiological pulmonary parameters are of central importance.

The timing of secondary definitive osteosynthesis within the DCO concept seems to not be advantageous before 5 days after the trauma. PV Giannoudis recommended secondary fracture fixation based on defined parameters (Table 4) .

Table 4 Physiologic derangaments wich indicate the potential need for damage control surgery

Significant bleeding asidosis pH<7.2
Hypothermia, temp<35^{0}C
Operative time>90 min
Coagulopathy as seen by either laboratory result or „nonsurgical,, bluding
Lactate>5mmol/L

Key factors in patient selection for damage control

Critical factors:

Severe metabolic acidosis(pH<7.30)

Hypothermia (temperature <35^{0}C)

Resuscitation and operative time>90 minutes

Coagulopathy as evidenced by development of nonmechanical bleeding

Massive transfusion (> 10 units packets of red blood sells).

Table 5 Patients categorization

Clinical	Clinical parameter	Patients status

criteria		Stable	Borderline	Unstable	In Extremis
Shock	Systolic blood pressure (mmHg)	≥100	80-100	< 90	<70
	Blood units given/ in 2hr	0-2	2-8	5-15	>15
	Lactate levels(mg/dL)	< 2.0	2.5	>2.5	Severe acidosis
	Base deficit level (mmoli/L)	Normal range	No date	No date	>6-8
	Urinary output (ml/h)	>150	50-150	< 100	< 50
	ATLS Classification	I	II-III	III-IV	IV
Coagulation	Platelet count (mm^3)	> 10000/L	90000-11000/L	70000-90000	< 70000
	Factor II/V	90-100%	70-80%	50-70%	<50%
	Fibrinogen (g/dL)	>1	1	<1	DIC
	D-Dimer(μg/ml)	Normal range	Abnormal	Abnormal	DIC
Temperature	^{0}C	< 34	33-35	30-32	≤ 30
Soft tissue injuries	AIS Chest Trauma Scores	1 sau2	≥ 2	≥ 2	≥ 3
	Lung Function (PaO_2/FiO_2)	350-400	300-400	200-300	< 200
	Abdominal Trauma Abdominal trauma /Moor	None < II	Slight < III	Moderate III	Severe III or IV
	Abdominal trauma (AO)	A	B or C	C	C
	External(AIS)	1 or 2	2 or 3	3 or 4	Crush injury

Note: AIS – abbreviated injury score, ATLS – advanced trauma life support, PaO_2 – partial pressure of oxygen in arterial blood , :FiO2- fraction of inspired oxygen.

Damage Control Resuscitation is defined as a systematic approach to major exsanguinating trauma incorporating several strategies to decrease mortality and morbidity [109,131,139]:

1. Permissive hypotension (Minimal Normotension)
2. Hemostatic resuscitation (Massive Transfusion Protocol)
3. Hemorrhage control (Damage Control Surgery).

Initial Assessment: Advanced Trauma Life Support (ATLS) Protocol

The treatment of bleeding is to stop the bleeding. Damage control resuscitation is a management strategy of which goal is to enable survival of the trauma patient until bleeding is controlled while keeping the risk of iatrogenicity to a minimum. Damage control resuscitation is part of ATLS AB.CDE protocol that ensures oxygenation of the cells:

- Airway: airway is most often secured by orotracheal intubation. When orotracheal intubation is impossible and airway has to be secured, cricothyroidotomy is a DC procedure. C-spine is protected by a cervical collar.

- Breathing: trauma patient is given 100% O_2. The SaO_2 is monitored. If a pleural effusion (pneumo- and/or haemothorax) is present, a chest tube is placed. A sucking thoracic wound is treated by a vented chest seal.

- Circulation: control of bleeding is initially achieved, depending on situations, by direct pressure eventually enhanced by haemostatic dressings, by tourniquet placement or by placement of a pelvic sling. ECG and blood pressure are monitored non-invasively. Two large-bore intravenous lines or one intraosseous line is placed. Crystalloid perfusion is started. In case of hemorrhagic shock, permissive hypotension and transfusion of red blood cell unit (RBC) (O Rh- then type specific) and early plasma administration are recommended. A FAST echography is performed to look for intraperitoneal bleeding and cardiac tamponade.
- Disability: GCS score is calculated, pupillary reactivity and symmetry are checked, and focal neurological deficits are searched.
- Exposure: patient's dresses are removed, and a logroll is performed to allow complete examination including the back. Body temperature is monitored.

Fluid replacement in balanced resuscitation –initial fluid replacement with up to 1L crystalloid. Titrate small bolus (250 ml) fluid administration to achieve permissive hypotension SBP to 80 – 90 mmHg or normal mentation or palpable radial pulse (>80 mm Hg) or brachial pulse (> 60 mmHg),until definitive control of bleeding is obtained. Role of fluid challenge (250-500 ml) in testing to stratify responder to fluid resuscitation

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Targeted Blood Pressure with Permissive Hypotension and Restrictive Fluid Administration

The concept of damage control resuscitation aims to achieve a lower than normal blood pressure, also called 'permissive hypotension', and thereby avoid the adverse effects of early aggressive resuscitation using high doses of fluids while there is a potential risk of tissue hypoperfusion during short periods. Permissive hypotension and restrictive fluid administration are therefore reciprocal components of this approach; initial fluid administration is delayed or minimized, and less aggressive resuscitative end points are used. A targeted systolic blood pressure (SBP) of 80-90 mmHg is recommended until major bleeding has been stopped in the initial phase following trauma without brain injury. In patients with severe traumatic brain injury (GCS <8), maintenance of a mean arterial pressure >80 mmHg is recommended. This approximately equates to aiming for the restoration of a palpable radial pulse. A restrictive fluid administration strategy is recommended to achieve target blood pressure until bleeding can be controlled. Such an

approach decreases both the severity and incidence of dilution coagulopathy and as such complements a strategy of hemostatic resuscitation. Second, this reduces fluctuations in, and elevation of, systolic blood pressure which may disrupt the premature blood clot forming in areas of injury causing further bleeding.Damage control resuscitation Multidisciplinary approach to the management of critically injured, updated European guidelines recommends [Figure3]:
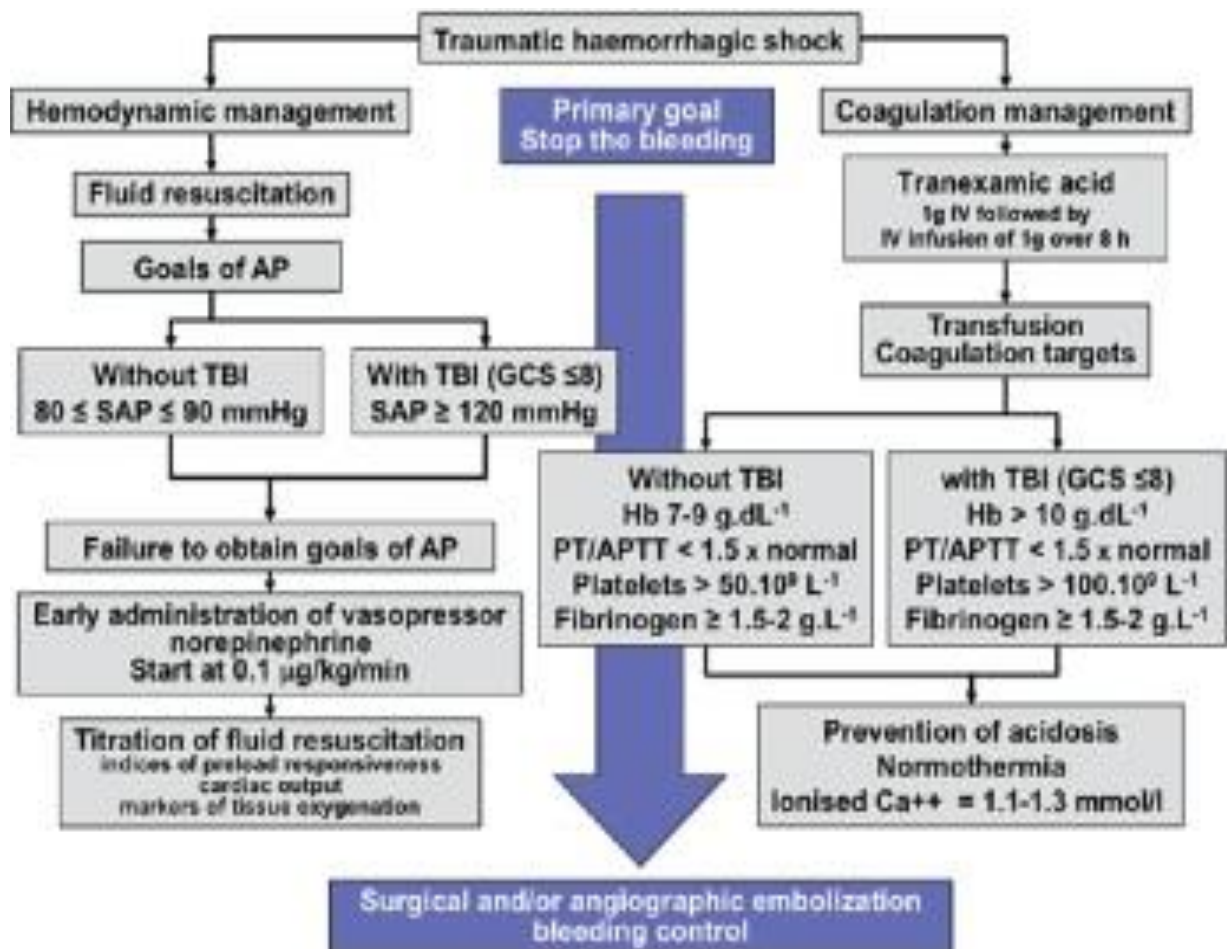
Figure 3: Flow chart of initial management of traumatic hemorrhagic shock. In the acute phase of traumatic hemorrhagic shock, the therapeutic priority is to stop the bleeding. As long as this bleeding is not controlled, the physician must manage fluid resuscitation, vasopressors, and blood transfusion to prevent or treat acute coagulopathy of trauma (AP = Arterial pressure, SAP = Systolic arterial pressure, TBI = Trauma brain injury, Hb = Hemoglobin, PT = Prothrombin time, APTT = Activated partial thromboplastin time).

- Time elapsed between injury and operation should be minimized for patients in need of urgent surgical bleeding control (Grade IA).

- Patients presenting with hemorrhagic shock and an identified source of bleeding should undergo an immediate bleeding control procedure unless initial resuscitation measures are successful (Grade IB).

- Early imaging (FAST or computed tomography) for detection of free fluid in patients with suspected torso trauma (Grade IB). If FAST is positive, it should be followed by immediate intervention.

- A target SBP of 80-100 mmHg until major bleeding is stopped in the initial phase without TBI (Grade IC). Low volume approach is contraindicated in TBI as adequate perfusion pressure is crucial to ensure tissue oxygenation of injured central nervous system.

- Target MAP of 65 mmHg or more, in controlled hypotensive resuscitation.

- Adjunct tourniquet uses to stop life-threatening bleeding from open extremity injuries in the presurgical setting.

- Initial normoventilation of trauma patients if there are no signs of imminent cerebral herniation. A low partial pressure of arterial carbon dioxide on admission to the emergency room is associated with a worse outcome in trauma patients with TBI. Hyperventilation and hypercapnia cause intense vasoconstriction with decreased cerebral blood flow and impaired tissue perfusion.

- Hemorrhagic shock with identified source of bleeding - initiate immediate bleeding control procedure.

- Serum lactate and base deficit measurement to estimate and monitor extent of bleeding and shock (Grade IB). Serum lactate is diagnostic parameter and prognostic marker of hemorrhagic shock. The amount of lactate produced by anaerobic glycolysis is an indirect marker of oxygen debt, tissue hypo-perfusion and the severity of hemorrhagic shock. Base deficit gives indirect estimation of acidosis due to impaired perfusion. Repeated lactate determinations represent a reliable prognostic index for patients with circulatory shock.

- DCR should be employed in severely injured patient presenting with deep hemorrhagic shocks, signs of ongoing bleeding and coagulopathy, hypothermia, acidosis, inaccessible major anatomical injury.

- Crystalloid should be applied initially for bleeding trauma patients (Grade IB). Hypertonic saline (HTS) to be considered for hemodynamically unstable patients (Grade 2B). Addition of colloid to be considered within the prescribed limits for each solution in hemodynamically unstable patients (Grade 2C).

- Early FFP in patients with massive bleeding (Grade IB). Platelets to be administered to maintain the count above 50×10^9 /L (Grade IC). However, maintain the count above 100

$\times 10^9$/L in patients with multiple trauma who are severely bleeding or have traumatic brain trauma (Grade 2C).

- Tranexamic acid 10-15 mg/kg followed by infusion of 1-5 mg/kg/h (Grade IB).
- Target hemoglobin of 7-9 gm% (Grade IC).

Monitoring of ionized calcium during massive transfusion (Grade IC). Calcium chloride to be administered if ionized calcium levels are low or electrocardiographic changes suggests hypocalcemia (Grade 2C).

Vasopressor Agents

Vasopressors may be required transiently to sustain life and maintain tissue perfusion in the presence of life-threatening hypotension, even when fluid expansion is in progress and hypovolemia has not yet been corrected. If used, it is essential to respect the recommended objectives for SBP (80-90 mmHg) in patients without traumatic brain injury. Norepinephrine is the agent of choice to restore and maintain target arterial pressure in hemorrhagic shock.

Management of coagulopathy in trauma patients

DCS is a resuscitation strategy that was devised to avoid these physiological disorders. DCR directly addresses the trauma-induced coagulopathy immediately upon patient admission [21] or in the pre-hospital setting [22]. DCR consists of balanced resuscitation, hemostatic resuscitation, and prevention of acidosis, hypothermia, and hypocalcemia.

Balanced resuscitation

The patient's response to the rapid infusion of isotonic fluid or blood is the indicator of the need for surgical or interventional hemostatic procedures. Aggressive fluid resuscitation was the initial fluid therapy recommended for many decades. However, this approach may contribute to increased blood loss and higher mortality [23].

Increasing evidence has shown that aggressive crystalloid-based resuscitation strategies are associated with cardiac and pulmonary complications [25], gastrointestinal dysfunction, coagulation disturbances, and disorders of immunological and inflammatory mediators [26]. Disturbances in cell volume then disrupt numerous regulatory mechanisms responsible for controlling the inflammatory cascade. For these reasons, an alternative approach to the treatment of hemorrhagic patients was recently proposed and practiced. The approach was introduced as permissive hypotension, delayed resuscitation, or controlled resuscitation. The aim of these resuscitation strategies is not hypotension but rather to balance the risk of decreased tissue perfusion with the benefits from the prevention of coagulopathy.

In 1994, Bickell and colleagues investigated the benefit of delayed fluid resuscitation in a randomized controlled trial. Five hundred eighty-nine adult patients with penetrating injuries and a pre-hospital systolic blood pressure of less than 90 mmHg were enrolled in the trial [27]. The

application of delayed fluid resuscitation increased the survival rate of of the patients from 62 to 70%.

After this report, several randomized or retrospective studies concerning balanced resuscitation were reported; however, the benefit to mortality varied among the studies [28, 29, 30, 31]. Duke et al. retrospectively compared cohorts with standard and restricted fluid resuscitation and reported that restricted fluid resuscitation showed a survival benefit [31].

When evaluating the effects of balanced resuscitation, these results should be interpreted cautiously. A recent Cochrane database analysis on crystalloids versus colloids published in 2013 that the resuscitation using colloids compared with crystalloids reduces the risk of death in patients with trauma, burns or following surgery. The use of HES may increase mortality. [38] Cochrane review concluded that since colloid use is not associated with improved survival, and they are considerably more expensive than crystalloids, it is hard to see how their continued use in clinical practice can be justified. [39] Further clinical trials of colloid use need to justify carefully the potential for patient benefit.

The tenth edition of the Advanced Trauma Life Support emphasizes the concept of balanced resuscitation, and the term "aggressive resuscitation" has been eliminated. The standard use of 1 L of crystalloid resuscitation as the starting point for all resuscitation has been modified to the initiation of 1 L of crystalloid infusion. Early use of blood and blood products for patients in shock is emphasized [32].

The most recent randomized controlled trial to evaluate the efficacy of balanced resuscitation was reported in 2015 [33]. This multicenter study was performed in 19 emergency medical services systems in the USA and Canada. The controlled resuscitation resulted in a reduction of early crystalloid resuscitation volume and an increase in the early transfusion of blood products. Although mortality at 24 h was not different among all patients, it improved in the subgroup with blunt trauma. The controlled resuscitation strategy can be successfully and safely implemented in a civilian environment beginning with the out-of-hospital setting and extending into early hospital care.

Hemostatic resuscitation

In 2007, Borgman and Holcomb et al. reported a survival benefit for the high ratio of plasma to red blood cell (RBC) in patients who received massive transfusions at a combat support hospital [34]. The most recent randomized trial to evaluate the suitable ratio of plasma to RBCs for patients with severe trauma and major bleeding was performed in the pragmatic, randomized optimal platelet and plasma ratios (PROPPR) study [44], in which 680 patients were randomized to receive either a 1:1:1 or 1:1:2 ratio of plasma, platelets, and RBCs. Although the mortality was not significantly different between the two groups, more patients in the 1:1:1 group achieved

hemostasis. Exsanguination, which was the predominant cause of death within the first 24 h, was significantly decreased in the high-ratio group.

Red Blood Cell Transfusion

In the *European* guideline, the Hb threshold for PRBCs transfusion is set to 7-9 g/dL where in US guideline Hb is set to 7 g/dL. These recommendations are based on studies showing that PRBCs transfusions can be associated with increased mortality, lung injury, increased infection rate and renal failure in injured patients and mainly on the *Transfusion Requirements in Critical Care* (TRICC) study demonstrating no efficacy of liberal approach (Hb threshold of 10-12 g/dL) versus restricted approach (7-9 g/dL) on mortality. For patients with concomitant hemorrhagic shock and traumatic brain injury, recent studies demonstrate no beneficial effect of a higher Hb threshold for RBCs transfusion on mortality or neurological outcomes but a higher risk of thromboembolic events, even if a higher Hb improves local cerebral oxygenation.

Plasma and Platelet

Transfusion in Hemostatic Resuscitation

The recent PROPPR randomized clinical trial compared 1:1:1 FFP-PLT-PRBCs ratio to 1:1:2 in severe trauma patients without survival bias. Unfortunately, the results showed a no statistically significant reduction in mortality for the 1:1:1 ratio group, letting the question open. The *European* guideline proposes to transfuse 1 FFP every two PRBCs during the initial management of patients with expected massive hemorrhage, continued with goal-directed therapy based on standard laboratory (PT or aPTT inferior to 1.5 times the normal controls) and/or viscoelastic tests.

Fibrinogen, a key component in the coagulation cascade, is the first and; most depleted factor in hemorrhagic trauma patients.

Platelet depletion or dysfunction in trauma patients needs to be addressed by platelet transfusion. The *European* guideline proposes to transfuse platelets if platelet count is less than 50.10^9/L in trauma patients or less than 100.10VL in case of ongoing bleeding or traumatic brain injury.

Viscoelastic Techniques and Administration of Concentrated Factors.

To adapt the treatment of hemostasis after the initial phase, viscoelastic techniques (VETs) may be very useful. VETs have been developed for several years and represent a comprehensive assessment of clot formation based on the mechanisms originating coagulopathy, including, in a second stage, inflammatory phenomena.

According to the latest *European* guideline, VETs are accepted as alternative to standard coagulation tests to guide the treatment of posttraumatic coagulopathy (grade 1C).

Principles of Clot Viscoelastic
Property Studies

Clot formation is assessed with ROTEM® (Tern GMBH, Munich, Germany) or with TEG® (Haemoscope Corporation, Niles, Illinois, USA). These tools explore dynamics of clot development, stabilization and dissolution (fibrinolysis).; The measured parameters are time (s), amplitude (mm) or angles.

TEG® and ROTEM® allow a rapid and accurate diagnosis of hyperfibrinolyses but will lack sensitivity to assess the intensity of fibrinolysis especially if minor or moderate.

Damage Control Resuscitation Once Bleeding Has Been Stopped

This step is devoted to reverse the sequelae of hypotension-related metabolic failure and support physiological and biochemical restoration.

Increasing power of damage control. Damage control should be started in the field by the paramedics who are trained to stop bleeding with local pressure or tourniquets, administer oxygen and combat hypothermia. The race against the clock starts. The emergency team in the field should strive for only minimal vascular filling, the objective being to obtain a systolic blood pressure of 90 mmHg; tranexamic acid should be administered. O-negative and then type-specific PRBC transfusions are started with the objective of obtaining hemoglobin of 9 g/dL (according to European guideline); coagulation disorders are corrected by administration of fibrinogen, coagulation factors and platelet concentrates. The patient is transferred rapidly to the operating room (or angiography suite, as necessary). When bleeding has been arrested, blood pressure should return to normal. Damage control resuscitation should be pursued until preset objectives of hemoglobin, temperature and coagulation parameters are attained. The comparison with naval damage control can be made in that not only should the water inflow be stopped, but the vital functions of the vessel must be restored as well (electricity, communications, propulsion, rudder) Invasive monitoring devices are generally used to guide fluid administration and normalize hemodynamics. Abramson and colleagues did show that serum lactate clearance correlates well with patient survival and that the ability to clear lactate to normal levels within 24 h was paramount to ensuing patient survival. Immediate and aggressive core rewarming not only improves perfusion but also helps reverse coagulopathy. All of the warming maneuvers initiated in the trauma bay and operating theatre should be duplicated in the intensive care unit. Gentilello showed that failure to correct a patient's hypothermia after a damage control operation is a marker of inadequate resuscitation or irreversible shock.

Rewarming

In DCR, hypothermia should be managed in conjunction with the efforts to correct the trauma-induced coagulopathy. It is essential to rewarm the torso using passive warming measures, such

as insulting foil, blankets, and the removal of wet clothes. The initial fluid resuscitation should be carried out with warmed infusions at a fluid temperature of 40–42 °C. Heated air inhalation, gastric or body cavity lavage with warmed fluids, and heat radiation are widely performed as well as the standardized use of warming measures with rapid infusers. The temperature in the emergency room and the operating room should be raised, at best to a thermally neutral range (28–29 °C)

Reversing acidosis

Reversal of metabolic acidosis in the trauma patient is better obtained through fluid and blood resuscitation and vasopressor support with surgical control of hemorrhage. Shock should be reversed and end-organ perfusion is restored . Because vital signs such as blood pressure and heart rate are not adequate to evaluate peripheral tissue perfusion, several endpoints of resuscitation are addressed. Base deficit and lactate levels are the reliable indices with which to evaluate the adequacy of the resuscitation and end-organ perfusion, and correlate with the mortality of trauma patients.

Tranexamic acid

The clinical randomization of an antifibrinolytic in significant hemorrhage 2 (CRASH-2) study, a large multi-center randomized controlled trial, investigated the effect of tranexamic acid on mortality and blood product requirements in trauma patients with hemorrhagic shock .The study was undertaken in 274 hospitals in 40 countries. More than 20,000 adult trauma patients were randomized to receive either tranexamic acid or placebo within 8 h of injury. All-cause mortality and the risk of death due to bleeding were significantly decreased with the administration of tranexamic acid. Maximal beneficial effects were achieved if it was given within the first 3 h of injury.

Fibrinogen concentrates

Fibrinogen plays a central role in the coagulation process. In patients with blood loss, fibrinogen has been reported to decrease more rapidly under critically low concentrations than the other coagulation factors. Thus, the supplementation of fibrinogen is a measure that makes sense when treating the coagulopathy of trauma patients. The effect of the administration of fibrinogen concentrates on outcome was investigated by matched-pairs analysis using the German Trauma Registry. Although 30-day mortality was comparable, 6-h mortality was significantly lower in the patients receiving fibrinogen. The fibrinogen concentrates might have delayed the cause of death from early hemorrhagic collapse to late multiple organ failure.

Prothrombin complex concentrate

Recently, prothrombin complex concentrate, derived from human plasma and contains variable amounts of factors II, VII, IX, and X, is used to correct coagulopathy. Goal-directed coagulation management using thromboelastometry was used to evaluate requirements of clotting factors .The

administration of fibrinogen concentrate alone or in combination with prothrombin complex concentrate resulted in a significant improvement of fibrin polymerization and shorter clotting time. Schochl et al. used fibrinogen concentrate and prothrombin concentrate complex as first-line therapies for coagulopathy based on thromboelastography in a study of 131 severely injured patients.

Calcium

Calcium acts as an important cofactor in the coagulation cascade. Low levels of ionized calcium at admission are associated with increased mortality and an increased requirement for massive transfusion. Citrate, which is used as an anticoagulant in blood product components, chelates calcium and exacerbates the hypocalcemia, particularly when used in the FFP. The faster the transfusion is given, the faster the reduction of the calcium concentration occurs. An ionized calcium concentration of less than 0.6–0.7 mmol/L could lead to coagulation defects. In addition, contractility of the heart and systemic vascular resistance are diminished under decreased ionized calcium levels. Because of its combined beneficial cardiovascular and coagulation effects, the calcium concentration should be monitored periodically with every ten units of transfusion, and it is recommended that a concentration of at least 0.9 mmol/L be maintained.

Massive transfusion protocol

Massive transfusion is typically defined as the transfusion of ten or more units of packed red blood cells within the first 24 h of injury. It is important for the resuscitation staff to identify the patients who might require massive transfusion early in the process of initial resuscitation. Following the prediction of massive transfusion, blood products should be delivered in a quick and timely manner at a high ratio of plasma, RBCs, and platelets. The protocol includes patient selection for activation of the MTP, description of the staff who should declare the activation, and the means by which the resuscitation team and the blood bank are informed of the protocol's activation.

Remote DCR

The concept and practice of the DCR is recently applied in the pre-hospital setting and named as remote DCR (RDCR). Not only the fixed-ratio coagulation therapy using the high ratio of plasma and platelets to pRBC but also the coagulation factor concentrate-based treatment is proposed in the RDCR. It includes three major components to a step-wise approach to achieve hemostasis: (1) stop (hyper)fibrinolysis, tranexamic acid; (2) support clot formation, fibrinogen concentrate; and (3) increase thrombin generation, prothrombin complex concentrate. Although RDCR warrants further investigation concerning its effect on the mortality or the blood products requirement, and the assessment of the patient's coagulation function in the instrument limited environment, the tranexamic acid has been implemented in the RDCR in the British, Norwegian, and Israeli civilian ambulance services. A prospective cohort study in the civilian trauma center demonstrated

reduction in mortality and multiple organ failure for patients treated with tranexamic acid in the subgroup of patients with shock .The updated European guideline suggests the administration of the first dose of tranexamic acid in route to the hospital as a grade 2C recommendation..

Changes of surgical strategy in DCR

The severely hemorrhagic patient has a limited amount of physiologic reserve before irreversible derangement, organ damage, and collapse occur. DCR restores this reserve, allowing more definitive treatment that results in decreased postoperative complications and improved outcomes .DCS is now incorporated as a component of DCR and should not be practiced in isolation . DCR as a structured intervention should begin immediately after rapid initial assessment in the emergency room and progresses through the operating theater into

Pre-hospital management	Start damage control resuscitation. Evaluation of possible bleeding points. Control of external bleeding: use of tourniquets for limbs with massive bleeding, scalp suturing, etc. Shortening of time to arrival in hospital in order to facilitate early bleeding control.	Hemostatic resuscitation
Emergency room	Re-evaluation and control of external bleeding, with identification of possible internal bleeding sites to decide surgery or interventional radiology.	
Operating room	Perform procedures needed to control bleeding points, with immediate blood flow restoration and contamination control.	
Intensive Care Unit	Patient stabilization, completion of the resuscitation process, warming, correction of acid-based imbalances and coagulopathy, and optimization of ventilation and hemodynamic condition.	
Operating room	Definitive surgical repair, which should be done once full patient stabilization and resuscitation has been achieved (variable time window).	

DCR strategy is the measure that directly addresses trauma-induced coagulopathy. Although several concerns, such as the plasma to RBCs ratio, the method of achieving balanced resuscitation, and the administration of other coagulation factors, are not completely resolved, it is now the most beneficial measure for treating trauma-induced coagulopathy, and it can change the treatment strategy of trauma patients. The effect of the reversal of coagulopathy in the massively hemorrhagic patient may shift the operative strategy from one of DCS to definitive surgery. Debate continues regarding the strategy of fluid management in trauma. Hemorrhagic

shock remains a leading cause of morbidity and mortality worldwide. Time-consuming procedures in the field should be avoided, and rapid transport to definitive care should be aimed at. Fluid choice has not been shown to affect the outcome in trauma, however large volume of the crystalloid resuscitation need to be avoided. In the absence of TBI, target SBP of 70-90 mmHg, normal mentation and peripheral pulses in case of uncontrolled hemorrhage should be aimed at. Normotension should be the aim in the presence of TBI. Tranexamic acid should be given to all the patients with penetrating trauma who need transfusion. MTP with fixed ratios should be given. Patients with penetrating trauma for whom definitive care is immediately available may benefit from damage control surgery. While DCR requires further study, the early literature seems to be promising.

Conclusions

1. Damage Control Surgery (DCS) is defined as the planned temporary sacrifice of normal anatomy to preserve the vital physiology. This is a concept in which the initial surgery becomes part of the resuscitation process rather than part of the curative process.

2. Once DCS was established, it was quickly marketed into other disciplines, including but not limited to neck, vascular, orthopedic, thoracic and military injuries. Although each discipline uses DCS in a slightly different manner, it is clear that the DCS approach leads to improved survival in patients with either blunt or penetrating injures who are approaching physiologic exhaustion.

3. It consists of 3 parts including the initial abbreviated laparotomy, ICU resuscitation and subsequent reoperation for definitive resuscitation This process serves to limit the physiological exposure to an unstable environment, allowing better resuscitation and outcome in the critically ill trauma patients.

4. Permissive hypotension - also known as "Hypotensive" or "Balanced" resuscitation - is a strategy of restricting fluid resuscitation until hemorrhage is controlled, while accepting a limited period of suboptimal organ perfusion. It is ensured by restricted fluid resuscitation to a volume sufficient to maintain a radial pulse. In polytrauma patients with head injuries, the importance of maintaining cerebral perfusion pressure is well recognized, consequently permissive hypotension is currently contraindicated in this setting.

5. DCR is a potent tool to hinder and even reverse the lethal triad. Damage control resuscitation currently includes early blood product transfusion, immediate arrest and/or temporization (i.e., TIVS and balloon tamponade) of ongoing hemorrhage, and restoration of blood volume and physiologic/hematologic stability. As a result, DCR addresses the early coagulopathy of trauma, avoids massive crystalloid resuscitation and leaves the

peritoneal cavity open when a patient approaches physiologic exhaustion without improvement.

6. Future evolution of the DCR concept will include further elucidation of personalized resuscitations (individual blood product ratios based on point of care testing) as well as introduction of hybrid angiography operating suites in centers with resource availability. Hypotensive Resuscitation Strategies prior to definitive hemorrage control.

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