

# Uncontrolled bleeding in patients with major abdominal trauma



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## Uncontrolled bleeding in patients with major abdominal trauma

*Haemodynamically instability after severe abdominal injuries requires a new therapeutic strategy. European guidelines recommend: reduced time, non-invasive investigations, avoid massive volemic replacement before surgery.*

*The primary aim of Damage Control Resuscitation protocol is to prevent the lethal triad: hypothermia, acidosis and coagulopathy. The treatment includes contemporary: permissive hypotension, haemostatic resuscitation, and Damage Control Surgery (DCS).*

*Systolic pressure below the physiological limits maximize the benefits of resuscitation and haemostasis, decreasing vessel clots expulsion.*

*Haemostatic resuscitation uses blood components and substitutes, to allow volemic replacement and to avoid trauma-induced coagulopathy (25% - 30% of complex trauma). The use of PRBCs and plasma 1 to 1 is an independent survival predictor in patients undergoing DCS.*

*Military haemostatic resuscitation protocol suggests massive transfusion using 10 or more PRBCs during 24 or 6 hours if 3 or more triggers are present: pressure > 90, hemoglobin > 11 g, temperature < 35.5°C, INR > 1.5, base deficit <math>\leq 6</math>. Joint Theater Trauma Registry demonstrated if we maintain PAS around 70-80 mmHg, using platelets, plasma PRBCs (1-1-1) and limiting crystalloids (250 cc), haemocomponents utilization decrease, mortality is reduced 65 % vs 19 % and Abdominal Compartment Syndrome incidence is limited.*

*When bleeding persists despite 10 PRBCs are infused, rFVIIa is recommended and Tranexanic Acid is essential in the drug list. Contemporary DCS performs packing for bleeding solve, intestinal diversion to avoid contamination and temporary wall closure to limit abdominal tension.*

KEY WORDS: Major abdominal trauma, Traumatic induced coagulopathy, Uncontrolled bleeding.

Uncontrolled bleeding, according to the European guidelines published in 2010, is bleeding that results in the complete loss of circulating blood volume (7% of total body volume in adults and 8-9% in children) within 24 hours or 50% within 3 hours, with a bleeding rate of 150 ml/min.<sup>1</sup> This extremely serious condition is the most common cause of death in cases of both a civil-

ian and a military setting. Patients with major abdominal trauma have a systolic blood pressure (BP) <90 mmHg, a Glasgow coma scale (GCS) score <8, a high organ injury scale (OIS) score due to injury severity score (ISS) >25, and an Acute Physiology and Chronic Health Evaluation (APACHE) score >19. Formerly these trauma victims died either immediately after the traumatic injury or while being transported to the emergency room (ER) but today, due to improved and more rapid service >10% are still alive on arrival at the hospital. A new strategy is needed for treating these patients who have very severe lesions and are hemodynamically unstable due to massive blood loss. First, the time required for admission to the ER should be reduced to a mini-

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mum, only investigations that directly affect treatment should be performed, and massive volume replacement before surgery should be considered useless and even harmful<sup>2</sup>. Grade 1 A recommendations in the European guidelines<sup>1</sup> state that patients with significant free intra-abdominal fluid who are hemodynamically unstable must be taken to the operating room (OR) immediately in order to minimize the time that elapses between injury and surgery and to achieve surgical control of bleeding as quickly as possible. This protocol of damage control resuscitation attempts to combat tissue hypoperfusion, deficits of coagulation factors and hypoxia due to massive hemorrhage, by the administration of fluids and red blood cells (RBCs) and by emergency explorative laparotomy. The primary goal of this treatment is to prevent the development of hypothermia hypocoagulation and metabolic acidosis, a "lethal triad"<sup>3</sup>.

Recent studies have shown that the presence of this triad creates a vicious pathophysiological circle since hypothermia inhibits platelet aggregation and increases pooling of platelets in the spleen while acidosis aggravates coagulation disorders, and stimulates the degradation of fibrinogen. The final result is a higher mortality rate<sup>4</sup>.

Damage control resuscitation in the setting of uncontrolled bleeding after major trauma is a protocol consisting of three surgical treatment strategies carried out simultaneously; permissive hypotension, hemostatic resuscitation and damage control surgery<sup>5</sup>. Together these new approaches to the treatment of victims of complex trauma have improved survival rates. Maintaining systolic BP below physiological limits, unless there are coexisting endocranial lesions which necessitate a BP of around 100 mmHg, makes it possible to maximize the metabolic benefits of resuscitation and improve hemostasis while reducing the risk of rebleeding caused by dislodging of clots. In the early years of this century Scalea demonstrated that maintaining systolic BP at around 70 mmHg instead of 100 mmHg during the reanimation phase of patients with severe bleeding had no negative effect on survival<sup>6</sup>.

Hemostatic resuscitation has been shown to optimize the reintegration of the blood supply with hemocomponents and hemoderivatives and to combat trauma-induced coagulopathy (TIC) which is present in 25-40% of patients with complex trauma<sup>7</sup>. As regards the former, it has been repeatedly demonstrated that transfusing packed red blood cells (PRBCs) and fresh frozen plasma in a 1:1 ratio together with a moderate use of crystalloids is an independent predictive factor for survival in patients undergoing damage control laparotomy<sup>8</sup>. The higher the ratio the greater the possibility of survival. In patients with TIC, especially in a military setting, the hemostatic resuscitation protocol calls for massive transfusion (MT) consisting of the transfusion of 10 or more units of PRBCs in the first 6 or 24 hours. In military protocols the presence of at least three of the following

triggers for MT, systolic BP >90 mmHg, hemoglobin level > 11g/dl, body temperature <35.5°C, International Normalized Ratio (INR) >1.5, and base deficit  $\geq$  6.0, makes necessary MT<sup>9</sup>. Scalea, after evaluating data of military trauma victims in Iraq and Afghanistan concluded that, in cases of critical bleeding after complex trauma, new resuscitation protocols called for maintaining a systolic BP of 70-80 mmHg, limiting the use of crystalloids, and transfusion of concentrated platelets, fresh frozen plasma and PRBCs in a 1:1:1 ratio<sup>10</sup>.

A retrospective analysis of 708 military trauma victims who underwent MT, published by the Joint Theater Trauma Registry in 2011, shows that the transfusion of RBCs, plasma and platelets in a 1:1:1 ratio and limitation of crystalloid administration to approximately 250 ml, made it possible to limit the use of hemocomponents and reduce the mortality rate from 65% to 19%<sup>11</sup>.

It was also found that the frequency of Abdominal Compartment syndrome (ACS) decreased because the reduced use of crystalloids practically eliminated capillary leakage and the resultant interstitial edema, which are key factors in the development of a "fourth space" and the rise in intra-abdominal pressure<sup>11</sup>.

As regards hemoderivatives, the new European guidelines recommend (grade 2C) considering the administration of recombinant activated Factor VII (rFVIIa) in initial doses of 200  $\mu$ g/Kg, followed by two doses of 100  $\mu$ g/Kg after 1 hour and after 3 hours, if critical bleeding persists in spite of an intensive use of hemocomponents (<10 units of RBCs)<sup>1</sup>. In clinical practice it has been shown that use of rFVIIa should be targeted. Acidosis inhibits rFVIIa: the procoagulant effect of rFVIIa is severely compromised at a pH <7.3<sup>4</sup>.

Hemoderivatives that are useful and less expensive are prothrombin complex PCCs registered in Italy as Uman Complex (Kedrion, Castevecchio Pascoli, Ital), Beriplex P/N (CSL Behring, Ottawa, Canada), Protromplex Tim 3®-Baxter-Immuno Vienna, Austria, Confidex (CLS Behring Marburg Germany), which contain some coagulation factors (II, IX and X and sometimes VII) and may also contain the anticoagulant proteins C and S. Associated with fibrinogen PCCs seem to normalize blood coagulation and increase clot strength. This cocktail of coagulation factors was initially used in the management of congenital or acquired anomalies in vitamin K-dependent coagulation factors and in cases of over-treatment with coumarin derivatives. European guidelines now recommend that PCCs be used even in cases of major bleeding and administered by slow (20 min.) intravenous infusion of 30-40 UI/Kg, and up to 50 UI/Kg in patients with an INR > 4. It must be kept in mind that an infusion of 1 UI/Kg can cause the prothrombin time (PT) to increase by 1%.

To date no cases of accidental thrombotic events have been reported after administration of PCCs in patients with uncontrolled bleeding after major abdominal trauma. This can be in great part attributed to the fact that

they do not contain thrombin or activated clotting factors and do contain small doses of heparin/antithrombin to prevent activation of clotting factors in vitro.

The United Nations added tranexamic acid to the list of essential drugs after the results of the pilot phase of the CRASH 2 trial were published<sup>12</sup>. This randomized controlled trial conducted on 20,000 randomized patients in 274 centers in 40 countries, and has so far provided encouraging data regarding the treatment of critical bleeding and without any reports of accidental thrombotic events.

To monitor coagulation in patients with uncontrolled bleeding the standard tests have been used, PT INR, and activated partial thromboplastin time (aPTT), but over time it became evident that these were not entirely effective in identifying TIC and were, moreover, time-consuming since it takes on average 78-88 minutes to obtain the best results. Today, in centers specialized in the treatment of uncontrolled bleeding, rotational thromboelastometry/thromboelastography (ROTEM/TEG) in use in the 1970s but then abandoned is again in the spotlight. With ROTEM/TEG precise information about the general coagulation status of a patient can be ascertained rapidly by evaluating the speed of clot formation and clot quality<sup>13</sup>.

In the surgical phase of resuscitation of these patients anesthesia management must follow the rules of damage control. Induction, sedation and neuromuscular block should be performed smoothly and fluctuations in systolic BP should be avoided. Pain management is essential and dissociative anesthesia should be used. This normally involves the administration of limited doses of fentanyl (approximately 1/5 of the normal dose). Care should be taken to avoid hypertensive peaks which can dislodge fibrin clots that are not yet stabilized<sup>11</sup>.

Damage control surgery simultaneously treats hemorrhage by means of packing, contamination by closure of the damaged bowel or by bowel diversion, and the subsequent (and predictable) increase in intra-abdominal pressure by means of temporary abdominal closure (TAC)<sup>5</sup>.

Packing, for compression hemostasis, is most often used in patients with major vascular lesions associated with parenchymal rupture, complex liver trauma, especially when complicated by laceration of the retrohepatic vena cava, complex pancreaticoduodenal injuries, and pelvic hematoma, especially when it is due to open fractures of the pelvis<sup>14</sup>.

Biological or synthetic glue, hemostatic gel and various types of topical hemostatic agents can be useful adjuncts to treatment. A new hemostatic wound dressing, Stasilon® (Entegriion, Research Triangle Park, NC, USA) containing fibers derived from bamboo, is currently recommended, and has been used with excellent results in military settings<sup>15</sup>. Treatment of retroperitoneal hematoma, according to the anatomical and topographical classification proposed by V.Selivanov<sup>16</sup>, should consist of surgical intervention for those in zone I (the central zone, both supra- and sub-

mesocolic), computed tomography angiography (CTA) and further angiographic procedures for those in zone II (right and left lateral), and conservative management for those in zone III (pelvis).

Pelvic packing after complex pelvic fractures associated with multifocal arterial and venous bleeding should be preceded by stabilization of the pelvis. This can be accomplished with various methods, using either direct intraperitoneal access via an open abdomen or preperitoneal access when it is not necessary to open the abdomen<sup>17</sup>.

Definitive control of arterial bleeding by means of percutaneous embolization, should follow packing not precede it since angiographic intervention before surgery is considered "time consuming"<sup>18</sup>.

The contribution made by interventional angiography is important in the reanimation phase (stage 2 of 3-stage treatment) for achieving hemodynamic stability.

The third stage, in which packing is removed, is problematic. It is especially important that this stage does not last more than 72 hours because after this time period the risk of infection steadily increases and also because of pack removal, which must be preceded by ample irrigation of the dressing with physiological solution and petroleum jelly oil in order to prevent dislodging of blood clots and rebleeding<sup>19,20</sup>.

In conclusion, in recent years the increasingly routine use of damage control resuscitation protocols has made it possible to reduce the use of hemocomponents and hemoderivatives, to limit the administration of crystalloids, and therefore to avoid post-resuscitation edema and creation of a "fourth space", with a notable reduction of ACS.

In addition this had led to less dilutional coagulopathy, less complications, and, because of improvements in anesthesia management, longer operating times, and earlier extubation are possible. These changes result in a higher overall survival rate<sup>10</sup>.

TAC is now the strategy most often used by army surgeons and it has revolutionized the surgical approach to victims of abdominal trauma, reducing the incidence of ACS and undergoing repeated modifications in response to technological developments

At the same time, however TAC is associated with the use of a large amount of hemocomponents and hemoderivatives, a longer stay in the intensive care unit, numerous interventions which lead to multiple complications, most commonly hemorrhage, enteric fistulas, and planned ventral hernias.

The treatment duration and hospital stay of TAC patients are long, and so this treatment method is complex and very expensive.

For these reasons, some authors, above all Americans, who recently performed a retrospective study on a large number of trauma cases reported in the literature, concluded that open abdomen appears to be used too frequently and often inappropriately<sup>21</sup>

It is therefore logical to ask oneself if increasing familiarity with damage control resuscitation may not in time lead to a reduction of TAC, thus permitting more selective use of open abdomen treatment and a renewed interest in primary closure <sup>22</sup>.

### Riassunto

L'instabilità emodinamica dopo traumi addominali gravi richiede una nuova strategia terapeutica. Le linee guida europee raccomandano: riduzione dei tempi, garantire indagini non invasive, evitare un recupero volemico massivo prima del trattamento chirurgico.

Lo scopo primario della "Damage Control Resuscitation" è prevenire la triade letale: ipotermia, acidosi, coagulopatia che porta alla formazione di un circolo vizioso fisiopatologico fatalmente ingravescente.

Il trattamento prevede l'attuazione contemporaneamente dei protocolli di ipotensione permissiva, rianimazione emostatica, Damage Control Surgery (DCS).

Molteplici studi militari e civili nell'ultimo decennio hanno dimostrato che negli emorragici critici il mantenimento di una pressione sistolica (PAS) a livelli sub fisiologici non incide negativamente sulla prognosi e permette una migliore emostasi, riducendo il rischio di espulsione dei coaguli dai vasi danneggiati.

La rianimazione emostatica utilizza emocomponenti e emoderivati, per il recupero volemico e per evitare la coagulopatia indotta dal trauma (25-40% dei politraumi). L'uso di Globuli rossi concentrati (pRBC) e plasma fresco congelato (FFP) nella proporzione 1 a 1 è un fattore indipendente di sopravvivenza dei pazienti che si sottopongono alla DCS.

Il protocollo militare di rianimazione emostatica in uso prima in Iraq e poi in Afganistan prevede la necessità di trasfusioni massive (MT) con 10 o più sacche di pRBC in 24 ore o in 6 ore quando presenti tre o più dei seguenti triggers: pressione arteriosa sistolica >90mmHg, emoglobina >11g/dl, temperatura <35.5 °C, INR>1.5, deficit di basi ≥6.

Il Joint Theater Trauma Registry ha dimostrato, con uno studio retrospettivo su 708 traumi militari sottoposti a MT, che se si mantiene la PAS vicina a valori di 70-80 mmHg, usando concentrati piastrinici (PC), FFP e pRBC nella proporzione di 1-1-1 e limitando i cristalloidi (circa 250 cc), si riduce l'utilizzo degli emocomponenti, contemporaneamente si limita l'incidenza della Sindrome Compartimentale Addominale e si diminuisce la mortalità dal 65% al 19%.

Quando il sanguinamento persiste a dispetto delle 10 sacche di pRBC infuse, è raccomandato l'impiego del rFVIIa o, in casi particolari del Complesso Protrombinico Concentrato (PCC). Un recente studio prospettico policentrico (Crash 2) ha dimostrato che l'utilizzo dell' Acido Tranexanico si è dimostrato essenziale nel fermare le emorragie e scervo di eventi trombo embolici indesiderati.

Se la fase critica emodinamica non si risolve, qualsiasi altra procedura sia diagnostica che terapeutica va considerata time-consuming e deve essere posticipata rispetto alla chirurgia in emergenza

Il trattamento chirurgico deve essere limitato alla sola chirurgia di Damage Control (DCS) utilizzando il packing per arrestare il sanguinamento, la diversione intestinale o il solo affondamento dei monconi per evitare la contaminazione e la chiusura temporanea della parete per limitare la tensione addominale.

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