CHAPTER 2

The clinical challenge of treating imminent exsanguination in trauma patients

This chapter is based on:

[A ‘blind’ transfusion policy in patients with acute severe blood loss].
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Prologue

The care of trauma patients with life-threatening hemorrhage is teamwork of which the final responsibility is borne by the trauma surgeon. To assure the best possible outcome, critical decision-making requires not only good knowledge and skills in trauma surgery and preservation of vital functions but also (team) leadership and governance throughout the trauma chain of survival. The trauma patient population is extremely heterogeneous. Each trauma patient is unique because of the immense diversity of factors that determine the condition and outcome of the patient. Due to the impact of different trauma mechanisms, one or more anatomical structures and/or one or more organ systems and/or vital functions can be damaged or deranged to a smaller or larger extent. Moreover, these derangements may appear in great variety of combinations. The heterogeneity in the trauma patient population is even more increased when patient factors such as age, co-morbidity, intoxication and different prehospital scenarios are added to the equation. In each case, trauma care demands a holistic but multidisciplinary approach of the patient as opposed to subdivision into treatment of single organs or systems without maintaining overview and so, omitting the establishment of priorities and best practice in the process of care. Trauma care is complex and time is a critical factor. So, successful trauma care requires preparation, organization, communication and teamwork on a national, regional and institutional level. In the Netherlands, care along the trauma chain of survival has been successfully organized through a national system of regional trauma networks. This system is being used as a template to organize care in chains of survival for other medical emergencies such as patients with stroke or myocardial ischemia. It may be superfluous to point out but ongoing education, training, audit and research are essential to improve the care of the injured. To illustrate the complexity of caring for a trauma patient on the brink of exsanguination, the case of an unfortunate horseman is dissected below.
An obstinate horse

A 54-year old horserman hit his saddle hard when his horse started bucking. He was able to dismount but soon after the accident he was found to be in shock and transported to the Emergency Department (ED). On admission, he was in profound hemorrhagic shock with a blood pressure of 80/60 mmHg and a pulse rate of 140 beats per minute. The pelvic X-ray showed a fracture of the anterior-posterior compression type (so-called ‘open book’-fracture) (Figure 1).

Figure 1. Pelvic X-ray taken during resuscitation in the emergency department showing traumatic symphysiolysis (a) and anterior diastasis (b) of both sacro-iliac joints (so-called ‘open book’-fracture). (Figure adapted from Frölke et al. with permission.)
Initial volume resuscitation consisted of intravenous infusion of 2000 mL of crystalloid fluids. An ultrasound examination according to FAST (Focused Assessment with Sonography for Trauma) revealed free intra-abdominal fluid. The patient, under suspicion of having a life-threatening intra-abdominal bleeding, was promptly transported to the operating room (OR). An emergency laparotomy was performed. The laparotomy revealed no intra-abdominal injuries but a large retroperitoneal hematoma was noted. Packing of the hematoma with gauzes to achieve tamponade of the retroperitoneum was not considered at that moment. Open reduction and internal fixation of the symphysiolyis was performed by plate osteosynthesis (Figure 2). In the intensive care unit (ICU), despite efforts to warm the patient and after transfusion of 35 units of packed red blood cells (PRBC), 10 units of fresh frozen plasma (FFP) and 4 units of platelet concentrates (PLTs; each constituted from 5 donors), hypothermia (core temperature of 34.5 °C) and an ongoing need for transfusion persisted. Systolic blood pressure fluctuated around 80 mmHg. In order to restore coagulation; fibrinogen, desmopressine, tranexamic acid and calcium were administered. Laboratory tests showed a hemoglobin (Hb) level of 4.8 mmol/L (normal values 8.1-10.7 mmol/L) and a prolonged activated partial thromboplastin time (aPTT) of 89 s (normal values 25-40 s), a prolonged prothrombine time (PT) of 51 s (normal values 8-13 s) and a platelet count of $22 \times 10^9$/l (normal values 150-400 $10^9$/l).

Arterial blood gas analysis showed acidosis with pH 7.14 (normal values 7.38-7.43) and a base deficit (BD) of $-16$ mmol/L (normal values $-2 - +2$ mmol/L). In order to stop ongoing bleeding, the decision was made to perform a relaparotomy. Just before transportation to the OR, coagulation factor recombinant factor VIIa (rFVIIa) was administered in a dose of 90 μg/kg. During laparotomy, massive intra-abdominal blood clots were evacuated and, again, a large retroperitoneal hematoma was identified. Diffuse bleeding (‘oozing’) from the pelvic cavity was tamponaded through packing of this cavity with gauzes (Figure 2).

Thereafter, because of suspicion of ongoing arterial bleeding in the pelvic cavity, the patient was moved to the angiography suite. Angiography of the pelvis showed extravasation of contrast (‘blush’) originating from the internal pudendal artery, which is indicative of active bleeding. The interventional radiologist successfully embolized this artery (Figure 2).
Figure 2. X-ray taken during procedural fluoroscopy of the pelvis showing (a) gauzes with radiopaque threads in the pelvic cavity ('packing'), (b) internal fixation with plate osteosynthesis of the symphysis (note the reduction of the symphysiolyis shown in figure 1 and (c) active bleeding (extravasation of contrast: ‘blush’) from the left internal pudendal artery which is being embolized by intra-arterial deposition of (d) coils (‘coiling’). (Figure adapted from Frölke et al. with permission)

Thereafter, systolic blood pressure stabilized around 100/60 mmHg with a pulse rate of 100 beats per minute. However, in ICU, transfusion of 10 units of PRBC, 6 units of FFP and 2 units of PLT’s were administered during several hours afterwards. In the meanwhile, the hemoglobin level had reached 6.9 mmol/L, the aPTT was 51 s, the PT was 24 s and the platelet count was $54 \times 10^9/l$. At that moment, arterial blood gas analysis showed a metabolic improvement (pH 7.33 and BD -4 mmol/L) and the body core temperature had increased to 36 °C. Two days later, the patient was returned to the OR to remove
the packing with gauzes. Large blood clots were noticed but no active bleeding was seen and the gauzes were removed without any problems. During the next 15 days, the patient developed the adult respiratory distress syndrome (ARDS) but recovered and was transferred to the ward. His recovery was complicated further by a surgical site infection. After two weeks on the ward, the patient was discharged and transferred to a rehabilitation center.

Commentary

The trauma chain of survival

‘A 54 year old horsemans hit his saddle hard when his horse started bucking. He was able to dismount but soon after he was found to be in shock and transported to the Emergency Department’. In trauma, the unexpected needs to be expected. Seemingly, minor events may have serious consequences that will manifest later on by clinical deterioration. The trauma mechanism of a ‘bucking horse’ may seem odd, but recently a small case series of similar patients has been reported. Injuries are sustained outside the hospital and often the time to definitive care within a trauma center can be substantial, even in a densely populated country without great outdoors such as the Netherlands. As time is a critical factor in managing life-threatening hemorrhage in trauma, acute care is like running a relay race along the trauma chain of survival and starts in the field. Care of the bleeding trauma patient is handed over between the following links of this chain: pre-hospital trauma care (emergency medical services (EMS), mobile medical team (MMT)); emergency trauma care (in the ED); operative trauma care (in the operating room (OR)); intensive care (in ICU); post-operative care (on the clinical ward); rehabilitation and outpatient care (in the rehabilitation center and/or outpatient clinic).

The three mainstays of treatment of life threatening hemorrhage in trauma

‘At admission, he was in profound hemorrhagic shock with a blood pressure of 80/60 mmHg and a pulse rate of 140 beats per minute. The pelvic X-ray showed a fracture of the anterior-posterior compression type (so-called ‘open book’-fracture). Initial volume resuscitation was performed intravenous infusion 2000 mL of crystalloid fluids. An ultrasound examination according to FAST (Focused Assessment with Sonography for Trauma) revealed free intra-abdominal fluid. The patient, under suspicion of having a life-threatening intra-abdominal bleeding, was promptly transported to the operating room (OR).’
The three mainstays of treatment of life-threatening hemorrhage in trauma\textsuperscript{4,5} are:

I) \textit{Stop the bleeding (hemorrhage control)}

While securing the airway and achieving effective ventilation and oxygenation, source(s) of bleeding need to be localized as quickly as possible to stop traumatic hemorrhage.\textsuperscript{6} In case of blunt trauma, as opposed to penetrating injuries where the probable anatomical location of the bleeding is indicated by the presence of external wounds, a pragmatic approach is warranted through searching for \textit{blood on the floor and four places more}. ‘Blood on the floor’ refers to external blood loss from open fractures (including maxillofacial fractures) and external wounds (e.g. lacerations of the scalp). ‘Four places more’ refers to four body compartments where significant blood loss due to trauma may occur: 1) extremities (closed long bone fractures), 2) chest (injuries of internal organs and/or blood vessels), 3) abdomen (injuries of internal organs and/or blood vessels) and 4) pelvic cavity (fractures of the pelvis have been referred to as ‘killing fractures’ because exsanguination can occur from the accompanying massive blood loss).\textsuperscript{7} External blood loss and the presence of long bone fractures can be diagnosed by physical examination. Evidence of occult blood loss, especially in blunt trauma, can be found by rapid screening of the chest, abdomen and pelvis through chest X-ray, FAST and pelvic X-ray in ED. All measures to stop the bleeding need to be applied, varying from digital pressure, tourniquets and splinting to provisional hemostatic suturing and pressure bandaging. The next step will be ‘damage control’\textsuperscript{8} surgical procedures (in OR) to get control of internal bleedings.

II) \textit{Volume support (restoration of the circulating blood volume)}

In massive blood loss, volume suppletion is initiated by administration of intravenous fluids\textsuperscript{6} (e.g. crystalloid and/or colloids). However, massive blood loss with severe hemorrhagic shock requires early, massive transfusion of blood products to restore perfusion, oxygen transport and coagulation. The depth of hemorrhagic shock, the patient response to initial therapy, control of hemorrhage and concomitant injuries, in particular traumatic brain injury, dictate resuscitation and goals regarding endpoints of resuscitation should be set.

III) \textit{Correction of coagulopathy}

Massive blood loss, profound hemorrhagic shock and subsequent resuscitation cause or enhance coagulopathy through the mechanisms of hemodilution, consumption and loss of coagulation factors, hyperfibrinolysis, hypothermia, acidosis and hypoperfusion.\textsuperscript{9,10} Aggressive treatment to correct
coagulopathy is needed to prevent exsanguination from non-surgical bleeding ('oozing') and may require measures beyond the early administration of FFP and PLTs such as the administration of procoagulants (e.g. rFVIIa) and antifibrinolytic agents (tranexamic acid).

**Damage control surgery**

‘An emergency laparotomy was performed. The laparotomy revealed no intra-abdominal injuries but a large retroperitoneal hematoma was noted. Packing of the hematoma with gauzes to achieve tamponade of the retroperitoneum was not considered at that moment. Open reduction and internal fixation of the symphysiolyis was performed by plate osteosynthesis.’

Therapeutic goals need to be set during resuscitation taking the actual physiological condition of the patients into account. To provide for attainment of the specific awareness, knowledge and skills that are needed for successful resuscitation in trauma, international master classes are organized for surgeons and anesthetists. To prevent further deterioration of the trauma due to acidosis, hypothermia and coagulopathy, abbreviated surgical techniques to stop bleeding and/or prevent contamination and quick, closure techniques are used to limit time spent in the OR. These techniques consist of packing (gauze tamponade of solid organs and/or pelvic cavity), ligation/coagulation of bleeding vessels, suturing and/or (partial) resection of bleeding solid organs or extremities, occlusion of larger blood vessels and/or wounds in solid organs with Foley-catheters, rapid external/internal fixation of long bone and/or pelvic fractures, shunting of damaged, larger blood vessels (with plastic tubes). Definitive surgical repair of injuries can be performed in a later stage, after homeostasis has been achieved in the ICU.¹¹

**‘Blind’ transfusion of blood products and the lethal triad**

‘In the intensive care unit, despite efforts to warm the patient and after transfusion of 35 units of packed red blood cells (PRBC), 10 units of fresh frozen plasma (FFP) and 4 units of platelet concentrates (PLTs; each constituted from 5 donors), hypothermia (core temperature of 34.5°C) and an ongoing need for transfusion persisted. Systolic blood pressure fluctuated around 80 mmHg. In order to restore coagulation; fibrinogen, desmopressine, tranexamic acid and calcium were administered. Laboratory tests showed a hemoglobin (Hb) level of 4.8 mmol/L (normal values 8.1-10.7 mmol/L) and a prolonged activated partial thromboplastin time (aPTT) of 89 s (normal values 25-40 s), a prolonged prothrombine time (PT) of 51 s (normal values 8-13 s) and a platelet count of 22 x 10⁹/L (normal values 150-400
Arterial blood gas analysis showed acidosis with a pH 7.14 (normal values 7.38 – 7.45) and a base deficit (BD) of –16 mmol/L (normal values -2 + 2 mmol/L).

During or after elective surgery, massive blood loss can be estimated reliably since the starting point is a situation of normovolemia. Guidelines for transfusion of blood components in these situations are based on the effects of hemodilution in normovolemic situations. Moreover, in elective cases, it is possible to anticipate the need for the administration of fluid and blood products in case of hemorrhage and fluid shifts and the patient seldom reaches a state of tissue hypoperfusion.\textsuperscript{12} So, these guidelines for normovolemic situations are of no value in case of massive blood loss in trauma where the amount of lost blood volume is unknown and the patient is presented in hypovolemic shock. Transfusion of blood components needs to be started ‘blindly’: i.e. empirical and not indicated by laboratory tests. Standard laboratory tests (e.g. for coagulation) are time-consuming and may show ‘pseudo-normalization’ (due to warming of the samples when tested).\textsuperscript{13} Also, standard laboratory tests do not give information about the actual formation, strength and lysis of blood clots. However, massive transfusion in trauma can be life saving and administration of blood products should be started immediately.\textsuperscript{14,15} Ideally, for ‘blind’ transfusion, protocols with algorithms (with fixed blood product ratio’s) and sound logistics (in cooperation with the blood bank) are needed to provide for early and rapid administration of not only PRBC but also of FFP and PLT’s in sufficient amounts, under hectic circumstances.\textsuperscript{1} In addition to massive transfusion, in order to counteract the so-called ‘lethal triad’ of acidosis (shock), coagulopathy and hypothermia\textsuperscript{16} that promotes further bleeding, other measures should be taken such as warming of the patient and administration of specific procoagulants when indicated.

**Stop the bleeding with all means**

‘In order to stop ongoing bleeding, the decision was made to perform a relaparotomy. Just before transportation to the OR, the coagulation factor recombinant factor VIIa (rFVIIa) was administered in a dose of 90 \( \mu \)g/kg. During laparotomy, massive intra-abdominal blood clots were evacuated and, again, the large retroperitoneal hematoma was identified. Diffuse bleeding (‘ooze’) from the pelvic cavity was tamponaded through a packing of this cavity with gauzes. Thereafter, because of suspicion of ongoing arterial bleeding in the pelvic cavity, the patient was moved to the angiography suite. Angiography of the pelvis showed extravasation of contrast (‘blush’) originating from the internal pudendal artery, which is indicative of active bleeding. This artery was successfully embolized by the interventional radiologist.’
rFVIIa was originally developed for treatment of hemorrhage in hemophiliacs but its potential, beneficial effect in life-threatening hemorrhage in trauma patients promoted off-label use in case of sustained traumatic coagulopathy and imminent exsanguination when conventional therapy (including surgery) failed.\textsuperscript{17} Since then, several clinical trials have been performed to elucidate the role of rFVIIa and other procoagulants as adjuncts to massive transfusion in hemorrhaging trauma. A pelvic fracture solely may lead to exsanguination. The blunt force that acts on the bony pelvic ring may disrupt soft tissue structures such as the pelvic floor and the presacral venous plexus. Low pressure (venous) bleeding can be effectively dealt with by packing the pelvic cavity\textsuperscript{18} and (provisional) stabilization of the pelvic ring. Arterial bleeding can be stopped by ligation of blood vessels. After packing, ongoing blood loss may be caused by the much more rare (higher pressure) bleeding from pelvic arteries. Transcatheter arterial embolization of bleeding vessels\textsuperscript{19} is a very effective means to stop this type of hemorrhage and requires, besides a 24/7 interventional radiology service, a more 'stable' patient that can be transferred to the angiography suite.

\textbf{The bleeding has stopped: definitive surgery and coping with complications}

‘Thereafter, systolic blood pressure stabilized around 100/60 mmHg with a pulse rate of 100 beats per minute. However, in ICU, transfusion of 10 units of PRBC, 6 units of FFP and 2 units of PLTs were administered during several hours afterwards. In the meanwhile, the Hb-level had reached 6.9 mmol/l, aPTT was 51 s, PT was 24 s and the platelet count was $54 \times 10^9$/L. At that moment, arterial blood gas analysis showed pH 7.33 and BD -4 mmol/L and core body temperature was 36°C. Two days later, the patient was returned to the OR to remove the packing with gauzes. Large blood clots were noticed but no active bleeding was seen and the gauzes were removed without any problems. During the next 15 days, the patient developed adult respiratory distress syndrome (ARDS) but recovered and was transferred to the ward. His recovery was complicated further by a surgical site infection. After two weeks on the ward, the patient was discharged and transferred to a rehabilitation center’

Within 24 to 48 hours after the bleeding has stopped and homeostasis has been achieved, removal of packs, definitive surgical procedures (anastomosis, resection) and closure of body cavities (if possible) is performed.\textsuperscript{11} In case of polytrauma, multiple sessions in OR may be needed thereafter for definitive treatment of e.g. fractures or closure of the abdomen. All sorts of complications can disrupt the clinical course. Common are complications related to the type and severity of injuries, surgical procedures and the degree of physiological derangement. Moreover, massive transfusion in trauma is independently
associated with increased infections\textsuperscript{20} and the post-injury multiple organ dysfunction syndrome (MODS)\textsuperscript{21}. After discharge from ICU the patient and his/her family will experience more and more the long and difficult road of rehabilitation that often may take more than one year post-injury. Intensive therapy and support are needed to resume pre-injury activities (despite permanent disabilities) and to prepare the patient for return into society.

**Epilogue**

Life-threatening hemorrhage in trauma is a complex but treatable disease provided that care and care providers along the trauma chain of survival are well prepared on national, regional, institutional and individual levels. After having secured the airway and establishment of adequate oxygenation and ventilation, all efforts must be directed at rapid hemorrhage control, volume support and coagulation management. Critical decision-making is a team effort under the final responsibility of the trauma surgeon.
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