■ INSTRUCTIONAL REVIEW: TRAUMA

Strategies for the management of haemorrhage following pelvic fractures and associated trauma-induced coagulopathy

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Exsanguination is the second most common cause of death in patients who suffer severe trauma. The management of haemodynamically unstable high-energy pelvic injuries remains controversial, as there are no universally accepted guidelines to direct surgeons on the ideal use of pelvic packing or early angio-embolisation. Additionally, the optimal resuscitation strategy, which prevents or halts the progression of the trauma-induced coagulopathy, remains unknown. Although early and aggressive use of blood products in these patients appears to improve survival, over-enthusiastic resuscitative measures may not be the safest strategy.

This paper provides an overview of the classification of pelvic injuries and the current evidence on best-practice management of high-energy pelvic fractures, including resuscitation, transfusion of blood components, monitoring of coagulopathy, and procedural interventions including pre-peritoneal pelvic packing, external fixation and angiographic embolisation.

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Injuries to the pelvis that result from high-energy trauma can be devastating, and patients often have other associated injuries. In haemodynamically unstable patients, early identification of the source of bleeding is crucial for effective resuscitation.[1] With improvements in pre-hospital triage patients often arrive in a trauma centre within the golden hour, thus prompt intervention is paramount.[2] Despite mortality rates between 10% and 60% for patients with a haemodynamically unstable pelvic fracture, evidenced-based guidelines for their management are not universally agreed upon and local protocols predominate.[3-8] Whether early angio-embolisation or pre-peritoneal pelvic packing should take precedence in the management of these injuries remains controversial.[9] Additionally, the optimal algorithm for resuscitation, which prevents or halts the progression of the trauma-induced coagulopathy (TIC), is yet to be determined.[10-14]

In severely injured patients, haemorrhage is the second most common cause of death[15,16] after brain injury, and is potentially preventable. The immediate reduction of pelvic volume via the application of a pelvic binder (circumferential compression) or external fixator results in a tamponade effect and can prevent further bleeding from venous or bony sources. This technique can be life-saving and is an essential part of initial resuscitation in the emergency department (ED).[17-22] Regardless of the specific algorithm followed by an institution, a multidisciplinary approach in the management of these patients is essential, including the involvement of general trauma surgeons, orthopaedic surgeons and specialists in intensive care.[23] The aim of this paper is to present the current evidence behind the various – and at times controversial – resuscitative strategies and procedural intervention for the management of haemodynamically unstable pelvic fractures and highlight some of the pearls and potential pitfalls.

Classification of high-energy injuries to the pelvic ring

Pelvic fractures are present in between 10% and 20% of patients who sustain high-energy blunt trauma, and account for 3% to 8% of all skeletal injuries.[24] The most common mechanism of injury is a motorcycle accident, followed by a road traffic accident involving a pedestrian, a fall from height, a road traffic accident and a crush injury. These fractures are also associated with significant long-term morbidity.[24,25]

Several classification systems have been described, based on the site of the fracture, the stability of the pelvis, the mechanism of injury and the direction of force applied. The most commonly used systems are the Tile[26] and the

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Young–Burgess[27] classifications.[28] The Tile system classifies fractures according to their stability, which is provided primarily by the posterior ligamentous complex. Type A fractures are completely stable with an intact posterior complex, type B are vertically stable but rotationally unstable (i.e. partially stable), and type C are both vertically and rotationally unstable. Type B fractures are further subdivided into B1 (open-book), B2 (lateral compression) and B3 (bilateral).

The Young–Burgess system is based primarily on the direction of the force causing the injury, and classifies them as anteroposterior compression (APC), lateral compression (LC), vertical shear (VS) and combined mechanism (CM).[27] The APC and LC types are further divided into three subcategories based on the extent of ligamentous disruption. APC types II and III, LC type III and VS fractures are characterised by major ligamentous disruption. The VS fractures include the isolated vertical force vectors, and CM fractures include pelvic ring disruptions that do not fall into a single category.

As well as providing a classification, the Young–Burgess system was designed to assist in identifying posterior ring injuries, to predict associated injuries and their resuscitation requirements, and predict mortality rates.[27] Several studies have shown that, of all pelvic fractures, APC type III fractures required the most transfused blood, probably owing to bilateral disruption of the sacral venous plexus and possible associated iliac artery injury; this is followed by LC type III, VS and CM fractures.[27,29,30] However, recent studies have questioned the predictive value of both classification systems. In one study evaluating both systems, no statistical correlation was identified between mortality rates and classification subgroups.[31] When injuries were classified into larger subgroups – partially stable (Tile B1/B2/B3 and LC I/APC I) and unstable (Tile C1/C2/C3 and LC II/LC III/APC II/ APC III/VS/CM) – a significantly higher mortality rate was noted for unstable Young–Burgess fractures.[31] Similarly, Manson et al[30] highlighted that by dividing the Young–Burgess classification into stable and unstable types, the predictive power of the classification increased with regard to mortality, transfusion requirements and non-orthopaedic injuries. Taking into account the inherent weaknesses of these classification systems, an individualised patient-specific approach must be employed to consider the patient's haemodynamic stability, the response to resuscitation, the mechanical stability of the pelvis and the associated injuries.

Patients who sustain a pelvic fracture can be categorised into two groups. First, those who are haemodynamically normal, having sustained a stable fracture with moderate ligamentous disruption. Their management involves osteoligamentous reconstruction on a non-urgent, semi-elective basis. This group comprises the majority of patients who sustain a fracture of the pelvis. Second, those with haemorrhagic shock from a displaced or unstable pelvic fracture necessitating a multidisciplinary team approach for emergent control of bleeding and pelvic stabilisation. This group accounts for < 10% of all those who sustain a fracture of the pelvis.

Mortality in the latter group can be stratified into three broad categories: exsanguination, brain injury and multiple organ failure. In the acute setting, within 24 hours from injury, death is due to haemorrhage and shock. In the subacute or late setting, death is due to the systemic inflammatory response to the trauma, with resultant adult respiratory distress syndrome (ARDS) and multiple organ failure.[32-34] Death due to an injury to the brain can occur at any time during the hospital stay. The presence of an associated open pelvic injury (i.e. a fracture with direct communication to the environment owing to disruption of the overlying skin, vagina or rectum) increases the mortality rate substantially, with rates > 50% having been reported.[35]

Bleeding pelvic fractures. Mortality rates in haemodynamically unstable patients with a pelvic fracture range from 18% to 40%. Death within the first 24 hours of injury commonly results from blood loss.[10,34] In patients with multiple injuries the source of bleeding is not always clear, and exclusion and/or management of blood loss from the chest and/or abdomen should be prioritised. Blood loss from pelvic fractures comes from three major sources: veins, arteries and cancellous bone. The low-pressure pelvic venous plexus is the most common source of bleeding, and is responsible for about 80% of bleeds in unstable pelvic fractures. Cadaveric studies suggest that it is the medium-sized vessels around the sacroiliac joints that are responsible for most bleeding.[36-38]

Haemodynamic instability from arterial bleeding occurs in between 10% and 15% of unstable pelvic fractures, hence a knowledge of the arterial anatomy allows angio-embolisation to be used to control actively bleeding vessels.[3,39]

Haemorrhage from fractured cancellous bone can be controlled by bony approximation and stabilisation.[36,37]

The retroperitoneal space can contain up to 4000 ml to 5000 ml of blood, and bleeding will continue until tamponade occurs. Physiological tamponade does not occur until the combined intrapelvic and retroperitoneal pressure exceeds the intravascular pressure. However, in an unstable pelvis with ligamentous disruption, tamponade is not feasible. Without its bony containment the retroperitoneal space will continue to expand, as it no longer functions as a closed system.[40]

Several authors have evaluated the use of fracture patterns to predict arterial injury, but the results are controversial. Some studies have reported that higher rates of transfusion are associated with APC type III and VS fractures,[27,29,41-43] and rarely, a posterior fracture along the sacroiliac joint may disrupt the main iliac trunk, with catastrophic haemorrhage.[44] Other studies report major pelvic bleeding with less severe patterns of fracture.[41,42,45,46] These differences are probably due to the fact that radiographs can only capture the displacement at the time of imaging, without any correlation with the maximum degree of displacement experienced at the time of injury.

Acute resuscitation strategies

Uncontrolled haemorrhage accounts for up to 40% of all deaths following major trauma.[16] Thus, hemorrhage control is paramount to prevent early in-hospital death in these patients. The principles and practice of resuscitation have evolved over the past three decades, as we have developed a better understanding of the pathophysiology involved in haemorrhagic shock and subsequent trauma-induced coagulopathy (TIC). Traditionally, aggressive fluid resuscitation was used to restore blood volume. However, it has become apparent that flooding a patient with crystalloids may be counterproductive. This may promote continued bleeding by increasing the intraluminal pressure at the fracture site, particularly in penetrating trauma, causing blood clots to dislodge. Additionally, 'over-resuscitation' can dilute clotting factors and lead to hypothermia, which will exacerbate any coagulopathy. The concept of 'permissive hypotension' theoretically avoids the adverse effects of aggressive fluid resuscitation while maintaining low but adequate tissue perfusion in the short term.[47] However, in injuries to the brain or spine 'permissive hypotension' is contraindicated, as ensuring adequate tissue oxygenation of the central nervous system overrides the risk of continued haemorrhage.[48] In one retrospective study, the incidence of coagulopathy was noted to increase as the volume of intravenous fluid administration increased, up to 70% in patients who received > 4000 ml of fluid (crystalloid:colloid ratio 1.6:1).[49] Recently published European guidelines for the management of haemorrhage following major trauma recommend maintaining a systolic blood pressure of 80 mmHg to 100 mmHg. However, other recently published articles report that the concept of 'permissive hypotension' cannot be universally applied as the optimal blood pressure remains unknown.[50,51] Additionally, this approach must be used cautiously in elderly patients, particularly in those with chronic hypertension.

Trauma-induced coagulopathy

In unstable pelvic fractures, as with any high-energy trauma, the development of TIC occurs in 25% to 40% of patients, and is directly related to the injury severity score (ISS).[52,53] Although a common sequela, its treatment remains a challenge. Several factors have been identified as contributing to TIC, including the severity of the injury, haemorrhagic shock, haemodilution, clotting factor consumption, and impaired formation of thrombus. Additionally, bleeding and tissue hypoperfusion lead to the lethal triad of acidosis, hypothermia and coagulopathy.[14,54] It was therefore commonly accepted that hypothermia and acidosis were intimately associated with TIC. Over the last decade, however, the concept of the endogenous coagulopathy of trauma has begun to mature and includes a cell-based model of coagulation.[55,56] In brief, this model abandons the traditional thinking of coagulation as being driven by enzymatic cascades, and introduces interactions between specific cell surface receptors and plasma components resulting in the formation of a clot. Furthermore, this model considers coagulation as occurring in three overlapping steps: 1) initiation, which occurs on tissue factor-bearing cells (primarily vascular sub-endothelial cells which are not normally exposed to blood and leukocytes in response to inflammatory mediators), 2) amplification and 3) propagation; the latter two processes occur on the surface of platelets. This cell-based model introduced a paradigm shift in the management of TIC. More recently, the hypothesis of TIC driven by protein C activation has begun to emerge. Proteins C and S, thrombomodulin and antithrombin are well-known endogenous anticoagulants. The idea of excessive protein C activation stems from reports of patients presenting with TIC within a short time of injury which was not correlated to clotting factor consumption, as was traditionally thought, but rather due to hypoperfusion and tissue injury.[57,58] In brief, sustained hypoperfusion is associated with an increased endothelial expression of thrombomodulin. This increases the availability of thrombomodulin-bound thrombin complexes on endothelial cells to activate protein C. Activated protein C then functions as an anticoagulant by rendering activated Factors V and VIII inactive, thereby reducing the overall generation of thrombin and its downstream procoagulant effects.[59] At this point, TIC is thought to consists of three elements:

- Impaired thrombin generation, which most agree is at least partially due to the activation of the anticoagulant protein C pathway, as a result of hypoperfusion.[57,60]

- Hyperfibrinolysis is a critical component of TIC in some patients. However, a mechanistic link between TIC and fibrinolysis remains largely unknown. At this point, a decrease in plasminogen activator inhibitor-1 (PAI-1) is the focus of attention, as this is the principal inhibitor of tissue plasminogen activator (tPA). Although low PAI-1 levels have been reported in trauma patients with an associated increase in protein C activity,[57,61,62] the mechanistic link has not been established.[63] The key breakthrough will come from differentiating pathological, uncontrolled fibrinolysis leading to uncontrolled haemorrhage and death, from physiological lysis directed by haemostasis during injury in order to preserve vascular patency.

- Although early platelet dysfunction is involved in TIC, the mechanistic link between early platelet dysfunction and TIC remains a mystery.[64]

The diagnosis of TIC is made both clinically on the basis of generalised 'non-surgical' bleeding and with laboratory markers. The historical laboratory diagnosis includes prothrombin time (PT)/international normalised ratio (INR) and an activated partial thromboplastin time (aPTT) > 1.5 times the normal rate.

Although clinical data suggest that PT/INR and aPTT correlate poorly with bleeding, in many institutions these tests remain the routine method of diagnosing TIC. Another shortcoming of both INR/PT and aPTT is that they are performed in platelet-poor plasma assays, and

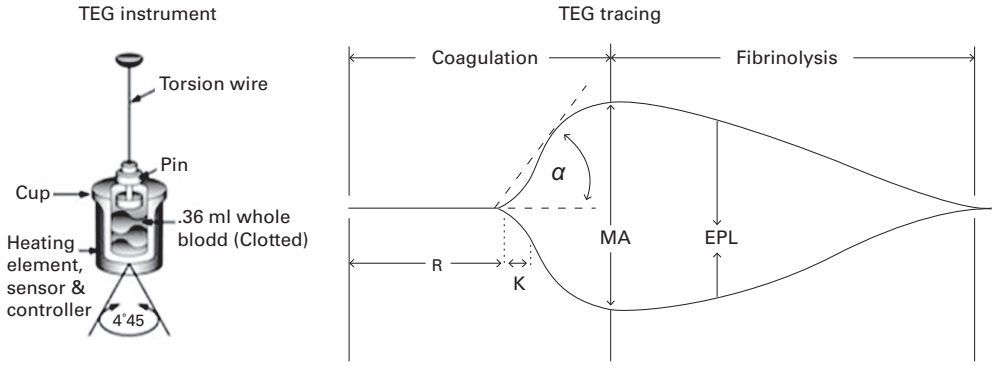

Fig. 1

Thromboelastography instrument and tracing. The instrument diagram illustrates the cup where the whole blood sample is placed and the pin attached to a torsion wire. The tracing begins with a linear segment from the start of the test to the formation of the first fibrin strands, resulting in stress being placed on the torsion wire and causing the tracing to split. The progressive deviation of the tracing reflects the formation of the clot (TEG, thromboelastography; R, reaction time; K, coagulation time (min); α, angle formed between horizontal and tangent line of the slope between reaction and coagulation time (°); MA, maximum amplitude (mm); EPL, percentage lysis). TEG® images: TEG® Instrument, TEG® tracing and TEG® interpretation of tracing shapes are used with the permission of the Haemonetics corporation. TEG® and Thrombelastograph® are registered trademarks of Haemonetics Corporation in the US, other countries or both.

were designed to monitor anticoagulation therapy and screen for heritable coagulopathies, thus ignoring any cell-based interactions. Viscoelastic assays of coagulation, although not new, take into account the cell-based model of haemostasis.

'Point-of-care' monitoring of coagulation by thromboelastography (TEG). One of the challenges in the management of TIC is the inadequate diagnosis and real-time monitoring of treatment using traditional plasma-based laboratory coagulation tests, PT/INR and aPTT, as they are time-consuming and offer only a limited assessment of the coagulation cascade as they are confined to the initiation of clot formation. Owing to these limitations the use of rapid 'point-of-care' TEG is gaining popularity.[65-67] It offers several advantages over traditional PT and aPTT tests.[67,68]

- The activated clotting time (ACT) from the rapid TEG can be obtained at the bedside or in the laboratory, within five minutes, and provides a rapid guide for the initiation of massive transfusion. It also gives physicians a real-time assessment, allowing for clinical decisions to be made concurrently.

- The subsequent measurements of the α angle (fibrinogen), maximum amplitude (platelets), and percentage lysis (fibrinolysis) provide invaluable information about the management of transfusion, in a goal-directed manner.

- A more complete assessment of the coagulation cascade can be obtained, as the test is done using whole blood and so the combined influences of packed red blood cells (PRBC), platelets (PLT), leukocytes, and plasma clotting factors on the formation of a clot are accounted for.

- The endpoints, i.e. clot time, strength and lysis rate (discussed below), are clinically relevant.

In brief, the TEG analyser consists of two mechanical components separated by a blood specimen (a cup and a pin/torsion wire suspended within the specimen). Once the specimen is in place, the temperature is adjusted to match the patient and the cup begins to oscillate. As the clot begins to form between the pin and the blood specimen, the developing fibrin strands in turn pull the wire as the specimen oscillates. This tensioning of the wire generates a signal that is plotted, resulting in the characteristic TEG tracing seen in Figure 1.

The various components of the TEG tracing (Fig. 1) are the reaction time (R, minutes), i.e. the time interval between initiation of the test to the time when the clot produces a 2 mm amplitude-tracing shift. The rapid TEG assay uses tissue factor as a clot activator, thus R time is represented as ACT. The R time and ACT are representative of the initial enzymatic clotting factor activity. The coagulation time (K, minutes) is the time interval between the R time and the time when the clot produces a 20 mm amplitude tracing. The α-angle (α, °) is the angle formed between the horizontal and the tangent line of the slope between the R and K time. The K and α-angle represent the rate at which the clot strengthens, mostly by the cleaving of fibrinogen by thrombin. The maximum amplitude (MA, mm) represents the point at which the strength of the clot reaches its maximum reading on the TEG tracing. This represents the end-result of maximal platelet–fibrin interaction via GPIIb-IIIa receptors (i.e. integrin complexes found on PLT and function as receptors for fibrinogen; thereby, aiding in PLT activation). The strength of the clot (G, dynes/cm^2) is calculated from the TEG tracing amplitude [(A, mm); G = (5000 × A) / (100 – A)] and represents 'global' strength owing to the clot's exponential relationship with A. The percentage lysis (EPL, %) represents the percentage of clot that has been lysed at a given time point and is a marker of fibrinolytic activity. This is now more commonly presented as percentage of clot lysed at 30 minutes following maximal clot strength (LY30, %).

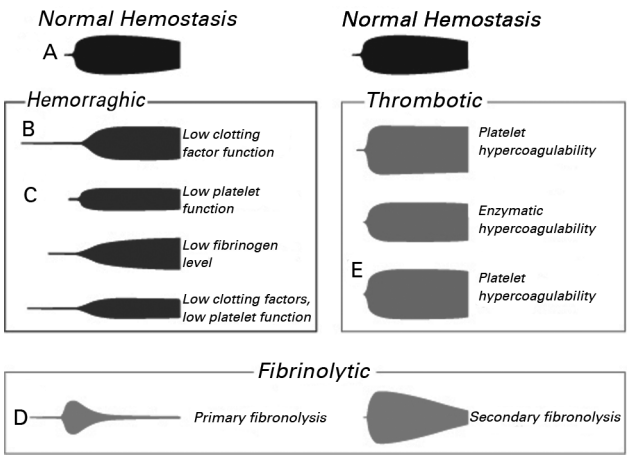

Fig. 2

Characteristic thromboelastographic (TEG) tracings seen in trauma patients. A - Normal TEG tracing. B - Anticoagulation caused by coagulation factor deficiency or inhibition leading to a prolonged R time. C - Platelet dysfunction or pharmacological inhibition leading to a decreased maximum amplitude (MA). D - Hyperfibrinolysis. E - Hypercoagulability leading to shortened R and K times, with a concomitant elevated α-angle and MA (R, reaction time (min); K, coagulation time (min); α, angle formed between the horizontal and the tangent line of the slope between the R and K time (°), MA, maximum amplitude (mm). Labels have been added to facilitate interpretation. TEG® images: TEG® Instrument, TEG® tracing and TEG® interpretation of tracing shapes are used with the permission of the Haemonetics corporation. TEG® and Thrombelastograph® are registered trademarks of Haemonetics Corporation in the US, other countries or both.

Rapid-TEG reference values:
- TEG-ACT: 0 s to 110 s
- K time: 1 min to 2 min
- α-angle: 66° to 82°
- MA: 54 mm to 72 mm
- G value: 5.3 dynes/cm^2 to 12.4 dynes/cm^2
- LY30: < 3%

Figure 2a illustrates a normal TEG tracing and several profiles with characteristic coagulation abnormalities. Enzymatic inhibition of coagulation factors by inhibition or depletion results in a prolonged R time (delayed initiation of clot formation) with normal K time and α-angle (normal fibrinogen), and normal MA (normal platelet function; Fig. 2B). Platelet dysfunction results in a normal R time with a primarily decreased MA (Fig. 2C). Clinically significant fibrinolysis has been defined as an EPL value > 15% and results in a TEG tracing with a steep tapering curve immediately following the MA (Fig. 2D).[54] Additionally, one study proposes the use of a cut-off LY30 value ≥ 3% to define clinically relevant fibrinolysis, as in patients meeting the criteria for massive transfusion it was a strong predictor of increased mortality and the need for massive transfusion.[69] However, its use in the general, widely heterogeneous trauma population is yet to be determined, as this cut-off provides low sensitivity but high specificity. In case of hyperfibrinolysis, antifibrinolytic agents such as tranexamic acid or α-aminocaproic acid, should be considered. Hypercoagulability results in shortened R and K times with a concomitant elevated a-angle and MA (Fig. 2E).

Use of tranexamic acid in trauma. The presence of hyperfibrinolysis in patients sustaining severe injuries is associated with high mortality rates – up to 100% in cases of fulminant lysis – with complete clot lysis within 30 minutes.[69-73] Tranexamic acid (TXA), a synthetic lysine derivative, is an antifibrinolytic agent that exerts its action by binding to the lysine domain of plasminogen, preventing its activation by plasmin, which is responsible for the dissolution of the fibrin clot.[74] The CRASH-2 trial was a large multinational randomised controlled trial on the effects of early treatment with TXA on 28-day hospital mortality, vascular events and transfusion requirements in severely injured adults.[75] The inclusion criterion was significant haemorrhage, defined as a systolic blood pressure < 90 mmHg, pulse >110 beats per minute, or both. There was a small but significant reduction in death from haemorrhage for those treated with TXA compared with the placebo group (4.9% *vs* 5.7%, respectively; p = 0.008). Although this study was interpreted by some as providing evidence for the routine use of TXA in bleeding trauma patients, important limitations are worth noting. First, the differences in the rates of mortality were small. Second, the enrolment criteria were broad; thus, an isolated pulse of 110 would qualify for entry into the study, and there was no laboratory determination of fibrinolysis. In fact, only half of the patients required a red cell transfusion, and there was no difference in the volume of transfusion between the two groups. Furthermore, this benefit was most notable when TXA was administered within one hour of injury, but when it was administered more than three hours after injury the mortality rate increased.

The use of TXA in trauma patients remains controversial. In adult trauma patients with haemorrhagic shock and evidence of fibrinolysis on TEG using a LY30 value > 3%, we favour using 1 g TXA intravenously (i.v.) over ten minutes, then 1 g i.v. over eight hours.[76]

Packed red blood cells (PRBC). RBCs not only provide tissue oxygenation but are also involved in coagulation and haemostasis by contributing to PLT activation and the generation of thrombin.[77] However, no prospective randomised trials have been conducted in trauma patients to identify the optimal haematocrit or levels of haemoglobin (Hb) required for haemostasis. From one prospective study, the Transfusion Requirements in Critical Care (TRCC) trial, the re-analysis of 203 trauma patients showed that using a conservative transfusion regimen (Hb trigger < 7.0 g/dl) rather than a more liberal transfusion regime (Hb trigger < 10 g/dl) resulted in fewer transfusions with no increase in adverse outcomes.[78] Although there is little high-quality scientific evidence, recent studies have shown that in patients with brain injuries, a higher level of Hb was associated with improved cerebral oxygenation. One study showed that an increase in Hb from 8.7 g/dl to 10.2 g/dl resulted in improved cerebral oxygenation in 74% of patients.[79,80] The current consensus is that a level > 10 g/dl should be maintained in patients involved in major trauma with ongoing coagulopathy.

Unfortunately, studies that have addressed blood transfusion in major trauma have suffered from several limitations. All of these retrospective studies have a survival bias, as it is unclear whether increased transfusions 'truly' increase the rate of survival or whether patients who survive have more time to receive them. Additionally, > 80% of RBC transfusions occur within six hours of presentation, whereas most studies report on blood products and/or the ratio received within a 24-hour period, potentially worsening the survival bias. Although a target Hb > 7 g/dl is recommended for patients resuscitated in the intensive care unit (ICU), it is the general consensus that the target in those with a coagulopathy should be > 10 g/dl.

Fresh-frozen plasma (FFP). In the last few years there has been a major shift towards the earlier and aggressive use of FFP and PLTs in conjunction with RBC transfusion, away from the traditional resuscitation with a large volume of crystalloid. This strategy was initially based on the use of fresh whole blood by military trauma specialists in the early 1980s, and recent experience from the Iraq and Afghanistan conflicts where a goal ratio of FFP to PLT to RBCs of 1:1:1 was used as part of the protocol of massive transfusion, showing up to a 50% decrease in mortality compared with the traditional methods of resuscitation.[81,82] A recent meta-analysis and a multicentre study of major trauma in civilian patients reported improved rates of survival in those who received a higher FFP and/or PLT to RBC ratio during their resuscitation. One study of 466 massively transfused patients reported that a ratio of FFP to RBC ≥ 1:2 was associated with an improved six-hour, 24-hour and 30-day survival compared with those who received a ratio ≤ 1:2.[83-85] However, as with studies on RBC transfusions, significant limitations exist.

The exact dose and timing of FFP administration remains controversial; however, most guidelines recommend the early use of FFP in patients with significant bleeding in the presence of TIC.[11,13,14,51] More recently, studies demonstrating the development of TIC shortly after major injury have revived interest in the timing of the administration of FFP, as well as other blood components.[86,87] A prospective randomised multicentre trial evaluating the effect of FFP as the first fluid to be administered in patients at risk of TIC is currently under way.[88] The idea is to expand on the benefits seen with early FFP administration in the emergency department, with the hope that mortality rates will decrease if FFP is given earlier, at the scene of the trauma. For now, a target ratio of FFP to RBC of 1:2 is recommended for trauma patients with massive haemorrhage, and TEG-guided transfusion should be undertaken when the ACT is > 110 s.

Platelets (PLTs). No evidence is currently available to guide the triggers for platelet transfusion in trauma. Although there is a high incidence of thrombocytopenia in major trauma patients, no absolute platelet count that predicts the development of TIC has yet been found.[89] Most guidelines have been based on medical conditions leading to thrombocytopenia, where no risk of haemorrhage has been noted until the PLT count drops to < 50×10^9/l.[90] Although there is no consensus, a higher threshold of 100×10^9/l has been suggested in patients with severe brain injury and those with significant bleeding following major trauma.[13,91] A recent meta-analysis showed an improved rate of survival in major trauma patients who received a higher PLT to RBC ratio during their resuscitation. Patients who had a PLT to RBC ratio ≥ 1:2 had an improved 30-day survival compared with those who had a ratio ≤ 1:2.[84] Recent studies suggest that PLT dysfunction, rather than the absolute PLT count, may play a larger role in TIC than was previously thought. Patients may have increased fibrin degradation products, secondary to disseminated intravascular coagulation and/or fibrinolysis, that can interfere with platelet function, therefore higher PLT thresholds have been suggested.[13,92-94] As with RBC and FFP, survival bias and confounding factors make the data from these studies difficult to interpret. Therefore, when possible, individualised goal-directed therapy is favoured over empirical PLT transfusions.[50] A target PLT count of > 50×10^9/l is recommended for trauma patients. In those with severe bleeding or a brain injury a PLT count of > 100×10^9/l has been suggested. TEG-guided transfusion should be undertaken when MA is < 50 mm. Based on the best evidence, 1 unit of apheresis PLT (4 to 6 pooled units) per 5 units of RBC is recommended.

Adverse effects of empirical transfusion protocols. Although the early and appropriate use of blood products (FFP, PLTs and RBCs) in trauma patients appears to have an impact on survival, their over-zealous use may not be the safest strategy. Allogeneic transfusions are not benign interventions and adverse reactions are well described; these include infectious, immunological, allergic, anaphylactic and haemolytic reactions.[95,96] In addition, blood transfusions in trauma patients have been shown to be an independent risk factor for mortality, admission to ICU, postoperative infection and multiple organ failure.[97-101] One study in a level I trauma centre demonstrated that blood transfusion was an independent risk factor for post-injury multiple organ failure, with a dose-dependent association, and this relationship was present despite the inclusion of other indices of shock. Several recent studies have found an association between FFP and PLT use and an increased risk of transfusion-related acute lung injury and multiple organ failure; this is thought to be due to the increased immunological and allergic reaction and the resultant systemic inflammatory response.[95,96,99] A study involving 1440 critically injured patients found that early FFP administration was an independent risk factor for the development of multiple organ failure, in addition to the previously described RBC transfusion risk. This study demonstrated an increased risk of multiple organ failure with an increased absolute amount of FFP and FFP:RBC ratio transfused.[99] Therefore, it is essential to administer blood components only when physiologically necessary, and not empirically or with laboratory evidence of coagulopathy, without differentiation between impaired PLT function, fibrin production

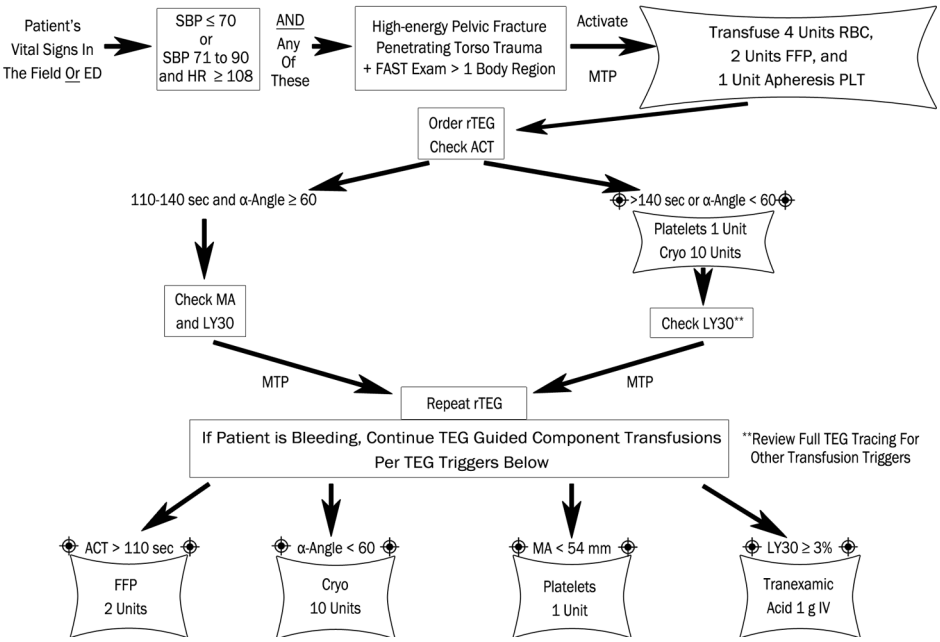

Fig. 3

The Denver Health Medical Center massive transfusion activation protocol, with thromboelastography (TEG)-guided blood component resuscitation guidelines. (ACT, activated clotting time; Cryo, cryoprecipitate; FAST, focused assessment with sonography for trauma; FFP, fresh-frozen plasma; LY30, clot lysed at 30 minutes; MTP, massive transfusion protocol; PLT, platelets; RBC, red blood cells; rTEG, rapid-TEG).

and excessive fibrinolysis. Although blood component transfusions play an integral role in the management of TIC, it would seem wise to proceed with caution with empirical ratio transfusions.

Massive transfusion protocols

Massive transfusion protocols have been implemented in many level I trauma centres as a means to improve product availability and the rate of survival (Fig. 3).[102] Massive transfusion has been commonly defined as the administration of > 10 units PRBCs within 24 hours. However, because 80% of the blood products transfused during massive transfusion occurs within six hours of presentation, the definition of massive transfusion is shifting to 10 units of RBCs within six hours of injury, in order to encompass the time frame of acute haemorrhage.[85] Although improved survival rates have been seen since the implementation of massive transfusion protocols, this has been attributed to the simultaneous increase in the ratio of FFP to RBC.[81,83,84,103] One study comparing survival rates and FFP:RBC ratios before and after the implementation of a massive transfusion protocol found that although the mortality rate decreased from 45% to 19%, the FFP:RBC ratio remained unchanged at 1:1.8. However, there was a significantly improved mean time to the first administration of RBC (115 *vs* 71 minutes) and FFP (254 *vs* 169 minutes).[103]

This begs the questions: 'Is the timing of plasma and PLT transfusions more important than the actual ratio of FFP and PLTs to RBCs?' and 'Does care based on a protocol improve outcomes?'

'Damage control' surgery

The principle of 'damage control' surgery was first described by Stone, Strom and Mullins in 1983,[104] in the context of abdominal trauma. In their original article, mostly dealing with penetrating abdominal trauma, they described performing an initial abbreviated laparotomy with abdominal packing to prevent additional bleeding, with interval correction of physiological disturbances and coagulopathy before definitive surgical treatment. In their experience, this was a life-saving technique in otherwise non-salvageable scenarios. Damage control surgery involves addressing life-threatening injuries (haemorrhagic control) first, followed by stabilisation and physiological restoration. Once the patient has been stabilised and the coagulopathy corrected, definitive surgery can be contemplated. Damage control orthopaedics includes external stabilisation of pelvic and long bone fractures. This approach minimises operating time and blood loss while facilitating nursing care and early mobilisation.[105]

Although several studies have shown improved outcomes with decreased ARDS, pulmonary complications and mortality rates, with early fracture fixation (within 24 hours),[106-108] in certain circumstances a delayed approach has been shown to be better.[109-112] In brief, these circumstances include polytrauma patients with severe brain, chest or abdominal injuries; haemodynamically unstable patients or those *in extremis*; those with an injury severity score (ISS) ≥ 15 or incompletely resuscitated (serum lactate > 4.0 mmol/l or base excess ≤ 5.5 mEq/l).[113] In addition, damage control orthopaedics has also been advocated in patients with subclinical or

occult hypoperfusion, defined as normalisation of vital signs with resuscitation but with a persistent serum lactate > 2.5 mmol/l, as the rate of post-operative complications in these patients was increased.[114,115]

Regarding pelvic injuries, initial surgical intervention includes the application of either an anterior external fixator using the quick, fluoroscopic-free but less stable iliac crest route or the more time-consuming but stable supra-acetabular route; or a pelvic C-clamp with possible concurrent pelvic packing.[116] The rationale for early pelvic stabilisation is to reduce pelvic volume, stabilise bony elements, and encourage tamponade to control blood loss. In addition, it allows these critically injured patients to be transferred promptly to the ICU for continued resuscitation.

The use of external fixators has been shown to reduce pelvic volume and appose bone fragments successfully, thereby limiting the amount of blood loss.[27,117] An open-book pelvis can be closed in this way, provided that the posterior complex is intact. In patients with a posterior complex injury, sufficient stability cannot be restored using an external fixator, unless its use is combined with traction or a pelvic C-clamp.[118] Pelvic C-clamps, however, should only be used when the correct surgical expertise is available, as perforation of the spinal canal and rectum has been reported.[119-121] One study comparing external fixators and pelvic C-clamps in vertically unstable cadaveric pelvic fractures showed that an external fixator provided better anterior stability, and the pelvic clamp better posterior stability.[118] If pelvic packing is to be performed simultaneously, the external fixator should be applied first to stabilise the pelvis and facilitate the tamponade effect of the packs, as pelvic packing is thought to be more effective with a stable pelvis, providing the mechanical foundation.[25,47]

'Damage control' surgery techniques must be considered as life-saving, and so should be performed expeditiously and effectively.

The rationale for pelvic packing. Several authors have attempted to compare the efficacy of pelvic packing with that of angiographic embolisation in unstable pelvic fractures.[3,4,8,25,47] However, such a comparison is not appropriate, as the time to angiography is significantly longer and dependent on the local facilities. Therefore, in institutions where both options are available, patients with more haemodynamic instability (i.e. those who have not responded to resuscitation) are more likely primarily to undergo emergent pelvic packing rather than 'delayed' angio-embolisation. Thus, institutions who have adopted pre-peritoneal pelvic packing as part of their protocol for treating pelvic fractures have placed it as the first step, unless there are clear indications of arterial bleeding, with angio-embolisation as a second step if haemodynamic instability persists.[3,4]

The technique used for packing has been described previously.[47] Briefly, in patients in whom pelvic stabilisation is indicated, a C-clamp or external fixator is placed prior to pelvic packing. A 6 cm to 8 cm midline incision is made about the symphysis pubis, and the rectus abdominis fascia is divided to access the inner pelvis. The bladder is retracted to one side and the pelvic brim is palpated as posteriorly as possible; then, three laparotomy swabs (packs) are placed sequentially deep to the brim. This is followed by three more on the opposite side of the bladder, for a total of six within the true pelvis. Many authors have advocated this technique of pelvic packing.[119,122,123] One disadvantage is the risk of infection in the pelvic space, which appears to be related to the number of times the packs are exchanged. Our rate of infection in the pelvic space is 46% in patients requiring re-packing, compared with 6% if the packs were removed.[3] One retrospective review reported pelvic packing to be superior to angiography in terms of earlier intervention – with the time to packing at 45 minutes compared with 135 minutes for angio-embolisation – and reduced blood transfusions.[8] However, direct comparisons between packing and angiography are difficult owing to the heterogeneity of injury severity and complexity in different studies, and the absence of randomised prospective studies.[120] In 85% of exsanguinating pelvic ring injuries the source of bleeding is the retroperitoneal venous plexus and bony fragments,[38] and so arterial interventions would be ineffective. The routine performance of arterial embolisation in haemodynamically unstable patients, in whom arterial bleeding occurs in only 15% of exsanguinating pelvises, causes the likely source of bleeding to be missed and wastes precious time. Pelvic packing is a rapid and effective procedure that can be done at the time of applying the external fixator. Another advantage of pelvic packing is that the patient can undergo several operative procedures simultaneously, including, for example, exploratory laparotomy, thereby saving valuable time and minimising the surgical burden. In fact, 87% of patients who are candidates for pelvic packing need some other operative intervention.[3] If haemodynamic stability is not achieved following pelvic packing and external fixation, with more than four units of RBCs required and a normal coagulation profile, a source of arterial bleeding should be explored by arteriography. Most recently, the concept of the 'trauma hybrid operating room' (THOR) has been advocated, in which trauma surgeons, trained in endovascular techniques, can perform an on-table angio-embolisation of arterial bleeding.[124,125] In selected cases with clear evidence of arterial bleeding requiring embolisation, using this strategy can avoid the time-consuming and often costly transportation to an interventional radiology suite prior to or following operative intervention. External pelvic fixation can be performed simultaneously with angio-embolisation in the operating theatre. However, as with any new technique, prospective studies will be needed in order to validate the use of this hybrid approach. The trauma algorithm at our institution (Fig. 4) applies to all patients presenting in shock with a pelvic fracture, and those who remain unstable despite the transfusion of two or more units of RBCs will be taken to the operating theatre urgently for pelvic packing and external fixation.[3]

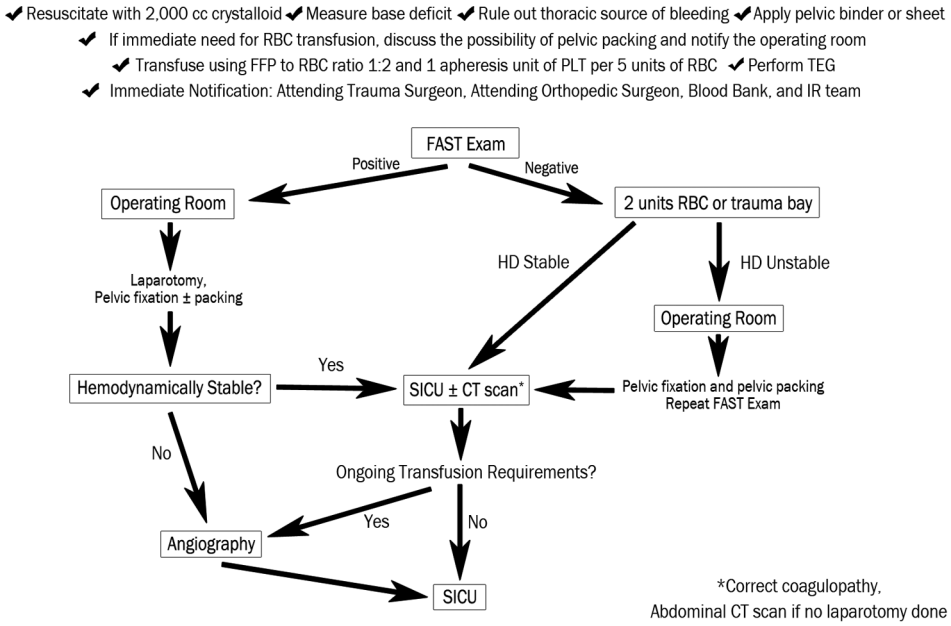

Fig. 4

The Denver Health Medical Center algorithm for the management of all high-energy pelvic injuries. (FAST, focused assessment with sonography for trauma; FFP, fresh-frozen plasma; HD, haemodynamically; PLT, platelets; RBC, red blood cells; SICU, surgical intensive care unit; TEG, thromboelastography).

The role of interventional angio-embolisation. In the management of arterial bleeding associated with unstable pelvic fractures success rates between 85% and 100% have been reported following arterial embolisation.[43] Embolisation can be selective to a bleeding artery or non-selective with embolisation of the internal iliac artery. This procedure can be performed independently or after other forms of treatment have been undertaken, such as pelvic packing and the application of an external fixator. However, the role of embolisation is debated, as most bleeding is secondary to venous injury, and even when embolisation is successful, the reported rate of mortality remains high.[123,126-128]

In addition, significant complications have been reported with pelvic embolisation, including a negative angiographic result (i.e. where no bleeding vessel was found on angiogram) and need for re-embolisation.[129-131] One study of patients with pelvic fractures undergoing angio-embolisation reported a complication rate of 11%, with gluteal muscle necrosis being the most common, and including impotence and necrosis of the bladder and skin. Patients undergoing bilateral embolisation had a 100% complication rate.[129] Therefore, bilateral and non-selective embolisation is not recommended. One study on 97 trauma patients requiring angiography reported that about a quarter of patients undergoing angio-embolisation developed contrast-induced nephropathy, and 21% had a negative angiographic result (i.e. where no bleeding vessel was found on angiogram).[131] Therefore, referring patients empirically to angiography is inappropriate. Although angio-embolisation has been used for over three decades in the management of these patients, delays in obtaining embolisation remain and yet it remains a part of routine care in most centres in the United States.[120]

Haemodynamic instability associated with a pelvic fracture poses the difficult question to the surgeon of whether to proceed to the operating theatre for pelvic packing and external fixation, or to transfer the patient to the interventional suite for arterial embolisation.[27] The presence of an arterial 'blush' on a contrast-enhanced CT scan or the presence of intra-abdominal pathology may influence this decision. In regards to the presence of a haematoma or arterial 'blush' on a CT scan, one study demonstrated that in patients with a haematoma (70% (26/37)), no haematoma (83% (5/6)), blush (83% (5/6)) or no blush (71% (22/31)) on a CT scan at the time of angiography had a positive result (i.e. where a 'true' bleeding vessel was found on the angiogram). The authors concluded that the presence or absence of a pelvic haematoma or arterial 'blush' should not alter the indications for pelvic angiography.[132] Nonetheless, a multidisciplinary discussion should be held between the interventional radiologist, the intensivist and the surgical team.

Conclusions

The management of high-energy injuries to the pelvic ring is still debated and should include a multidisciplinary approach, including trauma surgeons, orthopaedic surgeons, intensivists, and, if applicable, the interventional radiologist.

Protocols for the management of a pelvic fracture should focus on stopping haemorrhage, managing the TIC, the identification of associated injuries and restoration of haemodynamic stability.

Permissive hypotension with a systolic blood pressure between 80 mmHg and 100 mmHg may be considered in a patient with an unstable pelvic fracture in the absence of an associated brain injury.

To avoid exacerbating coagulopathy, normothermia should be maintained while minimising crystalloid infusion in all patients with a pelvic fracture.

In all haemodynamically unstable patients, immediate application of a pelvic binder or circumferential pelvic compression should be performed, especially those with an APC type II or III open-book injury.

Early transfusion in the resuscitation process of higher FFP and PLT to RBC ratios (i.e. ≥ 1:2) appears to improve the rate of survival in patients with significant haemorrhage. However, whenever possible, resuscitation should be goal-directed using TEG.

The mechanism of injury determines the type of fracture, and guides the choice of external fixation, including the use of a pelvic C-clamp, to promote optimal fracture stability.

Pelvic packing should be performed after external fixation and pelvic stabilisation.

If bleeding continues, arterial sources should be sought and controlled using angiography and angio embolisation.

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