Review

Management of bleeding in major burn surgery

Harald Welling [a,*], Sisse Rye Ostrowski [b], Jakob Stensballe [a,c], Martin Risom Vestergaard [c], Søren Partoft [f], Jonathan White [g], Pär Ingemar Johansson [a,d,e]

[a] Section for Transfusion Medicine, Rigshospitalet, Capital Region Blood Bank, Copenhagen University Hospital, Copenhagen, Denmark
[b] Department of Clinical Immunology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[c] Department of Anaesthesiology, Centre of Head and Orthopaedics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[d] Department of Surgery, Division of Acute Care Surgery, Centre for Translational Injury Research (CeTIR), University of Texas Medical School at Houston, TX, USA
[e] Centre for Systems Biology, The School of Engineering and Natural Sciences, University of Iceland, Iceland
[f] Department of Burn Surgery, Centre of Head and Orthopaedics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[g] Department of Intensive Care, Abdominal Centre, Copenhagen University Hospital, Rigshospitalet, Denmark

ARTICLE INFO

ABSTRACT

Major burn surgery is often associated with excessive bleeding and massive transfusion, and the development of a coagulopathy during major burn surgery is associated with increased morbidity and mortality. The aim of this study was to review the literature on intraoperative haemostatic resuscitation of burn patients during necrectomy to reveal strategies applied for haemostatic monitoring and resuscitation. We searched PubMed, EMBASE, and CENTRAL for studies published in the period 2006–2017 concerning bleeding issues related to burn surgery i.e. coagulopathy, transfusion requirements and clinical outcomes. In a broad search, a total of 1375 papers were identified. 124 of these fulfilled the inclusion criteria, and six of these were included for review. The literature confirmed that transfusion requirements increases with burn injury severity and that haemostatic monitoring by TEG® (thrombelastography) or ROTEM® (rotational thromboelastometry) significantly decreased intraoperative transfusions and was useful in predicting and goal-directing haemostatic therapy during excision surgery.

Resuscitation of bleeding during major burn surgery in many instances was neither standardized nor haemostatic. We suggest that resuscitation should aim for normal haemostasis during the bleeding phase through close haemostatic monitoring and resuscitation. Randomised controlled trials are highly warranted to confirm the benefit of this concept.

* Corresponding author at: Capital Region Blood Bank, Section for Transfusion Medicine, Rigshospitalet, University Hospital of Copenhagen, Blegdamsvej 9, 2100 Copenhagen, Denmark.
E-mail addresses: harald.sorwad.welling@regionh.dk, haraldwelling@gmail.com (H. Welling), sisse.rye.ostrowski@regionh.dk (S.R. Ostrowski), jakob.stensballe@regionh.dk (J. Stensballe), martin.risom.vestergaard.01@regionh.dk (M.R. Vestergaard), soeren.partoft@regionh.dk (S. Partoft), jonathan.oliver.white@regionh.dk (J. White), per.johansson@regionh.dk (P.I. Johansson).

Contents

1. Introduction

Following a major burn of >20% total body surface area (TBSA), the early post-injury and the later intraoperative necrectomy phases are characterized by major perturbations in haemostasis and risk of coagulopathy during surgery [1].

More than 10 years' research in trauma-induced coagulopathy has revealed several distinct types of endogenously driven coagulopathies; acute traumatic coagulopathy (ATC), driven by tissue injury and hypoperfusion [2] and disseminated intravascular coagulation (DIC), with a haemorrhagic phenotype, all of which are associated with poor outcome, increased mortality, and morbidity [3–6].

Burn patients may differ significantly in their haemostasis from trauma patients due to the excessive inflammatory response and tissue damage present before the occurrence of (surgical) bleeding. Given that coagulopathy is closely linked to inflammation and perturbations in the microvasculature [7–9], the complexity of the coagulopathy in severely burned patients emphasizes the risks of the patients and the importance of viewing and treating the coagulopathy of severe burn patients as its own entity [10,11].

Coagulopathy may be diagnosed according to conventional plasma-based assays, such as international normalized ratio (INR) applying a ratio of 1,2–1,5 as a definition of hypocoagulability [12,13] or it may be diagnosed by whole blood-based viscoelastic haemostatic assays, such as thrombelastography (TEG[1]) and rotational thromboelastometry (ROTEM) with distinctive patterns of hypocoagulability, hypercoagulability, or hyperfibrinolysis being identified [14]. TEG/ROTEM are whole blood based assays that record the initiation, velocity of formation and strength of and ensuing lysis of the blood clot in whole blood [15].

In multiple studies, TEG/ROTEM have demonstrated superiority in predicting the need for blood transfusion and reducing transfusion requirements in trauma patients [16–18] and TEG/ROTEM are superior to conventional plasma-based analysis e.g. activated thromboplastin time (aPTT) and INR in their ability to differentiate between, and diagnose clinically relevant coagulopathies as well as in predicting bleeding risk, transfusion requirements, and mortality for patients with coagulopathy [7,19–21]. Based on this, the viscoelastic assays appear appropriate for monitoring burn patients, as hypercoagulability and hyperfibrinolysis are not readily identified by conventional coagulation assays [22].

Despite risk of coagulopathy and excessive bleeding during burn surgery, there is no consensus on the management of intraoperative resuscitation and no guidelines for treatment of these patients even when coagulopathy during surgery is recognized.

The American [23], Australian [24], European [25], and UK burn associations' guidelines [26-29] do not specifically address haemostatic resuscitation in respect to necrectomy, which highlights the need for a standardized haemostatic intraoperative resuscitation and monitoring regime for these patients.

Here, we review the literature on intraoperative haemostatic resuscitation of burn patients during necrectomy to reveal the evidence for strategies applied for haemostatic monitoring and resuscitation.

2. Methods

2.1. Eligibility criteria

For this review, PubMed, EMBASE and CENTRAL were searched for original publications accepted for publication

---

[1] TEG: thrombelastography, ROTEM: rotational thrombelastometry, ATC: acute traumatic coagulopathy, DIC: disseminated intravascular coagulation, PCC: prothrombin complex concentrate, TXA: tranexamic acid, rFVIIa: recombinant factor VIIa.

in the period 2006–2017. In a manual search using respectively "burn surgery", "TEG", "ROTEM", "coagulopathy", "resuscitation", and "bleeding", 1375 articles were found. Only papers on adult human subjects published in English were considered. Studies including patients with a TBSA of 20% or more were included.

Papers on paediatric burn patients, Jehovah's witnesses, case-reports, or animal studies were excluded. Also, studies solely focusing on electrical burn injuries were excluded due to the complexity and organ damage characteristic of this specific burn aetiology. Likewise, studies of patients with significant inhalational injury in addition to skin burns were not included due to the complications associated hereto and the heterogeneity of inhalational burn injuries.

Lastly, we reviewed the abstracts of these articles and excluded articles not relevant to intraoperative burn care. This manuscript adheres to the applicable PRISMA guidelines.

A total of six studies were included for assessment in this review (Fig. 1).

2.2. Data

Data from the studies were extracted manually in assessing and studying the trials individually. Reference lists of the selected studies were also studied to reveal relevant articles not found in the initial search.

3. Results

Of the six included articles, three were retrospective studies, one was a prospective observational study and two were randomized clinical trials. Table 1 provides a short overview of included papers.

3.1. Blood transfusion in burn surgery

In a 62-month retrospective study, Yogore et al. reported intraoperative blood loss to be the major cause for transfusion at a larger American burn centre. Red blood cell (RBC) transfusion increased with TBSA whereas fresh frozen plasma (FFP) was not routinely transfused, but was reserved for acquired coagulopathies, DIC or clinical bleeding with prolonged PT or aPTT. Platelets were transfused preope ratively at less than $50,000 \times 10^9$/L. Patients with a 40% TBSA burn received volumes of RBC, FFP, platelets and apheresis platelets vastly exceeding all other groups and these patients had the highest rate of surgical procedures, blood loss and comorbidities such as sepsis and coagulopathy (DIC) [30]. It was not stated what percentage of these patients were surgical patients, but it is assumed that this group had a high rate of surgery.

Lu et al. confirmed the association between TBSA and RBC and FFP transfusion in a single-centre retrospective cohort
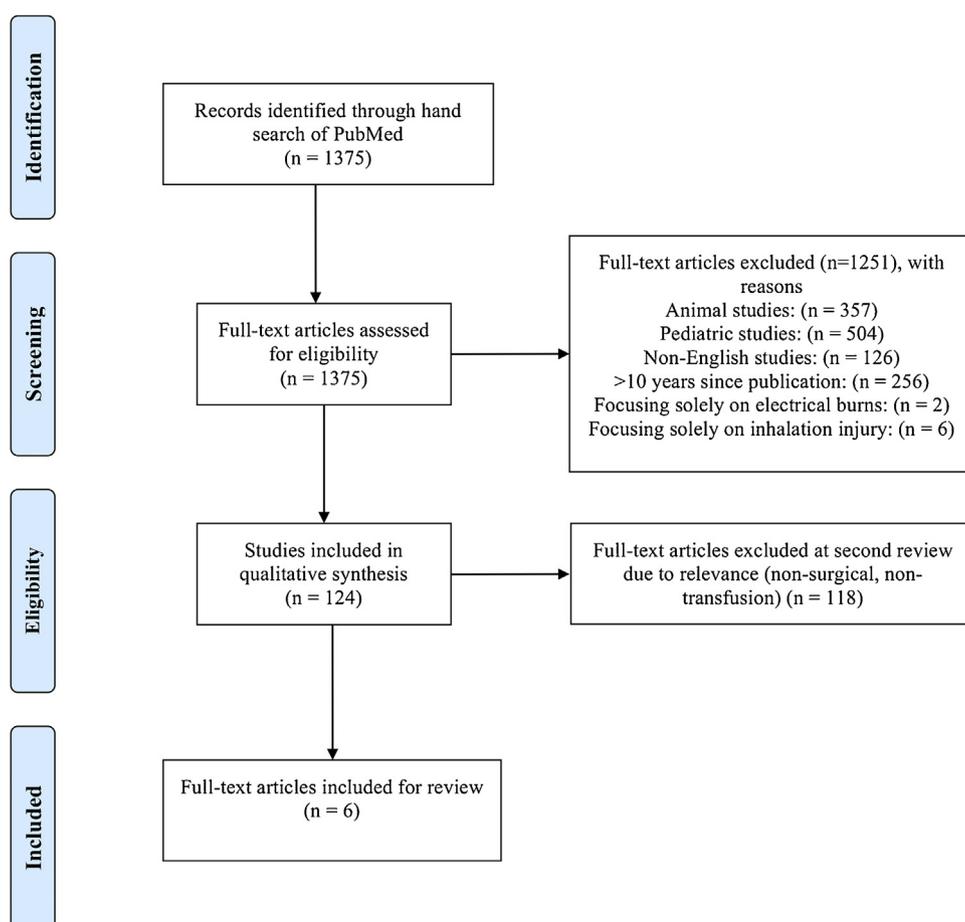

Fig. 1 – Data extraction flow diagram. Six studies were included for review.

Table 1 – Overview of literature.						
Authors	Year	Origin	Multi/single centre	No. of pts.	TBSA	Monitoring
Randomised controlled trials						
Johansson et al. [21]	2006	Denmark, Copenhagen	Single	18	Scheduled for excision and grafting of 10+	Recombinant FVIIa or placebo is given at first skin incision and again 90 min later. Outcome monitored as difference in amount of RBCs administered during and 24 h after surgery and postoperative complications.
Schaden et al. [34]	2012	Austria, Vienna	Single	30	29+	Control group: coagulation management performed according to clinician's discretion. Algorithm group: standardized treatment based on Austrian guidelines for trauma-induced coagulopathy using point-of-care ROTEM (EXTEM, FIBTEM, APTEM). Outcome parameter: amounts of RBC transfused on day of surgery.
Prospective/observational studies						
Pidcoke et al. [33]	2015	USA, Texas	Single	36	Scheduled for excision and grafting	Platelet count, haemostasis with ROTEM (FIBTEM, EXTEM, APTEM), platelet aggregation monitored with multiplate.
Retrospective studies						
Lu et al. [31]	2013	US, North Carolina	Single	89	15-65	Measuring blood utilization and evaluating relationship between this and clinical variables (anticoagulant usage and mortality).
Kwan et al. [32]	2006	Canada, Toronto	Single	172	20+	Comparison of outcome (MODS, mortality, general clinic) in patients treated before/after a restrictive transfusion strategy was adapted.
Yogore et al. [30]	2006	USA, Chicago	Multi	1615	Full ratio	Reviewing blood bank service utilization over 62 months at an urban burns centre

study of 89 consecutive burn patients with >15% TBSA. Bleeding patients in this centre were transfused RBCs aiming for a haemoglobin level of 6,2 mmol/l. Major burn patients may pre-emptively have been resuscitated with RBCs up to a haemoglobin level of 5,6–6,2 mmol/l in anticipation of significant intraoperative bleeding. FFP was administered in the event of active bleeding and INR > 1,5 and a prolonged aPTT. Patients who received therapeutic anticoagulation received 5–8 times more RBC and 2–4 times more plasma compared to those only on prophylactic anticoagulation. In a multivariate logistic regression analysis, there was no association between mortality and numbers of transfusions. However, those transfused with a greater volume of RBCs displayed a trend towards higher survival (odds ratio: 0.89; 95% CI: 0.76, 1.03; p: 0.13) while those transfused with a greater volume of FFP showed a trend towards higher mortality (odds ratio: 1.37; 95% CI: 0.99, 1.88; p: 0.055) [31].

Kwan et al. assigned subjects to groups based on time of treatment due to the adoption of a transfusion trigger of 7.0 g/dl (6,3 mmol/l) in 1999 at the burn unit investigated. Patients treated in the two years before 1999 were assigned the liberal transfusion group (LIB) and patients treated in the years after made up the restrictive transfusion groups (REST). Outcomes were reviewed for patients with >20% TBSA. A restrictive transfusion strategy effectively reduced the amount of transfused blood products in the operating room with significantly improved survival and less organ failure. Based on their data, they suggested that a transfusion trigger of 7.0 g/dl (6,3 mmol/l) was safe and at least as effective as a liberal transfusion strategy. There was no significant difference in length of hospital stay between the two groups (LIB: 45 ±88 days vs. REST: 44±38 days, p 0.942). The incidence of coagulopathy or any reduction in the severity of bleeding during surgery was not assessed in this study [32].

None of the papers included for this review specified a fixed intraoperative fluid resuscitation strategy or addressed the management of hypothermia or acidosis during necrectomies.

3.2. Blood components: protocols and balanced therapy

In an institutional board-approved prospective observational study, Pidcoke et al. found that balanced blood component therapy with a 1:1:1 ratio was not routinely used for actively bleeding burn patients during surgery at the investigated burn centre [33]. ROTEM, platelet count and impedance aggregometry were measured. It is not stated in this review what respective triggers were for transfusion of RBCs, FFP and platelets.

3.3. Monitoring haemostasis and goal-directing haemostatic therapy

In a randomised controlled single-centre study of thirty consecutive burn patients randomized to either coagulation management according to clinician's discretion or to a standardized treatment for management of coagulopathy by point-of-care ROTEM, Schaden et al. found a significant difference in the administration of perioperative blood products between the control group and the algorithm group. Transfusion of RBC was similar in the two groups whereas the

standard group received more FFP and platelets compared to the algorithm group (no patients in the algorithm group received platelets or FFP) [34].

The ROTEM analyses revealed that hyperfibrinolysis as a cause of hypofibrinogenaemia did not seem to be a contributing factor to the coagulation deficiencies observed in burn patients. Conversely, the fibrinogen level rose within 24h after injury and high baseline levels were confirmed on the third day after injury, just before surgery. Fibrinogen administration did not differ between standard and algorithm groups, and no prothrombin complex concentrate (PCC) or tranexamic acid (TXA) was administered in either of the two groups [34].

Pidcoke et al. recorded number, component type, volume and age of transfused blood products during burn excisions at a large US burn centre. Clinical data including morbidity, outcome and length of stay was not recorded. Units of RBCs, FFP, platelets and cryoprecipitate were collected to sample the remains of the bag and tubing. Aliquots of the original volume of each blood product were combined to produce a composite sample that contained identical ratios of the blood products transfused to the patient. The mixed samples of transfusate from the patients produced abnormally weak clots, with clot strengths below the reference range (49–71 mm) even when platelets were present in platelet-RBC-ratios greater than 1:1, indicating a platelet function deficit. Even undiluted platelet concentrates displayed significantly abnormal results in accordance with previous findings of stored platelets. Platelet aggregation data showed that those with the highest baseline platelet counts received fewer transfusions. The majority of patients received RBCs and platelets alone.

Pidcoke et al. also found that platelet factor and thromboxane B2 were elevated in patients after burn injury, suggesting that platelet activation and turnover contributed significantly to impaired platelet function in burn patients. Furthermore, they reported that burn patients had increased levels of factor VIII and fibrinogen before surgery. While factor VIII was consumed rapidly during excision of the burn wound, platelet count and factor levels decreased during surgery [33].

3.4. Pro-haemostatics

In a single-centre, double-blinded randomised controlled trial including 18 consecutive patients with >10% TBSA, Johansson et al. showed that recombinant factor VIIa (rFVIIa) significantly reduced the total number of blood products transfused to patients during surgery. Surgery was performed at a median of 10 days after burn injury in the rFVIIa-group. Patients were randomised to receive either placebo or 40 μg/kg rFVIIa at first skin incision and again 90 min later. Preoperative PT-INR values were within the normal range in both groups, but shortened after rFVIIa-administration from a median of 1,20–<0,70. The rFVIIa group had a lower incidence of multiple organ failure and infectious morbidity and a dampening of the IL-6 elevation. No thromboembolic events were recorded in this study [35].

4. Discussion

The present review of the literature confirmed that burn surgery is associated with excessive transfusion requirements

but that most institutions do not apply protocolled monitoring and treatment. A more generalised approach to this patient group is applied by most institutions, including supportive measures mitigating hypothermia and acidosis, but not addressing intraoperative coagulation monitoring. This highlights the need for randomised controlled trials on the (intraoperative) management of major burn patients.

Outcome in haemorrhaging trauma patients has improved significantly through the implementation of haemostatic resuscitation comprising the use of balanced blood products, hypotensive resuscitation and limited crystalloid and colloid administration. Patients presenting with major burns to necrectomy present a major challenge with regard to haemostatic resuscitation, yet our review of the literature was unable to identify any studies reporting an effect of balanced blood product transfusion in adult burn patients during surgery. Furthermore, protocols distributed by burn associations and other authoritative bodies in this field have not evaluated resuscitation of burn patients during surgery [23–25,29].

4.1. Coagulopathy in burn surgery

The work of Pidcoke et al. confirmed earlier results documenting a significant decrease of platelet levels and coagulation factor levels during surgery. It is notable that platelet dysfunction is an independent predictor of mortality in trauma patients [36,37], and in patients with burns, platelet count often decreases 3–5 days after admission [38,39]. There is emerging evidence that platelet dysfunction is a feature of coagulopathy of trauma and may contribute to the clinical coagulopathy observed in burn patients during surgery [40] emphasizing the need for adequate monitoring of this.

4.2. Pro-haemostatics in burn surgery

One study demonstrated that administration of antifibrinolytics and fibrinogen did not seem be of benefit in burn patients undergoing surgery, as coagulopathy did not seem to be related to hypofibrinogenemia [34]. This finding is very different from non-burn trauma patients with substantial bleeding, as fibrinogen seems to be the factor depleted first during massive haemorrhage [41]. Importantly, these data also support the hypothesis that even if patients are hypercoagulable at the time of surgery due to high fibrinogen levels, abnormally low platelet counts or function and low coagulations factor levels may significantly contribute to clinical coagulopathy [33] but this requires confirmation. Though one study indicated that rFVIIa might be useful in the surgical setting of burns for reducing blood loss [35] and preventing coagulopathy [42], prohaemostatic therapy is neither habitually used in these patients, nor actively investigated on this indication. However, in light of more recent publications [43], rFVIIa should not be administered to burn patients in a clinical setting until a phase III study has published new data to support the use. Furthermore, for all prohaemostatic agents, the risk of thromboembolic complications in the face of the hypercoagulable and inflamed patient should be weighted against the risk of critical on-going bleeding.

4.3. Haemostatic monitoring burns surgery patients

Despite the overwhelming heterogeneity in the burn population literature in, amongst other variables, TBSA, resuscitation regime, severity of injury, and timing of surgery, there is substantial evidence that burn patients present with a wide range of haemostatic profiles including normo-, hyper-, and hypocoagulability and hyperfibrinolysis, which can all be detected by TEG/ROTEM. Management of haemostatic monitoring in general have shifted towards VHA testing with TEG/ROTEM being increasingly popular. Furthermore, two recent studies investigating haemostasis monitoring during burn surgery using TEG/ROTEM (Table 1) [33,34] demonstrated reduced transfusion requirement in both studies, emphasizing that TEG/ROTEM monitoring may be advantageous for haemostatic monitoring of burn patients. This is in alignment with the findings for other surgical procedures with complex coagulopathies [21] and in alignment with a Cochrane review concluding that blood product requirements and blood loss were significantly reduced by implementation of TEG/ROTEM in surgical patients [44].

The use of TEG/ROTEM as an addition to standard laboratory tests has not been investigated [45]. For this reason, it is difficult to examine the accuracy of VHA predictions of conventional laboratory values of blood samples. A disadvantage of TEG/ROTEM equipment may be its requirement for regular calibration by trained personnel.

The implementation of standardized near point of care haemostatic monitoring utilizing VHA's together with ongoing haemostatic resuscitation may be a beneficial strategy in these patients undergoing necrectomy.

The present review has several limitations: for practical reasons, only studies published in English were reviewed which may increase the risk of (language) bias. Also, only patients with a TBSA of >20% were included. Importantly, in some studies, patients with extensive burns who did not survive were excluded from the studies, which may bias the outcome. Finally, the review is based on a limited literature on intraoperative burn resuscitation, which may heighten the risk of publication bias.

5. Conclusion

The haemostatic profile of burn patients is very heterogeneous and changes remarkably from the time of burn injury to the time of surgery. Although burn patients are hypercoagulable shortly after admission and during recovery, coagulopathy is a relevant concern during major burn surgery due to the substantial blood loss and concomitant inflammation, hypothermia, and haemodilution. There is absence of current literature endorsing the practice of intra-operative hemostatic monitoring during major burn surgery, and explicit national or international guidelines or protocols on the topic are lacking.

There is evidence that TEG/ROTEM guided goal-directed therapy during excision surgery may reduce or correct coagulopathy, hereby reducing transfusion requirements. This may be due to the ability of TEG/ROTEM to reveal both hyper- and hypocoagulability, including hypofibrinogenemia and hyperfibrinolysis, which may be relevant causes of coagulopathy in burn patients.

International guidelines describing how to resuscitate and manage and monitor haemostatic therapy during necrectomy of major burn patients are required, and a larger randomised controlled trial on the subject is highly warranted.

Declarations of interest

REFERENCES

[1] Meshulam-Derazon S, Nachumovsky S, Ad-El D, Sulkes J, Hauben DJ. Prediction of morbidity and mortality on admission to a burn unit. Plast Reconstr Surg 2006;118(1):116–20.

[2] King DR, Namias N, Andrews DM. Coagulation abnormalities following thermal injury. Blood Coagul Fibrinolysis 2010;21(7):666–9.

[3] Lier H, Krep H, Schroeder S, Stuber F. Preconditions of hemostasis in trauma: a review. The influence of acidosis, hypocalcemia, anemia, and hypothermia on functional hemostasis in trauma. J Trauma 2008;65(4):951–60.

[4] Douning LK, Ramsay MA, Swygert TH, Hicks KN, Hein HA, Gunning TC, Suit CT. Temperature corrected thrombelastography in hypothermic patients. Anesth Analg 1995;81(3):608–11.

[5] Martini WZ, Holcomb JB. Acidosis and coagulopathy: the differential effects on fibrinogen synthesis and breakdown in pigs. Ann Surg 2007;246(5):831–5.

[6] Martini WZ. Coagulation complications following trauma. Mil Med Res 2016;3:35.

[7] Mitra B, Wasiak J, Cameron PA, O'Reilly G, Dobson H, Cleland H. Early coagulopathy of major burns. Injury 2013;44(1):40–3.

[8] Lavrentieva A. Coagulopathy in burn patients: one part of a deadly trio. Burns 2015;41(3):419–20.

[9] Lavrentieva A. Replacement of specific coagulation factors in patients with burn: a review. Burns 2013;39(4):543–8.

[10] Lavrentieva A, Kontakiotis T, Bitzani M, Papaioannou-Gaki G, Parlapani A, Thomareis O. Early coagulation disorders after severe burn injury: impact on mortality. Intensive Care Med 2008;34(4):700–6.

[11] Levi M, van der Poll T, Buller HR. Bidirectional relation between inflammation and coagulation. Circulation 2004;109(22):2698–704.

[12] Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. J Trauma 2003;54(6):1127–30.

[13] Mitra B, Tullio F, Cameron PA, Fitzgerald M. Trauma patients with the 'triad of death'. Emerg Med J 2012;29(8):622–5.

[14] Meng ZH, Wolberg AS, Monroe 3rd DM, Hoffman M. The effect of temperature and pH on the activity of factor VIIa: implications for the efficacy of high-dose factor VIIa in hypothermic and acidotic patients. J Trauma 2003;55(5):886–91.

[15] Duchesne JC, McSwain Jr. NE, Cotton BA, Hunt JP, Dellavolpe J, Lafaro K. Damage control resuscitation: the new face of damage control. J Trauma 2010;69(4):976–90.

[16] Davenport RA, Brohi K. Cause of trauma-induced coagulopathy. Curr Opin Anaesthesiol 2016;29(2):212–9.

[17] Frith D, Goslings JC, Gaarder C, Maegele M, Cohen MJ, Allard S. Definition and drivers of acute traumatic coagulopathy: clinical and experimental investigations. J Thromb Haemost 2010;8(9):1919–25.

[18] Davenport R, Manson J, De'Ath H, Platton S, Coates A, Allard S. Functional definition and characterization of acute traumatic coagulopathy. Crit Care Med 2011;39(12):2652–8.

[19] Lu RP, Ni A, Lin FC, Ortiz-Pujols SM, Adams SD, Monroe 3rd DM. Major burn injury is not associated with acute traumatic coagulopathy. J Trauma Acute Care Surg 2013;74(6):1474–9.

[20] Park Martini WZ, Dubick MA, Salinas J, Butenas S, Kheirabadi BS. Thromboelastography as a better indicator of hypercoagulable state after injury than prothrombin time or activated partial thromboplastin time. J Trauma 2009;67(2)266–75 discussion 275-6.

[21] Johansson PI, Stissing T, Bochsen L, Ostrowski SR. Thrombelastography and tromboelastometry in assessing coagulopathy in trauma. Scand J Trauma Resusc Emerg Med 2009;17:45.

[22] Roberts HR, Hoffman M, Monroe DM. A cell-based model of thrombin generation. Semin Thromb Hemost 2006;32(Suppl. 1):32–8.

[23] American Burn Association. Practice guidelines for burn care. J Burn Care Rehabil 2001 The United States of America.

[24] Government of South Australia, R.A.H., Burns Unit, Greenwood J. First aid and emergency management of adult burns. Australia: [73_TD$DIFF]Royal Adelaide Hospital and The Government of Southern Australia; 2011.

[25] European Burns Association (EBA), Brychta P, Magnette A, et al. European Practice Guidelines for Burn Care. 2011.

[26] Reikvam H, Steien E, Hauge B, Liseth K, Hagen KG, Storkson R. Thrombelastography. Transfus Apher Sci 2009;40(2):119–23.

[27] Fries D, Innerhofer P, Schobersberger W. Time for changing coagulation management in trauma-related massive bleeding. Curr Opin Anaesthesiol 2009;22(2):267–74.

[28] Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion 2005;45(9):1413–25.

[29] The National Network for Burn Care. National burn care standards. England: [75_TD$DIFF]NHS (National Health Services) UK; 2013.

[30] Yogore 3rd MG, Boral L, Kowal-Vern A, Patel H, Brown S, Latenser BA. Use of blood bank services in a burn unit. J Burn Care Res 2006;27(6):835–41.

[31] Lu RP, Lin FC, Ortiz-Pujols SM, Adams SD, Whinna HC, Cairns BA, et al. Blood utilization in patients with burn injury and association with clinical outcomes (CME). Transfusion 2013;53(10)2212–21 quiz 2211.

[32] Kwan P, Gomez M, Cartotto R. Safe and successful restriction of transfusion in burn patients. J Burn Care Res 2006;27(6):826–34.

[33] Pidcoke HF, Isbell CL, Herzig MC, Fedyk CG, Schaffer BS, Chung KK, et al. Acute blood loss during burn and soft tissue excisions: an observational study of blood product resuscitation practices and focused review. J Trauma Acute Care Surg 2015;78(6 Suppl. 1):S39–47.

[34] Schaden E, Kimberger O, Kraincuk P, Baron DM, Metnitz PG, Kozek-Langenecker S. Perioperative treatment algorithm for bleeding burn patients reduces allogeneic blood product requirements. Br J Anaesth 2012;109(3):376–81.

[35] Johansson PI, Eriksen K, Nielsen SL, Rojkjaer R, Alsbjorn B. Recombinant FVIIa decreases perioperative blood transfusion requirement in burn patients undergoing excision and skin grafting—results of a single centre pilot study. Burns 2007;33(4):435–40.

[36] Brown LM, Call MS, Margaret Knudson M, Cohen MJ, Holcomb JB, Wade CE, et al. A normal platelet count may not be enough: the impact of admission platelet count on mortality and transfusion in severely injured trauma patients. J Trauma 2011;71(2 Suppl. 3):S337–42.

[37] Stansbury LG, Hess AS, Thompson K, Kramer B, Scalea TM, Hess JR. The clinical significance of platelet counts in the first 24 h after severe injury. Transfusion 2013;53(4):783–9.
Gille J, Klezcewski B, Malcharek M, Raff T, Mogk M, Sablotzki A, et al. Safety of resuscitation with Ringer's acetate solution in

[38] severe burn (VolTRAB)—an observational trial. Burns 2014;40 (5):871–80.

[39] Kowal-Vern A, Walenga JM, Sharp-Pucci M, Hoppensteadt D, Gamelli RL. Postburn edema and related changes in interleukin-2, leukocytes, platelet activation, endothelin-1, and C1 esterase inhibitor. J Burn Care Rehabil 1997;18(2):99–103.

[40] Wohlauer MV, Moore EE, Thomas S, Sauaia A, Evans E, Harr J, et al. Early platelet dysfunction: an unrecognized role in the acute coagulopathy of trauma. J Am Coll Surg 2012;214(5):739-46.

[41] Hiippala ST, Myllyla GJ, Vahtera EM. Hemostatic factors and replacement of major blood loss with plasma-poor red cell concentrates. Anesth Analg 1995;81(2):360-5.

[42] Levi M, Ten Cate H. Disseminated intravascular coagulation. N Engl J Med 1999;341(8):586–92.

[43] Simpson E, Lin Y, Stanworth S, Birchall J, Doree C, Hyde C. Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia. Cochrane Database Syst Rev 20123: Cd005011.

[44] Wikkelso A, Wetterslev J, Moller AM, Afshari A. Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) to monitor haemostatic treatment in bleeding patients: a systematic review with meta-analysis and trial sequential analysis. Anaesthesia 2017;72(4):519–31.

[45] Whiting P, Al M, Westwood M, Ramos IC, Ryder S, Armstrong N, et al. Viscoelastic point-of-care testing to assist with the diagnosis, management and monitoring of haemostasis: a systematic review and cost-effectiveness analysis. Health Technol Assess 2015;19(58)1–228 v–vi.