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Effect of a factor-based coagulation management on blood product use after major burn injury: A retrospective cohort study

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ARTICLE INFO

Article history:
Accepted 18 August 2021

Keywords:
Burns
Hemorrhage
Patient Blood Management
Point-of-care systems
Coagulation algorithm

ABSTRACT

Background: Transfusion of allogenic blood products was shown to be associated with more adverse events and a higher mortality in severely burned patients. This study investigated the impact of a goal-directed and factor-based coagulation algorithm on blood product use and clinical outcomes in severely burned patients.
Methods: This retrospective cohort study included adult patients admitted to the burn center of the University Hospital Zurich with major burn injuries compromising 20–80% of total body surface area. We compared two 3-year periods, one before the introduction of a goal-directed coagulation and transfusion algorithm (period 1: 2009–2011) and one after (period 2: 2016–2018). We applied linear and logistic regression models adjusted for confounders.
Results: We analyzed 36 patients (27.8% female) versus 42 patients (14.3% female) in period 1 and 2, respectively. Comorbidities and burn types were comparable between both collectives. Treatment according to the coagulation algorithm resulted in an overall reduction of 33 units of red blood cells (95% CI −52.8 to −12.9, $p = 0.002$), 9 units fresh frozen plasma (95% CI −14.7 to −2.6, $p = 0.006$) and 1.4g fibrinogen (95% CI −2.2 to −0.5, $p = 0.001$) per patient. We observed less infections (61.8% vs. 41.5%, $p = 0.11$) and a reduced mortality (38.9% vs. 26.8%, $p = 0.33$) during the algorithm treated period, although not significant.

Abbreviations: ABSI, Abbreviated Burn Severity Index; BMI, Body Mass Index; CCI, Charlson Comorbidity Index; HIT, heparin-induced thrombocytopenia; ICU, intensive care unit; INR, International Normalized Ratio; ISS, Injury Severity Score; SAPS II, Simplified Acute Physiology Score II; TBSA, total body surface area; 4-factor PCC, 4-factor prothrombin complex concentrate.

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https://doi.org/10.1016/j.burns.2021.08.015

Conclusion: Treatment of severely burned patients with a goal-directed coagulation algorithm reduced blood product use and resulted in target-oriented administration of coagulation factors to improve outcomes.

1. Introduction

Severely burned patients suffer from life threatening conditions and are at high risk to develop a coagulopathy [1]. These patients are exposed to volume resuscitation, hypothermia and surgical interventions that further influence coagulation and blood loss. The inflammatory mechanism initiated by the injury itself has profound effects on the coagulation cascade that can lead to burn-induced coagulopathy [2]. Burn-induced coagulopathy has unique aspects compared to non-burn trauma coagulopathy as changes occur once burn patients have received large amounts of fluids after admission [3]. Further, this is part of the lethal triad hypothermia, acidaemia and coagulopathy, which in trauma and burn injury is associated with significant mortality [4].

Before the introduction of the goal-directed and factor-based coagulation algorithm [5] as part of patient-blood management for severely burned patients at the University Hospital Zurich, patients were often treated according to historically fixed transfusion strategies (e.g. red blood count and fresh frozen plasma in a ratio of 1:1) [6]. This management was frequently accompanied by an untargeted use of available coagulation factors. Such rigid transfusion patterns generated a high transfusion demand and delay of coagulation alteration recognition [7]. Further, patients receiving intensive care were more likely to be exposed to allogeneic transfusions [8]. We could recently show that transfusions in severely burned patients is independently associated with an increased infection rate, thromboembolic morbidity and a prolonged hospital stay [9].

Point-of-care guided hemostatic resuscitation with target guided coagulation factor therapy is already the gold standard in trauma patients [10]. Despite the mentioned indications before, clear recommendations for severely burned patients are lacking [11,12] with only few studies addressing burn victims in particular [13–15]. According to the review of Welling et al. [15], no observational or retrospective study addresses algorithm based hemostatic management of severely burned patients to date. The aim of this study was therefore to investigate the impact of a goal-directed and factor-based coagulation algorithm on blood poduct use and clinical outcomes in severely burned patients.

2. Methods

The study was reviewed and approved by the independent ethics committee of Zurich (BASEC Nr. 2019-01589) and was conducted in accordance with medical research principles specified in the Declaration of Helsinki as well as the guidelines of Good Clinical Practice. Patients with declined General Consent ("Further use of health-related personal data and biological material for research") were not included in the study.

2.1. Setting

The University Hospital of Zurich (USZ) is a tertiary care referring hospital and serves as one of two certified burn centers in Switzerland. Within the framework of highly specialized medicine, every year, about 70 severely burned patients receive treatment at this clinic. In 2012, the burn intensive care unit at USZ implemented a compulsory transfusion and coagulation management with a focus on a goal-directed and factor-based algorithm. This approach has been assessed on trauma patients [5,16]. The algorithm (Fig. 1 [5]) applies point-of-care viscoelastic as well as standard laboratory tests to bleeding patients, aiming to substitute specific coagulation factors in an individualized manner with restrictive transfusion triggers. Whenever possible, a thorough past medical history on patient factors and medication affecting coagulation was held. Further, samples for platelet count, factor V and factor XIII activity are sent to the laboratories and a point-of-care rotational thrombelastometry analysis (ROTEM®, Instrumentation Laboratory, Bedford, MA, U.S.A.) and arterial blood gas analysis are performed. ROTEM® measurements include EXTEM (tissue factor-activated extrinsic pathway), INTEM (ellagic acid-activated intrinsic pathway), FIBTEM (containing platelet inhibitor cytochalasin D, evaluating the contribution of fibrinogen to clot formation), APTEM (containing aprotinin to inhibit plasmin to evaluate fibrinolysis) or HEPTEM in case of heparin use. Further, patient physiology is maintained (e.g., normothermia, normocalcaemia, normal acid-base status). According to the laboratory results, the pathologies are specifically treated according to the guidelines of the algorithm (Fig. 1) [5]. In an active bleeding situation the target haematocrit-range is 0.21–0.24.

2.2. Participants and study design

In this retrospective and observational single center study, we compared two 3-year periods, one before the introduction of the factor-based goal-directed coagulation and transfusion algorithm and one after full implementation and training. The first period ran from January 2009 to December 2011 and the second period from January 2016 to December 2018. The latter time point was chosen to ensure full establishment of the algorithm. In both cohorts, we included adult patients with major burn injuries compromising 20 and 80% of total body surface area (TBSA) primarily admitted to the burn intensive care unit at the USZ. We excluded patients with documented refusal of informed consent, age below 18, and patients who

Patient history	Perform point-of-care and laboratory coagulation assays
1. Medication • Platelet inhibition • Heparin • Oral anticoagulation (vitamin-K antagonists, Xa or IIa inhibitors) 2. Available laboratory values 3. Past medical history (e.g.): • HIT • Von Willebrand disease • Liver disease	1. **ROTEM®** (EXTEM, INTEM, FIBTEM, APTEM), HEPTEM in case of heparin use 2. Laboratory coagulation • Anti-Xa (screening for heparin and Xa inhibitors) • TT (screening for dabigatran) • PT (screening for vitamin-K antagonists or factor deficiency), CoaguChek® • Factor V (liver failure or factor deficiency) • Factor XIII (factor deficiency) 3. Impedance aggregometry in case of platelet inhibition
Patient physiology (target values)	**Management**
Normothermia (≥ 35.0° C) Normocalcaemia (Ca^{2+} ≥ 1.15 mmol.l^{-1}) Normal acid-base status (pH > 7.2) Haematocrit (0.21-0.24) Permissive hypotension -MAP 55-65 mmHg prior to surgical / interventional source control -MAP 80-90 mmHg in case of TBI	Active warming Calcium i.v. Fluid resuscitation with balanced crystalloid solution. Gelatin may be considered RBC transfusion Permissive hypovolaemia / hypotension Vasopressors combined with volaemia correction
Detect low fibrinogen	**Management**
FIBTEM ≤ 7 mm	**Fibrinogen** 2-4 g i.v. (after 6 g of Fibrinogen, administer factor XIII, 15 U.kg^{-1} i.v.)
Detect fibrinolysis	**Management**
EXTEM / INTEM: Clot lysis after MCF and **APTEM**: normal = Hyperfibrinolysis	**Tranexamic acid** • Bolus: 15 mg.kg^{-1} i.v. (consider empiric use) • Consider continuous infusion 1 – 2 mg.kg^{-1}.h^{-1}
Ongoing bleeding	**Management**
Factor XIII activity < 60% **Platelet count/function** • **EXTEM / INTEM MCF < 40 mm** • **Platelet count** ≤ 50.000.μl^{-1} (≤ 100.000.μl^{-1} in cardiac surgery or TBI) • **Platelet function (Impedance aggregometry)** INR > 2.3 (Quick`s value < 30%) Factor V activity < 20%	Factor XIII 15 U.kg^{-1} i.v. Platelet concentrate Consider desmopressin 0.3 µg.kg^{-1} (max 16 µg) in case of aspirin (like) platelet dysfunction Four-factor prothrombin complex concentrate (slow continuous infusion of small repeated doses – e.g. 500 IU) FFP (2-4 units)
Detect heparin	**Antagonise heparin**
INTEM (CT/CFT) or ACT prolonged and **HEPTEM or heparinase-ACT** normal	**Protamine** (1:1) to antagonise heparin
Special circumstances	**Consider**
Seek haematologist advice	rFVIIa 60 mcg kg^{-1} von Willebrand factor concentrate Idarucizumab

Fig. 1 – Original coagulation algorithm of the University Hospital Zurich [5], with kind reprint permission from John Wiley and Sons Publisher.
Abbreviations: ACT, activated clotting time; CFT, clot formation time; CT, clotting time; FFP, fresh frozen plasma; HIT, heparin induced thrombocytopenia; INR, international normalized ratio; IU, international units; i.v., intravenous; MAP, mean arterial pressure; MCF, maximum clot firmness; PT, prothrombin time; RBC, red blood cells; rFVIIa, recombinant-activated factor VII; TBI, traumatic brain injury; TT, thrombin time.

underwent cardiopulmonary resuscitation before arrival at the hospital. Patients who received initial care at another hospital prior to referral (secondary admissions) were also excluded (Fig. 2).

2.3. *Data collection and variables*

Medical records of all included patients were reviewed. Based on the intensive care discharge reports, the previously defined

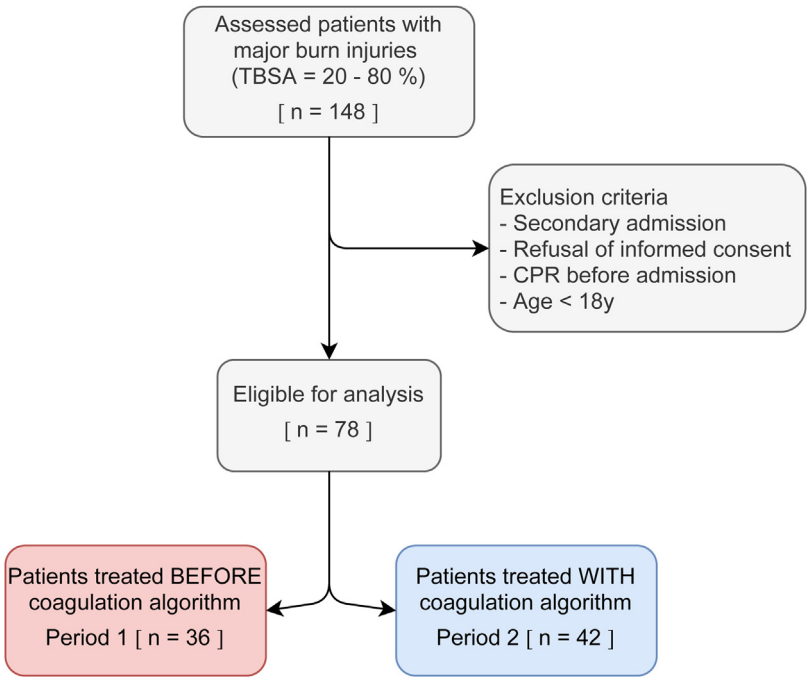

Fig. 2 – Flowchart of patient selection.

variables of medical conditions and clinical outcomes were assigned to the corresponding cases. To characterize the patient cohorts we determined the following scores: Charlson Comorbidity Index (CCI) [17], Injury Severity Score (ISS) [18], Abbreviated Burn Severity Index (ABSI) [19], and Simplified Acute Physiology Score II (SAPS II) [20]. Parameters, such as age, sex, length of hospital stay, number of transfused units of packed red blood cells, fresh frozen plasma, and platelet concentrate, were extracted from the hospital's clinical information system. We recorded the laboratory parameters at the day of admission, before the first surgical procedure, and at the day of discharge from intensive care unit (ICU).

2.4. *Outcome*

The primary endpoint was the delivery of allogeneic blood transfusions. As secondary outcomes, we compared the use of coagulation factors and clinical outcomes such as multi-organ failure, sepsis, infections, thromboembolic events, length of ICU and hospital stay, and in-hospital mortality.

2.5. *Statistical analysis*

We present descriptive tables with a comparison of the two time periods using a Mann–Whitney test for continuous variables and Fisher's exact test for nominal variables. We calculated odds ratios to compare the two periods with respect to the binary variable of patients receiving allogenic transfusions or coagulation factors. For adjusted comparisons, we used linear models for continuous data and logistic regression models for binary data to compare the two periods with respect to the key outcomes mortality, transfusion data and coagulation factors and quantify the differences. All models were additionally adjusted for sex, age, ABSI and CCI scores. For the analysis of laboratory values over time, we used mixed linear models with a random intercept for each patient to see if a difference between the courses of these values between the two periods was present. Analyses were done with R version 3.6.2 [21].

3. Results

We screened 148 patients with major burn injuries (TBSA 20% –80%) treated during the defined periods at the University Hospital of Zurich. In the first period before the implementation of the factor-based coagulation management, 36 patients (27.8% female) matched inclusion criteria, compared to 42 patients (14.3% female) in the second period. The prevalence of comorbidities and injury severity was comparable. We observed an almost identical distribution of burn types including third-degree burns between the two periods. Patients admitted in the second period had a larger burned total body surface area (Table 1).

Treatment according to the coagulation algorithm resulted in a lower number of patients receiving fresh frozen plasma and fibrinogen (Table 2). After adjustment for confounders, it also resulted in an overall reduction of 33 units of packed red blood cells (95% CI -52.8 to -12.9, $p = 0.002$), 9 units fresh frozen plasma (95% CI −14.7 to −2.6, $p = 0.006$) and 1.4 g fibrinogen (95% CI −2.2 to −0.5, $p = 0.001$) per patient (Table 3). Platelet concentrate transfusions and the administration of 4-factor prothrombin complex concentrate or coagulation factor XIII was comparable between both periods.

Patients showed the same baseline hemoglobin level (median 144 g/L) in both time spans (Table 1), though during hospitalization, a different progression was observed. Patients treated according to the coagulation algorithm showed a

Table 1 – Characteristics of patients treated before and with the coagulation algorithm.

	Before algorithm	With algorithm	*p*-value
	Period 1 [n = 36]	Period 2 [n = 42]	
Patient characteristics			
Age (years)	53.0 (40.5–74.2)	52.0 (33.5–57.8)	0.29
BMI (kg/m^2)	26.2 (19.3–28.0)	24.7 (22.5–27.8)	0.32
Sex (female)	10 (27.8)	6 (14.3)	0.17
Type of burn			1.00
Scald	7 (19.4%)	9 (21.4%)	
Burn	24 (66.7%)	27 (64.3%)	
High-current	4 (11.1%)	5 (11.9%)	
Chemical	1 (2.8%)	1 (2.4%)	
Third-degree burn	23 (65.7%)	27 (65.8%)	1.00
Scores			
Charlson comorbidity index	1.0 (0.0–4.0)	1.0 (0.0–1.5)	0.37
Injury Severity Score (pts)	18.0 (16.0–25.0)	16.0 (10.0–25.0)	0.41
Total body surface area (%)	30.0 (30.0–50.0)	40.0 (30.0–50.0)	0.79
ABSI (pts)	9.0 (7.0–10.0)	8.0 (7.0–11.0)	0.24
SAPS II (pts)	32.0 (15.0–51.5)	31.0 (21.0–43.0)	0.80
First laboratory value at admission			
Hemoglobin (g/L)	144 (133–154)	144 (136–153)	0.60
Platelets (G/l)	275 (212–376)	221 (190–271)	0.02
INR (unit)	1.1 (1.0–1.2)	1.1 (1.1–1.2)	0.18
Creatinine (μmol/L)	92.0 (66.0–103.0)	85.0 (72.0–103.0)	0.87
eGFR (ml/min)	88.7 (64.6–97.8)	95.5 (66.8–108.5)	0.31

Data presents as median and interquartile range (IQR). Categorical variables as number and percentage (%). Abbreviations: ABSI, Abbreviated Burn Severity Index; BMI, Body Mass Index; SAPS II, Simplified Acute Physiology Score II; INR, International Normalized Ratio.

significantly higher hemoglobin level before the first surgery (Fig. 3). At discharge from burn intensive care unit, hemoglobin levels did not differ significantly (median period 1: 85 g/L vs. period 2: 90 g/L, $p = 0.66$) in univariate comparison. However, the adjusted model showed an overall higher hemoglobin level of 10 g/L for the cohort receiving treatment according to the coagulation algorithm compared to the cohort treated before (95% CI 0.17–1.73, $p = 0.023$) **(Table S2 and S3 in supplement)**.

Patients treated according to the coagulation algorithm (period 2), had fewer infections and the duration of intensive care therapy as well as the total length of hospital stay were shorter. The percentage of in-hospital mortality (period 1: 38.9% vs. period 2: 26.8%, $p = 0.33$) was lower including the adjusted comparison of in-hospital mortality (OR 0.58, 95% CI 0.13–2.39, $p = 0.45$) **(Table S1.1 in supplement)** in the cohort treated according to the coagulation algorithm, although not significant. The incidence of thromboembolic events was comparable between both cohorts. Table 4 gives a detailed overview of the occurrence of observed complications during both periods.

4. Discussion

This retrospective study analyzed 78 adults admitted to the burn center of the University Hospital Zurich with major burn injuries. We compared the need for blood products in patients treated before and after the introduction of a goal-directed and

Table 2 – Differences in the number of patients receiving allogeneic blood products and coagulation factors between the periods during the length of hospital stay.

	Period 1 [n = 36]	Period 2 [n = 42]	Odds ratio [95% CI]	*p*-value
Allogenic transfusions				
Red blood cells	26 (72.2%)	23 (54.8%)	0.47 [0.18 to 1.19]	0.11
Fresh frozen plasma	14 (38.9%)	4 (9.5%)	0.17 [0.04 to 0.53]	<0.01
Platelet concentrate	2 (5.6%)	2 (4.8%)	0.85 [0.10 to 7.39]	0.87
Coagulation factors				
4-factor PCC	4 (11.1%)	2 (4.8%)	0.40 [0.05 to 2.18]	0.31
Coagulation factor XIII	17 (47.2%)	17 (40.5%)	0.76 [0.31 to 1.87]	0.55
Fibrinogen	11 (30.6%)	4 (9.5%)	0.24 [0.06 to 0.79]	0.03

Data reported as number and percentage (%). **Period 1** refers to the patient cohort before the introduction and **Period 2** to the cohort treated according to the coagulation algorithm.
Abbreviation: 4-factor PCC, 4-factor prothrombin complex concentrate.

Table 3 – Adjusted models for the comparison of transfused allogeneic blood products and administered coagulation factors between the periods.

	Coefficient	95% confidence interval	*p*-value
Allogenic transfusions			
Red blood cells (units)	−33	−52.8 to −12.9	0.002
Fresh frozen plasma (units)	−9	−14.7 to −2.6	0.006
Platelet concentrate (units)	0	−0.7 to 0.2	0.300
Coagulation factors			
4-factor PCC (IU)	−61	−141.9 to 19.7	0.140
Coagulation factor XIII (IU)	−1211	−2443.7 to 20.9	0.054
Fibrinogen (g)	−1.4	−2.2 to −0.5	0.001

The coefficients represent the difference for the patients treated according to the coagulation algorithm (period 2) in comparison with patients treated before (period 1). The models are adjusted for age, sex, the Abbreviated Burn Severity Index (ABSI) and Charlson Comorbidity Index. Abbreviation: 4-factor PCC, 4-factor prothrombin complex concentrate.

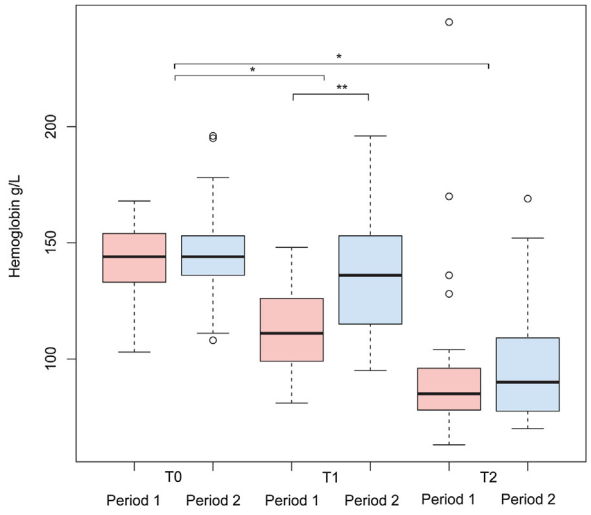

Fig. 3 – Boxplots for hemoglobin levels over time. Comparing the patient cohort treated before (Period 1 = red) and with the coagulation algorithm (Period 2 = blue) between the course of different values over three time points T0 (baseline at admission), T1 (before the first surgical intervention), and T2 (discharge from ICU).
***Mixed linear models for a difference of T0 and T1, T0 and T2 ($p < 0.0001$, each), overall difference between period 1 and period 2 ($p = 0.02$). ** Unadjusted comparison at T1 between period 1 and period 2 ($p = 0.0005$); unadjusted comparison at T0 and T2 n.s. Level of significance 0.05.**

factor-based coagulation algorithm. We observed a reduction of the number of patients receiving allogenic fresh frozen plasma transfusions and fibrinogen as well as the overall amount of transfused packed red blood cells, fresh frozen plasma, and administration of fibrinogen.

Transfusion of allogenic blood products is associated with adverse events [22]. In relation to severely burned patients, the recently published study by Kaserer et al. demonstrated that transfusion of allogeneic blood products is associated with an increased rate of infection and thromboembolic morbidity as well as a prolonged hospital stay [9]. Our data shows that the use of a coagulation algorithm for severely burned patients reduces the amount of transfused red blood cells and fresh frozen plasma during the length of hospitalization. The trial of Schaden et al. [14] reported reduced transfusion use during surgical burn wound excision, using a similar approach. Concerning platelet concentrate transfusion, the portion of transfused patients as well as the number of transfusions did not differ between the two periods. However, the amounts administered were very small, making a detection of any differences less likely. It should be noted that the level of platelets in period 2 was significantly lower (median period 1: 275 G/I vs. period 2: 221 G/I, $p = 0.02$).

The recent meta-analysis of Santos et al. [23] reported significant reduction in mortality in the perioperative period of surgical patients treated with hemostatic assays. The Cochrane review of Wikkelsø et al. [24] mentioned evidence for the application of viscoelastic guided transfusion strategies to improve morbidity in patients with bleeding. Our data support the conclusion in which the algorithm-treated cohort showed lower overall infection rates. Especially urinary tract infections were significantly reduced in the patient group treated according to the coagulation algorithm. Further, no more complications occurred during the algorithm-based treatment compared with the treated cohort before, such as thromboembolic events. To the contrary, fewer antifungal therapies were administered and the duration of intensive care treatment was noticeably shorter. In addition to fewer allogeneic transfusions, we observed in the cohort treated according to the coagulation algorithm a reduced number of patients receiving fibrinogen. This is an important finding, as one would assume that more fibrinogen is administered due to the algorithm protocol. In Switzerland, fibrinogen concentrate was licensed in 1992, 4-factor PCC in 2004 and factor XIII concentrate in 2003. Until the introduction of the coagulation algorithm these factor concentrates were used empirically and not goal-directed in addition to FFP transfusion for coagulation management. Cryoprecipitate is not availble in Switzerland. A cornerstone of the coagulation algorithm are repetitive point-of-care measurements to identify, quantify and monitor patient's fibrinogen levels. We interpret the reduced fibrinogen administration as a resulted of a target-oriented

Table 4 – Descriptive of complications and outcome of patients treated before and according to the coagulation algorithm.

	Before algorithm	With algorithm	*p*-value
	Period 1 [n = 36]	Period 2 [n = 42]	
Surgeries (frequency)	4.0 (2.0–9.5)	3.0 (2.0–6.0)	0.33
Multi-organ failure	4 (11.8%)	6 (14.6%)	1.00
Sepsis	15 (44.1%)	16 (39.0%)	0.81
Positive blood culture	17 (50.0%)	18 (43.9%)	0.65
Overall infection rate	21 (61.8%)	17 (41.5%)	0.11
Respiratory	17 (50.0%)	17 (41.5%)	0.49
Skin	18 (52.9%)	12 (29.3%)	0.06
Osteomyelitis	1 (2.8%)	1 (2.4%)	1.00
Abdominal	2 (5.9%)	2 (4.9%)	1.00
Urinary	14 (41.2%)	4 (9.8%)	<0.01
Antibiotic drugs	21 (61.8%)	22 (53.7%)	0.49
Antifungal drugs	14 (38.9%)	6 (14.3%)	0.02
HIT	0 (0%)	3 (7.3%)	0.25
Thrombo-embolic events	5 (14.7%)	7 (17.1%)	1.00
Duration			
Length ICU (days)	22.0 (5.0–48.2)	12.0 (3.0–30.0)	0.13
Length of stay (days)	29.0 (16.5–56.0)	23.0 (11.0–54.0)	0.49
In-hospital mortality	14 (38.9%)	11 (26.8%)	0.33

Data presents as median and interquartile range (IQR). Categorical variables as number and percentage (%). Abbreviations: HIT, heparin-induced thrombocytopenia; ICU, intensive care unit.

administration of coagulation factors. The trial of Schaden et al. [14] found no difference in fibrinogen administration between standard and algorithm group. The review for management of bleeding in major burn surgery does not mention other studies concerning fibrinogen therapy [15].

Despite seeing the same hemoglobin value at admission (T0) as well as a similar one at discharge from the ICU (T2), the hemoglobin level remained significantly higher before the first surgical intervention (T1). Also, the adjusted model showed an overall higher amount of hemoglobin in the period treated according to the coagulation algorithm. In our study, the portion of women declined from 27.8% in period 1–14.3% in period 2. Although the gender difference is not statistically significant, it has to be taken into account that women may have a higher prevalence of preexisting anemia [25]. The recent post-hoc analysis of Turan et al. [26] described postoperative anemia as a risk factor for non-fatal myocardial infarction and all-cause mortality.

A predefined coagulation protocol (algorithm) facilitates decision making and improves outcomes. Of course, several factors influence these events, for which we could not correct the analysis. Nonetheless, the study provides further evidence for the use of a goal directed coagulation algorithm to improve the treatment of severely burned patients.

4.1. *Limitations*

This was a retrospective study, which can only indicate a possible association. We compared two cohorts that are four years apart. This interval was required for implementation of the algorithm and team training. To the best of our knowledge, other therapy standards did not change during the observation periods; however, some minor adaptations may have been applied. Transfusion practice may has changed over the last 15 years. At the University Hospital Zurich, transfusion strategies were not more restrictive in the cohort treated according to the coagulation algorithm. We registered the same median hemoglobin value at admission in both periods and observed a numerically higher hemoglobin value at ICU discharge in period 2. The adjusted model showed a higher overall hemoglobin level of 10 g/L for patients treated according to the coagulation algorithm. We explain this by a lower blood loss due to a better coagulation management. Our patient collective was limited, though very comparable in terms of demographics, medical comorbidities, and burn patterns. In addition, we adjusted our analysis for the ABSI, which was recently proven for its accuracy [27]. Further, with the adjustment for the Charlson Comorbidity Index, we reduced other confounders in order to focus on the impact of transfusions in our outcomes.

5. Conclusion

Treatment of severely burned patients with a goal-directed and factor-based coagulation algorithm reduced blood product use and led to a target-oriented administration of coagulation factors to improve patient's outcomes.

Author contributions

Concept and design: AK, SDS, DRS, and JAP. Acquisition of data: NP. Review of data: SDS. Statistical analysis: JB. Drafting of the manuscript: SDS and AK. All authors analyzed and interpreted the results, critically edited the manuscript, approved the final version to be submitted, and agree to be accountable for the accuracy and integrity of the work.

Conflict of interest

SDS, NP and JB have no conflicts of interests to declare. AK received honoraria for lecturing from Bayer AG Switzerland. DRS's academic department is receiving grant support from the Swiss National Science Foundation, Berne, Switzerland, the Swiss Society of Anesthesiology and Reanimation (SGAR), Berne, Switzerland, the Swiss Foundation for Anesthesia Research, Zurich, Switzerland, Vifor SA, Villars-sur-Glâne, Switzerland and Vifor (International) AG, St. Gallen, Switzerland. DRS is co-chair of the ABC-Trauma Faculty, sponsored by unrestricted educational grants from Novo Nordisk Health Care AG, Zurich, Switzerland, CSL Behring GmbH, Marburg, Germany, LFB Biomédicaments, Courtaboeuf Cedex, France and Octapharma AG, Lachen, Switzerland. DRS received honoraria / travel support for consulting or lecturing from: Danube University of Krems, Austria, US Department of Defense, Washington, USA, European Society of Anesthesiology, Brussels, BE, Korean Society for Patient Blood Management, Seoul, Korea, Korean Society of Anesthesiologists, Seoul, Korea, Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis, Paris, France, Baxalta Switzerland AG, Volketswil, Switzerland, Bayer AG, Zürich, Switzerland, B. Braun Melsungen AG, Melsungen, Germany, Boehringer Ingelheim GmbH, Basel, Switzerland, Bristol-Myers-Squibb, Rueil-Malmaison Cedex, France and Baar, Switzerland, CSL Behring GmbH, Hattersheim am Main, Germany and Berne, Switzerland, Celgene International II Sàrl, Couvet, Switzerland, Daiichi Sankyo AG, Thalwil, Switzerland, Haemonetics, Braintree, MA, USA, Instrumentation Laboratory (Werfen), Bedford, MA, USA, LFB Biomédicaments, Courtaboeuf Cedex, France, Merck Sharp & Dohme, Kenilworth, New Jersey, USA, PAION Deutschland GmbH, Aachen, Germany, Pharmacosmos A/S, Holbaek, Denmark, Pfizer AG, Zürich, Switzerland, Pierre Fabre Pharma, Alschwil, Switzerland, Portola Schweiz GmbH, Aarau, Switzerland, Roche Diagnostics International Ltd, Reinach, Switzerland, Sarstedt AG & Co., Sevelen, Switzerland and Nümbrecht, Germany, Shire Switzerland GmbH, Zug, Switzerland, Tem International GmbH, Munich, Germany, Vifor Pharma, Munich, Germany, Neuilly sur Seine, France and Villars-sur-Glâne, Switzerland, Vifor (International) AG, St. Gallen, Switzerland, Zuellig Pharma Holdings, Singapore, Singapore. JAP received grant support from the Swiss National Science Foundation. JAP received honoraria/travel support from Mediwound (Rüsselsheim, Germany), Integra Lifesciences (Saint Priest, France), Polymedics (Denkendorf, Germany), Nanomedic Technologies (Lod, Israel).

Acknowledgment

The authors thank Dr. Clara Castellucci for proofreading the manuscript.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.burns.2021.08.015.

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