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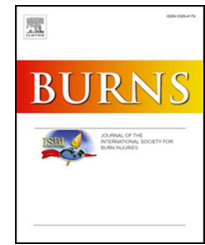
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Changes in coagulation and temperature management in burn patients – A survey of burn centers in Switzerland, Austria and Germany

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ABSTRACT

Background: Severely burned patients suffer from both coagulopathy and hypothermia, with a lack of international consensus and appropriate treatment guidelines. This study examines recent developments and trends in coagulation and temperature management in European burn centers.

Methods: A survey was sent to burn centers in Switzerland, Austria and Germany in 2016 and again in 2021. The analysis was performed using descriptive statistics, with categorical data reported in absolute numbers (n) and percentages (%) and numerical data reported as mean and standard deviation.

Results: The rate of completed questionnaires was 84 % (16 of 19 questionnaires) in 2016 and 91 % (21 of 22 questionnaires) in 2021. The number of global coagulation tests performed has decreased over the observation period in favor of single factor determination and bed-side point-of-care coagulation tests. This has also led to increased administration of single factor concentrates in therapy. Although many centers had a defined treatment protocol for hypothermia in 2016, coverage increased such that in 2021 all centers surveyed had such a protocol. The body temperature was measured more consistently in 2021; thus, hypothermia was more actively sought, detected and treated.

Conclusion: A point-of-care guided, factor-based coagulation management and the maintenance of normothermia have gained importance in the care of burn patients in recent years.

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Abbreviations: ABA, American Burn Association; DAV, Deutschsprachige Arbeitsgemeinschaft für Verbrennungsmedizin; FFP, Fresh frozen plasma; ICU, Intensive care unit; ISBI, International Society for Burn Injuries; ROTEM, Rotational thromboelastometry

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1. Introduction

Severely burned patients are at increased risk of presenting with or developing coagulopathy and hypothermia [1]. If both are present, two of the three factors from the lethal triad of hypothermia (body temperature ≤ 35.5 °C), acidosis (arterial pH ≤ 7.25) and coagulopathy (derangement of hemostasis resulting in either excessive bleeding, clotting or elevated INR) are met. The lethal triad with increased overall mortality is known primarily in trauma patients, but was shown to be also a mortality predictor in burn patients [2–4]. However, the treatment of severely burned patients is complex on multiple levels and differs significantly from trauma patients. Airway management, fluid resuscitation, wound care, infection control, coagulation management and the preservation of normothermia play an essential role in the care of burned patients. Deviations in these treatment areas lead to increased morbidity and mortality [1,5–9]. The systemic inflammation caused by burn injuries can lead to burn-induced coagulopathy, which challenges the clinician during hospital admission and subsequent multiple surgeries [10,11]. In addition, hypothermia, often a limiting factor for surgical interventions, occurs due to widespread disruption of the skin's barrier function and consequently limited temperature maintenance [12]. While the importance of appropriate diagnostic tools and treatment algorithms for coagulation disorders in trauma patients is well established, there is a lack of consensus concerning guidelines for burn patients [13–15].

To study this topic more in depth, we sent out a survey regarding coagulation and temperature management to burn centers in Switzerland, Austria and Germany in 2016 and 2021. The aim of this study is to present the current status and recent developments in the diagnosis and management of coagulopathy and hypothermia in burned patients.

2. Methods

2.1. Study setting and data collection

The Cantonal Ethics Committee of Zurich in Switzerland waived the study after review (BASEC No.: Req-2020–01242).

This is a researcher-initiated, multi-center, international study investigating physicians' experience and opinions on current therapy for coagulopathy and hypothermia in burn patients in their respective centers. The study was conducted from 2016 to 2021 in burn centers of the "Deutschsprachige Arbeitsgemeinschaft für Verbrennungsmedizin" (DAV), including affiliated burn centers in Germany, Austria and Switzerland. All centers were certified in their respective country. Participation was voluntary and without monetary compensation.

2.2. Survey

We sent out an anonymous questionnaire, created using SurveyMonkey (SVMK Inc., San Mateo, California, USA), by e-mail to the burn centers in 2016 and 2021. For both time points the questionnaire was identical. It contained 11 questions on the current status of diagnosis and treatment of coagulation disorders in burn patients and five questions on monitoring and management of body temperature. Single- or multiple-choice responses were entered with no time limit. Diagnostic coagulation questions included coagulation management at entry, intraoperatively and during follow-up. The coagulation tests available for selection were as follows: Measurement of platelets, INR/Quick, prothrombin time, thrombin time, fibrinogen, viscoelastic coagulation tests (e.g. ROTEM), platelet aggregometry (e.g., Multiplate), factor V, factor XIII and other. When asked about products used to correct coagulation disorders, participants could select the following: red cell concentrates, platelet concentrates, fresh frozen plasma (FFP), erythropoietin, intravenous application of iron (e.g., ferinject), tranexamic acid, fibrinogen, 4-factor prothrombin complex concentrate, factor XIII concentrate, recombinant coagulation factor VIIa, other. When asked about temperature management, the following measures could be selected: minimize exposed skin sites, pre-warmed drapes/blankets, temperature management system, warmed infusions, room temperature control, direct admission to burn unit, other.

2.3. Statistical analyses

Only descriptive statistics were applied to analyze the surveys. Categorical data are reported in absolute numbers (n) and percent (%) and numerical data as mean and standard deviation (\pm SD). All statistical analyses were performed with Excel (Microsoft Corporation).

3. Results

The return rate of completed questionnaires was excellent, with 84 % (16 of 19 questionnaires) in 2016 and 91 % in 2021 (21 of 22 questionnaires), respectively.

The frequency of conducted coagulation assessments at hospital admission was 68.14 % in 2016 and 72.7 % in 2021, intraoperative 21.0 % in 2016 and 18.2 % in 2021, and during further treatment 42.1 % in 2016 and 40.9 % in 2021. The frequency of global coagulation tests performed at admission was 58.8 % in 2016 and 45.5 % in 2021. Intraoperatively, global coagulation tests were carried out in 50.0 % in 2016 and 47.6 % in 2021 and during further treatment 50.0 % in 2016 and 59.1 % in 2021. Viscoelastic coagulation tests (e.g., ROTEM) were performed during at admission in 17.7 % (2016) vs. 4.5 % (2021), intraoperatively in 18.8 % (2016) vs. 62.0 % (2021) and during further treatment in 6.3 % (2016) vs. 22.8 % (2021). The

results of the survey questions concerning coagulation assessment are summarized in Fig. 1.

In 2021, 91 % of all centers had a protocol for reducing the use of allogeneic blood products compared to 63.2 % in 2016. The availability of all blood or coagulation products listed in the survey has increased remarkably within five years. The results of the survey questions concerning coagulation management are summarized in Fig. 2.

In 2016, 94 % of the burn centers had a hypothermia prevention guideline. This increased to 100 % in 2021. Body temperature at admission was measured in 68.8 % in 2016 and 90.9 % in 2021, intraoperatively in 62.5 % in 2016 and 81.8 % in 2021 and postoperatively in 50.0 % in 2016 and 77.3 % in 2021. Preventive physical measures such as minimizing exposed skin areas were applied in 86.7 % in 2016 and 100 % in 2021. The ambient room temperature was adjusted in 100 % in 2016 and 95.45 % in 2021, the use of pre-warmed blankets was 53.3 % in 2016 and 90.9 % in 2021. If despite the preventive measures, relevant hypothermia of $< 36^{\circ}\text{C}$ occurred, the operation may be terminated prematurely in 2021 (18.2 % in 2021 vs. 0 % in 2016). Fig. 3.

4. Discussion

In this study, we could show that between 2016 and 2021, coagulation and temperature management gained importance in the burn centers of Switzerland, Austria and Germany.

In the past, patients were frequently transfused according to historically fixed regimens and coagulation factors were not administered in a targeted approach [16–19]. Guidelines by the American Burn Association (ABA) and the International Society for Burn Injuries (ISBI) advise on a wide variety of burn care related topics, including but not limited to emergency care, airway stabilization, fluid substitution, wound care, infections and nutrition. Furthermore, in the ISBI Practice Guidelines for Burn Care, Part 2 from 2018, the risks related to the transfusion of blood products are discussed and restrictive use of these products is recommended. However, information concerning the application of point-of-care coagulation tests is not included and in case of massive bleeding, a transfusion strategy of 1:1:1 red blood cell units: plasma transfusions: platelet transfusions is advised [20]. Due to the increasing awareness of potential side effects of allogeneic blood transfusions, a trend toward algorithm-based and targeted administration of coagulation factors, as already the gold standard in trauma care, has become apparent in recent years in Europe [21]. This has not only reduced the number of allogeneic blood products administered but also reduced the associated side effects, including infections [22]. Where fixed transfusion regimens for red blood cells, platelet concentrates and fresh frozen plasma used to predominate, a clear trend toward targeted, factor-based coagulation management is emerging, as there is evidence that this reduces transfusions of allogeneic blood products [17,18,22]. Targeted substitution of blood and coagulation products is part of Patient Blood Management protocols and has already been established and validated in the peri-

operative setting and trauma care, as it improves patient outcomes and reduces costs [23–25]. It is not surprising that due to the positive results in other areas, transfusion and coagulation algorithms are also being introduced successfully in burn care [26,27]. Not only can limited blood products be used sparingly, but the associated side effects are reduced. Burn patients show altered hemostasis due to disseminated intravascular coagulation and increased proinflammatory cytokines, leading to a hypercoagulable state and thus increased thromboembolic events [23]. Successful implementation and enforcement of Patient Blood Management can reduce these dreaded thromboembolic complications and infections, as shown by Sahli et al. [22]. This study compared two time periods, one before and one after the implementation of a goal-directed coagulation and transfusion algorithm based on point-of-care and conventional laboratory tests focusing on specific factors. The applied coagulation and transfusion algorithm is already published in the study [22].

In order to enable the targeted administration of coagulation factors, a detailed prior analysis of the actual state of blood coagulation is necessary. Point-of-care coagulation tests, in Europe predominately rotational thromboelastometry (ROTEM), are firmly established in trauma care and perioperatively in liver or heart interventions [28,29]. Viscoelastic tests are increasingly being used in the treatment of burn patients. However, only 17 % in the survey said viscoelastic tests are used upon admission, while > 60 % during surgery. These results reflect the fact that directly after an isolated burn injury, blood loss is not a major issue. Coagulation factors are upregulated within hours and predispose burn patients to a hypercoagulable state [1]. In addition, extravasation of water in the sense of redistribution results in hemoconcentration [30]. Consequently there is rarely a significant (hypo)coagulopathy to be expected at admission of burn patients. However, due to the extensive bleeding during large tangential excisions coagulopathy becomes important during further surgery and coagulation needs to be re-assessed timely and frequently. In combination with the nowadays widely available diagnostics and supplementation of individual factors, e.g., factor XIII, a trend toward factor-based management can be clearly identified in the period covered by this study. All available coagulation factors were administered more frequently in 2021 than in 2016 (fibrinogen 37.5 % in 2016 vs. 72.7 % in 2021; prothrombin complex concentrate 50.0 % in 2016 vs. 72.3 % in 2021; factor XIII concentrate 43.8 % in 2016 vs. 72.7 % in 2021; recombinant factor VIIa 12.5 % in 2016 vs. 72.7 % in 2021).

Temperature management is important in the care of severely burned patients. Due to the extensive skin injuries and surgical interventions with large wound areas, maintaining normothermia can be challenging [31]. Therefore, many burn patients are hypothermic at hospital admission or develop a hypothermia during extended surgeries [32]. To date, the impact of hypothermia in burn patients is controversial. In an animal model with rats, mild hypothermia was shown to be potentially beneficial for survival [33]. In addition, the evidence for many measures to maintain normothermia, especially raising room temperature, is insufficient and subject to

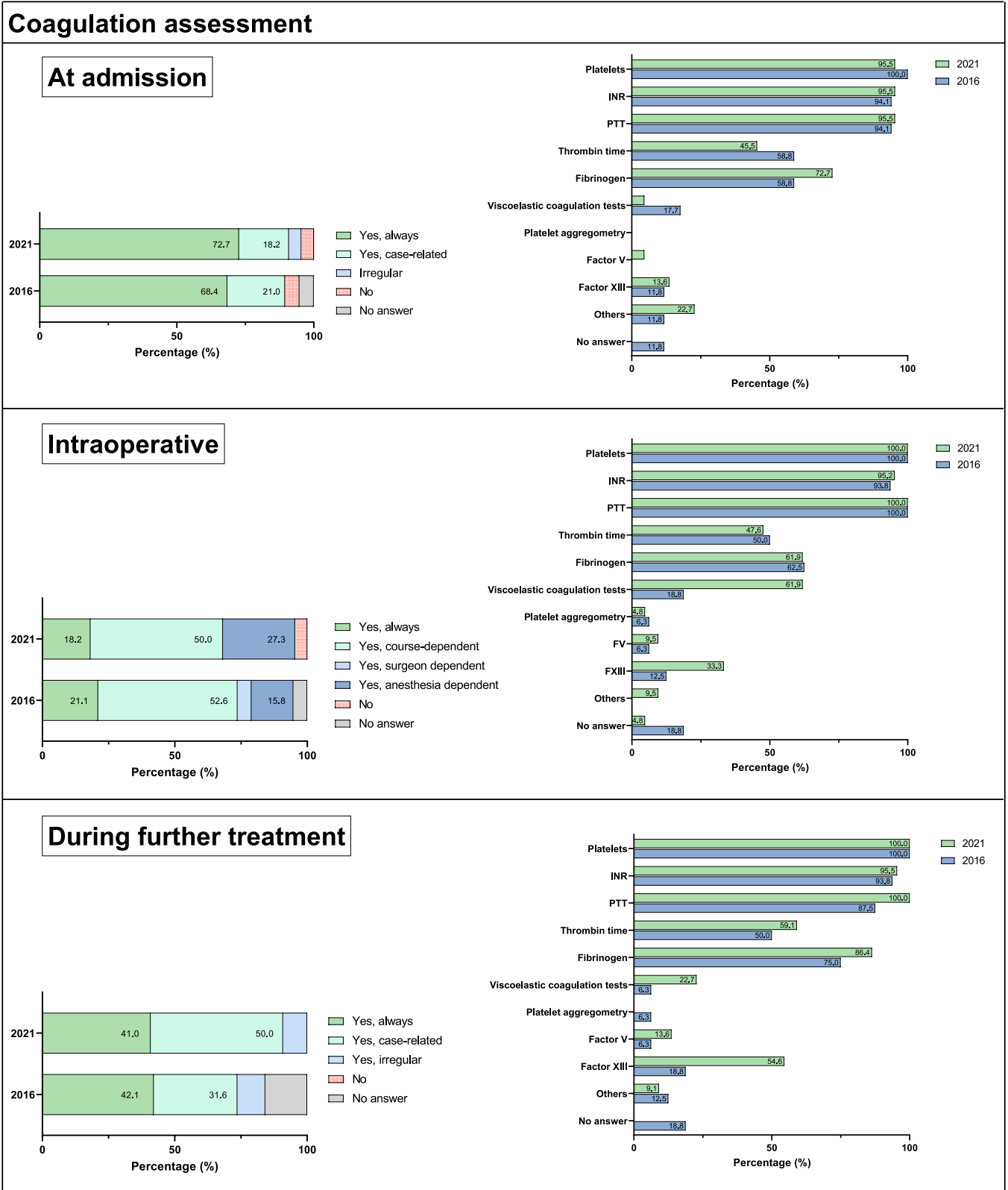


Fig. 1 – Presentation of the results of the questions asked in the questionnaire regarding the coagulation assessment at three different time points. On the left, each with a simple selection of whether a coagulation assessment is performed and, if so, under what conditions. The right-hand side shows which coagulation tests are performed. These could be selected with multiple selection.

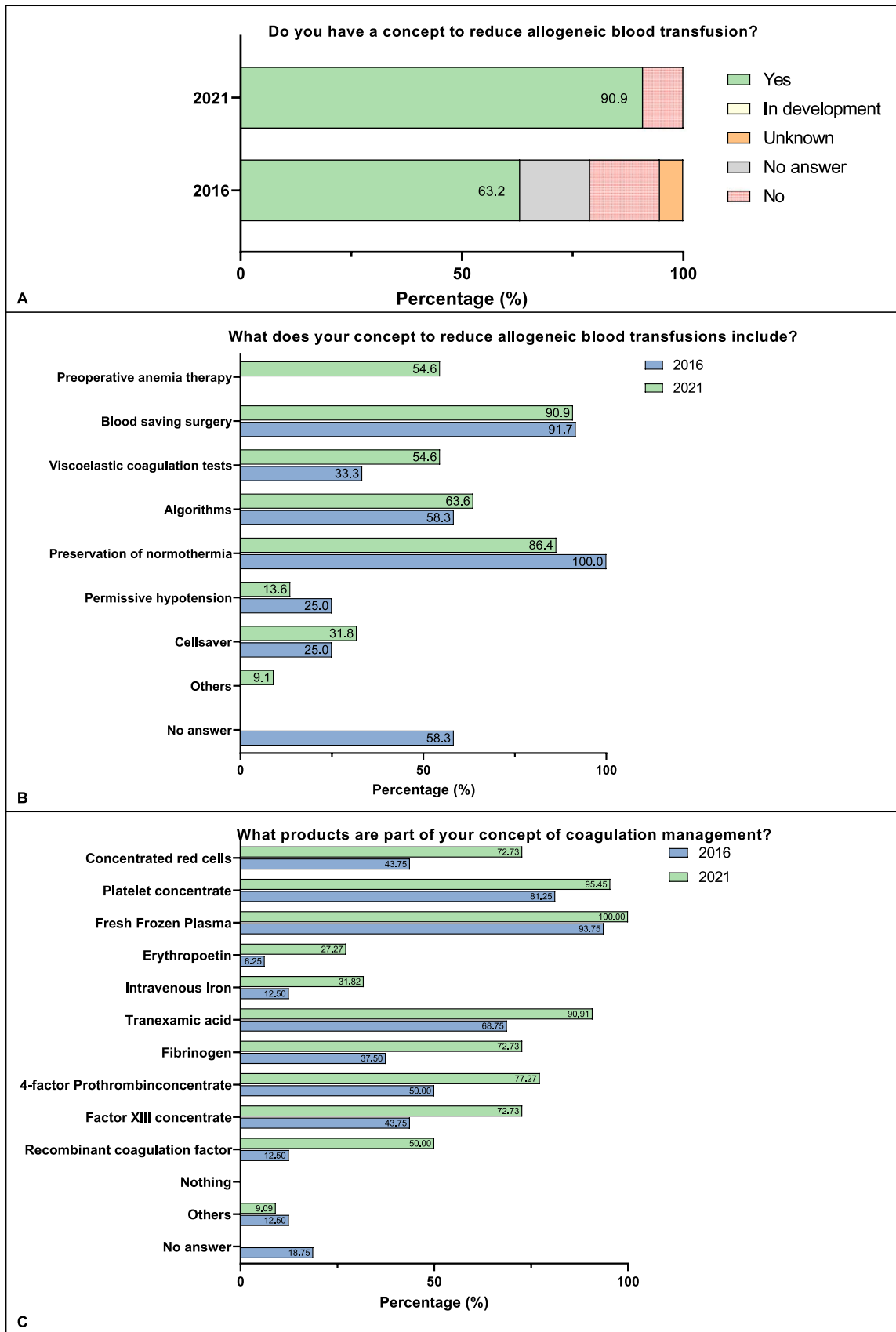


Fig. 2 – Presentation of the results of the questions related to blood coagulation management. A: Answer as single choice. B/ C: Multiple choice from given list.

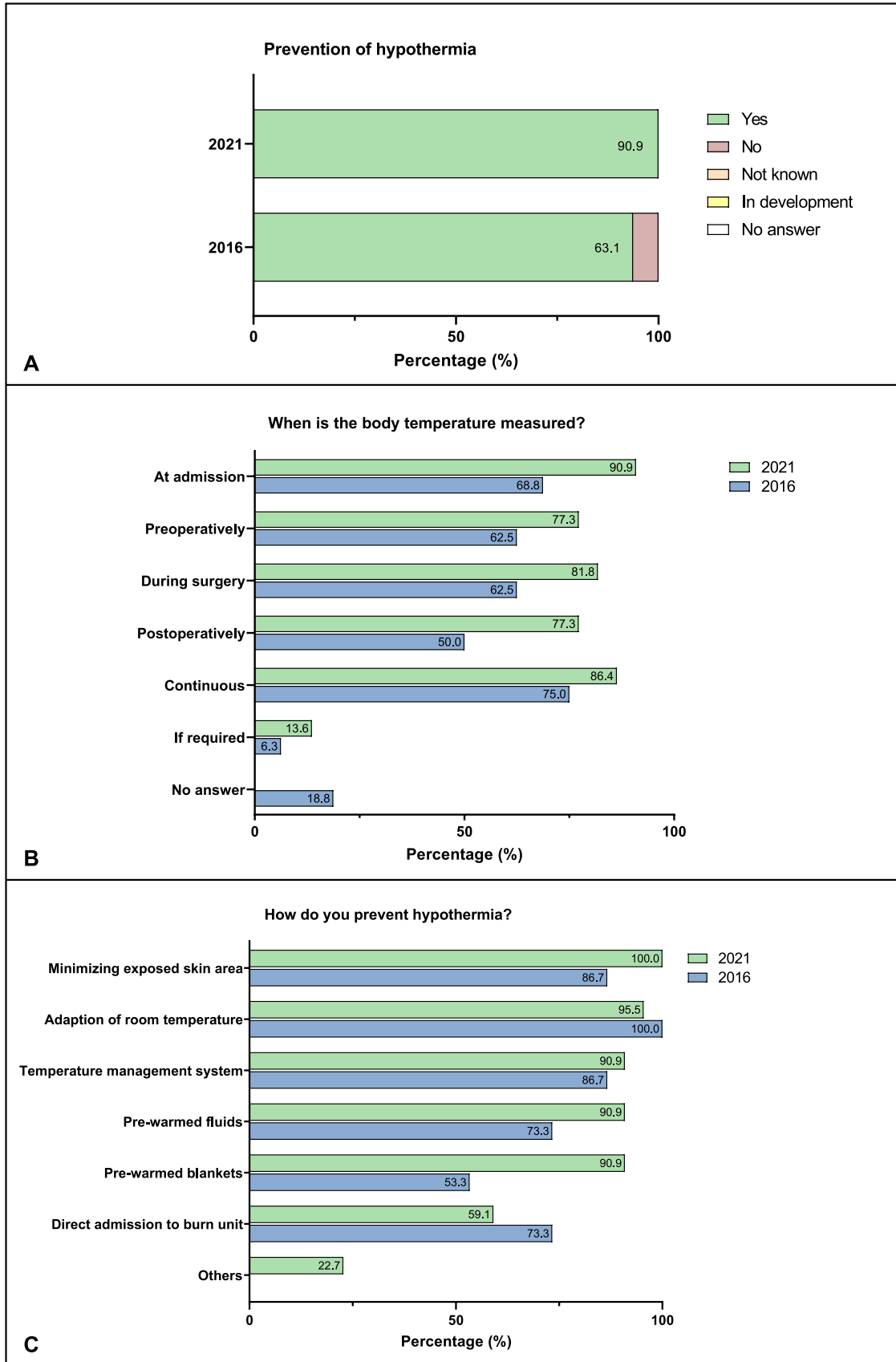


Fig. 3 – Presentation of the results of the hypothermia questions. A: Single choice. B/C: multiple choice from given list.

further research [34]. On the other hand, it was shown that hypothermia is associated with coagulopathy, increased infection rates, hemodynamic instability, increased length of ICU stay and mortality [35–37]. Moreover, maintaining normothermia during surgery was shown to reduce blood transfusions and wound infections [38]. The focus on hypothermia prevention was increased during the surveyed period. These results are in line with previous published surveys regarding temperature management in Europe and the United States [39,40]. In 2021, all surveyed centers had guidelines to prevent hypothermia underlining the clinical importance of temperature management in severely burned patients. At the University Hospital Zurich, for example, temperature management comprises continuous monitoring of the body temperature, radiant heaters in the resuscitation bay, pre-warmed operating theaters, heated infusions, forced-air heating blankets and pre-warmed blankets. In selected patients, we use esophageal warmers with good results so far. Furrer et al. showed the feasibility of using an esophageal heat exchanger tube, commonly used in the cooling of patients with myocardial ischemia, to maintain the body temperature in severely burned patients [41]. However, studies comparing the effectiveness of the esophageal heat exchanger tube to other warming methods are lacking.

4.1. Limitations

This study presents results based on the individual opinions of clinicians and their respective institutions. Due to the statements' subjectivity and individuality, it is impossible to draw conclusions about burn care more generally. Nevertheless, the clinicians' opinions are important because they provide a high level of experience and insight into daily clinical practice. With this study, due to the lack of patient data, no recommendations for action can be made, but trends in treatment can be identified. Due to the close collaboration, our survey was sent to burn centers in the German speaking area only. The importance of hypothermia control and coagulation management have been known for many years and our questionnaire did examine the changes in protocols over a five-year period. However, we did not assess when exactly certain coagulation and hypothermia management measures were implemented in the respective burn center.

5. Conclusion

Coagulation management and maintenance of normothermia have gained importance in European burn centers during the observation period. The trend is clearly toward factor-based, goal-directed coagulation management and the establishment of algorithms as part of Patient Blood Management. In addition, all surveyed burn centers have recognized the importance of temperature maintenance and have hypothermia guidelines.

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CRedit authorship contribution statement

CR contributed to data collection, data preparation and interpretation, drafting and critical revision of the manuscript. SA did the artwork, contributed to interpretation, drafting and critical revision of the manuscript. CR and SA contributed equally to this study. DRS contributed to data interpretation and critical revision of the manuscript. JAP and AK designed the study, provided the data, contributed to data interpretation and critical revision of the manuscript. All authors revised and approved the final manuscript.

Conflicts of interests

CR, SA, MA and LM have no conflicts of interests to report. Dr. Spahn's academic department is receiving grant support from the Swiss National Science Foundation, Berne, Switzerland, the Swiss Society of Anesthesiology and Perioperative Medicine (SSAPM), Berne, Switzerland, the Swiss Foundation for Anesthesia Research, Zurich, Switzerland, Vifor SA, Villars-sur-Glâne, Switzerland and Vifor (International) AG, St. Gallen,

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