



Guidelines

Management of severe thermal burns in the acute phase in adults and children^{☆,☆☆}



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ARTICLE INFO

Article history:

Available online 5 March 2020

Keywords:

Severe burns
Intensive care
Guidelines

ABSTRACT

Objectives: To provide recommendations to facilitate the management of severe thermal burns during the acute phase in adults and children.

Design: A committee of 20 experts was asked to produce recommendations in six fields of burn management, namely, (1) assessment, admission to specialised burns centres, and telemedicine; (2) haemodynamic management; (3) airway management and smoke inhalation; (4) anaesthesia and analgesia; (5) burn wound treatments; and (6) other treatments. At the start of the recommendation-formulation process, a formal conflict-of-interest policy was developed and enforced throughout the process. The entire process was conducted independently of any industry funding. The experts drew up a list of questions that were formulated according to the PICO model (Population, Intervention, Comparison, and Outcomes). Two bibliography experts per field analysed the literature published from

[☆] With the collaboration of the following societies: Francophone Society of Burns (Société francophone de brûlologie – SFB), French Society of Emergency Medicine (Société française de médecine d'urgence – SFMU), Association of French-Speaking Paediatric Anaesthesiologists and Intensivists (Association des anesthésistes-réanimateurs pédiatriques d'expression française – ADARPEF).

^{☆☆} Text approved by the SFAR Clinical Reference Committee (15/05/2019) and the SFAR Board of Directors (24/05/2019).

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January 2000 onwards using predefined keywords according to PRISMA recommendations. The quality of data from the selected literature was assessed using GRADE[®] methodology. Due to the current paucity of sufficiently powered studies regarding hard outcomes (i.e. mortality), the recommendations are based on expert opinion.

Results: The SFAR guidelines panel generated 24 statements regarding the management of acute burn injuries in adults and children. After two scoring rounds and one amendment, strong agreement was reached for all recommendations.

Conclusion: Substantial agreement was reached among a large cohort of experts regarding numerous strong recommendations to optimise the management of acute burn injuries in adults and children.

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Introduction

Burn injuries are common and mostly accidental. The majority of cases are not serious and may be treated as outpatients. In France, severe burns are responsible for about 10,000 hospitalisations annually, half of which require stays at specialised burns centres ([Annex 1](#)). Although these more severe burns are associated with relatively low mortality, they induce considerable morbidity with physical, psychological, and social consequences, long hospital stays and a significant use of resources.

The incidence of burns is four times higher in children than in adults: burn injuries account for about 25% of all paediatric hospitalisations. The most common cause is hot liquids.

The recommendations herewith aim to provide a rational therapeutic approach to managing severe burn injuries in adults and children.

Although an official definition of severe burns is lacking, the experts who produced these recommendations consider both life-threatening and function-threatening burns as severe burns and propose the following criteria to define them:

- in adults ([Annex 2A](#)):
 - one of the following criteria: total body surface area (TBSA) burned > 20%, deep burns > 5%, presence of smoke inhalation, deep burns in areas that might lead to functional sequelae (face, hands, feet, perineum), burns from high-voltage electricity,
 - TBSA < 20% AND one or more of the following criteria: age > 75 years, severe comorbidities, known or suspected smoke inhalation, deep circular burns, superficial burns in function-sensitive areas (face, hands, feet, perineum, skin folds), TBSA > 10%, deep burn 3–5%, burns from low-voltage electricity, chemical burns (e.g. hydrofluoric acid);

- in children ([Annex 2B](#)):
 - one of the following criteria: TBSA > 10%, deep burns > 5%, infants (< 1 year of age), severe comorbidities, smoke inhalation injuries, deep burns in function-sensitive areas (face, hands, feet, perineum, flexure lines), circular burns, electrical or chemical burn.

This highly practical categorisation aims to optimise the triage, thereby promoting the efficient usage of the limited number of beds at burns centres across the country ([Annex 1](#)). We also propose guidelines on how to manage major complications during the acute phase, namely, haemodynamic and respiratory failure, hypothermia and pain.

Since the management of severe burns is multidisciplinary, these recommendations are intended for all healthcare providers caring for severely burned patients during the first 48 hours after injury (i.e. prehospital and emergency staff, anaesthesiologists and anaesthetist nurses, intensivists and caregivers in non-specialist centres and paediatricians). These recommendations are also intended for surgeons since escharotomies or very early excisions may be required within 48 hours of injury. These recommendations have been drafted by specialists from all over Europe. Finally, the recommendations only address the treatment of thermal burns: treatment of electrical and chemical burns is excluded.

Purpose of the recommendations

The purpose of these recommendations for professional practice (RPP) was to produce a decision-making framework for the management of thermal burns in the acute phase. The experts endeavoured to produce a minimum number of recommendations that highlight the main management principles in the six predefined fields. The well-known basic universal rules of good clinical practice were excluded from these recommendations.

Recommendation fields

The recommendations relate to six fields:

- assessment, admission to specialised centres, and telemedicine;
- haemodynamic management;
- airway management and smoke inhalation;
- anaesthesia and analgesia;
- local treatment;
- other treatments.

Methods

These guidelines are the result of work by a group of experts who were brought together by the SFAR, SFB, SFMU, and ADARPEF. All experts completed a conflict-of-interest declaration before beginning their contribution. The organising committee's first step was to define the objectives of the recommendations and the methodology to be used. The organising committee then defined the six fields that would be targeted by this RRP and its related questions. The resulting recommendations were then modified and finally validated by the experts.

When possible, the questions were formulated according to Patients – Intervention – Comparison – Outcome (PICO) format. Patients with severe burn injuries form the population that is the subject of all these recommendations ("P" of the PICO format).

The literature analysis was conducted according to the GRADE method (Grade of Recommendation Assessment, Development

and Evaluation). This analysis showed that there are currently very few studies with enough power to accurately measure the effects of treatment on the most important outcome variable, namely, mortality. The methodological quality of these few studies was mostly poor. Therefore, prior to writing these guidelines, the experts decided to adopt the recommendations for professional practices (RPP) format rather than the recommendations formalised by experts (RFE) format. The GRADE method was still used to compile the tables summarising the data in the literature. As a result, the level of evidence for each bibliographic reference was determined based on the type of study involved. The level of evidence for each article could be re-evaluated on the basis of the methodological quality of the study, whether the different studies had consistent results, whether the evidence was direct or not, cost analyses, and the significance of the benefits observed in the study.

The recommendations were then drafted using the SFAR's RPP terminology, namely, "the experts suggest doing" or "the experts suggest not doing". Proposed recommendations were presented to the experts and discussed one by one. The aim of these discussions was not necessarily to obtain a single convergent opinion from the experts for each proposal but, rather, to identify the points on which the experts agreed, disagreed, or were undecided. Thus, each recommendation was evaluated by each expert and scored on a scale of 1 (complete disagreement) to 9 (complete agreement). The collective rating of the experts was then determined using the GRADE method. A recommendation was validated when:

- at least 70% of the experts expressed a concurring opinion;
- fewer than 20% of the experts expressed a contrary opinion.

If a recommendation was not validated, it was reformulated and the new formulation was subjected to the same consensus-seeking process described above.

Field 1: assessment, admission to specialised centres, and telemedicine

Experts: Nicolas Donat (Clamart), Clément Hoffmann (Clamart), Mathieu Fontaine (Lyon), Thomas Leclerc (Clamart), and Hugues Lefort (Metz).

Question 1.1: What method should be used to measure the burned skin area?

R1.2 – The experts suggest that the standardised method of Lund and Browder (suitable for both adults and children) should be used to measure the total burned body surface area.

Rationale

It is crucial to measure the total burned body surface area (TBSA) soon after injury, as this variable directly impacts the clinical course and initial management, particularly fluid resuscitation in the first hours. As a result, this assessment is a cornerstone of the definition of severe burns ([Annex 2](#)). TBSA should only be evaluated for second- and third-degree burns.

Several TBSA measurement methods have been reported. Five studies ($n = 1944$ patients) showed that these methods often significantly under- or overestimate true TBSA [1–5].

Indeed, TBSA appears to be overestimated in 70–94% of cases. Consequently, the volume of fluids administered in the acute phase generally exceeds the requirements. Nevertheless, the Lund-

Browder chart ([Annex 3](#)) appears to be the most accurate method for TBSA quantification. The Wallace rule of nines ([Annex 3](#)) significantly overestimates TBSA and is not suitable for children [6]. However, in practice, especially in prehospital settings, the Lund-Browder method is not always easy and must be repeated during initial management. The assessment can be done manually or facilitated by existing smartphone applications (e.g. E-Burn, see [Annex 3](#)) [7,8]. This precise, repeated evaluation of the TBSA at the beginning of the patient's care prevents overtriage (which consumes inappropriate resources) and limits undertriage (which can lead to increased morbidity and mortality) [9].

While the Lund-Browder chart (paediatric version) is the reference method for TBSA measurement [5,10], the serial halving method could be used in the prehospital setting or in mass casualty situations [11]. An alternative is to use the open hand (i.e. the palm and fingers), which is equivalent to a TBSA of 1%. This practical method is simple to teach and use. It also limits overvaluation of the TBSA [12].

Question 1.2: Does specialist management improve the survival and functional prognosis of patients with severe burns?

R1.2.1 – The experts suggest that referral to a burn specialist should be sought to determine whether the patient should be admitted in a burns centre.

R1.2.2 – The experts suggest that telemedicine should be used to improve the initial assessment of severely burned patients.

R1.2.3 – If there is an indication for admission in a burns centre, the experts suggest that the patient should be admitted directly to the centre.

R1.2.4 – The experts suggest that an escharotomy should be performed if a deep burn induces compartment syndrome in the limbs or trunk that compromises the airways and respiration and/or circulation. Ideally, the escharotomy should be performed in a burns centre by an experienced provider.

Rationale for R1.2.1

Severe burns remain associated with long-term morbidity and mortality [13,14]. The main risk factors for mortality after severe burns are age, TBSA, and smoke inhalation [15–17]. Optimal management of these patients requires considerable resources as well as specialised multidisciplinary teams [18]. Several international studies have reported that a multidisciplinary approach is associated with better survival, facilitates rehabilitation, and reduces complications, length of hospital stay, and costs. These benefits have also been observed in other settings (e.g. neurosurgery or thoracic surgery) [19–21]. Burns centres have therefore opened all over France and elsewhere ([Annex 1](#)), and this is why the French-speaking Burns Society (Société francophone de brûlologie) has proposed indications for admission to these centres. Despite this, however, most burns patients in France (and elsewhere) are still managed by non-specialised teams [22–25]. The experts agree that, with severe burns, first responders should urgently request the opinion of a specialist to help determine the severity of the burn, measure the TBSA burned, initiate appropriate fluid resuscitation, and ensure appropriate management and referral of the patient. Advice from specialists is also required for burns involving certain anatomical areas (face, hands, feet, flexure lines, genitals or perineum). An expert opinion is also needed in special situations such as hyperalgesia or the need for special medico-social care or long-term rehabilitation.

Rationale for R1.2.2

When no burns specialists are readily available, telemedicine can reliably improve the measurement of TBSA burned and help to correctly characterise its severity. This in turn improves patient management because it not only prevents overtriage and unnecessary hospitalisation, but also reduces undertriage, which increases the risk of morbidity and mortality [26–29]. Telemedicine is particularly suitable for burns with non-life-threatening burns or when the degree of severity is uncertain [30,31]. Telemedicine also limits inappropriate patient transfers, which are associated with an increased risk of mortality [9]. It is necessary to have an interconnected system (synchronous or not) that allows images to be transferred, processed, and even archived rapidly so that there is no time-loss that might increase risks for the patient [32,33]. Such systems must meet the international recommendations for telemedicine practices [34].

Rationale for R1.2.3

If hospitalisation at a burns centre is required, direct admission should be preferred. Many studies have shown that burns centres are associated with better survival of burns patients. This has been attributed to their concentration of complementary areas in burn care, their specialisation in burn care techniques and the volume of patients admitted [35–39]. Certain retrospective studies with low levels of evidence have found conflicting results regarding survival [9,40,41]. However, several studies have shown that admission to a burns centre is associated with decreased morbidity, even in the long-term [42,43]. In addition, several prospective randomised clinical trials in adult populations have shown that early surgical excision and skin grafting, which are now routinely performed at most major burns centres around the world, significantly reduce morbidity, mortality and the length of hospital stay for severely burned patients [44]. Notably, the study by Ehrl et al. found that direct admission to a burns centre reduced the time to excision and the duration of mechanical ventilation [9]. Similarly, Pegg et al. showed that patients either directly admitted to a burns centre, or admitted secondarily yet with a shorter delay, had earlier excision, which in turn indirectly improved morbidity and mortality [15,45]. The negative impact of inhalation injuries on mortality also increases non-linearly with the transfer time [16]. The experts suggest that direct admission should be preferred if hospitalisation at a burns centre is required. A transition phase at a nearby institution should be considered if the burns victim exhibits haemodynamic or respiratory instability in the early stages and the transportation time is long ([Annex 2](#)).

Rationale for R1.2.4

Circumferential third-degree burns can induce constriction, which increases pressure inside the affected anatomical compartment. Depending on the affected body region, this pressure can lead to:

- acute limb ischemia with neurological disorders and downstream necrosis;
- thoracic or abdominal compartment syndrome with physiological consequences, namely, decreased cardiac output and pulmonary compliance, hypoxia, hypercapnia, acute renal failure, and mesenteric ischemia [46,47].

Escharotomy can decompress the subcutaneous tissue in cases of third-degree (and sometimes deep second-degree) circumferential burns [48]. No randomised controlled trials have evaluated the effect of escharotomy on burn-related compartment syndromes. However, although mostly retrospective and with small sample sizes, several cohort studies and case series suggest that, while escharotomy is relatively rarely performed, it does decrease intra-compartmental pressure and can both cure and prevent

compartment syndrome, decrease morbidity and improve functional outcomes [49–52]. The timing for escharotomy is rarely mentioned in the literature. There seems to be international agreement that escharotomy is rarely indicated immediately and that the only urgent indication is compromised airway movement and/or ventilation. It is also agreed that patients who exhibit intra-abdominal hypertension or circulatory impairment should undergo escharotomy within 48 hours of the emergence of these conditions [50–56].

Escharotomy carries a risk of complications, particularly haemorrhage and infection [50,57]. A poorly performed escharotomy is also associated with increased morbidity [57–60]. Therefore, the experts recommend that this procedure be performed only at a Burns Centre. If it is impossible to transfer the patient to a burns centre quickly, it is recommended that specialist advice be obtained before performing an escharotomy.

Field 2: haemodynamic management

Experts: Pauline Devauchelle (Lille), Nicolas Donat (Clamart), Clément Hoffmann (Clamart), Jeanne Jonquieres (Lyon), Thomas Leclerc (Clamart), Marie-Reine Losser (Nancy), and Sabri Soussi (Paris).

Question 2.1: Should intravenous fluid be administered early in the initial management of severe burns?

R2.1.1 – The experts suggest that adult burn patients with a total burned body surface area of $\geq 5\%$ and paediatric burn patients with a total burned body surface area of $\geq 10\%$ should receive 20 mL/kg of an intravenous crystalloid solution within the first hour of management.

R2.1.2 – The experts suggest that balanced crystalloid solutions should be used.

Rationale

Severe burn injuries induce early hypovolaemic shock due to inflammation, capillary leak syndrome and alterations in the microcirculation [61]. The severity of this shock and the rapidity of its onset were first described in the 1930s and have been observed repeatedly ever since, including after mass casualty accidents, such as the Los Alfaques disaster in 1978 [62,63]. These observations were confirmed in animal models. These models were also used to develop several formulae to calculate the initial fluid requirements. Baxter et al. and Asch et al. observed in animals that the nadir of cardiac output appears within the first 4 hours, before increasing [64,65]. Fluid resuscitation restores cardiac output more rapidly [65]. Observational studies then showed that a low cardiac output was associated with a worse outcome [66–68]. The timing of fluid resuscitation appears to be critical. One retrospective study has shown that children who undergo early fluid resuscitation (within 2 hours of being burnt) have reduced morbidity and mortality [69]. Consequently, the experts propose early administration of 20 mL/kg of crystalloid (within the first hour) to address the early hypovolaemic phase. No adjustment for TBSA is based on the difficulties and errors in accurately assessing it within the first minutes after injury.

Intravenous access should be obtained as soon as possible, preferably in unburned areas. If an intravenous access cannot be rapidly obtained, an intraosseous route is recommended [70]. Central femoral venous access should be considered as a last resort [71].

Historically, Ringer's or Hartmann's solutions have been the most commonly used for fluid resuscitation. These are balanced crystalloid solutions characterised by an electrolyte concentration

close to that of plasma, particularly regarding sodium and chloride concentrations [68,72]. There are very few data and no randomised controlled trials on other balanced solutions such as Ringer's Acetate solution [73,74]. Compared to balanced solutions, 0.9% NaCl is associated with a higher risk of hyperchloraemia and metabolic acidosis in other settings (e.g. major surgery or ICU populations). Moreover, ICU patients receiving 0.9% NaCl have a higher incidence of acute kidney injury than patients receiving balanced solutions [75,76]. In this context, it seems reasonable to propose Ringer's Lactate solution as the first-line balanced fluid resuscitation solution for burns victims [75,77–80].

Few observational studies have also investigated hypertonic solutions. Due to the paucity of these data, these solutions cannot yet be recommended for fluid resuscitation in burns patients.

Question 2.2: Should fluid resuscitation be guided by the total body surface area (TBSA) burned?

R2.2 – The experts suggest using a formula that includes at least the body weight and total burned body surface area to estimate the initial crystalloid infusion rate.

Rationale

Fluid resuscitation is a cornerstone in the initial management of severe burns [62,81,82] (Annex 4). Several formulae that predict fluid requirements are available (Evans et al., Baxter and Shires [Parkland formula], and Pruitt et al. [Brooke formula], supplementary files 4 and 5) [64,83–85]. These formulae estimate fluid requirements between 2 and 4 mL/kg/%TBSA over the first 24 hours post-burning. Unfortunately, these formulae have never been rigorously validated. None of them have been formally proven to achieve better outcomes than others. The Rule of Tens, an alternative to these classical formulae, is best suited to the prehospital phase and the first hours of care. It has not been clinically validated (validation in silico only) [86].

In children, several formulae have been proposed to calculate the total fluid intake required in the first 48 hours. All include TBSA. None of them have been formally evaluated and no studies comparing them have been reported [87]. As children differ from adults in having a higher body surface area/weight ratio, formulae developed for adults are probably not applicable to children. Indeed, burned children require a higher total fluid intake than adults in the first 48 hours: two retrospective studies reported a total fluid intake of about 6 mL/kg/%TBSA in children over that period [88,89]. For children with a burned TBSA of over 10%, several centres handle these paediatric specificities by calculating the daily basal fluid intake requirement according to Holliday and Segar's 4-2-1 rule and then adding this amount to the fluid requirement determined by the modified Parkland formula (between 3 and 4 mL/kg/%TBSA) [90,91]. However, two retrospective studies suggest that reducing total fluid intake levels in the subgroup of children with 10–20% of burned TBSA is associated with a shorter hospital stay and a lesser need for skin grafts [92,93]. Annex 4 indicates the recommended doses of crystalloid at various time points in the first 48 hours after injury.

Question 2.3: Should fluid resuscitation be adjusted for severe burns?

R2.3 – The experts suggest that in fluid resuscitation for severe burns, the infusion rate should be adjusted as soon as possible based on clinical and haemodynamic parameters.

Rationale

Resuscitation formulae provide an initial estimate of the amount of fluids required to compensate for fluids lost due to burn injuries, but these are inaccurate. Actual infusion rates must be adjusted to the clinical response and haemodynamic parameters to avoid either insufficient [69] or excessive fluid infusion (known as “fluid creep”) [94], as both of which are associated with increased morbidity [64,95,96].

The easiest and fastest way to adjust fluid resuscitation rates is based on hourly urine output. While not formally established, a urine output of 0.5–1 mL/kg/h is commonly targeted in adults with thermal burns. Other parameters may be used in combination with urine output, including arterial lactate concentration or advanced haemodynamic monitoring such as echocardiography, cardiac output monitoring and central venous pressure measurements. These seem to be particularly valuable in patients with haemodynamic instability and/or persistent oliguria despite resuscitation [97,98]. The impact of targeting specific haemodynamic parameters on outcome is unclear [99,100]. A computer-based decisional support system can also help with decision-making during the initial resuscitation phase and may limit the risk of over-resuscitation [101]. If hypotension persists despite appropriate fluid resuscitation, vasopressors can be used. However, the cardiac function and intravascular volume status should probably be evaluated as soon as possible using echocardiography or alternative haemodynamic monitoring [102]. In *Annex 5A*, the experts propose a haemodynamic management protocol for adults. Note that so far no algorithms have been prospectively validated.

A similar risk of under- and over-resuscitation exists for children. A retrospective study reported an increased length of mechanical ventilation time and a longer hospital stay with a positive fluid balance on Day 3 [103]. Urine output is considered as a key parameter to guide fluid resuscitation in children [104]. A retrospective study in children with TBSA > 30% reported that haemodynamic monitoring using transpulmonary thermodilution was associated with less fluid and lower morbidity [105]. *Annex 5B* proposes a fluid resuscitation algorithm in children.

Question 2.4: *Should albumin be used for fluid resuscitation in severe burns?*

R2.4 – The experts suggest administering human albumin to severe burns patients with a total burned body surface area of over 30% after the first 6 hours of management.

Rationale

A recent international survey of intensive care unit physicians showed that more than 30% of responders frequently or systematically used colloids in the early phase of severe burn management. The most commonly used colloid was human albumin (more than 60% of respondents) [72,106]. In theory, colloids can increase oncotic pressure, thereby decreasing fluid leakage and reducing the volume of crystalloids administered in the initial phase of severe burn management. As a result, colloid administration could reduce the complications related to fluid overload, which include acute respiratory distress syndrome, congestive acute kidney injury, and abdominal compartment syndrome, thereby potentially improving the prognosis [107,108]. Human albumin may also have an anti-inflammatory and antioxidant activity [106].

A recent meta-analysis initially found that, when patients with severe burns were given albumin within the first 24 hours, their survival did not improve. However, when two studies with a high risk of bias were excluded, the meta-analysis showed that albumin administration significantly reduced mortality (odds ratio = 0.34; 95% confidence interval = 0.19–0.58; $P < 0.001$) [109]. Another meta-analysis showed that albumin administration within the first 24 hours in severe burns patients also significantly reduced abdominal compartment syndrome from 15.4% in the non-treated control group to 2.8% in the albumin-treated group ($P < 0.05$): the odds ratio was 0.19 (95% confidence interval = 0.07–0.5). However, the two groups did not differ significantly in terms of mortality, acute kidney injury, or respiratory complications [110]. Several studies, most of them observational, showed that 5% albumin administration reduced administered crystalloid volumes and decreased the incidence of organ failure and mortality for patients with a TBSA of ≥ 20 –30% [110–114]. However, the small ($n = 42$) multicentre controlled study by Cooper et al. was unable to detect a significant difference between the 5% albumin group and the control group in terms of organ failure [115].

Notably, a multicentre study on patients without burns who had severe sepsis or septic shock did not find that 20% albumin administration (with a serum albumin target of > 30 g/L) reduced mortality relative to the control group either. However, the patients in the septic shock subgroup who received albumin did have a lower net fluid balance and less mortality than the controls [116].

Since the very high volumes of crystalloids administered to burns patients is associated with iatrogenic injuries, the experts suggest that severe burns patients should receive enough albumin to maintain albumin levels at > 30 g/L. The albumin doses that achieve this are generally around 1–2 g/kg/day. This may help to decrease the infused volumes of crystalloid and the resulting morbidity.

In paediatric settings, albumin administration has been empirically included in certain resuscitation protocols (Galveston and Cincinnati). Although this approach is still controversial, it seems to reduce paediatric fluid needs. A study on children with a TBSA of $> 15\%$ showed that, compared to late administration (12 hours post-burning), early administration (8–12 hours post-burning) of 5% albumin decreased crystalloid administration, the incidence of fluid creep, and the length of hospital stay [117]. Similarly, a retrospective observational study in paediatric patients who required progressive increases in crystalloid administration found that albumin administration normalised the ratio of fluid volume to urinary output [118].

The experts would like to remind readers that the European Medicines Agency (EMA) and the National Agency for Drug Safety (ANSM) contraindicate the use of hydroxyethyl starches in severe burns (ansm.sante.fr/S-informer/Informations-de-securite-Lettres-aux-professionnels-de-sante/Solutions-pour-perfusion-a-base-d-hydroxyethylamidon-HEA-nouvelles-mesures-visant-a-renforcer-les-restrictions-existantes-Lettre-aux-professionnels-de-sante).

Field 3: airway management and smoke inhalation

Experts: Damien Barraud (Metz), Pauline Devauchelle (Lille), Hugues Lefort (Metz), Matthieu Legrand (Paris), Marie-Reine Lossier (Nancy), Olivier Pantet (Lausanne, Switzerland), and Sandrine Wiramus (Marseille).

Question 3.1: Should patients with facial burns be routinely intubated?

R3.1.1 – The experts suggest that patients with burns involving the face or neck should not be routinely intubated.

R3.1.2 – The experts do suggest considering intubating patients with burns involving the entire face if one (or more) of the following features are also present:

- 1) A deep and circular burn on the neck,
- 2) Symptoms of airway obstruction (i.e. change in voice, stridor, laryngeal dyspnea),
- 3) The burns are very extensive (i.e. total burned body surface area $\geq 40\%$).

Rationale

The literature on the intubation criteria in burns patients and the morbidity and mortality associated with intubation and mechanical ventilation is poor. However, the data do show that burns patients have a high risk of unnecessary intubation in the prehospital setting. A study from Cai et al. in patients with various TBSAs who were intubated in the prehospital setting showed that the intubation was considered unnecessary in nearly one third of patients [119]. Similar rates were observed in two other studies [120,121]. Cai et al. also reported that the reason for intubation in the prehospital setting was fear of an airway obstruction in three quarters of patients. Such unnecessary intubations come at a cost: Cai et al. reported that patients who were intubated in the prehospital setting had more complications compared to patients who were intubated only after they arrived at a burns centre. However, their duration of mechanical ventilation was shorter (median: one hour [IQR: 1.0–4.0] versus four hours [2.0–8.0]) and they had shorter length of hospital stays [119].

These data reflect the poorly defined criteria for prehospital intubation. Nevertheless, the experts agree that, if patients with severe burns have non-specific indications for intubation (i.e. severe respiratory distress, severe hypoxia or hypercapnia, and coma), they should be intubated without delay. The experts also agree that patients with severe burns involving the whole face should be intubated if one or more of the following criteria are met:

- the burn is a deep circular neck burn and/or;
- symptoms of airway obstruction exist (i.e. voice modification, stridor, and laryngeal dyspnea) are present, and/or;
- the patient has a very extensive burn (i.e. TBSA $\geq 40\%$).

In particular, patients with face/neck burns who were exposed to vapours or who inhaled smoke should be closely monitored due to the risk of glottis oedema and respiratory distress [122,123]. Note that a difficult intubation procedure should be implemented in these patients [124]. In patients with no immediate indication for orotracheal intubation, the clinical situation should be re-evaluated on a regular basis during their transport and after hospital admission (Annex 4).

The same applies in children. It should be noted that tracheal intubation is not recommended in the absence of respiratory distress in children who have been burned by hot fluid, even if the burns involve the face and/or skull and/or neck.

Question 3.2: Should a bronchial flexible fibroscopy be routinely performed in smoke inhalation?

R3.2 – The experts suggest that, if smoke inhalation is suspected, bronchial fibroscopy should not be performed outside burns centres to avoid transfer delays.

Rationale

Smoke inhalation should be suspected in the event of fire in an enclosed space, presence of soot on the face, dysphonia, dyspnea, wheezing, and/or blackish sputum. Bronchial flexible fibroscopy is generally considered as the gold standard for diagnosing smoke inhalation. Chest X-rays and blood gas analyses are not indicative of the diagnosis [125]. The severity of the lesions observed during bronchoscopy (using grading scores) [126–128] is correlated with morbidity, length of stay in the intensive care unit, duration of mechanical ventilation and severity of hypoxemia [126–138]. However, an urgent indication for intubation depends primarily on proximal lesions of the airways. Although common practice, the impact of fibroscopy on outcomes is uncertain. In one retrospective study, systematic, repeated completion of fibroscopies during the hospital stay was associated with shorter lengths of stay and mortality [139]. These results were not confirmed in a small randomised study ($n = 33$) [140]. Fibroscopy should probably only be performed in patients who have already been intubated, due to the risk of clinical deterioration after the procedure. Since it is not clear how bronchial fibroscopy affects the patient's prognosis or treatment, it should not delay transfer to a burns centre.

Inhalation syndrome is rare in children: the incidence before the age of 12 is 4.5%. This is because most children are burned by scalding [141]. Nevertheless, smoke inhalation increases paediatric mortality three-fold and raises the risk of morbidity, especially respiratory and infectious problems [142,143]. These deleterious effects of smoke inhalation are even observed when the TBSA is $< 10\%$: children with a TBSA $< 10\%$ and smoke inhalation are 10 times more likely to die than similar children without smoke inhalation [144]. As with adults, fibroscopy is considered as the gold standard for diagnosis, but its impact on treatment or prognosis is not clear [125]. Again, its use in children, which may be complicated in young children, must not delay proper management of these patients.

Question 3.3: Should hydroxocobalamin be administered routinely in cases of smoke intoxication?

R3.3.1 – The experts suggest that hydroxocobalamin should not be routinely administered after smoke inhalation.

R3.3.2 – The experts suggest that administration of hydroxocobalamin should be restricted to adult patients with smoke inhalation and a high suspicion of severe cyanide poisoning and to children with smoke intoxication and moderate intoxication from cyanide.

Rationale

Smoke inhalation can be accompanied by cyanide poisoning, potentially lethal due to mitochondrial toxicity [145]. Hydroxocobalamin is the most widely available antidote for cyanide poisoning in France. Although experimental data suggest that hydroxocobalamin effectively counters the effects of cyanide

poisoning, there are insufficient data to confirm its efficacy in humans. The available observational studies lack a control group and therefore have a very low-level of evidence [146,147]. There is no evidence that hydroxocobalamin improves survival after smoke inhalation. Furthermore, hydroxocobalamin has been associated with nephrotoxicity due to oxalate nephropathy [148]. Therefore, hydroxocobalamin treatment should probably be restricted to cases of smoke inhalation in which serious cyanide poisoning is suspected with cardiac or respiratory arrest, shock, and/or coma. Since plasma lactate concentration is correlated with plasma cyanide concentrations, its measurement may guide the indications for hydroxocobalamin treatment: a cohort study showed that 83% of patients with cyanide poisoning exhibited plasma hyperlactatemia above 8 mmol/L [149]. The recommended dosage in adults is 5 g and 10 g for cardiac arrest (Annex 4A).

Children have higher alveolar ventilation per minute and a lower body mass index than adults. These differences contribute to their greater vulnerability to cyanide poisoning after smoke inhalation [150,151]. Given the seriousness of this poisoning, hydroxocobalamin (70 mg/kg, maximum 5 g) administration is recommended in the prehospital setting of smoke inhalation in children with signs of moderate cyanide poisoning (Glasgow Coma Scale [GCS] score $\leq$ 13, confusion, stridor, hoarse voice, polypnea, dyspnea, soot particles in the airways) or severe cyanide poisoning (GCS score $\leq$ 8, seizures, coma, mydriasis, severe haemodynamic disorders, collapse, respiratory depression) [152].

Question 3.4: Should hyperbaric oxygen therapy be systematically administered when there is suspicion of smoke inhalation?

R3.4 – The experts suggest that hyperbaric oxygen therapy should not be routinely administered for cases of suspected carbon monoxide poisoning after smoke inhalation.

Rationale

Two potential indications for one or more hyperbaric oxygen therapy (HBOT) sessions in severely burned patients have been proposed. The first is after suspected or proven carbon monoxide (CO) poisoning secondary to smoke inhalation: in such cases, HBOT is thought to prevent or reduce the neurological sequelae of this poison. The second indication is to promote the healing of burn wounds.

A systematic review of six studies by the Cochrane group in 2011 did not find any evidence that HBOT might decrease the neurological sequelae of CO poisoning [153]. Nevertheless, in 2016, the European Committee of Hyperbaric Medicine (ECHM) stated that patients with CO poisoning who have a high risk of medium or long-term neurological sequelae should be treated with HBOT, regardless of their carboxyhaemoglobin level at admission. These are patients with an altered state consciousness and/or neurological, respiratory, cardiac or psychological symptoms. HBOT is also recommended for CO-poisoned pregnant women regardless of their clinical presentation upon admission. These recommendations were designated by the ECHM as type 1 recommendations, and HBOT is strongly recommended as a primary treatment method (grade B evidence) [154]. However, two international societies (the American College of Emergency Physicians and the International Society for Burn Injuries) reached more conservative conclusions. They stated that HBOT is often contraindicated in severe burns patients, owing to frequent haemodynamic or respiratory instability in the acute phase, creating technical

difficulties with HBOT carrying significant risks [52,155]. The experts of the current recommendations suggest that the indication for HBOT should be evaluated on a case-by-case basis. Factors to consider in these assessments include whether the patient is a child or a pregnant woman, the severity of both the poisoning and the burn, stability of the patient, whether the HBOT equipment can be initiated within an acceptable time frame, and whether a specialised team is present to ensure the best safety conditions. No studies comparing normobaric oxygen therapy with a placebo in smoke inhalation patients with CO poisoning have been reported. However, since the physiological and pharmacological basis for normobaric oxygen therapy in CO poisoning is very well known and widely accepted [156], all three societies recommend oxygen therapy for this indication. Therefore, all patients with suspected or confirmed CO poisoning after smoke inhalation should be treated with oxygen without delay, via a high concentration mask, or 100% FiO₂ for 6 to 12 hours, if mechanically ventilated.

With regard to the healing of severe burn injuries, a systematic review by the Cochrane group reported that the scientific evidence supporting HBOT for this indication is old, limited, and of very low-level evidence [159]. In their 2016 statement, the ECHM suggested that early HBOT (within the first 6 hours) could be an optional therapy for second-degree burns involving $> 20\%$ TBSA, especially if the burns involve the face, neck, or perineum [154]. It was considered that HBOT in this setting could reduce deep extension of the burn and improve healing (type 3 recommendation, namely, HBOT can be considered as a possible measure but the evidence for it is only grade C) [157]. None of the three international societies of burns (the American Burn Association, the European Burn Association, and the International Society for Burn Injuries) provide recommendations for this indication. The results of an ongoing study may soon provide additional answers (NCT00824551). In the meantime, the experts of the current recommendations have agreed that HBOT is not indicated for burn wound healing.

In children, the ECHM recommends that any child suspected of CO poisoning should immediately receive 100% oxygen, starting at the first aid stage. This is a Type 1 recommendation supported by grade C evidence [156]. Moreover, the ECHM states that all children with CO intoxication who exhibit impaired consciousness and/or neurological, cardiac, respiratory, or psychological symptoms should be treated with HBOT, regardless of the carboxyhaemoglobin value at hospital admission. This is a type 1 recommendation that is supported by grade B evidence [154]. The experts of the current recommendations agree on these statements.

Field 4: anaesthesia and analgesia

Experts: Mathieu Jeanne (Lille) and Antoine Roquilly (Nantes).

Question 4.1: Should combinations of analgesics be used to control pain in patients with severe burns?

R4.1.1 – The experts suggest that multimodal analgesia can be used but all analgesic medications must be titrated on the basis of validated comfort and analgesia assessment scales.

R4.1.2 – The experts suggest that titrated intravenous ketamine can be combined with other analgesics to treat severe burn-induced pain.

R4.1.3 – The experts suggest that, if the patient is stable, non-pharmacological techniques should be combined with analgesic drugs for dressings, where appropriate.

Rationale

The pain caused by burns or the care of burns (i.e. dressings) is often very intense and difficult to treat and can represent an indication for admission to a burns centre. The use of written protocols for the management and regular assessment of pain should be encouraged [158].

Burn injuries trigger inflammation, hypermetabolism and capillary leakage, which lead to hypovolaemia and may increase the risk of adverse effects from analgesics or sedative drugs [159]. Titrating drugs is therefore likely to reduce the risk of under- and overdosing [160]. Ketamine is an effective drug for burn-induced pain and can limit morphine consumption.

In 2008 and 2012, the French Society of Emergency Medicine (SFMU) and the SFAR produced sedation and analgesia guidelines respectively [161,162].

The lack of good quality data on lidocaine prevents drawing up any recommendations for its use in burns patients [163].

Locoregional anaesthesia techniques may be used in burns patients when applicable [164].

Finally, non-pharmacological treatments such as cooling limited burned surfaces (see Q5.1) and covering burns with a fatty substance (e.g. Vaseline and dressings) might improve pain control. Moreover, virtual reality or hypnosis techniques may reduce the intensity of pain and the patient's anxiety. For patients without life-threatening injuries, burn management conditions must be adapted to the use of these techniques [165].

The experts would like to stress that the sedation and analgesia algorithms of the SFAR and SFMU recommendations apply to severely burned patients.

Pain induced by burns or dressing changes is often short lasting. Short-acting opioids and ketamine are probably the best drugs for the management of burn-induced pain. Inhaled nitrous oxide can be useful, especially when no intravenous access is available. The haemodynamic effects of alpha-2 receptor agonists make them difficult to use in the acute phase. Finally, in highly painful injuries or procedures, general anaesthesia is an effective option [166].

Field 5: local treatment

Experts: Damien Barraud (Metz), Mathieu Fontaine (Lyon), Laetitia Goffinet (Nancy), Jeanne Jonquieres (Lyon), Matthieu Legrand (Paris), Célia Lucas (Paris), and Anne-Françoise Rousseau (Liège, Belgium).

Question 5.1: Should we routinely cool severe burns?

R5.1 – The experts suggest that burns in adults with total burned body surface area < 20% and children with total burned body surface area < 10% should be cooled in absence of shock.

Rationale

Cooling burns can limit their deepening. A study by Wood et al. on 2320 patients (> 16 years old, median TBSA 5.5%) reported that cooling times of less than 40 minutes significantly reduced the need for skin grafting ($P < 0.001$ for 20–39 min of cooling) [167]. Similarly, the study by Harish et al. on 4900 patients with a TBSA of < 10% (mean TBSA 1.9%) reported that early cooling with tap water significantly reduced the depth of burns, although not the need for skin grafting [168]. Experimental animal studies also suggest an impact of cooling on burn depth [169–171]. Cooling burns can also reduce pain [172].

A 20-minute cooling was associated with a shorter hospital stay, a lower risk of admission to continuing care, and a lower need for grafts in burns with < 25% TBSA [167,168]. However, cooling was not associated with lower mortality. In adults, burns should probably be cooled for 20 minutes within 3 hours of sustaining the burn [167,173]. While cooling is typically done with 15 °C water, there are also other cooling techniques [174].

Cooling carries a risk of hypothermia. Three studies involving 1172 patients found no association between cooling and the occurrence of hypothermia [175–177]. However, a study of 622 children showed that hypothermia after cooling was a risk factor in those with a TBSA of > 10% [178]. Other studies suggested that external cooling did not bear a risk of hypothermia in children if their TBSA was < 15% [178,179]. The TBSA that is significantly associated with a risk of harm remains uncertain. However, the experts propose that in the absence of shock, a TBSA of over 10–15% in children and 20–25% in adults should discourage external cooling.

Question 5.2: Should a dressing be applied in the initial phase?

R5.2 – The experts suggest that burn wounds should be covered in the initial phase to reduce the risk of hypothermia and microbial contamination. The dressing should be maintained until expert advice can be obtained.

Rationale

Burn wound dressings can reduce pain, protect the wound from external contamination, and limit heat loss. Wound care is by no means a priority and should be performed only after a well-conducted resuscitation. If the patient cannot be transferred to a burns centre within a few hours after injury, a dressing is probably required. Ideally, a burns specialist should be consulted to define the most appropriate dressing for the clinical situation and whether blisters should be flattened or excised.

Burn wound care should be performed in a clean environment and will mostly require deep analgesia or general anaesthesia. The wounds should be cleaned with tap water, isotonic saline solution, or an antiseptic solution before applying the dressing [180,181]. The type of dressing depends on the TBSA, the local appearance of the wound, and the patient's general condition (Annex 6). There is little evidence that one type of dressing is superior to others. However, it seems that silver sulfadiazine is associated with prolonged healing if used for a long time on superficial burns [182]. An antiseptic dressing may be appropriate for large or contaminated burns. Topical antibiotics should not be used as first-line treatment but dedicated to infected wounds only.

When applying the dressing, particularly on the limbs, it is necessary to prevent the bandages from inducing a tourniquet effect. In the case of circular dressings, distal perfusion should be monitored. Ideally, dressings should be re-evaluated daily.

External cooling devices (e.g. Water-Jel dressings) should not be used for prolonged periods, to limit the risk of hypothermia. Accordingly, severe burns patients should not be transported to the hospital with external cooling devices. Burn wounds can be covered in the prehospital phase by sterile gauze, interface dressings, or non-adhesive dressings. However, the application of such simple dressings should not delay other resuscitation interventions.

Question 5.3: Should antibiotic prophylaxis be administered routinely in severe burns patients?

R5.3 – The experts suggest that antibiotic prophylaxis should not be administered routinely to burns patients.

Rationale

Infections are a major complication of severe burns and a leading cause of death in these patients. However, it remains unclear whether burns patients should receive local antibiotic prophylaxis, systemic antibiotic prophylaxis before surgery and during the perioperative period, and/or systemic antibiotic prophylaxis outside the surgical period [183]. The question regarding local antibiotic prophylaxis has already been addressed in R5.2. The question regarding the use of systemic antibiotic prophylaxis before surgery is beyond the scope of these recommendations (excision graft surgery is very rarely performed or indicated in the first 48 hours, especially when patients are not hospitalised at a burns centre). The level of evidence for the use of systemic antibiotic prophylaxis is low [184] with only three small randomised clinical trials. Two trials reported that systemic antibiotic prophylaxis did not reduce the risk of infection [185] and the third ($n = 40$) suggested that antibiotic prophylaxis might decrease the risk of pneumonia [184]. A cohort study based on Japanese data suggested that systemic antibiotic prophylaxis in the subgroup of mechanically ventilated burns patients might decrease the risk of death [186]. Thus, the impact of systemic antibiotic prophylaxis on outcome (i.e. infections and death) remains uncertain. The experts suggest that systemic antibiotic prophylaxis should be avoided, especially given the risk of selecting multidrug-resistant bacteria in severe burns patients [187].

Field 6: other treatments

Experts: Marie-Reine Losser (Nancy), Célia Lucas (Paris), Olivier Pantet (Lausanne, Switzerland), and Anne-Françoise Rousseau (Liège, Belgium).

Question 6.1: Should enteral nutrition be started early in severe burns?

R6.1 – The experts suggest starting nutritional support within 12 hours after burn injury. The oral or enteral routes are preferred to the parenteral route.

Rationale

Early initiation of oral or enteral nutrition (within the first 6 to 12 hours) is associated with attenuation of the neuro-hormonal stress response and the hypermetabolic response [188,189], increased production of immunoglobulins [190], reduced incidence of stress ulcers, and reduced risk of energy and protein deficiency [191,192]. Daily energy requirements are determined by using predictive formulas specific to burns patients. For adults, the Toronto formula is used whereas the Schofield formula is used for children [193–195] (Annex 7). The protein requirements are 1.5–2 g/kg/day for adults and up to 3 g/kg/day for children [196,197].

Glutamine (or alpha-ketoglutarate) supplementation appears to be associated with reduced gram-negative bacteraemia, a shorter hospital length of stay, and decreased hospital mortality [198,199]. In both adults and children, micronutrient supplementa-

tion should probably be given early. The main trace elements are copper, zinc, and selenium. The main vitamins that should be supplemented are vitamins B, C, D, and E [200–207]. These supplements reflect the high micronutrient requirements of burns patients, which cannot be covered by oral or enteral nutrition [208,209].

Question 6.2: Should thromboprophylaxis be given?

R6.2 – The experts suggest that thromboprophylaxis should be routinely prescribed for severe burns patients in the initial phase.

Rationale

Hypercoagulability is frequently observed in burns patients due to elevations in platelet counts, fibrinogen and levels of factors V and VIII, which are associated with a drop in antithrombin III and proteins C and S [210]. Retrospective cohorts show that burns patients who lack thromboembolic prophylaxis have a high incidence of deep vein thrombosis (0.9–5.9%) [211–214]. The equivalent range in burns patients with prophylaxis is 0.25–2.4% [215–219]. In the largest retrospective study currently available, which includes 33,637 patients with or without prophylaxis, the incidence of thromboembolic events was 0.61% [220]. Prospective studies of patients with and without prophylaxis who were routinely investigated by Doppler ultrasound for deep vein thrombosis yielded even higher incidences, ranging from 6.1% to 23.2% [221–224]. The risk of thromboembolic events increases with age, TBSA, depth of burns, presence of central venous access (including femoral access), duration of mechanical ventilation and the need for intensive care hospitalisation and multiple transfusions [220,223,224]. One randomised controlled trial ($n = 96$) showed that enoxaparin was superior to placebo for preventing thromboembolic events (0% vs. 8%, $P = 0.021$) [225]. Side effects are scarce: bleeding rarely occurs [215,225] and the incidence of heparin-induced thrombopenia is estimated at 2.7% with unfractionated heparin and 0.1–0.2% with low molecular weight heparin [218,226]. It is therefore reasonable to apply thromboprophylaxis in burns patients [227]. These doses have been proposed to be higher than in other medical or surgical ICU patients due to a higher risk of thrombosis, lower levels of antithrombin III [228], increased volume of distribution, and increased renal clearance in these patients. For this reason, measuring anti-Xa activity has been suggested [229]. Mechanical thromboprophylaxis can be used for the unburned area in patients with a contraindication for heparin.

In paediatrics, thromboprophylaxis is indicated in pubescent patients and if a central venous catheter is in place.

Disclosure of interest

Conflicts of interest of the SFAR Experts in the 5 years before the date of validation by the SFAR Board of Directors: Matthieu Legrand reports lecture fees from Baxter and Fresenius and consulting fees from Novartis. Mathieu Jeanne reports a conflict of interest with MDMS (LOOS, France). Antoine Roquilly reports working as a consultant for MSD and bioMerieux.

Conflicts of interest of the SFB Experts in the 5 years before the date of validation by the SFB Board of Directors: none.

Conflicts of interest of the SFMU Experts in the 5 years before the date of validation by the SMU Board of Directors: Hugues Lefort reports working as a consultant for Ethypharm.

Conflicts of interest of the ADARPEF Experts in the 5 years before the date of validation by the ADARPEF Board of Directors: none.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.accpm.2020.03.006>.

References

- [1] Armstrong JR, Willand L, Gonzalez B, Sandhu J, Mosier MJ. Quantitative analysis of estimated burn size accuracy for transfer patients. *J Burn Care Res* 2017;38:e30–5.
- [2] Baartmans MGA, van Baar ME, Boxma H, Dokter J, Tibboel D, Nieuwenhuis MK. Accuracy of burn size assessment prior to arrival in Dutch burn centres and its consequences in children: a nationwide evaluation. *Injury* 2012;43:1451–6. <http://dx.doi.org/10.1016/j.injury.2011.06.027>.
- [3] Collis N, Smith G, Fenton OM. Accuracy of burn size estimation and subsequent fluid resuscitation prior to arrival at the Yorkshire Regional Burns Unit. A three-year retrospective study. *Burns* 1999;25:345–51.
- [4] Harish V, Raymond AP, Issler AC, Lajevardi SS, Chang L-Y, Maitz PKM, et al. Accuracy of burn size estimation in patients transferred to adult Burn Units in Sydney, Australia: an audit of 698 patients. *Burns* 2015;41:91–9. <http://dx.doi.org/10.1016/j.burns.2014.05.005>.
- [5] Sadideen H, D'Asta F, Moiemien N, Wilson Y. Does overestimation of burn size in children requiring fluid resuscitation cause any harm? *J Burn Care Res* 2017;38:e546–51. <http://dx.doi.org/10.1097/BCR.0000000000000382>.
- [6] Wachtel TL, Berry CC, Wachtel EE, Frank HA. The inter-rater reliability of estimating the size of burns from various burn area chart drawings. *Burns* 2000;26:156–70.
- [7] Godwin Z, Tan J, Bockhold J, Ma J, Tran NK. Development and evaluation of a novel smart device-based application for burn assessment and management. *Burns* 2015;41:754–60. <http://dx.doi.org/10.1016/j.burns.2014.10.006>.
- [8] Fontaine M, Ravat F, Latarjet J. The e-burn application – A simple mobile tool to assess TBSA of burn wounds. *Burns* 2018;44:237–8. <http://dx.doi.org/10.1016/j.burns.2017.09.020>.
- [9] Ehrh D, Heidekrueger PI, Ninkovic M, Broer PN. Effect of primary admission to burn centers on the outcomes of severely burned patients. *Burns* 2018;44:524–30. <http://dx.doi.org/10.1016/j.burns.2018.01.002>.
- [10] Gerverman J, Bittner EA, Friedstat JS, Moore M, Nozari A, Ibrahim AE, et al. Discrepancy in initial pediatric burn estimates and its impact on fluid resuscitation. *J Burn Care Res* 2015;36:574–9. <http://dx.doi.org/10.1097/BCR.0000000000000185>.
- [11] Jault P, Donat N, Leclerc T, Cirodde A, Davy A, Hoffmann C, et al. Les premières heures du brûlé grave. *J Eur Urgences Reanim* 2012;24:138–46. <http://dx.doi.org/10.1016/j.jeurea.2012.09.003>.
- [12] Hettiaratchy S, Papini R. Initial management of a major burn: II—assessment and resuscitation. *BMJ* 2004;329:101–3. <http://dx.doi.org/10.1136/bmj.329.7457.101>.
- [13] Wolf SE, Rose JK, Desai MH, Mileski JP, Barrow RE, Herndon DN. Mortality determinants in massive pediatric burns. An analysis of 103 children with > or = 80% TBSA burns (> or = 70% full-thickness). *Ann Surg* 1997;225:554–65. <http://dx.doi.org/10.1097/0000658-199705000-00012> [discussion 565–569].
- [14] Jackson PC, Hardwicke J, Bamford A, Nightingale P, Wilson Y, Papini R, et al. Revised estimates of mortality from the Birmingham Burn Centre, 2001–2010: a continuing analysis over 65 years. *Ann Surg* 2014;259:979–84. <http://dx.doi.org/10.1097/SLA.0b013e31829160ca>.
- [15] Muller MJ, Pegg SP, Rule MR. Determinants of death following burn injury: determinants of death following burn injury. *Br J Surg* 2001;88:583–7. <http://dx.doi.org/10.1046/j.1365-2168.2001.01726.x>.
- [16] Cassidy TJ, Edgar DW, Phillips M, Cameron P, Cleland H, Wood FM. Transfer time to a specialist burn service and influence on burn mortality in Australia and New Zealand: a multi-centre, hospital based retrospective cohort study. *Burns* 2015;41:735–41. <http://dx.doi.org/10.1016/j.burns.2015.01.016>.
- [17] Jeschke MG, Pinto R, Kraft R, Nathens AB, Finnerty CC, Gamelli RL, et al. Morbidity and survival probability in burn patients in modern burn care. *Crit Care Med* 2015;43:808–15. <http://dx.doi.org/10.1097/CCM.0000000000000790>.
- [18] Al-Mousawi AM, Mecott-Rivera GA, Jeschke MG, Herndon DN. Burn teams and burn centers: the importance of a comprehensive team approach to burn care. *Clin Plast Surg* 2009;36:547–54. <http://dx.doi.org/10.1016/j.cps.2009.05.015>.
- [19] MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med* 2006;354:366–78. <http://dx.doi.org/10.1056/NEJMs052049>.
- [20] Mirski M, Chang C, Cowan R. Impact of a neuroscience intensive care unit on neurosurgical patient outcomes and cost of care. *J Neurosurg Anesthesiol* 2001;13:83–92.
- [21] Kim MM, Barnato AE, Angus DC, Fleisher LA, Fleisher LF, Kahn JM. The effect of multidisciplinary care teams on intensive care unit mortality. *Arch Intern Med* 2010;170:369–76. <http://dx.doi.org/10.1001/archinternmed.2009.521>.
- [22] Dupont A, Paget L, Pasquereau A, Rigou A, Thélot B. Les victimes de brûlures : hospitalisations selon le PMSI. France métropolitaine. *Rev Epidemiol Sante Publique* 2016;64:S215. <http://dx.doi.org/10.1016/j.respe.2016.06.188>.
- [23] Klein MB, Nathens AB, Emerson D, Heimbach DM, Gibran NS. An analysis of the long-distance transport of burn patients to a regional burn center. *J Burn Care Res* 2007;28:49–55. <http://dx.doi.org/10.1097/BCR.0B013E31802C894B>.
- [24] Hagstrom M, Wirth GA, Evans GRD, Ikeda CJ. A review of emergency department fluid resuscitation of burn patients transferred to a regional, verified burn center. *Ann Plast Surg* 2003;51:173–6. <http://dx.doi.org/10.1097/01.SAP.0000058494.24203.99>.
- [25] Latifi N-A, Karimi H. Why burn patients are referred? *Burns* 2017;43:619–23. <http://dx.doi.org/10.1016/j.burns.2016.09.007>.
- [26] Blom L, Boissin C, Allorto N, Wallis L, Hasselberg M, Laflamme L. Accuracy of acute burns diagnosis made using smartphones and tablets: a questionnaire-based study among medical experts. *BMC Emerg Med* 2017;17:39. <http://dx.doi.org/10.1186/s12873-017-0151-4>.
- [27] McManus J, Salinas J, Morton M, Lappan C, Poropatich R. Teleconsultation program for deployed soldiers and healthcare professionals in remote and austere environments. *Prehosp Disaster Med* 2008;23:210–6 [discussion 217].
- [28] Warner PM, Coffee TL, Yowler CJ. Outpatient burn management. *Surg Clin North Am* 2014;94:879–92. <http://dx.doi.org/10.1016/j.suc.2014.05.009>.
- [29] Berkebile BL, Goldfarb IW, Slater H. Comparison of burn size estimates between prehospital reports and burn center evaluations. *J Burn Care Rehabil* 1986;7:411–2.
- [30] Freiburg C, Ignieri P, Sartorelli K, Rogers F. Effects of differences in percent total body surface area estimation on fluid resuscitation of transferred burn patients. *J Burn Care Res* 2007;28:42–8. <http://dx.doi.org/10.1097/BCR.0B013E31802C88B2>.
- [31] Wallace DL, Hussain A, Khan N, Wilson YT. A systematic review of the evidence for telemedicine in burn care: with a UK perspective. *Burns* 2012;38:465–80. <http://dx.doi.org/10.1016/j.burns.2011.09.024>.
- [32] Holt B, Faraklas I, Theurer L, Cochran A, Saffle JR. Telemedicine use among burn centers in the United States: a survey. *J Burn Care Res* 2012;33:157–62. <http://dx.doi.org/10.1097/BCR.0b013e31823d0b68>.
- [33] Boccara D, Bekara F, Soussi S, Legrand M, Chaouat M, Mimoun M, et al. Ongoing development and evaluation of a method of telemedicine: burn care management with a smartphone. *J Burn Care Res* 2018;39:580–4. <http://dx.doi.org/10.1093/jbcr/irx022>.
- [34] Jung E-Y, Kang HW, Park I-H, Park DK. Proposal on the establishment of telemedicine guidelines for Korea. *Healthcare Info Res* 2015;21:255. <http://dx.doi.org/10.4258/hir.2015.21.4.255>.
- [35] Sheridan RL. Burn care: results of technical and organizational progress. *JAMA* 2003;290:719–22. <http://dx.doi.org/10.1001/jama.290.6.719>.
- [36] Light TD, Latenser BA, Kealey GP, Wibbenmeyer LA, Rosenthal GE, Sarrazin MV. The effect of burn center and burn center volume on the mortality of burned adults—An analysis of the data in the national burn repository. *J Burn Care Res* 2009;30:776–82. <http://dx.doi.org/10.1097/BCR.0b013e3181b47ed2>.
- [37] Kastenmeier A, Faraklas I, Cochran A, Pham TN, Young SR, Gibran NS, et al. The evolution of resource utilization in regional burn centers. *J Burn Care Res* 2010;31:130–6. <http://dx.doi.org/10.1097/bcr.0b013e3181cb8ca2>.
- [38] Holmes JH, Carter JE, Neff LP, Cairns BA, d'Agostino RB, Griffin LP, et al. The effectiveness of regionalized burn care: an analysis of 6873 burn admissions in North Carolina from 2000 to 2007. *J Am Coll Surg* 2011;212. <http://dx.doi.org/10.1016/j.jamcollsurg.2010.12.044> [487–493.e6].
- [39] Hranjec T. Burn-center quality improvement: are burn outcomes dependent on admitting facilities and is there a volume-outcome “Sweet-Spot”? *Am Surg* 2012;78:559–66. <http://dx.doi.org/10.1016/j.burns.2017.11.003>.
- [40] Win TS, Nizamoglu M, Maharaj R, Smailes S, El-Muttardi N, Dziewulski P. Relationship between multidisciplinary critical care and burn patients survival: a propensity-matched national cohort analysis. *Burns* 2018;44:57–64. <http://dx.doi.org/10.1016/j.burns.2017.11.003>.
- [41] Palmieri TL, London JA, O'Mara MS, Greenhalgh DG. Analysis of admissions and outcomes in verified and nonverified burn centers. *J Burn Care Res* 2008;29:208–12. <http://dx.doi.org/10.1097/BCR.0b013e31815f31b4>.
- [42] Gomez M, Tushinski M, Jeschke MG. Impact of early inpatient rehabilitation on adult burn survivors' functional outcomes and resource utilization. *J Burn Care Res* 2017;38:e311–7. <http://dx.doi.org/10.1097/BCR.0000000000000377>.
- [43] Mason SA, Nathens AB, Byrne JP, Fowler RA, Karanickolas PJ, Moineddin R, et al. Burn center care reduces acute health care utilization after discharge: a population-based analysis of 1895 survivors of major burn injury. *Surgery* 2017;162:891–900. <http://dx.doi.org/10.1016/j.surg.2017.05.018>.
- [44] Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. *Burns* 2006;32:145–50. <http://dx.doi.org/10.1016/j.burns.2005.09.005>.
- [45] Pegg SP. Burn epidemiology in the Brisbane and Queensland area. *Burns* 2005;31:S27–31. <http://dx.doi.org/10.1016/j.burns.2004.10.004>.
- [46] Ivy ME, Atweh NA, Palmer J, Possenti PP, Pineau M, D'Aiuto M. Intra-abdominal hypertension and abdominal compartment syndrome in burn patients. *J Trauma* 2000;49:387–91.
- [47] Strang SG, Van Lieshout EMM, Breederveld RS, Van Waes OJF. A systematic review on intra-abdominal pressure in severely burned patients. *Burns* 2014;40:9–16. <http://dx.doi.org/10.1016/j.burns.2013.07.001>.
- [48] Blocker TG, Moyer CA. Delayed coverage of the burn wound and joint movement. In: Womack NA, editor. *On burns*. Springfield, Illinois: Charles C. Thomas; 1953. p. 172.
- [49] Hobson KG, Young KM, Ciraulo A, Palmieri TL, Greenhalgh DG. Release of abdominal compartment syndrome improves survival in patients with

- burn injury. *J Trauma* 2002;53:1129–33. <http://dx.doi.org/10.1097/01.TA.0000034227.90946.6D> [discussion 1133–1134].
- [50] Orgill DP, Piccolo N. Escharotomy and decompressive therapies in burns. *J Burn Care Res* 2009;30:759–68. <http://dx.doi.org/10.1097/BCR.0b013e3181b47cd3>.
 - [51] de Barros MEPM, Coltro PS, Hetem CMC, Vilalva KH, Farina JA. Revisiting escharotomy in patients with burns in extremities. *J Burn Care Res* 2017;38:e691–8. <http://dx.doi.org/10.1097/BCR.0000000000000476>.
 - [52] ISBI Practice Guidelines Committee, Ahuja RB, Gibran N, Greenhalgh D, Jeng J, Mackie D, et al. ISBI practice guidelines for burn care. *Burns* 2016;42:953–1021. <http://dx.doi.org/10.1016/j.burns.2016.05.013>.
 - [53] European Practice Guideline for Burn Care 2017. <https://www.euroburn.org/documents/>.
 - [54] Joint Trauma System Clinical Practice Guidelines. Burn Care 2016. [https://jts.amedd.army.mil/assets/docs/cpgs/JTS_Clinical_Practice_Guidelines_\(CPGs\)/Burn_Care_11_May_2016_ID12.pdf](https://jts.amedd.army.mil/assets/docs/cpgs/JTS_Clinical_Practice_Guidelines_(CPGs)/Burn_Care_11_May_2016_ID12.pdf).
 - [55] New Zealand National Burn Service. Escharotomy Guidelines n.d. <http://www.nationalburnservice.co.nz/assets/Documents/Policies-and-guidelines/01d76a6e70/escharotomy-guidelines.pdf>.
 - [56] Darton A, NSW ACI. Clinical Practice Guidelines: escharotomy for burn patients. n.d. https://www.aci.health.nsw.gov.au/_data/assets/pdf_file/0003/162633/Escharotomy_CPG_new_format.pdf.
 - [57] Pruitt BA, Dowling JA, Moncrief JA. Escharotomy in early burn care. *Arch Surg* 1968;96:502–7. <http://dx.doi.org/10.1001/archsurg.1968.01330220018003>.
 - [58] Brown RL, Greenhalgh DG, Kagan RJ, Warden GD. The adequacy of limb escharotomies-fasciotomies after referral to a major burn center. *J Trauma* 1994;37:916–20.
 - [59] Burd A, Noronha FV, Ahmed K, Chan JYW, Ayyappan T, Ying SY, et al. Decompression not escharotomy in acute burns. *Burns* 2006;32:284–92. <http://dx.doi.org/10.1016/j.burns.2005.11.017>.
 - [60] Salisbury RE, Taylor JW, Levine NS. Evaluation of digital escharotomy in burned hands. *Plast Reconstr Surg* 1976;58:440–3.
 - [61] Alvarado R, Chung KK, Cancio LC, Wolf SE. Burn resuscitation. *Burns* 2009;35:4–14. <http://dx.doi.org/10.1016/j.burns.2008.03.008>.
 - [62] Arturson G. The los alfaques disaster: a boiling-liquid, expanding-vapour explosion. *Burns* 1981;7:233–51. [http://dx.doi.org/10.1016/0305-4179\(81\)90104-2](http://dx.doi.org/10.1016/0305-4179(81)90104-2).
 - [63] Moyer CA, Margraf HW, Monafa WW. Burn shock and extravascular sodium deficiency—Treatment with Ringer's solution with lactate. *Arch Surg* 1965;90:799–811. <http://dx.doi.org/10.1001/archsurg.1965.01320120001001>.
 - [64] Baxter CR, Shires T. Physiological response to crystalloid resuscitation of severe burns. *Ann N Y Acad Sci* 1968;150:874–94.
 - [65] Asch MJ, Feldman RJ, Walker HL, Foley FD, Popp RL, Mason AD, et al. Systemic and pulmonary hemodynamic changes accompanying thermal injury. *Ann Surg* 1973;178:218–21.
 - [66] Soussi S, Deniau B, Ferry A, Levé C, Benyamina M, Maurel V, et al. Low cardiac index and stroke volume on admission are associated with poor outcome in critically ill burn patients: a retrospective cohort study. *Ann Intensive Care* 2016;6:87. <http://dx.doi.org/10.1186/s13613-016-0192-y>.
 - [67] Lorente JA, Ezpeleta A, Esteban A, Gordo F, de la Cal MA, Díaz C, et al. Systemic hemodynamics, gastric intramucosal PCO2 changes, and outcome in critically ill burn patients. *Crit Care Med* 2000;28:1728–35.
 - [68] Soussi S, Taccori M, De Tymowski C, Depret F, Chaussard M, Fratani A, et al. Risk factors for acute mesenteric ischemia in critically ill burns patients – a matched case control study. *Shock* 2019;51(2):153–60.
 - [69] Barrow RE, Jeschke MG, Herndon DN. Early fluid resuscitation improves outcomes in severely burned children. *Resuscitation* 2000;45:91–6.
 - [70] Soar J, Nolan JP, Böttiger BW, Perkins GD, Lott C, Carli P, et al. European Resuscitation Council Guidelines for Resuscitation 2015. *Resuscitation* 2015;95:100–47. <http://dx.doi.org/10.1016/j.resuscitation.2015.07.016>.
 - [71] Marichy J, Vaudelin T, Marin-Lafitte I, Gueugniaud P-Y, Couchard C. Transportation of burn patients. *Annals of the MBC* 1989;2.
 - [72] Soussi S, Berger MM, Colpaert K, Dunser MW, Guttormsen AB, Juffermans NP, et al. Hemodynamic management of critically ill burn patients: an international survey. *Crit Care* 2018;22:194. <http://dx.doi.org/10.1186/s13054-018-2129-3>.
 - [73] Gille J, Kleczewski B, Malcharek M, Raff T, Mogk M, Sablotzki A, et al. Safety of resuscitation with Ringer's acetate solution in severe burn (VolTRAB) – an observational trial. *Burns* 2014;40:871–80. <http://dx.doi.org/10.1016/j.burns.2013.11.021>.
 - [74] Aoki K, Yoshino A, Yoh K, Sekine K, Yamazaki M, Aikawa N. A comparison of Ringer's lactate and acetate solutions and resuscitative effects on splanchnic dysoxia in patients with extensive burns. *Burns* 2010;36:1080–5. <http://dx.doi.org/10.1016/j.burns.2010.04.002>.
 - [75] Semler MW, Self WH, Wanderer JP, Ehrenfeld JM, Wang L, Byrne DW, et al. Balanced crystalloids versus saline in critically ill adults. *N Engl J Med* 2018;378:829–39. <http://dx.doi.org/10.1056/NEJMoa1711584>.
 - [76] Sen A, Keener CM, Sileanu FE, Foldes E, Clermont G, Murugan R, et al. Chloride content of fluids used for large-volume resuscitation is associated with reduced survival. *Crit Care Med* 2017;45:e146–53. <http://dx.doi.org/10.1097/CCM.0000000000002063>.
 - [77] Yunus NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA* 2012;308:1566–72. <http://dx.doi.org/10.1001/jama.2012.13356>.
 - [78] Rochwerg B, Alhazzani W, Sindi A, Heels-Ansdell D, Thabane L, Fox-Robichaud A, et al. Fluid resuscitation in sepsis: a systematic review and network meta-analysis. *Ann Internal Med* 2014;161:347. <http://dx.doi.org/10.7326/M14-0178>.
 - [79] Soussi S, Ferry A, Chaussard M, Legrand M. Chloride toxicity in critically ill patients: what's the evidence? *Anaesthesia Crit Care Pain Med* 2017;36:125–30. <http://dx.doi.org/10.1016/j.accpm.2016.03.008>.
 - [80] Raghunathan K, Shaw A, Nathanson B, Stürmer T, Brookhart A, Stefan MS, et al. Association between the choice of IV crystalloid and in-hospital mortality among critically ill adults with sepsis. *Crit Care Med* 2014;42:1585–91. <http://dx.doi.org/10.1097/CCM.0000000000000305>.
 - [81] Underhill FP. The significance of anhydremia in extensive superficial burns. *J Am Med Assoc* 1930;95:852–7. <http://dx.doi.org/10.1001/jama.1930.02720120020006>.
 - [82] Cope O, Moore FD. A study of capillary permeability in experimental burns and burn shock using radioactive dyes in blood and lymph. *J Clin Invest* 1944;23:241–57. <http://dx.doi.org/10.1172/JCI101487>.
 - [83] Evans EI, Purnell OJ, Robinett PW, Batchelor A, Martin M. Fluid and electrolyte requirements in severe burns. *Ann Surg* 1952;135:804–17. <http://dx.doi.org/10.1097/00000658-195206000-00006>.
 - [84] Arturson – 1981 – The los alfaques disaster A boiling-liquid, expan.pdf n.d.
 - [85] Pruitt Jr BA, Wolf SE. An historical perspective on advances in burn care over the past 100 years. *Clin Plast Surg* 2009;36:527–45. <http://dx.doi.org/10.1016/j.cps.2009.05.007>.
 - [86] Chung KK, Salinas J, Renz EM, Alvarado RA, King BT, Barillo DJ, et al. Simple derivation of the initial fluid rate for the resuscitation of severely burned adult combat casualties: in silico validation of the rule of 10. *J Trauma* 2010;69(Suppl. 1):S49–54. <http://dx.doi.org/10.1097/TA.0b013e3181e425f1>.
 - [87] Romanowski KS, Palmieri TL. Pediatric burn resuscitation: past, present, and future. *Burns Trauma* 2017;5:26. <http://dx.doi.org/10.1186/s41038-017-0091-y>.
 - [88] Graves TA, Cioffi WG, McManus WF, Mason AD, Pruitt BA. Fluid resuscitation of infants and children with massive thermal injury. *J Trauma* 1988;28:1656–9.
 - [89] Merrell SW, Saffle JR, Sullivan JJ, Navar PD, Kravitz M, Warden GD. Fluid resuscitation in thermally injured children. *Am J Surg* 1986;152:664–9.
 - [90] Walker TLJ, Rodriguez DU, Coy K, Hollén LI, Greenwood R, Young AER. Impact of reduced resuscitation fluid on outcomes of children with 10–20% body surface area scalds. *Burns* 2014;40:1581–6. <http://dx.doi.org/10.1016/j.burns.2014.02.013>.
 - [91] Palmieri TL. Pediatric burn resuscitation. *Crit Care Clin* 2016;32:547–59. <http://dx.doi.org/10.1016/j.ccc.2016.06.004>.
 - [92] Walker SM, Franck LS, Fitzgerald M, Myles J, Stocks J, Marlow N. Long-term impact of neonatal intensive care and surgery on somatosensory perception in children born extremely preterm. *Pain* 2009;141:79–87. <http://dx.doi.org/10.1016/j.pain.2008.10.012>.
 - [93] Hollén L, Coy K, Day A, Young A. Resuscitation using less fluid has no negative impact on hydration status in children with moderate sized scalds: a prospective single-centre UK study. *Burns* 2017;43:1499–505. <http://dx.doi.org/10.1016/j.burns.2017.04.011>.
 - [94] Saffle JR. The phenomenon of “fluid creep” in acute burn resuscitation. *J Burn Care Res* 2007;28:382–95. <http://dx.doi.org/10.1097/BCR.0b013e318053D3A1>.
 - [95] Pruitt BA. Fluid and electrolyte replacement in the burned patient. *Surg Clin North Am* 1978;58:1291–312.
 - [96] Kelly JF, McLaughlin DF, Oppenheimer JH, Simmons 2nd JW, Cancio LC, Wade CE, et al. A novel means to classify response to resuscitation in the severely burned: derivation of the KMAC value. *Burns* 2013;39:1060–6. <http://dx.doi.org/10.1016/j.burns.2013.05.016>.
 - [97] Sanchez M, Garcia-de-Lorenzo A, Herrero E, Lopez T, Galvan B, Asensio M, et al. A protocol for resuscitation of severe burn patients guided by transpulmonary thermodilution and lactate levels: a 3-year prospective cohort study. *Crit Care* 2013;17:R176. <http://dx.doi.org/10.1186/cc12855>.
 - [98] Agarwal N, Petro J, Salisbury RE. Physiologic profile monitoring in burned patients. *J Trauma* 1983;23:577–83.
 - [99] Csontos C, Foldi V, Fischer T, Bogar L. Arterial thermodilution in burn patients suggests a more rapid fluid administration during early resuscitation. *Acta Anaesthesiol Scand* 2008;52:742–9. <http://dx.doi.org/10.1111/j.1399-6576.2008.01658.x>.
 - [100] Holm C, Mayr M, Tegeler J, Horbrand F, Henckel von Donnersmarck G, Muhlauer W, et al. A clinical randomized study on the effects of invasive monitoring on burn shock resuscitation. *Burns* 2004;30:798–807. <http://dx.doi.org/10.1016/j.burns.2004.06.016>.
 - [101] Salinas J, Chung KK, Mann EA, Cancio LC, Kramer GC, Serio-Melvin ML, et al. Computerized decision support system improves fluid resuscitation following severe burns: an original study. *Crit Care Med* 2011;39:2031–8. <http://dx.doi.org/10.1097/CCM.0b013e31821cb790>.
 - [102] Gueugniaud PY, Vilasco B, Pham E, Hirschauer C, Bouchard C, Fabreguette A, et al. [Severe burnt patients: hemodynamic state, oxygen transport and consumption, plasma cytokines]. *Ann Fr Anesth Reanim* 1996;15:27–35.
 - [103] Nagpal A, Clingenpeel M-M, Thakkar RK, Fabia R, Lutmer J. Positive cumulative fluid balance at 72 h is associated with adverse outcomes following acute pediatric thermal injury. *Burns* 2018;44:1308–16. <http://dx.doi.org/10.1016/j.burns.2018.01.018>.
 - [104] Stutchfield C, Davies A, Young A. Fluid resuscitation in paediatric burns: how do we get it right? A systematic review of the evidence. *Arch Dis Child* 2018;104:280–5. <http://dx.doi.org/10.1136/archdischild-2017-314504>.

- [105] Kraft R, Herndon DN, Branski LK, Finnerty CC, Leonard KR, Jeschke MG. Optimized fluid management improves outcomes of pediatric burn patients. *J Surg Res* 2013;181:121–8. <http://dx.doi.org/10.1016/j.jss.2012.05.058>.
- [106] Soussi S, Depret F, Benyamina M, Legrand M. Early hemodynamic management of critically ill burn patients. *Anesthesiology* 2018;129:583–9. <http://dx.doi.org/10.1097/ALN.0000000000002314>.
- [107] Klein MB, Hayden D, Elson C, Nathens AB, Gamelli RL, Gibran NS, et al. The association between fluid administration and outcome following major burn. *Ann Surg* 2007;245:622–8. <http://dx.doi.org/10.1097/01.sla.0000252572.50684.49>.
- [108] Markell KW, Renz EM, White CE, Albrecht ME, Blackburn LH, Park MS, et al. Abdominal complications after severe burns. *J Am Coll Surg* 2009;208:940–7. <http://dx.doi.org/10.1016/j.jamcollsurg.2008.12.023> [discussion 947–949].
- [109] Eljaiek R, Heylbroeck C, Dubois M-J. Albumin administration for fluid resuscitation in burn patients: a systematic review and meta-analysis. *Burns* 2017;43:17–24. <http://dx.doi.org/10.1016/j.burns.2016.08.001>.
- [110] Navickis RJ, Greenhalgh DG, Wilkes MM. Albumin in burn shock resuscitation: a meta-analysis of controlled clinical studies. *J Burn Care Res* 2016;37:e268–78. <http://dx.doi.org/10.1097/BCR.0000000000000201>.
- [111] Lawrence A, Faraklas I, Watkins H, Allen A, Cochran A, Morris S, et al. Colloid administration normalizes resuscitation ratio and ameliorates “fluid creep.” *J Burn Care Res* 2010;31:40–7. <http://dx.doi.org/10.1097/BCR.0b013e3181cb8c72>.
- [112] Park SH, Hemmila MR, Wahl WL. Early albumin use improves mortality in difficult to resuscitate burn patients. *J Trauma Acute Care Surg* 2012;73:1294–7. <http://dx.doi.org/10.1097/TA.0b013e31827019b1>.
- [113] Cochran A, Morris SE, Edelman LS, Saffle JR. Burn patient characteristics and outcomes following resuscitation with albumin. *Burns* 2007;33:25–30. <http://dx.doi.org/10.1016/j.burns.2006.10.005>.
- [114] Ennis JL, Chung KK, Renz EM, Barillo DJ, Albrecht MC, Jones JA, et al. Joint Theater Trauma System implementation of burn resuscitation guidelines improves outcomes in severely burned military casualties. *J Trauma* 2008;64:S146–51. <http://dx.doi.org/10.1097/TA.0b013e318160b44c> [discussion S151–152].
- [115] Cooper AB, Cohn SM, Zhang HS, Hanna K, Stewart TE, Slutsky AS, et al. Five percent albumin for adult burn shock resuscitation: lack of effect on daily multiple organ dysfunction score. *Transfusion* 2006;46:80–9. <http://dx.doi.org/10.1111/j.1537-2995.2005.00667.x>.
- [116] Caironi P, Tognoni G, Masson S, Fumagalli R, Pesenti A, Romero M, et al. Albumin replacement in patients with severe sepsis or septic shock. *N Engl J Med* 2014;370:1412–21. <http://dx.doi.org/10.1056/NEJMoa1305727>.
- [117] Müller Dittrich MH, Brunow de Carvalho W, Lopes Lavado E. Evaluation of the “early” use of albumin in children with extensive burns: a randomized controlled trial. *Pediatr Crit Care Med* 2016;17:e280–6. <http://dx.doi.org/10.1097/PCC.0000000000000728>.
- [118] Faraklas I, Lam U, Cochran A, Stoddard G, Saffle J. Colloid normalizes resuscitation ratio in pediatric burns. *J Burn Care Res* 2011;32:91–7. <http://dx.doi.org/10.1097/BCR.0b013e318204b379>.
- [119] Cai AR, Hodgman EI, Kumar PB, Sehat AJ, Eastman AL, Wolf SE. Evaluating pre burn center intubation practices: an update. *J Burn Care Res* 2017;38:e23–9. <http://dx.doi.org/10.1097/BCR.0000000000000457>.
- [120] Eastman AL, Arnold BA, Hunt JL, Purdue GF. Pre-burn center management of the burned airway: do we know enough? *J Burn Care Res* 2010;31:701–5. <http://dx.doi.org/10.1097/BCR.0b013e3181eebe4f>.
- [121] Romanowski KS, Palmieri TL, Sen S, Greenhalgh DG. More than one third of intubations in patients transferred to burn centers are unnecessary: proposed guidelines for appropriate intubation of the burn patient. *J Burn Care Res* 2016;37:e409–14. <http://dx.doi.org/10.1097/BCR.0000000000000288>.
- [122] Madhani DD, Steele NP, de Vries E. Factors that predict the need for intubation in patients with smoke inhalation injury. *Ear Nose Throat J* 2006;85:278–80.
- [123] Esnault P, Prunet B, Cotte J, Marsaa H, Prat N, Lacroix G, et al. Tracheal intubation difficulties in the setting of face and neck burns: myth or reality? *Am J Emerg Med* 2014;32:1174–8. <http://dx.doi.org/10.1016/j.ajem.2014.07.014>.
- [124] Conti BM, Fouché-Weber LY, Richards JE, Grissom T. Images in anesthesiology: video laryngoscopy for intubation after smoke inhalation. *Anesthesiology* 2017;127:709. <http://dx.doi.org/10.1097/ALN.0000000000001655>.
- [125] Deutsch CJ, Tan A, Smailes S, Dzielwulski P. The diagnosis and management of inhalation injury: an evidence based approach. *Burns* 2018;44:1040–51. <http://dx.doi.org/10.1016/j.burns.2017.11.013>.
- [126] Chou SH, Lin S-D, Chuang H-Y, Cheng Y-J, Kao EL, Huang M-F. Fiber-optic bronchoscopic classification of inhalation injury: prediction of acute lung injury. *Surg Endosc* 2004;18:1377–9. <http://dx.doi.org/10.1007/s00464-003-9234-2>.
- [127] Endorf FW, Gamelli RL. Inhalation injury, pulmonary perturbations, and fluid resuscitation. *J Burn Care Res* 2007;28:80–3. <http://dx.doi.org/10.1097/BCR.0b013e31802c889f>.
- [128] Ikonomidis C, Lang F, Radu A, Berger MM. Standardizing the diagnosis of inhalation injury using a descriptive score based on mucosal injury criteria. *Burns* 2012;38:513–9. <http://dx.doi.org/10.1016/j.burns.2011.11.009>.
- [129] You K, Yang H-T, Kym D, Yoon J, Haejun Y, Cho Y-S, et al. Inhalation injury in burn patients: establishing the link between diagnosis and prognosis. *Burns* 2014;40:1470–5. <http://dx.doi.org/10.1016/j.burns.2014.09.015>.
- [130] Ramon P, Wallaert B, Galizzia JP, Gesterman X, Voisin C. [Value of tracheo-bronchial endoscopy in facial burns]. *Rev Mal Respir* 1985;2:97–101.
- [131] Masanès M-J, Legendre C, Lioret N, Saizy R, Lebeau B. Using bronchoscopy and biopsy to diagnose early inhalation injury. *Chest* 1995;107:1365–9. <http://dx.doi.org/10.1378/chest.107.5.1365>.
- [132] Hassan Z, Wong JK, Bush J, Bayat A, Dunn KW. Assessing the severity of inhalation injuries in adults. *Burns* 2010;36:212–6. <http://dx.doi.org/10.1016/j.burns.2009.06.205>.
- [133] Mosier MJ, Pham TN, Park DR, Simmons J, Klein MB, Gibran NS. Predictive value of bronchoscopy in assessing the severity of inhalation injury. *J Burn Care Res* 2012;33:65–73. <http://dx.doi.org/10.1097/BCR.0b013e318234d92f>.
- [134] Albright JM, Davis CS, Bird MD, Ramirez L, Kim H, Burnham EL, et al. The acute pulmonary inflammatory response to the graded severity of smoke inhalation injury. *Crit Care Med* 2012;40:1113–21. <http://dx.doi.org/10.1097/CCM.0b013e3182374a67>.
- [135] Bai C, Huang H, Yao X, Zhu S, Li B, Hang J, et al. Application of flexible bronchoscopy in inhalation lung injury. *Diagn Pathol* 2013;8:174. <http://dx.doi.org/10.1186/1746-1596-8-174>.
- [136] Ching JA, Ching Y-H, Shivers SC, Karlinski RA, Payne WG, Smith DJ. An analysis of inhalation injury diagnostic methods and patient outcomes. *J Burn Care Res* 2016;37:e27–32. <http://dx.doi.org/10.1097/BCR.0000000000000313>.
- [137] Spano S, Hanna S, Li Z, Wood D, Cartotto R. Does bronchoscopic evaluation of inhalation injury severity predict outcome? *J Burn Care Res* 2016;37:1–11. <http://dx.doi.org/10.1097/BCR.0000000000000320>.
- [138] Aung MT, Garner D, Pacquola M, Rosenblum S, McClure J, Cleland H, et al. The use of a simple three-level bronchoscopic assessment of inhalation injury to predict in-hospital mortality and duration of mechanical ventilation in patients with burns. *Anaesth Intensive Care* 2018;46:67–73.
- [139] Carr JA, Phillips BD, Bowling WM. The utility of bronchoscopy after inhalation injury complicated by pneumonia in burn patients: results from the national burn repository. *J Burn Care Res* 2009;30:967–74. <http://dx.doi.org/10.1097/BCR.0b013e3181bfb77b> [PAP].
- [140] Carr JA, Crowley N. Prophylactic sequential bronchoscopy after inhalation injury: results from a three-year prospective randomized trial. *Eur J Trauma Emerg Surg* 2013;39:177–83. <http://dx.doi.org/10.1007/s00068-013-0254-x>.
- [141] Thoms BD. Patient and injury characteristics, mortality risk, and length of stay related to child abuse by burning: evidence from a national sample of 15,802 pediatric admissions. *Ann Surg* 2008;247:519–23. <http://dx.doi.org/10.1097/SLA.0b013e31815b4480>.
- [142] Kraft R, Herndon DN, Al-Mousawi AM, Williams FN, Finnerty CC, Jeschke MG. Burn size and survival probability in paediatric patients in modern burn care: a prospective observational cohort study. *Lancet* 2012;379:1013–21. [http://dx.doi.org/10.1016/S0140-6736\(11\)61345-7](http://dx.doi.org/10.1016/S0140-6736(11)61345-7).
- [143] Tan A, Smailes S, Friebe T, Magdum A, Frew Q, El-Muttardi N, et al. Smoke inhalation increases intensive care requirements and morbidity in paediatric burns. *Burns* 2016;42:1111–5. <http://dx.doi.org/10.1016/j.burns.2016.02.010>.
- [144] Travis TE, Moffatt LT, Jordan MH, Shupp JW. Factors impacting the likelihood of death in patients with small TBSA burns. *J Burn Care Res* 2015;36:203–12. <http://dx.doi.org/10.1097/BCR.0000000000000113>.
- [145] Walker PF, Buehner MF, Wood LA, Boyer NL, Driscoll IR, Lundy JB, et al. Diagnosis and management of inhalation injury: an updated review. *Crit Care* 2015;19:351. <http://dx.doi.org/10.1186/s13054-015-1077-4>.
- [146] Anseuw K, Delvaux N, Burillo-Putze G, De Iaco F, Geldner G, Holmström P, et al. Cyanide poisoning by fire smoke inhalation: a European expert consensus. *Eur J Emerg Med* 2013;20:2–9. <http://dx.doi.org/10.1097/MEJ.0b013e328357170b>.
- [147] Erdman AR. Is hydroxocobalamin safe and effective for smoke inhalation? Searching for guidance in the haze. *Ann Emerg Med* 2007;49:814–6. <http://dx.doi.org/10.1016/j.annemergmed.2007.03.006>.
- [148] for the PRONOBURN Study Group, Legrand M, Michel T, Daudon M, Benyamina M, Ferry A, et al. Risk of oxalate nephropathy with the use of cyanide antidote hydroxocobalamin in critically ill burn patients. *Intensive Care Med* 2016;42:1080–1. <http://dx.doi.org/10.1007/s00134-016-4252-4>.
- [149] Baud FJ, Haidar MK, Jouffroy R, Raphaelen J-H, Lamhaut L, Carli P. Determinants of lactic acidosis in acute cyanide poisonings. *Crit Care Med* 2018;46:e523–9. <http://dx.doi.org/10.1097/CCM.0000000000003075>.
- [150] Mintegi S, Azkuna B, Prego J, Qureshi N, Dalziel SR, Arana-Arri E, et al. International epidemiological differences in acute poisonings in pediatric emergency departments. *Pediatr Emerg Care* 2019;35:50–7. <http://dx.doi.org/10.1097/PEC.0000000000001031>.
- [151] Baud FJ, Barriot P, Toffis V, Riou B, Vicaute E, Lecarpentier Y, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med* 1991;325:1761–6. <http://dx.doi.org/10.1056/NEJM199112193252502>.
- [152] Mintegi S, Clerigie N, Tipo V, Ponticelli E, Lonati D, Burillo-Putze G, et al. Pediatric cyanide poisoning by fire smoke inhalation: a European expert consensus. Toxicology Surveillance System of the Intoxications Working Group of the Spanish Society of Paediatric Emergencies. *Pediatr Emerg Care* 2013;29:1234–40. <http://dx.doi.org/10.1097/PEC.0b013e3182aa4ee1>.
- [153] Buckley NA, Juurlink DN, Isbister G, Bennett MH, Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev* 2011;CD002041. <http://dx.doi.org/10.1002/14651858.CD002041.pub3>.
- [154] Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. *Diving Hyperb Med* 2017;47:24–32. <http://dx.doi.org/10.1016/j.annemerg-med.2007.10.012>.

- [155] Wolf SJ, Lavonas EJ, Sloan EP, Jagoda AS. Clinical policy: critical issues in the management of adult patients presenting to the emergency department with acute carbon monoxide poisoning. *Ann Emerg Med* 2008;51:138–52. <http://dx.doi.org/10.1016/j.annemergmed.2007.10.012>.
- [156] Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxyhemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. *Chest* 2000;117:801–8. <http://dx.doi.org/10.1378/chest.117.3.801>.
- [157] Villanueva E, Bennett MH, Wasiak J, Lehm JP. Hyperbaric oxygen therapy for thermal burns. *Cochrane Database Syst Rev* 2004. <http://dx.doi.org/10.1002/14651858.CD004727.pub2>.
- [158] Depetris N, Raineri S, Pantet O, Lavrentieva A. Management of pain, anxiety, agitation and delirium in burn patients: a survey of clinical practice and a review of the current literature. *Ann Burns Fire Disasters* 2018;31:97–108.
- [159] Porter C, Tompkins RG, Finnerty CC, Sidossis LS, Suman OE, Herndon DN. The metabolic stress response to burn trauma: current understanding and therapies. *Lancet* 2016;388:1417–26. [http://dx.doi.org/10.1016/S0140-6736\(16\)31469-6](http://dx.doi.org/10.1016/S0140-6736(16)31469-6).
- [160] Yamashita S, Kaneda K, Han T-H. Population pharmacokinetics of a propofol bolus administered in patients with major burns. *Burns* 2010;36:1215–21. <http://dx.doi.org/10.1016/j.burns.2010.03.003>.
- [161] Sauder P, Andreoletti M, Cambonie G, Capellier G, Feissel M, Gall O, et al. [Sedation and analgesia in intensive care (with the exception of new-born babies). French Society of Anesthesia and Resuscitation. French-speaking Resuscitation Society]. *Ann Fr Anesth Reanim* 2008;27:541–51. <http://dx.doi.org/10.1016/j.annfar.2008.04.021>.
- [162] Vivien B, Adnet F, Bounes V, Chéron G, Combes X, David J-S, et al. [Sedation and analgesia in emergency structure. Reactualization 2010 of the Conference of Experts of Sfar of 1999]. *Ann Fr Anesth Reanim* 2012;31:391–404. <http://dx.doi.org/10.1016/j.annfar.2012.02.006>.
- [163] Wasiak J, Mahar PD, McGuinness SK, Spinks A, Danilla S, Cleland H, et al. Intravenous lidocaine for the treatment of background or procedural burn pain. *Cochrane Database Syst Rev* 2014. <http://dx.doi.org/10.1002/14651858.CD005622.pub4>.
- [164] Town CJ, Johnson J, Van Zundert A, Strand H. Exploring the role of regional anesthesia in the treatment of the burn-injured patient: a narrative review of current literature. *Clin J Pain* 2019;35:368–74. <http://dx.doi.org/10.1097/AJP.0000000000000680>.
- [165] Scheffler M, Koranyi S, Meissner W, Strauß B, Rosendahl J. Efficacy of non-pharmacological interventions for procedural pain relief in adults undergoing burn wound care: a systematic review and meta-analysis of randomized controlled trials. *Burns* 2018;44:1709–20. <http://dx.doi.org/10.1016/j.burns.2017.11.019>.
- [166] Patterson DR, Hoffland HWC, Hoflund H, Espey K, Sharar S. Nursing Committee of the International Society for Burn Injuries. Pain management. *Burns* 2004;30:A10–5. <http://dx.doi.org/10.1016/j.burns.2004.08.004>.
- [167] Wood FM, Phillips M, Jovic T, Cassidy JT, Cameron P, Edgar DW, et al. Water first aid is beneficial in humans post-burn: evidence from a bi-national cohort study. *PLoS ONE* 2016;11:e0147259. <http://dx.doi.org/10.1371/journal.pone.0147259>.
- [168] Harish V, Tiwari N, Fisher OM, Li Z, Maitz PKM. First aid improves clinical outcomes in burn injuries: evidence from a cohort study of 4918 patients. *Burns* 2019;45:433–9. <http://dx.doi.org/10.1016/j.burns.2018.09.024>.
- [169] Bartlett N, Yuan J, Holland AJA, Harvey JG, Martin HCO, La Hei ER, et al. Optimal duration of cooling for an acute scald contact burn injury in a porcine model. *J Burn Care Res* 2008;29:828–34. <http://dx.doi.org/10.1097/BCR.0b013e3181855c9a>.
- [170] Yuan J, Wu C, Holland AJA, Harvey JG, Martin HCO, La Hei ER, et al. Assessment of cooling on an acute scald burn injury in a porcine model. *J Burn Care Res* 2007;28:514–20. <http://dx.doi.org/10.1097/BCR.0b013e3181855c9a>.
- [171] Cuttle L, Kempf M, Kravchuk O, Phillips GE, Mill J, Wang X-Q, et al. The optimal temperature of first aid treatment for partial thickness burn injuries. *Wound Repair Regen* 2008;16:626–34. <http://dx.doi.org/10.1111/j.1524-475X.2008.00413.x>.
- [172] Shulman AG. Ice water as primary treatment of burns. Simple method of emergency treatment of burns to alleviate pain, reduce sequelae, and hasten healing. *JAMA* 1960;173:1916–9.
- [173] Rajan V, Bartlett N, Harvey JG, Martin HCO, La Hei ER, Arbuckle S, et al. Delayed cooling of an acute scald contact burn injury in a porcine model: is it worthwhile? *J Burn Care Res* 2009;30:729–34. <http://dx.doi.org/10.1097/BCR.0b013e31818ac059b>.
- [174] Venter THJ, Karpelowsky JS, Rode H. Cooling of the burn wound: the ideal temperature of the coolant. *Burns* 2007;33:917–22. <http://dx.doi.org/10.1016/j.burns.2006.10.408>.
- [175] Singer AJ, Taira BR, HCT Jr, McCormack JE, Shapiro M, Aydin A, et al. The association between hypothermia, prehospital cooling, and mortality in burn victims. *Acad Emerg Med* 2010;17:456–9. <http://dx.doi.org/10.1111/j.1553-2712.2010.00702.x>.
- [176] Steele JE, Atkins JL, Vizcaychipi MP. Factors at scene and in transfer related to the development of hypothermia in major burns. *Ann Burns Fire Disasters* 2016;29:103–7.
- [177] Lönnecker S, Schoder V. [Hypothermia in patients with burn injuries: influence of prehospital treatment]. *Chirurg* 2001;72:164–7.
- [178] Baartmans MGA, de Jong AEE, van Baar ME, Beerthuisen GJLM, van Loey NEE, Tibboel D, et al. Early management in children with burns: cooling, wound care and pain management. *Burns* 2016;42:777–82. <http://dx.doi.org/10.1016/j.burns.2016.03.003>.
- [179] Cox SG, Martinez R, Glick A, Numanoglu A, Rode H. A review of community management of paediatric burns. *Burns* 2015;41:1805–10. <http://dx.doi.org/10.1016/j.burns.2015.05.024>.
- [180] Cooper DD, Seupaul RA. Is water effective for wound cleansing? *Ann Emerg Med* 2012;60:626–7. <http://dx.doi.org/10.1016/j.annemergmed.2012.06.011>.
- [181] Fernandez R, Griffiths R. Water for wound cleansing. *Cochrane Database Syst Rev* 2012;CD003861. <http://dx.doi.org/10.1002/14651858.CD003861.pub3>.
- [182] Wasiak J, Cleland H, Campbell F. Dressings for superficial and partial thickness burns. *Cochrane Database Syst Rev* 2008;CD002106. <http://dx.doi.org/10.1002/14651858.CD002106.pub3>.
- [183] Azzopardi EA, Azzopardi E, Camilleri L, Villalpalos J, Boyce DE, Dziewulski P, et al. Gram negative wound infection in hospitalised adult burn patients – systematic review and meta-analysis. *PLoS ONE* 2014;9:e95042. <http://dx.doi.org/10.1371/journal.pone.0095042>.
- [184] Avni T, Levkovich A, Ad-El DD, Leibovici L, Paul M. Prophylactic antibiotics for burns patients: systematic review and meta-analysis. *BMJ* 2010;340:c241. <http://dx.doi.org/10.1136/bmj.c241>.
- [185] Ramos G, Cornistein W, Cerino GT, Nacif G. Systemic antimicrobial prophylaxis in burn patients: systematic review. *J Hosp Infect* 2017;97:105–14. <http://dx.doi.org/10.1016/j.jhin.2017.06.015>.
- [186] Tagami T, Matsui H, Fushimi K, Yasunaga H. Prophylactic antibiotics may improve outcome in patients with severe burns requiring mechanical ventilation: propensity score analysis of a Japanese Nationwide Database. *Clin Infect Dis* 2016;62:60–6. <http://dx.doi.org/10.1093/cid/civ763>.
- [187] Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012;18:268–81. <http://dx.doi.org/10.1111/j.1469-0699.2011.03570.x>.
- [188] Mochizuki H, Trocki O, Dominioni L, Brackett KA, Joffe SN, Alexander JW. Mechanism of prevention of postburn hypermetabolism and catabolism by early enteral feeding. *Ann Surg* 1984;200:297–310.
- [189] Vivic VK, Radman M, Kovacic V. Early initiation of enteral nutrition improves outcomes in burn disease. *Asia Pac J Clin Nutr* 2013;22:543–7. <http://dx.doi.org/10.6133/apjcn.2013.22.4.13>.
- [190] Lam NN, Tien NG, Khoa CM. Early enteral feeding for burned patients—An effective method which should be encouraged in developing countries. *Burns* 2008;34:192–6. <http://dx.doi.org/10.1016/j.burns.2007.03.010>.
- [191] Chiarelli A, Enzi G, Casadei A, Baggio B, Valerio A, Mazzoleni F. Very early nutrition supplementation in burned patients. *Am J Clin Nutr* 1990;51:1035–9. <http://dx.doi.org/10.1093/ajcn/51.6.1035>.
- [192] Venter M, Rode H, Sive A, Visser M. Enteral resuscitation and early enteral feeding in children with major burns—Effect on McFarlane response to stress. *Burns* 2007;33:464–71. <http://dx.doi.org/10.1016/j.burns.2006.08.008>.
- [193] Allard JP, Pichard C, Hoshino E, Stechison S, Fareholm L, Peters WJ, et al. Validation of a new formula for calculating the energy requirements of burn patients. *J Parenter Enteral Nutr* 1990;14:115–8. <http://dx.doi.org/10.1177/0148607190014002115>.
- [194] Royall D, Fairholm L, Peters WJ, Jeejeebhoy KN, Allard JP. Continuous measurement of energy expenditure in ventilated burn patients: an analysis. *Crit Care Med* 1994;22:399–406.
- [195] Suman OE, Micak RP, Chinkes DL, Herndon DN. Resting energy expenditure in severely burned children: analysis of agreement between indirect calorimetry and prediction equations using the Bland-Altman method. *Burns* 2006;32:335–42. <http://dx.doi.org/10.1016/j.burns.2005.10.023>.
- [196] Cynober L, Barges L, Berger MM, Carsin H, Chiolerio R, Garrel D, et al. Recommendations nutritionnelles chez le grand brûlé Nutritional recommendations for severe burn victims. *Nutr Clin Metab* 2005;19:166–94. <http://dx.doi.org/10.1016/j.nupar.2005.07.001>.
- [197] Rodriguez NA, Jeschke MG, Williams F, Kamolz L-P, Herndon DN. Nutrition in burns: Galveston contributions. *J Parenter Enteral Nutr* 2011;35:704–14. <http://dx.doi.org/10.1177/0148607111417446>.
- [198] Lin J-J, Chung X-J, Yang C-Y, Lau H-L. A meta-analysis of trials using the intention to treat principle for glutamine supplementation in critically ill patients with burn. *Burns* 2013;39:565–70. <http://dx.doi.org/10.1016/j.burns.2012.11.008>.
- [199] van Zanten ARH, Dhaliwal R, Garrel D, Heyland DK. Enteral glutamine supplementation in critically ill patients: a systematic review and meta-analysis. *Crit Care* 2015;19:294. <http://dx.doi.org/10.1186/s13054-015-1002-x>.
- [200] Falder S, Silla R, Phillips M, Rea S, Gurfinkel R, Baur E, et al. Thiamine supplementation increases serum thiamine and reduces pyruvate and lactate levels in burn patients. *Burns* 2010;36:261–9. <http://dx.doi.org/10.1016/j.burns.2009.04.012>.
- [201] Barbosa E, Faintuch J, Machado Moreira EA, Gonçalves da Silva VR, Lopes Pereira MJ, Martins Fagundes RL, et al. Supplementation of vitamin E, vitamin C, and zinc attenuates oxidative stress in burned children: a randomized, double-blind, placebo-controlled pilot study. *J Burn Care Res* 2009;30:859–66. <http://dx.doi.org/10.1097/BCR.0b013e3181b487a8>.
- [202] Mayes T, Gottschlich MM, Khoury J, Kagan RJ. Investigation of bone health subsequent to vitamin D supplementation in children following burn injury. *Nutr Clin Pract* 2015;30:830–7. <http://dx.doi.org/10.1177/0885533615587720>.
- [203] Rousseau A-F, Foidart-Desalle M, Ledoux D, Remy C, Croisier J-L, Damas P, et al. Effects of cholecalciferol supplementation and optimized calcium intakes on vitamin D status, muscle strength and bone health: a one-year

- pilot randomized controlled trial in adults with severe burns. *Burns* 2015;41:317–25. <http://dx.doi.org/10.1016/j.burns.2014.07.005>.
- [204] Rousseau A-F, Damas P, Ledoux D, Lukas P, Carlisi A, Le Goff C, et al. Vitamin D status after a high dose of cholecalciferol in healthy and burn subjects. *Burns* 2015;41:1028–34. <http://dx.doi.org/10.1016/j.burns.2014.11.011>.
- [205] Rousseau A-F, Damas P, Ledoux D, Cavalier E. Effect of cholecalciferol recommended daily allowances on vitamin D status and fibroblast growth factor-23: an observational study in acute burn patients. *Burns* 2014;40:865–70. <http://dx.doi.org/10.1016/j.burns.2013.11.015>.
- [206] Klein GL, Herndon DN, Chen TC, Kulp G, Holick MF. Standard multivitamin supplementation does not improve vitamin D insufficiency after burns. *J Bone Miner Metab* 2009;27:502–6. <http://dx.doi.org/10.1007/s00774-009-0065-7>.
- [207] Klein GL, Chen TC, Holick MF, Langman CB, Price H, Celis MM, et al. Synthesis of vitamin D in skin after burns. *Lancet* 2004;363:291–2. [http://dx.doi.org/10.1016/S0140-6736\(03\)15388-3](http://dx.doi.org/10.1016/S0140-6736(03)15388-3).
- [208] Stucki P, Perez M-H, Cotting J, Shenkin A, Berger MM. Substitution of exudative trace element losses in burned children. *Crit Care* 2010;14:439. <http://dx.doi.org/10.1186/cc9198>.
- [209] Berger MM. Antioxidant micronutrients in major trauma and burns: evidence and practice. *Nutr Clin Pract* 2006;21:438–49. <http://dx.doi.org/10.1177/0115426506021005438>.
- [210] Sebastian R, Ghanem O, DiRoma F, Milner SM, Price LA. Pulmonary embolism in burns, is there an evidence based prophylactic recommendation? Case report and review of literature. *Burns* 2015;41:e4–7. <http://dx.doi.org/10.1016/j.burns.2014.06.018>.
- [211] Rue LW, Cioffi WC, Rush R, McManus W, Pruitt BA. Thromboembolic complications in thermally injured patients. *World J Surg* 1992;16:1151–5.
- [212] Harrington DT, Mozingo DW, Cancio L, Bird P, Jordan B, Goodwin CW. Thermally injured patients are at significant risk for thromboembolic complications. *J Trauma* 2001;50:495–9. <http://dx.doi.org/10.1097/00005373-200103000-00014>.
- [213] Mullins F, Mian MAH, Jenkins D, Brandigi C, Shaver JR, Friedman B, et al. Thromboembolic complications in burn patients and associated risk factors. *J Burn Care Res* 2013;34:355–60. <http://dx.doi.org/10.1097/BCR.0b013e31827819a1>.
- [214] Alyafi T, Alkahtani M, Alturki N, Ashi M. The incidence of the deep veins thrombosis among adult and pediatric Saudi patients with burns. *National Guard hospital between 2010/2015*. *Arch Clin Exp Surg (ACES)* 2019;8:1. <http://dx.doi.org/10.5455/aces.20180621121428>.
- [215] Fecher AM, O'Mara MS, Goldfarb IW, Slater H, Garvin R, Birdas TJ, et al. Analysis of deep vein thrombosis in burn patients. *Burns* 2004;30:591–3. <http://dx.doi.org/10.1016/j.burns.2003.12.019>.
- [216] Bushwitz J, LeClaire A, He J, Mozingo D. Clinically significant venous thromboembolic complications in burn patients receiving unfractionated heparin or enoxaparin as prophylaxis. *J Burn Care Res* 2011;32:578–82. <http://dx.doi.org/10.1097/BCR.0b013e31822dc3c7>.
- [217] Barret JP, Dziewulski PG. Complications of the hypercoagulable status in burn injury. *Burns* 2006;32:1005–8. <http://dx.doi.org/10.1016/j.burns.2006.02.018>.
- [218] Busche MN, Herold C, Krämer R, Knobloch K, Vogt PM. Evaluation of prophylactic anticoagulation, deep venous thrombosis, and heparin-induced thrombocytopenia in 21 burn centers in Germany, Austria, and Switzerland. *Ann Plast Surg* 2011;67:17–24. <http://dx.doi.org/10.1097/SAP.0-b013e31821bd4bc>.
- [219] Wahl WL, Brandt M-M. Potential risk factors for deep venous thrombosis in burn patients. *J Burn Care Rehabil* 2001;22:128–31. <http://dx.doi.org/10.1097/00004630-200103000-00008>.
- [220] Pannucci CJ, Osborne NH, Wahl WL. Venous thromboembolism in thermally injured patients: analysis of the national burn repository. *J Burn Care Res* 2011;32:6–12. <http://dx.doi.org/10.1097/BCR.0b013e318204b2ff>.
- [221] Wahl WL, Brandt M, Ahrns KS, Zajkowski PJ, Proctor MC, Wakefield TW, et al. Venous thrombosis incidence in burn patients: preliminary results of a prospective study. 41. *J Burn Care Rehabil* 2001;22:S66. <http://dx.doi.org/10.1097/00004630-200103002-00041>.
- [222] Wait M, Hunt J, Purdue J. Duplex scanning of central vascular access sites in burn patients. *Ann Surg* 1990;211:499–503. <http://dx.doi.org/10.1097/BCR.0b013e318204b2ff>.
- [223] Wibbenmeyer LA, Hoballah JJ, Amelon MJ, Chang PX, Loret de Mola RM, Lewis RD, et al. The prevalence of venous thromboembolism of the lower extremity among thermally injured patients determined by duplex sonography. *J Trauma* 2003;55:1162–7. <http://dx.doi.org/10.1097/01.TA.0000057149.42968.1D>.
- [224] Li Q, Ba T, Wang L-F, Chen Q, Li F, Xue Y. Stratification of venous thromboembolism risk in burn patients by Caprini score. *Burns* 2019;45:140–5. <http://dx.doi.org/10.1016/j.burns.2018.08.006>.
- [225] Ahuja RB, Bansal P, Pradhan GS, Subberwal M. An analysis of deep vein thrombosis in burn patients (Part 1): comparison of D-dimer and Doppler ultrasound as screening tools. *Burns* 2016;42:1686–92. <http://dx.doi.org/10.1016/j.burns.2016.08.005>.
- [226] Hejl CG, Leclerc T, Bagues L, Samson T, Foissaud V. Incidence and features of heparin-induced thrombocytopenia (HIT) in burn patients: a retrospective study. *Thromb Haemost* 2008;99:974–6. <http://dx.doi.org/10.1160/TH07-10-0625>.
- [227] Duranteau J, Taccone FS, Verhamme P, Ageno W. European guidelines on perioperative venous thromboembolism prophylaxis: intensive care. *Eur J Anaesthesiol* 2017;35:142–6. <http://dx.doi.org/10.1097/EJA.0000000000000707>.
- [228] Arevalo Velasco A, Del Campo Balsa T, Gomez Bajo C, Cuesta Garcia V, Garcia Muhoz S, Lopez Pastor A, et al. Hypercoagulation in burn patients – Efficacy of thromboembolic prophylaxis. *Ann Medit Burns Club* 1993;6:5.
- [229] Lin H, Faraklas I, Cochran A, Saffle J. Enoxaparin and antifactor Xa levels in acute burn patients. *J Burn Care Res* 2011;32:1–5. <http://dx.doi.org/10.1097/BCR.0b013e318204b346>.