

Pediatric burn injury: key points for the anaesthesiologist

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Abstract

Burns are the eleventh leading cause of deaths in childhood and the fifth most common cause of non-fatal childhood injury, and most often occur in children under 4. 80% to 90% of all severe burns occur in low to middle income countries. Anaesthesiologists are crucial members of the multi-disciplinary team caring for children with burns. Provision of adequate analgesia, sedation, anesthesia and intensive care treatment are roles of anaesthesiologists and non-physician anaesthetists. There are several anaesthetic challenges with managing the child with burns such as a potential difficult airway, challenging intravascular line placement, water and electrolyte disturbances, altered temperature regulation, sepsis, cardiovascular and respiratory insufficiency, altered pharmacokinetic and pharmacodynamics pathways. The majority of critical adverse events in burn injured patients are associated with the airway and hemodynamic instability. The specific anaesthetic technique required depends on the individual patient pathophysiology condition. With the progress in burn care trauma protocols and with the development of multidisciplinary teams at special burn units, outcomes have improved over the past two decades. This review provides insights into existing therapeutic approaches for the management of paediatric burns.

Key words: anaesthesia, intensive care, paediatric, burn injury**INTRODUCTION**

Burns are the eleventh leading cause of deaths in childhood and the fifth most common cause of non-fatal childhood injury¹. Children under 4 years are at highest risk of burn injuries, almost double that of all other pediatric age groups². Even though the global mortality rate associated with burn injury has decreased in past two decades, burns remain a significant source of morbidity and mortality in childhood^{3,4}.

It is crucial to understand how a child is different from an adult in size, body surface area, temperature regulation, skin thickness and metabolic rate^{5,6}. The younger the child, the greater the mortality because of deeper burns due to thinner skin, more complexity of fluid resuscitation, smaller upper airways, difficult vascular access and immature immune system⁷. The initial management is very important and should focus on the ABCDE algorithm⁸.

Improved outcomes in past decades can be attributed to advances in resuscitation, protocols for intensive care, improved coverage of wounds and treatment of infections, better treatments for inhalation injury and for hypermetabolic response⁹. Severe paediatric burns

may require long-term rehabilitation treatment and may be associated with psychosocial consequences. The goals of burn care are to preserve life and function, to limit physical and psychological sequelae and to provide social reintegration¹⁰.

CLASSIFICATION AND SCORING SYSTEMS

Burns may be caused by heat, chemicals, electricity, or radiation. The severity of burn injury can be characterized by the depth of the burn, the total body surface area (TBSA) of the burn, the location of burn injury and the presence of inhalation injury¹¹. Burns are classified according to of the burns into three main categories: first, second and third degree. First-degree burns are superficial and only affect the epidermis, where the skin is red and painful. These rarely require hospital treatment. Second-degree burns affect both the dermis and epidermis, and the skin may be swollen, red or white, have blisters and be very painful. Third-degree burns are the most severe and reach through the skin layer to the hypodermis. Nerves may be destroyed causing severe pain or numbness. Skin may look charred, raised, leathery and blistered.

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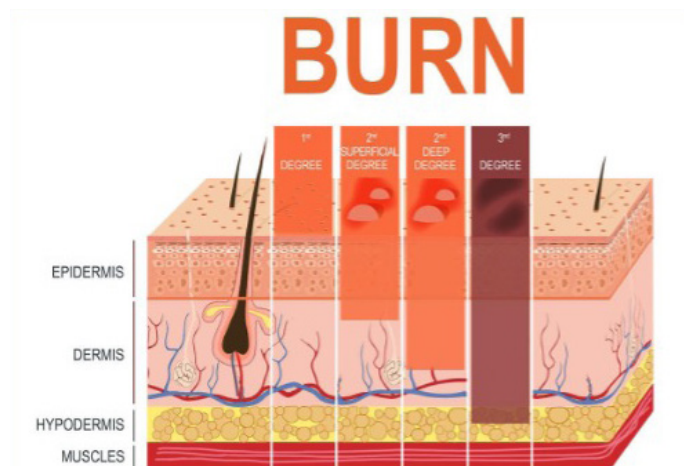


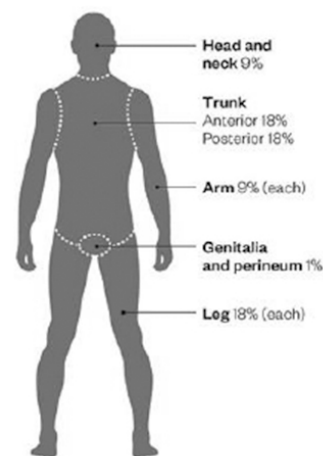
Figure 1. The skin structures affected by different degrees of burn. (Taken from Swiss Med Wkly. 2019;149:w20079) licensed under CC BY-NC-ND

To estimate the total body surface area (TBSA) burns in children, Lund and Browder charts may be used, which takes into account changes in the body proportions of growing children. In children, the head and neck occupy a larger, and the lower extremities occupy a smaller, proportion of the total body area. The rule of nine is useful for estimating burns in children older than 14 years. The area of the child's palm corresponds to approximately 1% of the total body surface area and this simple method can be useful when Lund and Browder charts are not available or when the burns are irregular in shape and non-confluent¹² (Figure 2).

Burns that affect more than 10% TBSA, or more than 5% TBSA of deep burns are considered to be serious as they are life-threatening. In neonates, a smaller TBSA causes more severe burn injury than in older children, due to the immaturity of the organ systems and the subsequent difficulty in maintaining homeostasis¹³.

For estimating the severity of burns are used two scoring systems: the Paediatric Risk of Mortality (PRISM) score and the Abbreviated Burn Severity Index (ABSI)¹⁴. The PRISM scoring system utilizes 14 variables including vital signs and lab values, which are collected over the first 24 hours after admission to hospital. The ABSI score is calculated from five variables (sex, age in years, inhalation injury, full thickness burn, total body surface area burned) that can be rapidly assessed at the time of admission, which eases calculation and allows for immediate prediction of mortality. Both PRISM and

Wallace rule of nines



Lund and Browder chart

Relative percentage of body surface area (% BSA) affected by growth

	half of head (a)	half of one thigh (b)	half of one lower leg (c)
0 yr	9½	2¾	2½
1 yr	8½	3¼	2½
5 yr	6½	4	2¾
10 yr	5½	4¼	3
15 yr	4½	4¼	3¼

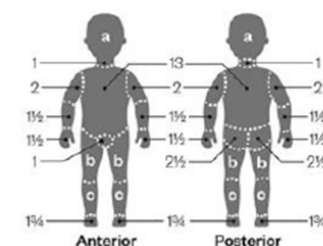


Figure 2. Body surface area estimation: Rule of nines and Lund and Browder chart.

ABSI scores predict mortality in children with severe burns, whether analysed alone or in a combined model. These scoring systems have advantages and disadvantages, so further validation of these scores need to be done with prospective studies. A detailed summary of these scoring systems is beyond the scope of this article.

PATHOPHYSIOLOGY

The skin serves as a barrier to protect the body from infection and to prevent heat and fluid losses. Therefore, destruction of this barrier by a burn injury can lead to infection and to altered heat and fluid regulation⁹.

Severe burn injury also induces the release of local and systemic mediators of inflammation. Local mediators, which include prostaglandins, leukotrienes, bradykinin, nitric oxide, histamine and oxygen free radicals, cause localized and systemic capillary leak with resultant oedema. Systemic mediators like interleukins and tumour necrosis factor alpha (TNF- α) cause a systemic inflammatory response that occurs almost immediately post injury. This liberation of pro-inflammatory mediators leads to the release of stress hormones that cause a hyper-metabolic state 3–5 days after the burn injury. Pathophysiologic changes occur in every organ systems and they can be divided into two phases: the acute phase, which resolves within 24–48h and the late or hypermetabolic phase¹⁵.

Table 1: Classification of burns according to severity

Minor	Moderate	Severe
<5% of body surface area	5-10% body surface area	> 10% of body surface area
<2% deep burns	2-5% deep burns	> 5% deep burns
	Suspected inhalational injury	Electric burns (electrocution)
	Circumferential burns	Inhalational injury
	Comorbidity (diabetes, etc.)	Burns of the face, hands, feet, perineum
		Significant associated trauma

INTRAHOSPITAL STRATEGIES IN TREATMENT

Early recognition and management of life-threatening injuries can have a significant impact on outcomes in burns. The mechanism of burns is extremely important, and if it occurred as a result of an explosion, traffic trauma or suspected joint injury, the priority is the evaluation of trauma. The primary and secondary examinations are done following Advanced Trauma Life Support standards¹⁶. After the primary assessment, a burn-specific secondary examination should be done in a way of estimation for the possibility of inhalation injury, intoxication with carbon monoxide and cyanide and accurate assessment of the burn wounds.

The management of burns can be considered in three phases. The first phase includes prehospital care and the early hospital phase: adequate and prompt first aid, assessment of the burns, resuscitation, escharotomies or fasciotomies and the management of inhalation injury. The second is the late hospital phase: wound care including burn surgeries, infection control management, maintenance of organ function and attenuation of hypermetabolism. The third phase is the long-term phase: management of persistent hypermetabolism, reconstruction and rehabilitation⁹.

AIRWAY MANAGEMENT: WHEN TO INTUBATE?

The airway of children is much smaller in diameter than adults and is very quickly endangered by oedema, so early intubation is advised if required. Intubation should never be postponed for more than a few hours in the case of cervicofacial burns, because the progressive oedema accelerates between the 4th and 8th hours to reach a maximum between the 12th and 36th hour post-burn¹⁷. Progressive unrecognized oedema can make intubation difficult and multiple failed attempts can worsen oedema in an already tight airway.

A high degree of suspicion for inhalation injury is essential. If the burn is a consequence of a fire, especially indoors, there is a possibility of inhalation injury to the respiratory tract.

Inhalation injury leads to oedema of the upper respiratory tract and chemical irritation of the lower respiratory tract. Clinical signs for inhalation injury are respiratory distress, hypoxemia, stridor, wheezing, oropharyngeal blistering, tongue swelling, carbonaceous sputum and singed eyebrows and nasal hairs. If there is any doubt about airway patency or the possibility for airway deterioration, the decision should be made for prompt endotracheal intubation. These patients should not be prophylactically intubated, neither to get prophylactic antibiotic therapy. Standard protocols for inhalation injury include bronchodilators, nebulised heparin, nebulised acetylcysteine and for extreme oedema, racemic adrenaline¹⁸.

The underlying mechanism in acute lung injury is impairment of alveolar membrane function, which often becomes apparent 24 to 48 hours after the initial burn injury. The treatment is similar to adult respiratory distress syndrome and is associated with increased morbidity and mortality¹⁹.

VASCULAR ACCESS

Venous access should be obtained as soon as possible, through intact skin if possible. A venous line may be placed through burned skin if unavoidable, but securing the cannula may be difficult. Placing

an intravenous line distal to a circumferential burn injury must be avoided because the constrictive effect that may develop can reduce venous return from distal parts of a limb. Two large peripheral venous lines are usually sufficient. In the case of failure to place a peripheral line, central venous access may be required and an intra-osseous needle may be required for resuscitation, but should be replaced within 24 hours^{20,21}.

FLUID RESUSCITATION: CRYSTALLOIDS AND COLLOIDS

Many formulas for fluid resuscitation in burns patients have been studied and all have the same goal: keeping sufficient organ perfusion. All formulas tend to fulfil two main rules: a) the minimum amount of fluid needed to maintain sufficient organ perfusion should be infused, and b) the volume needs to be carefully titrated to avoid under- and over-resuscitation. Optimal fluid resuscitation remains a matter of debate, with studies addressing not only the amount of fluid used in resuscitation, but also the type of fluid. No large prospective randomised trials have been done to establish whether crystalloids are better than colloids in resuscitation.

For initial fluid resuscitation in children with burns, crystalloids are the first choice during the initial 24 hours post-burn period²⁰. The Parkland Formula is most commonly used^{22,23}.

Total volume of crystalloid to be given in the first 24h = 4ml/kg body weight x % TBSA burned

However, recent data¹⁹ suggest the Parkland Formula may underestimate the fluid requirements in children younger than 3 years, patients with severe large and deep burns, those with associated inhalation injury, alcohol or drug use and electrical injury. Fluid balance can be challenging with under-resuscitation leading to multiple organ failure (MOF) and increased mortality. Over-resuscitation may lead to worsening of oedema, deteriorating gas exchange, pleural effusion, pericardial effusion, pulmonary oedema, acute respiratory distress syndrome, compartment syndrome, central neurological ischemia and multiple organ failure.

Oral hydration is most appropriate for burns with less than 10% TBSA in infants and children and with less than 15% TBSA for older children, if the injury does not interfere with a child's ability to take fluids by mouth. Enteral nutrition demands need to be carefully supervised due to gastric paresis and food aversion can disturb a child's ability to keep sufficient hydration and nutrition.

The optimal time to safely start using colloids is the subject of much debate. The time at which the protein leakage stops has been described differently in the literature. Capillary integrity is thought to have recovered 12 to 24 hours after the burn, and this is one of the strategies when to start using colloids. In the opinion of Cocks et al²⁵ albumin extravasation stops 8 h after burn injury. As claimed by Demling²⁶, capillary leakage of protein reduces remarkably about 12h after burn injury.

5% Albumin solutions may be started after 24 hours in a stable patient or 8 hours post-burn in a patient with difficult resuscitation at a dose of 0.75⁻¹g/kg/day in order to keep an albumin concentration >2.0g/dl. Serum albumin concentration should be monitored every 12 hours^{20,27}.

Acute changes in serum sodium levels can promote seizures, cerebral oedema and central pontine myelinolysis—each one is related to higher mortality risk²⁸.

One of the biggest challenges in fluid resuscitation is monitoring whether the infused volume is adequate. Formulas only ensure assessments of fluid demands, but reestablishment of intravascular volume must be controlled by indirect clinical signs such as capillary refill, heart rate, blood pressure and urine output. The satisfactory hourly urine output is the gold parameter for adequate fluid resuscitation, for children less than 30kg the goal is a urine output of 1ml/kg/h, and for children over 30kg the goal is urine output 0.5ml/kg/h²⁹. Hemodynamic targets are: systolic blood pressure values for children <1 month of age: 60mmHg, from 1 month to 10 years: 70+ (2 x years), and for older than 10 years: 90mmHg; mean arterial pressure (MAP) > 65mmHg. Global perfusion indicators (lactates, baseline deficit, central venous blood saturation) are more reliable than diuresis and correlate with burn rate and mortality²⁹.

ANALGESIA AND SEDATION OUTSIDE THE OPERATING ROOM

Analgesia should always be multimodal and multidisciplinary and include non-pharmacological and pharmacological methods with non-opioid and opioid analgesics. The pain burned patients experience may be divided into a 'background' pain and a 'breakthrough' pain associated with painful procedures. While background pain may be controlled with intravenous opioids via continuous infusion or patient or nurse-controlled analgesia (PCA/NCA) and/or less potent oral opioids, breakthrough pain may be treated with a variety of interventions³⁰. The intramuscular, subcutaneous and oral routes should be avoided because of unreliable systemic absorption associated with the shock state and delayed gastric emptying. In order to reduce the use of high opioid doses, other agents can be used as analgesic adjuncts, such as acetaminophen, ketamine, or an alpha-2 agonist, such as clonidine. Non-steroidal anti-inflammatory drugs are contraindicated in severe burns within the first 48 hours due to the increased risk of renal failure and gastric stress ulcers. Benzodiazepines may help with anxiety and avoid hypotension.

TEMPERATURE REGULATION

Hypothermia following burns can be significant and may result in worse outcomes. Children with large burns, full-thickness burns, inhalation injury or those who are intubated are at risk for hypothermia and benefit from any measures for temperature preserving³¹. The most critical time is during burn debridement and grafting, and many clinical practice guidelines recommend the ambient temperature should be increased in the operating room and intensive care unit. The use of an intravenous fluid warmer is a novel way in maintaining normothermia during the surgery in burn patients and may be more effective than conventional methods³².

HYPERMETABOLIC STATE: IMPORTANCE OF ADEQUATE NUTRITION

A burn injury results in a prolonged and persistent hypermetabolic response characterised by a 10- to 20-fold elevation in plasma catecholamines, cortisol and inflammatory mediators.

This response leads to twice-normal metabolic rates and whole-body catabolism. Adequate nutrition is therefore an essential part of burn care and should be initiated within 12h after injury³³. Early enteral nutrition mitigates catabolism and recommendations exist for nutrition that is high in glucose and amino acids, and low in fat with some unsaturated fatty acids.

Supplementation of single aminoacids, especially alanine and glutamine has debatable effect³⁵. Dietary components that have gained more recent attention are vitamins, micronutrients and trace elements and their replacement may reduce morbidity in patients with severe burns³⁶.

PREVENTING INFECTIONS

Infection remains the leading cause of death in patients with severe burns. Prophylactic parenteral administration of antibiotics is not recommended, but targeted therapy according to the results of microbiological analysis. Prophylactic systemic antibiotics can be convenient in patients with severe burns who require mechanical ventilation and in selected split-thickness skin grafting procedures³⁷. The use of topical antimicrobial agents is important in the treatment of local infections because systemic antibiotics do not reach burns in high concentrations due to vascular microthrombosis and the presence of oedema. Silver sulfadiazine with cerium nitrate is usually first line therapy and may be effective for up to 48 hours³⁸.

ANESTHESIA FOR SURGICAL PROCEDURES

Damaged tissue releases toxins and pro-inflammatory mediators responsible for systemic inflammatory response syndrome (SIRS) and hypermetabolism. Surgery may need to be performed on a regular basis, with an average of one operation every 5-7 days. The risks of septic shock, renal failure and multiple organ failure also increase exponentially with time³⁸.

Patients are often brought to the operating room in the early phase of burn injury, when they are undergoing significant fluid shifts with corresponding cardiovascular and/or respiratory instability³⁹. However unstable the child is, the operation should not be delayed as early wound excision and coverage with skin analogues within 72–168 hours, improves outcome in paediatric patients with acute burn without inhalation injury. Lower doses of anaesthetic drugs may be required as decreases in circulatory blood volume throughout the first phase (first 48h) of burn shock leads to reduction in renal and hepatic blood flow which prolongs the rate of drug distribution and the onset of clinical effects. In the following hypermetabolic state (after 48h), high blood flow to the liver and kidneys, decreased plasma albumin and an increased level of α -1-acid glycoprotein results in modulated protein binding and elevated renal clearance⁴⁰. The amount of albumin to which acidic and neutral drugs bind decreases, so the free fraction is higher, but the amount of α -acid glycoprotein that binds cationic drugs is doubled (lidocaine, propofol, muscle relaxants, some opioids) and thus the free fraction decreases.

General anaesthesia with the use of opioids, volatile or intravenous anaesthetics and muscle relaxants, is common choice of anaesthesia for burn excision and grafting. Propofol and thiopental are successfully used for induction with careful titration, in order to minimize dose-dependent respiratory and cardiac depression.

Etomidate is not a good choice due to the possibility of inducing adrenocortical suppression. Ketamine can be advantageous for the induction of hypovolemic patients because of sympathetic nervous system stimulation and may be useful for procedural sedation for a change of dressing⁴¹. Anaesthesia maintenance is reached with inhalational agents or with intravenous anaesthetics. Succinylcholine can be safely given within the first 24 hours of injury. However, should not be used after 48–72h post-burn injury, due to synthesis of extrajunctional receptors causing hyperkalaemia. There may also be a degree of resistance to nondepolarizing muscle relaxants⁴².

While regional anaesthesia techniques offer great benefits for pain control, it may be hard to find an intact skin area for regional anaesthesia in the child with severe burns⁴³.

CONCLUSION

Severe burn-related injuries require a multidisciplinary team assessment and management. Understanding and applying the principles of the initial approach in burned children can help to improve outcomes. Particular attention should be directed to airway management, fluid and metabolic requirements, and appropriate analgesia and sedation. New initiatives to tackle the problem of antibiotic resistance are required urgently.

REFERENCES:

- World Health Organization A WHO plan for burn prevention and care WHO, Geneva, Switzerland (2008).
- Sanabria Carretero P, Vogel C, Reinoso-Barbero F, López Gutiérrez JC. Resuscitation of the burned child in critical condition. *Rev Esp Anestesiol Reanim*. 1998 Aug-Sep; **45(7)**: 285-93.
- Strobel AM, Fey R. Emergency Care of Pediatric Burns. *Emerg Med Clin North Am*. 2018 May; **36(2)**: 441-458.
- Palmieri TL. Pediatric Burn Resuscitation. *Crit Care Clin*. 2016 Oct; **32(4)**: 547-59.
- Arbuthnot MK, Garcia AV. Early resuscitation and management of severe pediatric burns. *Semin Pediatr Surg*. 2019 Feb; **28(1)**: 73-78.
- Mehrotra S, Misir A. Special Traumatized Populations: Burns Injuries. *Curr Pediatr Rev*. 2018; **14(1)**: 64-69.
- Barcelos RS, Santos IS, Matijasevich A, Barros AJ, Barros FC, FrançaGV et al. Falls, cuts and burns in children 0-4 years of age: 2004 Pelotas (Brazil) birth cohort. *Cad Saude Publica*. 2017 Mar 9; **33(2)**: e00139115.
- Landsleitner B, Keil J. Burns and scalds in children. *Med Klin Intensiv med Nof med*. 2015 Jun; **110(5)**: 346-53.
- Jeschke MG, Herndon DN. Burns in children: standard and new treatments. *Lancet*. 2014 Mar 29; **383(9923)**: 1168-78.
- Meuli M, Lochbühler H. Current concepts in pediatric burn care: general management of severe burns. *Eur J Pediatr Surg*. 1992 Aug; **2(4)**: 195-200.
- Brusselsaers N, Monstrey S, Vogelaers D, Hoste E, Blot S. Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality. *Crit Care*. 2010; **14(5)**: R188.
- Kasten KR, Makley AT, Kagan RJ. Update on the critical care management of severe burns. *J Intensive Care Med*. 2011; **26(4)**: 223-236.
- Ugburo AO, Fadeyibi IO, Mofikoya BO, Akanmu ON, Temiye EO, Kanu OO et al. Neonatal burns in Lagos, South-Western Nigeria: Epidemiology and outcome of management. *Burns*. 2013 May; **39(3)**: 483-92.
- Berndtson AE, Sen S, Greenhalgh DG, Palmieri TL. Estimating severity of burn in children: Pediatric Risk of Mortality (PRISM) score versus Abbreviated Burn Severity Index (ABSI). *Burns* 2013; **39(6)**: 1048-53.
- Fuzaylov G, Fidkowski CW. Anesthetic considerations for major burn injury in pediatric patients. *Paediatr Anaesth*. 2009; **19(3)**: 202-11.
- Bouillon B, Probst C, Maegele M, Wafaisade A, Helm P, Mutschler M et al. Emergency room management of multiple trauma: ATLS® and S3 guidelines. *Chirurg*. 2013 Sep; **84(9)**: 745-52.
- Vivó C, Galeiras R, del Caz MD. Initial evaluation and management of the critical burn patient. *Med Intensiva*. 2016 Jan-Feb; **40(1)**: 49-59.
- Enkhbaatar P, Herndon DN, Traber DL. Use of nebulized heparin in the treatment of smoke inhalation injury. *J Burn Care Res*. 2009 Jan-Feb; **30(1)**: 159-62.
- Mehta M, Tudor GJ. Parkland Formula. 2020 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; Jan 2021.
- Bittner EA, Shank E, Woodson L, Martyn JA. Acute and perioperative care of the burn-injured patient. *Anesthesiology*. 2015; **122(2)**: 448-464. 55
- Saffle JI. The phenomenon of "fluid creep" in acute burn resuscitation. *J Burn Care Res* 2007; **28**: 382-95.
- van Duin D, Jones SW, Dibiasi L, Schmits G, Lachiewicz A, Hultman CS et al. Reduction in central line-associated bloodstream infections in patients with burns. *Infect Control Hosp Epidemiol*. 2014 Aug; **35(8)**: 1066-8.
- Greenhalgh DG. Burn resuscitation. *J Burn Care Res* 2007; **28**: 555-65.
- Greenhalgh DG. Burn resuscitation: the results of the ISBI/ABA survey. *Burns* 2010; **36**: 176-82.
- Cocks AJ, O'Connell A, Martin H. Crystalloids, colloids and kids: a review of paediatric burns in intensive care. *Burns* 1998; **24**: 717-24.
- Demling RH. Fluid resuscitation. In: Boswick Jr JA, editor. The art and science of burn care. Rockville: Aspen Publications, 1987.
- 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 Jun; **17(6)**: e280-6.
- Yowler CJ, Fratianne RB. Current status of burn resuscitation. *Clin Plast Surg* 2000; **27**: 1210.
- 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(1)**: 121-128.
- Gregoretti C, Decaroli D, Piacevoli Q, Mistretta A, Barzaghi N, Luxardo N et al. Analgo-sedation of patients with burns outside the operating room. *Drugs*. 2008; **68(17)**: 2427-43
- Ziegler B, Kenngott T, Fischer S, Hundeshagen G, Hartmann B, Horter J et al. Early Early hypothermia as risk factor in severely burned patients: A retrospective outcome study. *Burns*. 2019; **45(8)**: 1895-1900
- Prunet B, Asencio Y, Lacroix G, Bordes J, Montcriol A, D'Aranda E et al. Maintenance of normothermia during burn surgery with an intravascular temperature control system: a non-randomised controlled trial. *Injury*. 2012 May; **43(5)**: 648-52.
- Gore DC, Chinkes D, Sanford A, Hart DW, Wolf SE, Herndon DN. Influence of fever on the hypermetabolic response in burn-injured children. *Arch Surg* 2003; **138**: 169-74.
- 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.
- Berger MM, Pantet O. Nutrition in burn injury: any recent changes? *Curr Opin Crit Care*. 2016 Aug; **22(4)**: 285-91.
- Gamliel Z, DeBiaise MA, Demling RH. Essential microminerals and their response to burn injury. *J Burn Care Rehabil* 1996; **17**: 264-72.
- Ramos G, Cornistein W, Cerino GT, Nacif G. Systemic antimicrobial prophylaxis in burn patients: systematic review. *J Hosp Infect*. 2017 Oct; **97(2)**: 105-114.
- Yoshino Y, Ohtsuka M, Kawaguchi M, Sakai K, Hashimoto A, Hayashi M et al. The wound/burn guidelines - 6: Guidelines for the management of burns. Wound/Burn Guidelines Committee. *J Dermatol*. 2016 Sep; **43(9)**: 989-1010.

39. Bittner EA, Shank E, Woodson L, Martyn JA. Acute and perioperative care of the burn-injured patient. *Anesthesiology*. 2015;122(2): 448–464. Jul; **91(1)**: 320-2.
40. Steele AN, Grimsrud KN, Sen S, Palmieri TL, Greenhalgh DG, Tran NK. Gap analysis of pharmacokinetics and pharmacodynamics in burn patients: a review. *J Burn Care Res* 2015 May-Jun; **36(3)**: e194-211.
41. Harbin KR, Norris TE. Anesthetic management of patients with major burn injury *AANA J*. 2012; **80(6)**: 430-9.
42. Gronert GA. Succinylcholine hyperkalemia after burns. *Anesthesiology*. 1999 Jul; **91(1)**: 320-2.
43. Shank ES, Martyn JA, Donelan MB, Perrone A, Firth PG, Driscoll DN. Ultrasound-Guided Regional Anesthesia for Pediatric Burn Reconstructive Surgery: A Prospective Study. *J Burn Care Res*. 2016 May-Jun; **37(3)**: e213-7.