THE BURN PATIENT IN THE CRITICAL CARE DEPARTMENT. ITS OUTCOMES: A RETROSPECTIVE REVIEW FROM A SINGLE CENTER.

Department of emergency and critical care

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SUMMARY

Ramy Husein El-Ahmed

The burn patient in critical care. Its outcomes: A retrospective review from a single center.

Aim: The aim of this research work is to retrospectively review the outcomes of patients with large burns at the department of critical medicine in Kauno Klinikos.

Objectives: To report the outcomes of the patients: survival vs mortality, according to the following variables: demographic data (age, gender), severity of tissue damage (TBSA% affected by the burn, degree of the burn injury: I-II-III-IV), complications suffered (COHb levels included) and treatment strategy (including nutrition strategy, total amount fluid replacement therapy administered during the first 24 hours after admission).

Methods: The clinical outcomes of 29 patients admitted to the ICU [intensive care unit] unit between 2012 and December 2016 have met the inclusion criteria (%TBSA > 20%) after a review of ICU registries. The data was collected and analyzed using a standard Microsoft Excel spreadsheet and the statistical analysis was performed using a trial version of SPSS. A p value of < 0.05 was stated to be statistically significant.

Results: Out of the 29 patients, mortality was 51.72%. The mean age of non-survivors was 62 y.o., 44 y.o. for survivors. Male survivors accounted for 55%, while non-survivors 45%. Female survivors were 33.33% and non-survivors 66.66%. Average time in ICU was 43 days overall, 71 days for survivors and 17 days for non-survivors. The mean %TBSA [percentage of total body surface area affected by the burn, excluding the erythema alone] was 51%, being 36.5% for survivors, and 64.75% for nonsurvivors. 28 out of 29 patients reached a IIIº injury, out of those 15 did not survive (53.57%). The median of COHb [carboxylated hemoglobin] levels for survivors was 1.7% and for non-survivors 1.5%. The amount of fluids received during the first 24 hours was averaged 10.93L for survivors and 15.4L for nonsurvivors. The most common complication was inhalational injury (n=21) and the deadliest was MOF [multiple organ failure] (100% mortality). The mortality among those who received parenteral nutrition is higher (58.33%) than those who received enteral (53.33%). Some statistically significant prognostic values associated with an increase in mortality have been identified, such as age, %TBSA, fluid volume in the first 24h, development of pneumonia, shock and AKF [acute kidney failure].

Conclusions: It has been found that the following variables are associated with mortality: older age, extensive TBSA% affected by the burn, the development of shock, sepsis or acute kidney failure, and the volume of fluids administered during the first 24 hours after the burn (the last being an indirect prognostic factor, since it is linked to %TBSA).
CONFLICT OF INTEREST

There was not any conflict of interest.

SOURCES OF FUNDING

There was not any source of funding.

ABBREVIATIONS LIST:

TERMS
Simplified Acute Physiology Score (SAPS) 3: This is a score that has been developed to predict the hospital mortality rate in patients admitted to the general ICU [intensive care unit]. It uses epidemiological variables including the origin of the patient before an admission to the ICU, physiological variables and laboratory data from the first hour in the ICU. [29]

Acute physiology and chronic health evaluation (APACHE) II: This is a score that has been developed to predict the hospital mortality rate of patients admitted to the general ICU. It uses epidemiological variables, physiological variables and laboratory data from the first twenty four hours after the ICU admission. [29]

Abbreviated burn severity index (ABSI): This is a specific score that has been developed to predict the hospital mortality rate of burn patients. This consists of epidemiologic variables, such as age and gender, associated with the characteristics of burn trauma, such as inhalation injury, TBSA and the presence of a full thickness burn [29].

Ryan’s score: This is a specific score that has been developed to predict the hospital mortality rate of burn patients. This consists of three clinical variables: age greater than 60 years old, a TBSA greater than 40%, and the presence of inhalation injury. [29]

Cardiac index (CI): a haemodynamic parameter that relates the cardiac output (CO) from left ventricle in one minute to body surface area (BSA), thus relating heart performance to the size of the individual. The unit of measurement is liters per minute per square meter (L/min/m²).

PaO₂/FiO₂ ratio: the ratio of arterial oxygen partial pressure to fractional inspired oxygen.

LA50%: lethal burn area at which fifty percent of patients died.
ETHICS COMMITTEE CLEARANCE

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Vientisų studijų programa – MEDICINA
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DĖL PRITARIMO TYRIMUI

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VI k. stud. Ramy Hussein El-Ahmed (moks linenjo darbo vadovas: prof. Vidas Pilvinis, LSMUL
KK Intensyvios terapijos klinika) moks linenjo-tiriamojo darbo temos: „The burn patient in the
critical care department. Its outcomes: a retrospective review form a single center“ tiriamojo
darbo anotacija, kuri leidžia spręsti, jog planuojamame tyrimo neturėtų būti pažeistos tiriamojo
teisės, todėl šiam tyrimui pritariama.

Bioetikos centro vadovas

[Signature]

dr. Elmentas Peltiūs
INTRODUCTION

Burn is an important cause of morbidity and mortality. Severe cases carry a high risk of physical, emotional, cultural and economic burden, not only for the victims but also for society [1]. Burns are common and frequently involve small areas requiring only ambulatory treatment. However, more complex patients require hospitalization and intensive care unit (ICU) support [2]. This research work is aimed to deal with the outcomes of severely burn patients (>20% TBSA), in order to report the data on the outcomes of these critically ill burn patients in one of the largest ICU in Lithuania.

It is important to emphasize that due to the rarity of great burn injuries [3] as well as the existence of a mixed ICU unit instead of a specialized burn care center from where the data was obtained, the number of cases for the study is scarce. Knowledge regarding the clinical characteristics, risk factors for mortality, and outcomes of severe burn patients requiring intensive care in middle income countries is essential to assist in the decision-making process for care improvement and better resource allocation. Thus, the aim of this study was to characterize severe burn patients admitted to the Kauno Klinikos ICU, with the hypothesis that certain factors present on the patients early in the ICU admission make survivors diverge from non-survivors. Therefore, the parameters related to hospital mortality and rehabilitation discharge were analyzed as well.
AIM AND OBJECTIVES OF THE THESIS

The aim of this research work is to retrospectively review the outcomes of patients with large burns at the department of critical medicine in Kauno Klinikos.

Objectives:

Being the possible outcomes of the patients: survival vs mortality, the objectives of the thesis are:

1. To report outcomes on burn patients depending on their demographic data (age, gender).
2. To report outcomes on burn patients depending on the severity of tissue damage (TBSA% affected by the burn, degree of the burn injury: I-II-III-IV)
3. To report outcomes on burn patients depending on the complications suffered (COHb levels included).
4. To report outcomes on burn patients depending on the treatment strategy (including nutrition strategy, total amount fluid replacement therapy administered during the first 24 hours after admission)
LITERATURE REVIEW

Burns are injuries of skin or other tissue caused by thermal, radiation, chemical, or electrical contact. Burns are classified by depth (superficial and deep partial-thickness, and full-thickness) and percentage of total body surface area (TBSA) involved. Patients with large burns (> 20% TBSA) require fluid resuscitation.\(^8\)

Mortality rates for burn patients have been substantially reduced in the last few decades. The reduction in mortality with severe burn patients is mainly attributed to advancements in the areas of fluid resuscitation, nutritional support, pulmonary support, burn wound care, infection control, early tangential excision and skin grafting and the availability of multidisciplinary dedicated staff for the care of burn patients. As a result, burn patient mortality rates have been reduced by up to 50% in the last 40 years.\(^4\),\(^19\) Mortality rates, notwithstanding significant % TBSA and presence of inhalation injury, have significantly declined compared with previous benchmarks. Modern day surgical and medically intensive management has markedly improved to the point where we can expect patients younger than 55 years with severe burn injuries and inhalation injury to survive these devastating conditions.\(^5\) Proper evaluation and management, coupled with appropriate early referral to a specialist, greatly help in minimizing suffering and optimizing results.\(^7\)

Burn injury is a common cause of morbidity and mortality. In the United States, approximately 1.25 million people with burns present to the emergency department each year. Among these, 63,000 have minor burn injuries that are treated primarily in the emergency department and an additional 6000 sustain major burn injuries that require hospital admission.\(^6\),\(^7\)

Tissue burn involves direct coagulation and microvascular reactions in the surrounding dermis that may result in extension of the injury. Large injuries are associated with a systemic response caused by a loss of the skin barrier, the release of vasoactive mediators from the wound, and subsequent infection. This results clinically in interstitial edema in distant organs and soft tissues, with an initial decrease in cardiac output and the metabolic rate.\(^15\)

After successful resuscitation, a hypermetabolic response occurs, with near doubling of cardiac output and resting energy expenditure. Accelerated gluconeogenesis, insulin resistance, and increased protein catabolism accompany this response. Modification of this physiology has been proposed through the administration of beta-adrenergic blockade, beta-adrenergic supplementation, nonsteroidal anti-inflammatory agents, recombinant growth hormone, androgenic steroids, and insulin-like growth factor-1. Currently, data do not support the routine use of these therapies.\(^8\)

Burns cause protein denaturation and thus coagulative necrosis. Around the coagulated tissue, platelets aggregate, vessels constrict, and marginally perfused tissue (known as the zone of stasis) can extend around the injury. In the zone of stasis, tissue is hyperemic and inflamed. Damage to the normal epidermal barrier allows bacterial invasion and external fluid loss; damaged tissues often become edematous, further
enhancing volume loss. Heat loss can be significant because thermoregulation of the damaged dermis is absent, particularly in wounds that are exposed. [8,12]

Clinical assessment of burn extent and depth (paying special attention to facial burns) and bronchoscopy (in order to check tracheal damage) are important to evaluate in every severely burnt patient. [8,12]

Burn size is important to assess as it influences the size of the inflammatory response (vasodilatation, increased vascular permeability) and thus fluid shift from the intravascular volume. The size must be estimated to calculate fluid requirements. Ignore erythema. Burn depth determines healing time/scarring; assessing this may be hard, even when experienced. The big distinction is whether the burn is partial thickness (painful, red, and blistered) or full-thickness (insensate/painless; grey-white). Remember that burns can evolve, particularly over the 1st 48 hours. [12,23]

The percentage of TBSA involved is calculated; only partial-thickness and full-thickness burns are included in this calculation. For adults, the percentage TBSA for parts of the body is estimated by the rule of nines; for smaller scattered burns, estimates can be based on the size of the patient’s entire opened hand (not the palm only), which is about 1% of TBSA. Children have proportionally larger heads and smaller lower extremities, so the percentage TBSA is more accurately estimated using the Lund-Browder chart (see Figure no1) [8,14]

The Lund & Browder chart is accurate but time-consuming compared with the “Rule of nines”, although the latter generally overestimates burn area (better than underestimating). A modified rule of nines for children: from birth up to one year, surface area of the head and neck is 18% and each leg is 14%. For each year after, head loses 1% and each leg gains 0.5% - so adult proportions are reached approximately by age 10. [12]

![Figure no.1](https://example.com/image.png)

**Rule of nines (for adults(A)) and Lund-Browder chart (for children(B)) for estimating extent of burns.**

<table>
<thead>
<tr>
<th>Body Part</th>
<th>0 yr</th>
<th>1 yr</th>
<th>5 yr</th>
<th>10 yr</th>
<th>15 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>a = 1/2 of head</td>
<td>9 1/2</td>
<td>8 1/2</td>
<td>6 1/2</td>
<td>5 1/2</td>
<td>4 1/2</td>
</tr>
<tr>
<td>b = 1/2 of 1 thigh</td>
<td>2 3/4</td>
<td>3 1/4</td>
<td>4</td>
<td>4 1/6</td>
<td>4 1/2</td>
</tr>
<tr>
<td>c = 1/2 of 1 leg</td>
<td>2 1/2</td>
<td>2 1/2</td>
<td>2 3/4</td>
<td>3</td>
<td>3 1/4</td>
</tr>
</tbody>
</table>
Lethal burn area at which fifty percent of patients died (LA50%) was 36.5% and the greatest TBSA of all the patients who survived in our study was 57%. [29]

Burns cause both systemic and local complications. The major factors contributing to systemic complications are breakdown of skin integrity and fluid loss. Local complications include eschars and contractures and scarring. Meanwhile the most common systemic complications are hypovolemia and infection. Although others can happen, such as metabolic abnormalities (hypoalbuminemia, dilutional electrolyte deficiencies such as hypomagnesemia, hypophosphatemia, and hypokalemia; metabolic acidosis) Rhabdomyolysis or hemolysis can result from deep thermal or electrical burns of muscle or from muscle ischemia due to constricting eschars. Rhabdomyolysis causing myoglobinuria or hemolysis causing hemoglobinuria can lead to acute tubular necrosis and acute kidney injury. Ileus is also common after extensive burns. [8]

The greater the percentage of TBSA involved, the greater the risk of developing systemic complications. Risk factors for severe systemic complications and mortality include all of the following: Second- and third-degree burns of > 40% of TBSA, age > 60 yr or < 2 yr and the presence of simultaneous major trauma or smoke inhalation[8,9]

After initial treatment and stabilization, the need for hospitalization is assessed.

To determine the need for referral to a specialized burn unit, the American Burn Association devised a classification system. (table no.1) Under this system, burns can be classified as major, moderate and minor. Minor burns can typically be managed at home, moderate burns are often managed in hospital, and major burns are managed by a burn center. [10,11]

The management plan for patients with large burns that require inpatient care is usually determined by the physiology of the burn.

### American Burn Association severity classification [10]

<table>
<thead>
<tr>
<th>Minor</th>
<th>Moderate</th>
<th>Major</th>
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<tbody>
<tr>
<td>Adult &lt;10% TBSA</td>
<td>Adult 10–20% TBSA</td>
<td>Adult &gt;20% TBSA</td>
</tr>
<tr>
<td>Young or old &lt;5% TBSA</td>
<td>Young or old 5–10% TBSA</td>
<td>Young or old &gt;10% TBSA</td>
</tr>
<tr>
<td>&lt;2% full thickness burn</td>
<td>2–5% full thickness burn</td>
<td>&gt;5% full thickness burn</td>
</tr>
<tr>
<td>High voltage injury</td>
<td>High voltage burn</td>
<td></td>
</tr>
<tr>
<td>Possible inhalation injury</td>
<td>Known inhalation injury</td>
<td>Significant burn to face, joints, hands or feet</td>
</tr>
<tr>
<td>Circumferential burn</td>
<td>Other health problems</td>
<td>Associated injuries</td>
</tr>
</tbody>
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Table 1
injury. Management strategies for these patients generally require a coordinated approach that involves a specialized team. Hospitalization is divided into 4 general phases, including (1) initial evaluation and resuscitation, (2) initial wound excision and biologic closure, (3) definitive wound closure, and (4) rehabilitation and reconstruction. [7]

As described by the American College of Surgeons Committee on Trauma and the early management of severe burns protocol, before management of the burn wound can begin, evaluation of the burn patient is organized into a primary survey and secondary survey. [7,13]

In the primary survey, the burn patients systematically evaluated with an emphasis on support of the airway, gas exchange, and circulatory stability. [7,13] First evaluate the airway; this is an area of particular importance in burn patients. Early recognition of impending airway compromise, followed by prompt intubation, (when inhalation injury is highly suspected, it is preferable early expectant intubation) along with high-flow O$_2$ can be lifesaving. Recognize thoracic burns as they can restrict breathing movements and an escharotomy may be needed. Obtain appropriate vascular access, especially aimed for fluid resuscitation and place monitoring devices, then a complete a systematic trauma survey, including indicated radiographs and laboratory studies. [7,13]

In the secondary survey burn patients should then undergo a burn-specific secondary survey, which should include a determination of the mechanism of injury, an evaluation for the presence or absence of inhalation injury and carbon monoxide (probable in persons injured in structural fires) and or cyanide (from burning foam) intoxication, an examination for corneal burns, the consideration of the possibility of abuse, and a detailed assessment of the burn wound. [7,13]

Effective fluid resuscitation is one of the cornerstones of modern burn care and perhaps the advance that has most directly improved patient survival. Proper fluid resuscitation aims to anticipate and prevent rather than to treat burn shock. [2–4] The obvious challenge is to provide enough fluid replacement to maintain perfusion without causing fluid overload. [3, 5, 17]

Without effective and rapid intervention, hypovolemia/shock will develop if the burns involve > 15% to 20% total body surface area (TBSA). [18] Delay in fluid resuscitation beyond 2 hrs of the burn injury complicates resuscitation and increases mortality. [7, 16] The consequences of excessive resuscitation and fluid overload are as deleterious as those of under-resuscitation: pulmonary edema, myocardial edema, conversion of superficial into deep burns, the need for fasciotomies in unburned limbs, and abdominal compartment syndrome.

Given that the amount of fluids to be administered is directly proportional to the severity of the injuries, patients with major burns are the most difficult to manage. [34] Because the changes are different in every patient, fluid resuscitation can only be loosely guided by formulas. [7,16] The inherent inaccuracy of formulas requires continuous reevaluation and adjustment of infusions based on resuscitation targets.
For monitoring, the patient should be catheterized as the best single measure is the urine output – aim for more than 0.5mL/kg/hour. \[^{[21,33]}\]

Factors that influence fluid requirements during resuscitation besides TBSA burn include burn depth, inhalation injury, associated injuries, age, delay in resuscitation, need for escharotomies/fasciotomies, and use of alcohol or drugs. \[^{[21]}\]

It is not possible to accurately predict who will fail resuscitation, but patients who routinely require additional fluid include those with inhalation injury, electrical burns, those in whom resuscitation is delayed, and those using alcohol or illicit drugs. Patients making methamphetamine have larger, deeper burns and often require two to three times the standard Consensus formula resuscitation. There is significantly increased inhalation injury, nosocomial pneumonia, respiratory failure, and sepsis in these patients. \[^{[21]}\]

The use of excessive volumes for resuscitation is being documented with increasing frequency in many burn centers. \[^{[22]}\] Burn care providers have become more aggressive with the administration of benzodiazepines and narcotics, which may result in additional fluid demands. \[^{[21]}\]

Outreach education in burn care has contributed to a now common problem of excessive resuscitation given by first responders and non-burn physicians. Thus, many patients arrive at a burn center having received most of their first 8hr Consensus formula (Parkland Formula) requirements in just an hour or two. \[^{[21,22]}\]

Ideally, begin enteral feedings during resuscitation, except in patients with massive injuries or those who are underresuscitated and less likely to tolerate tube feedings because of ileus secondary to splanchnic underperfusion. \[^{[7]}\]

In general, fluid overload in critically ill patients is associated with worse outcomes, mainly in acute respiratory distress syndrome patients. In this way, in our patients, the higher cumulative fluid balance in the first seven days after an ICU admission was another factor associated with disease severity, and therefore was independently associated with mortality. This is known as fluid creep. \[^{[29]}\]

Concerns over administered fluid volumes are predicated on the belief that fluid volume can be critical to the development of organ failure, infections, and death. The potential problems of underresuscitation involve complications of inadequate perfusion, including hypovolemic shock, renal failure, and the conversion of partial thickness wounds to full thickness wounds. There has similarly been increasing emphasis on the potentially deleterious effects of massive volumes of fluid resuscitation, including extremity, orbital and abdominal compartment syndromes, acute respiratory distress syndrome (ARDS), prolonged periods of ventilator dependence, and increased mortality. \[^{[39]}\]

Nevertheless, Cancio et al reported that the Parkland formula underestimated fluid requirements in 84% of patients, and this includes above all major burns, where the Parkland formula by Baxter and Shires (3.7-4.3 mL/Kg/\%TBSA of crystalloid fluids within the first 24h. With this formula, half the volume is given in the first 8 hours postburn, with the remaining volume delivered over 16 hours) is found not to be effective enough. \[^{[39,40]}\]
The amount of excessive fluid received in excess of predicted affects the development of complications as shown here in Table 7. For fluids in excess of 25% of predicted volumes, the estimated increase in odds for adverse outcome were: ARDS (OR = 1.69; CI, 0.48–5.9), pneumonia (OR = 5.67, CI, 1.1–29.1), multiple organ failure (OR = 1.6; CI, 0.38–6.6), bloodstream infections (OR = 2.9; CI, 0.51–16.5), and death (OR = 5.33; CI, 1.4–20.4). In addition, all patients receiving >25% above predicted fluid volumes developed at least one of the adverse outcomes. These findings confirm the hypothesis that increasing volumes of fluid (or fluid creep as termed by Pruitt) may be associated with negative sequelae.

The combination of a body burn and smoke inhalation produces a marked increase in mortality and morbidity. Burn patients with inhalation injury have been shown to require increased fluids during resuscitation. The presence of inhalation injury was associated with a 44% increase in fluid requirements, which was remarkably uniform across all age groups and burn sizes. The degree of lung dysfunction caused by a smoke inhalation injury is accentuated by the presence of even a small body burn. Acute upper airway obstruction occurs in 20% to 33% of hospitalized burn patients with inhalation injury and is a major hazard because of the possibility of rapid progression from mild pharyngeal edema to complete upper airway obstruction. A carboxyhemoglobin level taken within 1 hr after injury is strongly indicative of smoke inhalation if >10%. Intubation itself is not without risk so should not be undertaken routinely simply because there are facial burns. The care of inhalation injury remains supportive. Even the gold standard of bronchoscopy within the first 24 hrs of admission cannot accurately predict the severity of inhalation injury. Roughly 70% of patients with inhalation injury will develop ventilator associated pneumonia. According to one study published in 2007, the most frequent cause of death for burn patients is inhalation injury. However, surprisingly, inhalation injury was not independently associated with increased mortality in the multivariate analysis, despite a great incidence of this type of injury.

Severe burn injury results in a prolonged hypermetabolic and catabolic state that persists as long as 1 year after injury. Early nutritional support has become a critical component of early management of injured patients to prevent ileus, stress ulceration, and the effects of hypermetabolism. International nutrition support guidelines advocate that enteral feedings should occur early in critically ill patients who have a functioning gastrointestinal tract, but what is considered early varies significantly. The Canadian Clinical Practice Guidelines recommend starting enteral nutrition (EN) within 24 to 48 hours after admission to the intensive care unit (ICU) in critically ill patients. The Eastern Association for the Surgery of Trauma recommends that intragastric feedings be started as soon as possible in burn patients after admission, because delayed enteral feeding (>18 hours) results in a high rate of gastroparesis and the need for intravenous
nutrition. Similarly, the American Burn Association (ABA) advocates early EN as soon as practical.\textsuperscript{[32,33]}

In one study\textsuperscript{[32]}, they evaluate the injury outcomes between those who received EN and those who did not. There was no increased incidence of gastrointestinal bleeding, abdominal compartment syndrome, need for laparotomy, or ventilator-associated pneumonia. They also evaluated the influence of early EN on time to ventilator-associated pneumonia development and found that early EN was not a significant predictor (adjusted hazard ratio [HR] = 1.23, \( P=0.41 \), 95\% confidence interval [CI] 0.74–2.04). In addition, length of mechanical ventilation, incidence of bloodstream and total infectious complications, multiple organ dysfunction syndrome, and survival were similar between the two groups. Patients fed early did have a shorter ICU LOS (40.7 vs 52.5 days, \( P=0.03 \)) and decreased wound infection rates (54.5 vs 80\%, \( P=0.01 \)).\textsuperscript{[32]}

In the same study, after adjustment for age, %TBSA burn, inhalation injury, and participating burn center, patients fed in the first 24 hours still had a shorter ICU LOS (adjusted HR =0.57, \( P=.03 \), 95\% CI 0.35–0.94) and lower wound infection risk (OR= 0.28, \( P=0.01 \), 95\% CI 0.10–0.76).\textsuperscript{[32]}

Other study\textsuperscript{[35]} shows that substantive caloric and protein deficits occur in burn patients, and there are associations between deficits and mortality, such that the greater the energy and protein deficits, the stronger the association with mortality. So, there was an association between death and energy (\( p = 0.02 \)) and protein (\( p = 0.027 \)) deficits regardless of feeding route. These associations between energy or protein deficits and mortality remained significant when adjusted for APACHE II. Glutamine administration was associated with survival when adjusted for APACHE II (\( p = 0.007 \)). When adjusting for protein administration the odds ratio and 95\% confidence intervals remained unchanged (\( p = 0.012 \)). Any hypoglycaemic episode during admission was also associated with mortality (\( p = 0.018 \)).\textsuperscript{[35]}

In a large systematic review\textsuperscript{[33]}, two studies reported, in part, on clinical outcomes (Chiarelli et al., 1990; Peck et al., 2004). The study by Chiarelli et al. (1990) showed no difference between the early and late fed groups for length of stay (69.2 ± 10.4 days versus 89.0 ± 18.9 days; \( P > 0.5 \)). Likewise with Peck et al. (2004) no significant differences, as reported by standard deviation (SD), were noted with the early and late fed groups in regards to number of infections (\( P=0.9 \)), days receiving antibiotics (\( P = 0.9 \)), ventilator days (\( P = 0.4 \)), intensive care unit days (\( P = 0.8 \)), length of acute stay days (\( P = 1.0 \)) and mortality (\( P = 0.7 \)). Regarding complications, two studies as well (Chiarelli et al., 1990; Peck et al., 2004) examined and reported on the complications of early enteral nutritional support. In the Chiarelli et al. (1990) study, intestinal complications were observed in two patients in the early fed group (toxic ileus and gastric micro-ulcerations) and in two patients in the late-fed group (vomiting and pseudomembranous colitis) between days 35 and 44. Thirty-three blood cultures were positive of various bacteria in seven late-fed patients, and five blood cultures were positive in early fed patients. Whereas Peck et al. (2004) noted that there were no significant differences, reported using SD, between the early and late groups with respect to tube feeding intolerance (\( P \leq 0.9 \)), incidence and duration of diarrhoea (\( P = 0.3 \)) aspiration events (\( P = 0.2 \)), or the need for total parental nutrition (\( P = 0.4 \)).\textsuperscript{[33]}

14
Practice Management Guidelines for the Management of Pain by the Committee on the Organization and Delivery of Burn Care of the American Burn Association recommends that once intravenous access is obtained and resuscitation started, intravenous opioids should be administered. Background pain is best managed through the use of long-acting analgesic agents. Breakthrough pain is addressed with short-acting agents via an appropriate route. Ketamine can be used for extensive burn dressing changes and procedures such as escharotomies. Anxiolytics such as benzodiazepines decrease background and procedural pain. For patients requiring mechanical ventilation, a propofol infusion will provide sedation but not analgesia. All medications should be given intravenously, orally, or rectally due to erratic absorption with intramuscular/subcutaneous administration. [26, 27, 28] It is estimated that up to 52% of burn patients have chronic pain. [37]

It has been proven that burn patients who are admitted to burn center with an in-hospital rehabilitation facility show better functional outcomes and shorter lengths of stay when compared to centers that do not have rehabilitation functions. [21,38] Interestingly, one study [18], unearth common initial clinical variables that will assist the physician to make an educated decision regarding the patient rehabilitation transfer potential. And, the variables found to predict rehabilitation most significantly were the execution of a surgical procedure, the length of stay in hospital and the existence of an inhalation injury. Also, shows that patients who were sent to rehabilitation were significantly more prone to be one of the following: extensively burned (40–89% TBSA, p < 0.0001), suffering from concomitant trauma (p < 0.0001), suffering from an inhalation injury (p < 0.0001), in need of ventilation (p < 0.0001), and in need of ICU treatment (p = 0.0005). [18]

In the study by Vieira de Campos et al. [29], when the general characteristics of the patients according to survival were evaluated, factors that were non-significantly associated with mortality were: age (too little sample (N=13, 8% of the total) of patients above 60 years old to statistically evaluate age as mortality factor), gender, type of injury other than burn, interval time from injury to admission, associated trauma (bone fractures, brain injury and chest and/or abdominal blunt trauma), comorbidities (stroke, diabetes mellitus, hypertension, alcohol or drug abuse). On the other hand, factors significantly associated with mortality were: SAPS3, APACHE II, ABSI, Ryan Score, SOFA points (denotes sequential organ failure assessment), systolic blood pressure at admission, %TBSA, fire burn, inhalation injury, suicide attempt, escharotomy. [29] Also during ICU days, at the 1st day Non-survival was related to higher dosages of norepinephrine (among patients who used vasopressors), higher cumulative fluid balances, lower diuresis and mechanical ventilation; and at the first week, we can add other factors related to non-survival such as higher creatinine values, lower platelets counts, and lower PaO2/FiO2 ratios. [29] In order to determine the factors associated with hospital mortality a logistic regression model was used and showed that in the ICU admission hierarchy exists an association
between mortality and a suicide attempt, higher SAPS 3 or TBSA. The first day hierarchy data added the urinary output to those variables. The first week hierarchy added the cumulative fluid balance to the factors associated with hospital mortality. [29]

Depending on the country income (low, middle or high) the final outcome for mortality differs. For example, in the present study [29], mortality for a similar TBSA% (28%) was higher when compared to Spain which yielded a 17.6% mortality rate in ICU for this kind of burn patients. [29] In accordance with this mortality varies considerably among different populations (range, 1.4% to 34%, with a decreasing trend over time), and clearly correlates with an increasing mean total burned surface area. [30]

In pediatric patients, the burn cutoffs were as follows: 60% (TBSA burned) for MOF, 55% for the presence of at least two burn wound infections/contaminations, 85% for sepsis, 55% for mortality, 60% for ARDS, and 65% for pneumonia. For adult patients, the cutoff burn size for MOF was around 50% TBSA burned. The cutoff for at least two burn wound infections/contaminations was around 45% TBSA, whereas the cutoff for sepsis was also around 50% TBSA burned. Mortality had a cutoff of approximately 45% TBSA burned. For pneumonia and ARDS, the cutoff was about 35% TBSA burned. These results indicate that the burn size associated with an increased risk for severe morbidity is approximately 40–50% TBSA burned. Elderly patients had the lowest survival cutoff at around 30% TBSA, but the results from this trial are non-conclusive because of low patient numbers. [36]

Pediatric patients also exhibited the quickest wound healing, as reflected by shorter ICU stays. Children stayed in the ICU an average of 0.5 days per percent burn, which is remarkably short. In contrast, adults stayed 1 day per percent burn. It is worth noting that length of stay used to be almost 2 days per percent burn (20), indicating that the implementation of protocolized care has shortened hospitalization. [36]

One large study, [39] connects several factors to survival at the first day, the first week and the first month after a burn injury. Its findings show that such factors as older age, increased %TBSA, elevated amount of fluids during the first 24 hours and a high injury severity score (ISS) are highly associated to mortality, as well as other factors such as low initial systolic blood pressure measurement, abnormal Glasgow coma scale (it was pointed that <13 point carry a significant risk factor for an elevated mortality), intubation, low SpO2, hypothermia and metabolic alkalosis all carry an elevated risk of mortality. Surprisingly, there was no an inverse relationship between inhalation injury and survival in contrast to previous studies. Interestingly, an elevated amount of fluid during the first 24 hours after injury even led to statistically significant long-term effects (at 6 month after injury) on mortality, being deleterious. [39]
METHODOLOGY AND METHODS

This is a retrospective study of 29 cases with severe burn injuries (>20% TBSA) who were treated at the intensive care unit of Kauno Klinikos, Lithuania. All patients were seen in the emergency room between 2012 and December 2016 and they were identified from emergency and intensive care unit case notes and registries. The collected data included: age, gender, ICU length-of-stay, localization, total area and degree of burn wound, nutrition strategy, treatment strategy, fluids administered during the first 24 hours after the burn injury, comorbidities, and COHb levels. The clinical outcomes collected were the discharge characteristics for survival (home-outpatient rehabilitation vs. inpatient rehab) and mortality. These data were reviewed and recorded in a datasheet and subsequently analysed using a standard Microsoft Excel spread sheet. For a more profound statistical analysis a free period version of SPSS (SPSS_Stats_trial_19_win64_en) was used. Continuous variables were reported as mean (SD) or median and categorical variables as count (n) and percentage. A two-sided p value < 0.05 was considered to be statistically significant. A logistic regression binary model was performed to determine if some of the independent variables were statistically significant for the prediction of the final outcome. For those whose p value was <0.05, the prognostic value has been calculated. The measure of association hereby used is the odds ratio with confidence intervals of 95%. It is important to point out that my small sample of cases could favor statistical implausible results.
## RESULTS

Overall demographics and patient characteristics: A total of 29 patients met the inclusion criteria and were included in the research work. The patients ranged in age from 23-86 years old, with a mean age of 53 years (SD 95%: ±19). The majority of the patients were male n=20 (69% of the total), while female patients were n=9 (accounting for 31% of the total). The average time they spent in the ICU department was 43 days.

<table>
<thead>
<tr>
<th>CASE</th>
<th>AGE</th>
<th>GENDER</th>
<th>ICU LOS (days)</th>
<th>%TBSA</th>
<th>BURN DEGREE</th>
<th>ALIVE</th>
<th>DEAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69</td>
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<td>40</td>
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<td></td>
</tr>
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<td>60</td>
<td>IIIº</td>
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<td></td>
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<tr>
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<tr>
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<td></td>
<td>yes</td>
</tr>
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<td>45</td>
<td>29</td>
<td>IIa-IIIº</td>
<td></td>
<td>yes</td>
</tr>
</tbody>
</table>

Table 2
(range: 1-142; SD95% ±41) and the mean ICU LOS (intensive care unit length of stay) for the survivors was 71 days (SD95,±37), while the mean ICU LOS for the non-survivors was 16.6 days (SD95,±22). The final TBSA% ranged from 20 until 95% with a mean of 51% (SD95% ±23%), and a median of 46%. The reported degrees of burn injuries were up to III°. Overall mortality in our ICU department for severely burnt patients was 51.72% (15 out of 29). Demographical data and injury characteristics for the combined population, survivors, and non survivors are shown in Table 2.

The most common type of injury was IIA-IIB-III° including several burn degrees distributed along the whole TBSA, and it was found in 14 patients overall (48,28%). 28 out of 29 patients reached a III° injury, out of those 15 did not survive (53,57%). While one patient reached up to IIB° injuries, and this one survived.

**Outcomes according to different variables:**

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>p value</th>
<th>OR [odds ratio]</th>
<th>95% CI [confidence interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>mean 44 (SD95, ±17)</td>
<td>mean 62 (SD95,±17)</td>
<td>0.0234</td>
<td>1.057</td>
<td>1.0076-1.1099</td>
</tr>
<tr>
<td>Male</td>
<td>55% (n=11)</td>
<td>45% (n=9)</td>
<td>0.2861</td>
<td>0.409</td>
<td>0.0792-2.1136</td>
</tr>
<tr>
<td>Female</td>
<td>33.33% (n=3)</td>
<td>66.66% (n=6)</td>
<td>0.2861</td>
<td>2.444</td>
<td>0.4731-12.629</td>
</tr>
<tr>
<td>III° injury</td>
<td>46.42% (n=13)</td>
<td>53.57% (n=15)</td>
<td>0.2967</td>
<td>1.432</td>
<td>0.4923-2.4423</td>
</tr>
<tr>
<td>%TBSA</td>
<td>mean 36.5 (SD95±11.2)</td>
<td>mean 64.75 (SD95,±22.8)</td>
<td>0.0100</td>
<td>1.098</td>
<td>1.0227-1.1796</td>
</tr>
<tr>
<td>COHb levels</td>
<td>mean 2.14 (SD95,±0.99)</td>
<td>mean 6.95 (SD95,±11.31)</td>
<td>0.5397*</td>
<td>1.071</td>
<td>0.8605-1.3325</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>p value</th>
<th>OR [odds ratio]</th>
<th>95% CI [confidence interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>COHb levels</td>
<td>median 1.7</td>
<td>mean 1.55</td>
<td>0.5397*</td>
<td>1.071</td>
<td>0.8605-1.3325</td>
</tr>
</tbody>
</table>

Table 3. *The median was used for calculating COHb levels p value.*

In table 3, it is shown how non-survivors were older and predominantly of female sex. They had more extensive burns (higher %TBSA), and apparently a higher COHb level in serum. Overall, they spent less time in the hospital.

Statistically, it has been found that several variables are independently associated with a higher risk of mortality (measured as odds ratio with a 95% confidence interval range). These variables which were statistically significant are: an increase in age, %TBSA burnt and the development of shock, sepsis or acute kidney failure. See table 3.

In figure 2, it is shown the most common complications that the patients suffered during their hospital admission. It’s remarkable that the totality of the patients who developed MOF died, as well as a big percentage of the patients who developed shock (mortality was 93,33%), sepsis (mortality was 83,33%) and AKF (mortality was 90%) also died.

Table 4 shows which complications are associated with a higher risk of mortality. These variables which were statistically significant are: the development of shock, sepsis or acute kidney failure.
Mainstays of treatment and its outcomes:

These are shown in figure 3, where we can observe how those received a determined type of treatment like fasciotomy, invariably died. Also it is seen a high mortality in those who received stress ulcer (mortality 83.33%) and thromboembolism (mortality 76.92%) prophylaxys, those who used opioids (mortality 80%), vasopressors
(mortality 90%), renal replacement therapies (mortality 88.98%) and finally those whose electrolyte disturbances (mortality 83.33%) were corrected.

The mortality among those who received parenteral nutrition is higher (58.33%) than those who received enteral (53.33%). Data is shown in figure 4.

Statistical analysis has shown that the nutrition strategy is not statistically significant (p-value is 0.0955) for the prediction of final outcome.

<table>
<thead>
<tr>
<th>Fluid volume</th>
<th>OVERALL</th>
<th>ALIVE</th>
<th>DEAD</th>
<th>p value</th>
<th>OR [odds ratio]</th>
<th>95% CI [confidence interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>13.9 liters</td>
<td>10.93 liters</td>
<td>15.4 liters</td>
<td>0.011028</td>
<td>1.314</td>
<td>1.0645-1.6226</td>
</tr>
<tr>
<td>SD</td>
<td>5.36 liters</td>
<td>3.7 liters</td>
<td>5.01 liters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>[6-24.5]</td>
<td>[6-19.8]</td>
<td>[8.08-24.5]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In table 5, an analysis of the fluid replacement therapy during the first 24 hours is shown. The mean fluid administered during the first 24 hours in liters was 13.9 liters (SD 95: ±5.36) with a range between 6 and 24.5 liters administered for the totality of cases. Also the characteristics of both the survival and the non-survival group are shown. The most used types of fluids where Ringer’s solution and NaCl 0.9% solution. Other fluids administered were NaHCO3 4.2% solution, dextrose 10% solution and KCl 7.45% solution, although these accounted for small amounts overall.

Type and volume of fluid replacement therapy administered during the first 24 hours after hospital is associated statistically with mortality.
DISCUSSION OF THE RESULTS

This case series has yielded a high mortality rate. More than half of the patients (51.72%) have not survived after hospitalization in the ICU department of our clinic in Kauno Klinikinine Ligonine. This could mainly be due to the fact that all our patients were of major severity in the ABA classification. \[10\]

Also there are studied factors associated with an increased mortality which were present in most of our patients, such as quite elevated age, with a mean of 53 years, a TBSA >20% with a median TBSA of 46%. The LA50% in this research work is 50%.

It is well studied that an increase in age or %TBSA is associated with mortality in burn patients, \[29,39\] Some hypothesis include that the loss of the protective skin barrier leads to massive loss of protein rich fluid, hypothermia, infection and pain, as well as immobility (with its indirect complications). \[42\]

It is relevant to emphasize that burn size is important to assess as it influences the size of the inflammatory response (vasodilatation, increased vascular permeability) and thus fluid shift from the intravascular volume. The size must be estimated to calculate fluid requirements. Ignore erythema. Burn depth determines healing time/scarring; assessing this may be hard, even when experienced. The big distinction is whether the burn is partial thickness (painful, red, and blistered) or full-thickness (insensate/painless; grey-white). Remember that burns can evolve, particularly over the 1st 48 hours. \[12\]

In the section of results, table 3 shows the outcomes for different variables. Again, age and TBSA% are higher on the patients who did not survive.

ICU length of stay was way shorter in the patients who did not survive, and I guess this is mainly due to the fact that surviving patients stayed in ICU a longer period because our sample contained severely burned patients who need and benefit from a special long-term care in our department, while the dead patients usually suffered from a prompt death. COHb levels have also been recorded, showing a higher average in those who did not survive. However, the sample was small (n=9) with an outlier in the mortality group. Because of this, the median was also calculated and now this one was a bit smaller for the mortality group.

Also the female: male mortality ratio was balancing for the female side, who had a 66.66% mortality in comparison with the 45% mortality for men, although a more thoughtful study including all the variables accompanying the male and female group, such as %TBSA, age, degree of injury, complications, etc should be evaluated in order to properly compare both groups and speculate if gender alone is a risk factor for mortality in this kind of patients. Nevertheless, some articles already hypothesize with the reasons for sex dimorphism, yet unknown. A possible theory relates to the differences in body composition between males and females. Females tend to have more extra-abdominal fat and consequently are at increased risk of split skin graft failure (following burn wound excision). \[42\]
Let’s emphasize that burn patients receive a larger amount of fluids in the first 24 h than any other trauma patients because of the pathophysiological mechanisms occurring in the injury.

In table 3 it is shown that patients who survived received a smaller amount of fluids during the 1st 24 hours after the burn injury than those who didn’t. This is supported by the strategy used by administering fluids (the use of the Parkland formula), where an increased in TBSA% leads to a greater administration of fluids. Since TBSA% is probably the greatest individual predictor of mortality, it is obvious that those patients who received more fluids were also those who had more probabilities to die. We do not acknowledge the amount of fluids the patients should have received during the first 24 hours by the Parkland formula, since the weight of the patients was not recorded. As a result, it was not possible to compare the fluids administered with the “ideal” of fluids which should have been administered for each patient, nor generate any hypothesis regarding fluid deficit or excess and their final outcome. In the section of results we described the amount and type of fluids received for each patient in the first 24h after the burn injury. Colloids are not used as recommended by current guidelines. Dextrose was added in those patients in whom hypoglycemia was a threat. The mean of fluid administered during the first 24 hours in liters was 13.9 liters (SD 95%: ±5.36) and the median was 12.5 liters. The total amount of fluids is associated with mortality according to a bivariate regression analysis (p value 0.011; OR [odds ratio] 1.314), as shown in table 3. We deduce that this statistical significance, which very similar to %TBSA, is extremely associated with the former and not with some complications related to the “fluid creep” since the amount of fluids given to the patient depends upon the percentage of TBSA affected by the burn.

The degree of the burn injury was also recorded. The outcome according to the degree is shown in table 3. The degree of the injury seems not to affect the final outcome in our results. By calculating the p value, the degree of burn injury was not significantly associated with mortality.

Nevertheless, it is interesting to point out the importance of a full-thickness injury (III-IVº) vs. a partial thickness injury (I-IIº), since one study found that the size of full-thickness, but not partial-thickness, burns was indeed independently associated with mortality, still giving importance to the degree of the burn as a factor to keep in mind while assessing an injury.

Burns cause both systemic and local complications. The major factors contributing to systemic complications are breakdown of skin integrity and fluid loss. Local complications include eschars and contractures and scarring. Meanwhile the most common systemic complications are hypovolemia and infection. Although others can happen, such as metabolic abnormalities (hypoalbuminemia, dilutional electrolyte deficiencies such as hypomagnesemia, hypophosphatemia, and hypokalemia; metabolic acidosis) Rhabdomyolysis or hemolysis can result from deep thermal or electrical burns of muscle or from muscle ischemia due to constricting eschars. Rhabdomyolysis
causing myoglobinuria or hemolysis causing hemoglobinuria can lead to acute tubular necrosis and acute kidney injury. Ileus is also common after extensive burns.\[8\]

When it comes to the complications suffered by our patients, it has been evaluated the most frequent ones and found inhalational injury (n=21), development of infection (n=15), shock (n=15) and acute respiratory failure (n=17) as the most common in our series. On the other hand, the most deadly complications were MOF (mortality 100%), AKF (mortality 90%), shock (mortality 93.33%) and sepsis (mortality 83.33%). Out of all the measure complications, the next have shown to be statistically significant independent prognostic values (shown extensively in table 2): shock (p value 0.0003), sepsis (p value 0.041) and AKF (p value 0.01).

For the inhalational injuries, other studies have proven an association between mortality and risk of mortality for those suffering this kind of injury.\[20\] In this research work, twenty one inhalational injuries were identified, which, although more common among those who died (52%), was not statistically associated with mortality in the bivariate regression analysis.

Regarding the treatment, the most common strategies, used in the totality of patients, included intubation and ventilation and antibiotics, while pain management, as a sum of opioid and non-opioid analgetics was used in 93% of the patients. Nevertheless, we believe there is certain inaccuracy or some omissions in the data from the case histories. For example, according to the registries, 18 patients were cleaned with antiseptics and dressed with bandages, however we believe this information is not reliable, and it is due to a lack of appropriate registration in the clinical case history of the patients, since all the patients should have been cleaned and dressed daily. The same can apply for other cornerstones of treatment in these severely burnt patients, such as in the use pain relief medications at some point during treatment.

Certain types of treatments strategies yielded a high mortality, probably due to the severity of the patient status and not due to complications regarding the administration of such treatment. These are fasciotomy, stress ulcer and thromboembolism prophylaxys, those who used opioids, vasopressors and renal replacement therapies, as shown in figure 3.

An appropriate nutrition in burn patients is essential, as the hypermetabolism occurring in these patients can lead to doubling of the normal resting energy expenditure, enteral nutrition should be started as soon as resuscitation is underway with a transpyloric feeding tube. Patients with burns > 20% TBSA will be unable to meet their nutritional needs with oral intake alone. Patients fed early have significantly enhanced wound healing and shorter hospital stays. In the rare case that precludes use of the gastrointestinal tract, parenteral nutrition should be used only until the gastrointestinal tract is functioning.\[21\]

In the present research work, it has been evaluated the outcome given the type of nutrition, which is shown in figure 4. It was also studied the possibility of a statistically
significant relation between the type of nutrition and final outcome, and was found that the type of nutrition given to the patient is not a predictor of mortality (p value 0.0955).

Interestingly, one study showed that patients fed early did have a shorter ICU LOS [ICU length of stay] (40.7 vs 52.5 days, \( P = 0.03 \)) and decreased wound infection rates (54.5 vs 80\%, \( P = 0.01 \)). \(^{[32]}\) This we assume it is among survivors who were discharged.

It would be engaging to perform a prospective study to determine extent of post burn morbidity in the survival group, as well as a prediction model for those patients who were sent to inpatient rehabilitation.
CONCLUSIONS

- Based on patients’ demographic data, an older age is directly associated with mortality, while the gender of the patient has not given any statistically significant results.
- Based on the severity of tissue damage, TBSA% affected by the burn is directly associated with mortality, the higher TBSA% the higher mortality.
- Based on the complications suffered, shock, sepsis and acute kidney failure are associated with higher mortality of burn patients.
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