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Prognostic factors in patients with burns

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Abstract

There are many various medical scales used in different clinical situations for scoring and prognostication the disease outcome. Burns are a group of heterogeneous disorders, which, depending on severity, may be treated in various settings – from outpatient clinic to intensive care units. Consequently they are also associated with different outcome. Over the years many scales and models were created to assess the prognosis and, in consequence, to help choosing the mode of treatment. Simultaneously constant improvement in intensive care reduces the predictive value of older models. In this paper authors searched the available literature for prognostic factors in burn patients as well as for clinical scales based on that disease.

Key words: prognostic factors, burns, clinical decision-making.

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INTRODUCTION

Prognostic models of patients sustaining various injuries are used in many areas of medical activities. On the clinical side, prognostic models enable optimization of the therapeutic decisions taken, e.g. a need of hospital admission or selection of a treatment centre reference level. On the reporting and scientific side, they enable objective evaluation of the therapy used, monitoring and comparison of therapeutic outcomes, and estimation of treatment costs; moreover, they are an important tool for scientific research [1, 2]. Despite significant advances in therapeutic methods, burns remain a significant public health problem worldwide. According to the World Health Organization, burns account for approximately 300,000 deaths a year throughout the world, the majority of which occur in less developed countries [3]. Data referring to the population of Poland are fragmentary and concern individual centres. An analysis of burns from the Łęczna centre reveals that 377 patients were hospitalized due to burns in the years 2013–2014 [4]. Data on paediatric patients treated in the Pediatric Surgery Clinic of Medical University in Białystok (outpatients and inpatients) demonstrate 357 cases within 6 years [5]. The present paper discusses the prognostic factors and the prognostic models based on them used in patients with burns.

MODELS BASED ON BURN CHARACTERISTICS

The first attempts to use a burn severity index were made in the early twentieth century by Weidenfeld, who also developed the method of estimating the total body surface area (TBSA) affected by a burn. He noticed a positive correlation between the skin surface affected and the risk of death [6, 7]. The idea of the burn severity index was expanded by Bull [8], who sought the possibility of objectively comparing the treatment outcomes achieved in various burn centres. He assessed the results of treatment in relation to the patients' age and the burn surface. Based on case series analysis, he assigned the specific probability of death to specific TBSA values and age. In turn, Baux [9] suggested the sum of TBSA values and age (referred to as the Baux score) as an index of burn severity. The Baux score was interpreted as correlating with the probability of death. The values exceeding 100 were defined as borderline, i.e. considered high, reaching 100% risk of death. The Baux score has gained wide international acceptance and is considered the gold standard for the assessment of burn severity and potential prognosis. Advances in therapy, including new methods of wound management, surgical techniques, antibiotic therapy, wider access to intensive care and specialized burn treatment centres, enabled changes in the interpretation of its values [10]. An attempt to validate the Baux score in the 21st century was undertaken by Roberts *et al*. [11], who compared the treatment outcomes in one specialist centre over 27 years. The obtained data indicate a progressive increase in the surface area affected by burns at which 50% of patients die. It corresponded to the Baux score 110, and the value above which the mortality rate was approaching 100% was estimated at 160 [11].

It should be emphasized that the authors of the above studies, when assessing the prognosis, did not consider the depth of burn. Burns of the first and second degree differ in pathophysiology from full thickness burns (third and greater degree). The latter usually require surgical interventions, which translates into a significant impact of third-degree burns on the predicted mortality [12, 13]. The Japanese Society for Burn Injuries recommends the use of two indices, i.e. the burn index (BI, burn area of full skin thickness + 0.5 remaining burn area) and the prognostic burn index (PBI = BI + age). The lack of wider recognition of this assessment in international guidelines is associated with limitations in clinical validation of indices and low availability of original publications: the studies were based on small groups and published in Chinese and Japanese [14, 15]. In 2015, both indices were evaluated in a group of 17,185 Japanese patients. The PBI was found to be significantly associated with mortality, and this relationship was most strongly expressed for the values > 85 [16].

The coexistence of inhalation injury is the subject of comprehensive research. On the one hand, it is associated with the development of complications, such as pneumonia and atelectasis [17]. On the other hand, it is an additional prognostic factor related to the unfavourable course of burn disease [18]. Osler *et al.* [19] attempted to supplement the original Baux score with the inhalation injury. They analysed the cases of 39,888 patients covering the years 2000–2007; the presence of inhalation injury was found to add to the risk the equivalent of 17 years or a burn with 17% higher TBSA, as compared to cases without inhalation injury. Due to the non-linear relationship between the obtained result and mortality, they additionally proposed a logistic model enabling its calculation. According to the authors, the obtained values should correspond to the results obtained in cases provided with the best available care at the time the scale was created. Another model including respiratory tract involvement, the abbreviated burn severity index (ABSI), was developed based on the analysis of 1352 burn cases. This analysis allowed the emergence of a total of 5 significant variables affecting the prognosis, i.e. gender, age, burn surface, the presence of a full thickness skin burn and the coexistence of inhalation injury. On this basis, a mortality probability model was created [20]. The model was validated by the authors themselves and in studies from other centres conducted in adult and paediatric populations [21, 22]. Lin *et al.* [23] proved the possibility of using ABSI as an indicator predicting the occurrence of acute respiratory distress syndrome. Despite numerous applications in clinical practice, there are casuistic reports emphasizing that its role is only auxiliary when choosing the management option, i.e. to cure a particular patient or provide only palliative care, especially that the treatment methods are constantly being improved [24]. Another model, also taking into account the presence of inhalation injury, was proposed in 1986 by Clark *et al.* [25]; compared with the ABSI this new model is based on a smaller number of parameters; it allows to predict the probability of death depending on the burn size, the patient`s age, and the presence of inhalation damage. Smith and Ryan developed similar scales based on their own material [26]. According to Smith, taking TBSA and age into account enables to predict mortality with an accuracy of 93%. Adding the presence of inhalation injury slightly improves the model's accuracy (93.3%). The above results are somewhat divergent from those cited earlier [19]. The model proposed by Ryan [1] is another attempt to simplify the assessment of a burn patient. It identifies 3 risk factors: age over 60 years, burns exceeding 40% TBSA and the presence of inhalation injury. Each subsequent risk factor increases the predicted mortality from 0.3% to 6%, 33% and 90%, respectively. McGwin [27] expanded these two models with the presence of pneumonia and of another injury coexisting with the burn. The advantage of his model was the use of two extensive databases, i.e. the National Burn Repository Report and National Trauma Data Bank, enabling the analysis of data of 68,661 patients. However, this model has been criticized because of poor evidence of a significant improvement in the predictive value, especially in the context of patients at high risk assessed with some other scales. For this reason, Thombs [28] proposes not to extend the existing models with the aforementioned 2 variables due to the lack of convincing evidence of a significant improvement in predictive value, compared to classic scales. The Ryan model [1] has been subjected to another improvement attempt. To improve predictability, the initial 60-year and 40% TBSA thresholds were categorized every 10 years and 10%, respectively. The model was developed based on the Belgian data from 1999–2003, covering a cohort of 5,246 patients with burns. Subsequently, it was validated on a group of 981 patients from 2004. During the validation according to the scale, 40 deaths were predicted, 42 patients died. This scale and its interpretation are presented in Table 1 [29]. Kim *et al.* [30] polemicized with the view on the importance of inhalation injury in the context of burn assessment. They pointed out the lack of an unambiguous definition; therefore, the diagnosis is based on history taking and simple observations during the physical examination, which makes it potentially subjective. In the analysis of risk factors in their group of patients, they were unable to prove the prognostic value of inhalation injury, or

TABLE 1. The Belgian Outcome in Burn Injury (BOBI) scale and corresponding probability of death. Based on [29]

Grade	0	1	2	3	4	
Age (years)	< 50	50–64	65–79	≥ 80		0–1
TBSA (%)	< 20	20–39	40–59	60–79	≥ 80	0–4
Inhalation injury	No			Yes		0–3
TOTAL						0–10

	0	1	2	3	4	5	6	7	8	9	10
Probability of death	0.1%	1.5%	5%	10%	20%	30%	50%	75%	85%	95%	99%

TBSA – the total body surface area (affected by a burn)

the value of carboxyhaemoglobin and the ratio of PaO_2 to FiO_2; however, the use of mechanical ventilation was prognostically significant. Therefore, the authors suggest to include the need for mechanical support of breathing instead of the presence of inhalation injury.

The previously mentioned role of predictive models as a method of selecting a treatment centre requires a scale characterised by maximum simplicity, with acceptable sensitivity and specificity. Godwin and Wood [31] attempted to improve the Baux score so that it could meet these requirements. They proposed a 3-point scale for assessing the severity of a patient's airway injury, where the patient: 1 – maintains saturation, assessed by pulse oximetry, while breathing atmospheric air, 2 – requires a mixture containing 40% oxygen to maintain saturation, 3 – does not maintain saturation despite using the mixture containing 40% oxygen. The addition of 20 times the degree of airway injury to the Baux score in the group with more than 30% TBSA increased the model sensitivity to 84%. At the same time, the specificity of the was 89%.

Bronchoscopy image of the airways

Due to the proven prognostic significance of the coexistence of inhalation injury, attempts were made to use an objective assessment of this burn complication in predicting mortality. The gradation criteria of bronchial tree injury were proposed by Endorf in 2007 [32]. They are listed in Table 2. The scale was evaluated in a group of 32 patients. The relationship between the value obtained on the scale and the occurrence of acute respiratory distress syndrome (ARDS), longer mechanical ventilation time, and the trend towards multi-organ failure and higher mortality were demonstrated. In the study group, there were no patients with a fourth-grade burn [33].

TABLE 2. Bronchoscopic criteria for assessing the inhalation injury in burned patients. Based on [32]

Grade	Description
0	Lack of carbon deposits, swelling, redness, excess of secretion, obstruction
1	Slight or speckled carbon deposits or redness in the proximal or distal bronchi
2	Medium-grade carbon deposits, redness, excess bronchial secretion with or without bronchial obstruction
3	Severe inflammation with fragile mucous membranes, abundant carbon deposits, bronchial secretions, bronchial tree obstruction (any trait or combination)
4	Features of mucosa exfoliation, necrosis, obstruction of the bronchial lumen (any feature or combination)

Spano had a larger group of patients subjected to bronchoscopic evaluation [34]; her retrospective analysis concerned 160 patients treated between 2007 and 2014. The bronchoscopic assessment of changes referred to as high grade (i.e. grade 3 and 4) was found to be associated with poorer oxygenation in the first post-injury days and longer mechanical ventilation. The author suggests that further research and evaluation should primarily include the differences found in scale-based assessment between individuals performing bronchoscopy, and only then comparing the results on a scale with the results of treatment.

Comorbidities

Comorbidities are another factor analysed as having an impact on the outcomes of burn disease treatment. In the study by Heredero *et al*. [35], a correlation between pre-existing chronic disease and mortality was demonstrated, which was most evident in patients with neurological diseases. A similar analysis of 2017 showed a higher probability of death among patients with multiple comorbidities. In the group of patients > 65 years, the comorbidity of chronic obstructive pulmonary disease was found to be significantly positively correlated with poor prognosis [36].

GENERAL RISK MODELS

The models described above were developed for patients with burns. There are also general scales designed for assessing patients in severe condition that can be used in burn cases. The Acute Physiology and Chronic Health Evaluation II (APACHE II) developed by Knauss in 1985 is one of such scales [37]. Its evaluation by Gomez *et al*. [38] in a group of patients with burns demonstrated that this scale, together with age, the surface of a full- as well as partial -thickness burn, and gender, was the strongest independent risk factor for death. Another analysis highlighted the clinical usefulness of the APACHE II score even though it did not include burn-specific variables [39]. The APACHE III scale developed in 1991 to revise the previous version, was also evaluated in the group of burn patients [40]. The retrospective analysis confirmed its usefulness in this group of patients. Nevertheless, the authors emphasize that a prospective analysis has still not been carried out [40].

The Sequential Organ Failure Assessment (SOFA) score is still another scale, developed to assess organ failure [41]. It was used by Nguyen *et al*. [42] in a group of patients with at least 40% TBSA involvement. Multi-organ failure syndrome was diagnosed in 45.30% of hospitalized patients and was also present in 60.37% of patients with concomitant inhalation injury. The authors showed high mortality of patients with the SOFA score of 6 and more. In addition, the severity of organ failure correlated with TBSA involvement, burn surface area of full skin thickness, and age.

An alternative scale for assessing organ failure is the Multiple Organ Dysfunction Scale (MODS) [43]. The Gomez analysis [38], mentioned above, did not show a significant correlation between the MODS value and mortality in the group of patients with burns. However, on the basis of validation of symptoms and scales, Gomez proposed the Fatality by Longevity, APACHE II Score, Measured Extent of Burn, and Sex (FLAMES) model which allows to predict the probability of death based on age, sex, APACHE II value, I–II and III degree burn surface. In a large comparative analysis with other scales already mentioned, the FLAMES model showed the highest adequacy (AUC 0.96) [38, 39].

LABORATORY TESTS

In addition to the above-mentioned indicators, numerous studies have been conducted on the use of morphological and biochemical determinants, including inflammatory markers, in predicting the course of burns. One of the inflammatory parameters determined was the level of procalcitonin, as its increase was observed in burned patients. In the study of patients with at least 30% TBSA, the highest value found on the first post-burn day correlated with the severity of the patient's condition, but not with the presence of inhalation injury. The authors failed to demonstrate a link between an early increase in procalcitonin levels and the developing septic process [44]. Similar conclusions were reached by Lavrentiev *et al*. [45], who proved the prognostic significance of the maximum value of procalcitonin concentration achieved during hospitalization based on serial daily determinations. Based on their data, they also proposed a cut-off value of 1.5 ng mL^{-1} as diagnostic for sepsis developing in a burned patient [45]. On the other hand, studies of the paediatric population showed too low sensitivity of procalcitonin concentration for the diagnosis of sepsis in burned children. C-reactive protein (CRP) and platelet counts in this population enabled to establish the diagnosis 0.8 days earlier than based on procalcitonin [46]. Moreover, serial measurements of interleukin 8 and 10 (IL-8, Il-10) were performed. Interleukin-8 showed the highest concentration immediately after the burn, while IL-10 reached its peak between the 5th and 9th day after injury. Higher concentration values indicated a lower probability of survival. Furthermore, the maximum values of IL-10 concentration showed statistically significant differences in the groups of patients with burns involving less and more than 50% of TBSA [47]. The maximum concentration of another cytokine, the tumour necrosis factor alpha (TNF-α), observed in a Japanese population study also correlated with mortality and, additionally, with the size of the body surface area that was burned [48]. In contrast to the above results, the Carsin findings [44] demonstrate that the TNF-α concentration did not increase significantly during the first 7 post-burn days. In another study, based on determinations of another interleukin, interleukin 1β, in the blood and the number of macrophages at the site of thermal injury, the septic predictor index was developed to predict the occurrence of septic complications in the study sample [49]. Nevertheless, according to some other authors the results obtained should be validated in a larger group of patients [50].

Platelet counts were also examined in connection with the development of sepsis and prediction of the disease course. Case reports and studies based on small groups of patients reported significant changes in platelet counts in burn patients [51, 52]. According to Gajbhiye *et al*., a decreasing trend in platelet counts was observed immediately after thermal injury; in survivors, an increasing trend was found during therapy. In fatal cases, the opposite tendency was observed – there was a continuous decrease in platelet counts, which did not correlate with the size of the burned area but remained associated with developing sepsis. The prognostic role of the sustained decreasing trend in platelet counts has also been confirmed in prospective studies [54]. In the group of patients studied by Pavic [55], in contrast to the Hindu group described above, decreases in platelet counts were significantly higher in patients with burns exceeding 10% TBSA, as compared to the group with a smaller burn area. Thus, there was a correlation with the size of the burned area. The authors suggest frequent platelet measurements between day 1 and 4 after burns, due to the highest dynamics during this period and the potential prognostic role. Peripheral blood cytometry in patients with 25–40% TBSA burns showed a reduction in T cell count and CD4/CD8 ratio, compared to the control group. This indicates the potential usefulness of T cell counts in the assessment of immunosuppression and indications for antibiotic therapy in burn patients [56].

The presence of neuroendocrine calcitonin-producing cells in the bronchial tree suggested the use of blood calcitonin values as a marker of bronchial tree injury, and thus of airway burns. In the study patients, calcitonin levels poorly correlated with TBSA, yet its levels determined for the first 3 days were significantly associated with mortality. Moreover, a correlation with the inhalation injury was shown, but its diagnosis was based solely on clinical suspicion resulting from risk factors [57]. A significant decrease in serum phosphate concentration is a documented factor increasing the mortality in patients with sepsis [58]. Hyperphosphataemia is a less common condition in patients with acute diseases, including burns. The presence of hyperphosphataemia on admission correlated with worse values of numerous indicators, such as the Glasgow coma scale, APACHE II, or average blood pressure. Clinically, this translated into higher 90-day mortality rates. Further analysis confirmed the independence of hyperphosphataemia in predicting death from other factors, such as the burn surface area [59].

An attempt was also made to develop a complex index based on laboratory measurements of selected serum proteins. Four acute phase proteins – CRP, orosomucoid/α1-acid glycoprotein, prealbumin and albumin – were evaluated to form the Prognostic Inflammatory and Nutritional Index (PINI). The PINI was validated in a group of paediatric patients with burns up to 20% TBSA, in whom it correlated with the burned TBSA [60]. Re-evaluation in the group of paediatric and adult patients demonstrated a correlation with mortality; moreover, the clinical usefulness of the index based solely on CRP and prealbumin determinations was proved.

CONCLUSIONS

There are numerous methods for prognosing the outcomes and estimating the risk of death among patients with burns. The models based on the specificity of burns mainly rely on the extent of skin burns, the co-occurrence of airway injury, and age, and allow to predict the course of the disease with high probability. The general scales used in patients requiring admission to the intensive care unit are also of high usefulness in burn patients, even though the specific factors associated with the presence of burn disease are not considered in them. The issue of objective assessment of bronchial tree bronchoscopy images is being studied yet the available findings are inconclusive. Despite numerous studies on laboratory determinations and the correlation of their results with prognosis, the costs of determinations should be considered. The cited study of Ryan [1] describes 37 patients with an intermediate risk of death, of which 11 who died were not qualified for resuscitation ("had do-not-resuscitate orders"). In the group of the remaining 26 patients, in whom resuscitation was a treatment option, five died. This highlights the auxiliary role of the scales, which only complement the clinical assessment carried out by physicians.

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