THE ROLE OF COMORBIDITIES ON OUTCOME PREDICTION IN ACUTE BURN PATIENTS

PLACE DES COMORBIDITÉS DANS LES CRITÈRES PRONOSTIQUES DES PATIENTS BRÛLÉS

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SUMMARY. Burn trauma is a leading cause of mortality and morbidity. None of the currently available formulas for mortality prediction take into account the impact of comorbidities on burn patients' outcome. In this study, we evaluate the impact of comorbidities on in-hospital mortality and prolonged length of hospital stay (≥30 days). A retrospective analysis of burn patients' medical records, over a 5-year period, was undertaken. A total of 677 patients were included. The mortality rate was 6.5%. Deceased patients and survivors with length of hospital stay (LOS) of 30 or more days were significantly older, had larger %TBSA burned, were more likely to have inhalation injury and comorbidities, and had higher Charlson Comorbidity Index (CCI) scores. On the multivariate logistic regression models, age, %TBSA burned, CCI score and the presence of inhalation injury were independently associated with mortality and prolonged LOS. In conclusion, the authors suggest that the inclusion of comorbidities should be considered on burn admission scores in an attempt to better predict burn mortality.

Keywords: comorbidities, burn, mortality

RÉSUMÉ. *Les brûlures sont responsables de morbidité et de mortalité élevées. Aucun des scores prédictifs actuels ne prend en compte les comorbidités des patients. Cette étude évalue leur impact sur le devenir et la durée d'hospitalisation prolongée (≥30 jours). Il s'agit d'une étude rétrospective fondée sur l'analyse des dossiers de 667 patients hospitalisés pendant une période de 5 ans, chez lesquels la mortalité s'est avérée être de 6,5%. Les patients décédés et à la durée de séjour ≥30 jours étaient significativement plus âgés, brûlés sur une plus grande surface, avaient plus fréquemment inhalé des fumées et avaient plus de comorbidités (reflétées par un score de Charlson- SCh- plus élevé). En analyse multivariée, l'âge, la surface brûlée, l'inhalation de fumées et le SCh était des facteurs indépendants de séjour prolongé et de mortalité. Les auteurs suggèrent donc d'inclure les comorbidités dans les scores prédictifs concernant les brûlés.*

Mots-clés : *comorbidités, brûlures, mortalité*

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Introduction

Burn injuries are a major cause of morbidity and mortality.[1] Despite the improvement in overall survival, mortality in patients with severe burn injuries remains high.[1,2] When burn injuries affect more than 15% of total body surface area (TBSA), a consequent acute phase response starts, potentially leading to a widespread systemic inflammation and eventually multiple organ failure. The final outcome depends on the patient's physiological reserve, which naturally decreases with age and comorbidities.[1]

The length of hospital stay (LOS) represents a severe burden for patients, families, providers and hospitals.[3] Many studies have shown that age, burn size and inhalation injury are major predictors of mortality and prolonged LOS following acute burn injury.[4] The role of comorbidities in relation to final outcome (in-hospital mortality and LOS), albeit less well studied, should not be ignored.[5]

During the last century, over 40 mortality prediction models for severe burn patients have been studied and validated.[6] The most widely used formulas are based on a small set of variables that can be easily screened for at time of admission of the burn patient.[6,7] Traditional models have used age and percentage of TBSA burned as their main predictors.[6,8] As burn care has evolved, new models included a wider variety of variables, like the presence of full thickness burn, inhalation injury and gender.[8] Besides the fact that none of the currently available formulas consider the impact of comorbidities on burn trauma outcome, they all tend to underestimate mortality.[1]

The Belgian Outcome in Burn Injury (BOBI) score is a user-friendly model that predicts the probability of death from acute burns soon after injury has developed, based on simple and objective clinical criteria (age, TBSA burned and inhalation injury) (*Table I*).[9]

One standardized method to score chronic comorbidities is the Charlson Comorbidity Index, also known as the CCI score (*Table II*). The standardized Charlson index has been reported to accurately predict the probability of mortality within 1 year. Each condition is given a score from 1 to 6. A higher score predicts the increased likelihood of mortality.[7,10]

Table I - The Belgian Outcome in Burn Injury (BOBI) score

	0	1	2	3	4	Score
Age (years)	<50	50-64	65-79	≥80	-	0-3
%TBSA	<20	20-39	40-59	60-79	≥80	0-4
Inhalation injury	No	-	-	Yes	-	0-3
Total	4.9%	-			-	0-10

Table II - Charlson comorbidity index score system

Comorbidity	Score
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Rheumatologic disease	1
Peptic ulcer disease	1
Mild liver disease	1
Diabetes without chronic complications	1
Diabetes with chronic complications	2
Hemiplegia or paraplegia	2
Renal disease	2
Solid tumor	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
AIDS/ HIV	6
Metastatic solid tumor	6
Maximum comorbidity score	37

The relative impact of pre-existing comorbidities on outcome following burn injury remains poorly studied.[7,11] Our purpose in this study is to assess the factors influencing in-hospital mortality and length of hospital stay and to analyze the relative impact of comorbidities, using the CCI score. We hypothesized that preexisting comorbidities would have a significant effect on burn injury outcome.

Materials and methods

Study design

A retrospective analysis of medical records of burn patients admitted to our Unit during a 5-year period (January 2014 - December 2018) was undertaken. All patients above the age of 18 years with acute burn injuries admitted to our Unit were included. Patients admitted to another facility for >24h prior to admission to the study center, and those with a non-burn diagnosis (necrotizing fasciitis and

Steven-Johnson syndrome/ toxic epidermal necrolysis) were excluded.

Baseline demographics, burn characteristics and comorbidities

The following data were collected for all patients: age, gender, burn mechanism, the presence or absence of inhalation injury, percentage of TBSA burned, LOS, in-hospital mortality, and the presence of comorbidities. Inhalation injury was diagnosed based on exposure to smoke in an enclosed space and clinical findings, which included carboxyhemoglobin levels and bronchoscopic findings. The CCI score and the BOBI score were calculated for each patient. The BOBI score ranges from 0 to 10 points, by dividing increasing age in 4 groups (0-3 points), TBSA in 5 groups (0-4 points) and presence of inhalation injury (3 points). It results in 11 risk categories, with probabilities of death ranging between <1% and >90%.[9]

Prolonged LOS was defined as LOS ≥30 days for patients who survived the burn injury.

Outcomes

The primary outcome for this study was to evaluate the impact of comorbidities (using the CCI score) on in-hospital mortality.

Two secondary outcomes were defined: to evaluate the discriminative power of the mortality prediction models, both BOBI and the new mortality prediction model (which includes preexisting comorbidities), and to assess the impact of comorbidities on prolonged length of hospital stay (≥30 days) among survivors.

Statistical analysis

Statistical analysis was carried out using STATA. Continuous variables were compared between two groups using the Mann-Whitney U test. The Chi-square test was used to assess association between discrete categorical variables. Multivariate logistic regression analysis was used to determine associations between categorical outcome variables and independent continuous or categorical predictor variables. A probability value of $p<0.05$ was considered statistically significant. The BOBI's discriminative power for mortality prediction in the study population was evaluated by assessing Receiver Operator Characteristics (ROC) curve. A ROC curve for the logistic regression model was also plotted and the area under the curve (AUC) was calculated to provide a measure of the model's discriminative ability. AUC ranges from 0 to 100%, where 100% indicates perfect discrimination and 50% indicates chance discrimination. Values above 80% are considered good discrimination. DeLong test was used to compare the AUC of both ROC curves.

Results

Patient demographics and burn injury characteristics are summarized in *Table III*. A total of 677 adult patients were included in the study, 54.8% of whom were male. The median age was 60 years old, the median percentage of TBSA burned was 7% and the median LOS was 15 days. 11.5% of patients had a diagnosis of inhalation injury and 57.5% of the patients had at least one comorbidity. The overall in-hospital mortality was 6.5%. The most common mechanism of burn trauma was flame injury (54.6%).

Deceased patients were significantly older ($p<0.001$), had larger %TBSA burned ($p<0.001$), were more likely to have inhalation injury ($p<0.00.1$) and comorbidities ($p<0.001$), and had higher CCI scores ($p<0.001$) when compared to patients who survived (*Table III*).

In a multivariate logistic regression model, age, %TBSA burned, CCI score, and the presence of in-

Table III - Baseline patient and injury characteristics

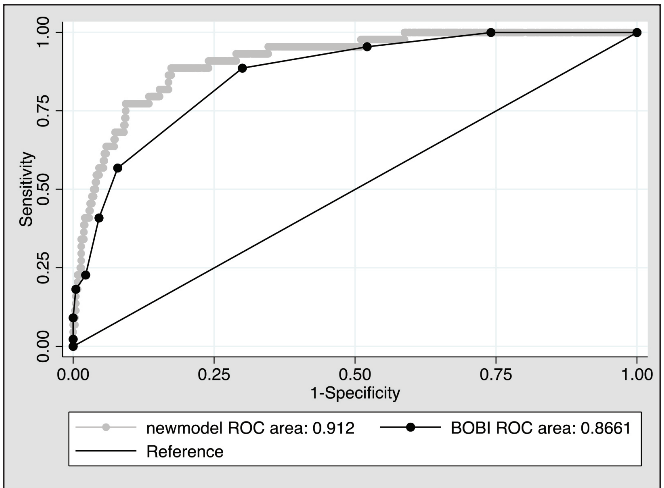
	All (n=677)	Non-survivors (n=44)	Survivors (n=633)	p-value
Age, median [IQR]	60 [44-76]	77 [65-83]	59 [44-74]	<0.001
Gender, male (%)	54.8	54.8	54.6	0.972
%TBSA, median [IQR]	7 [4-14.5]	28 [17-39]	7 [4-13]	<0.001
Inhalation (%)	11.5	40.9	9.5	<0.001
Comorbidities (%)	57.5	84.1	55.6	<0.001
CCI, median [IQR]	1 [0-2]	2 [1-3]	1 [0-2]	<0.001
Etiology (%)				
Fire/flame	54.6	77.3	53.1	<0.001
Scald	32.7	-	-	
Electrical	4.3	-	-	
Chemical	3.5	-	-	
Other	4.9	-	-	

halation injury (*Table IV*) were independently associated with in-hospital mortality.

Table IV - Factors influencing death (primary outcome): multivariate analysis

	OR	p-value
Age	1.07	<0.001
%TBSA	1.09	<0.001
Inhalation	2.94	0.021
CCI	1.56	<0.001

This logistic regression model provided a ROC curve with an area under the curve of 0.912, indicating that the model is excellent at discriminating between mortality and survival in our study population (*Fig. 1*).



	AUC	95% CI
Multivariate logistic regression model	0.912	0.872-0.952
BOBI score	0.866	0.818-0.915
		p-value=0.0542

Fig. 1 - Receiver operator characteristics (ROC) curve of fitted multivariate logistic regression model and of BOBI score for mortality prediction

A second ROC curve was plotted to evaluate the BOBI's discriminative power, with an area under the curve of 0.866 ± 0.025 (95% CI 0.818-0.915) (*Fig. 1*). BOBI, the mortality prediction model used at our Unit, showed a slightly lower discriminative power when compared to this new mortality prediction model based on the multivariate logistic regression (which accounts for the comorbidities using the CCI score), and this difference closely approaches statistical significance (p=0.054).

For the analysis of our secondary outcome, a baseline table between survivors who had a length of hospital stay <30 days and those who were hospitalized for 30 or more days is presented (*Table V*).

Table V - Baseline patient and injury characteristics among survivors

	Survivors with prolonged LOS (n=110)	Survivors with LOS <30 days (n=523)	p-value
Age, median [IQR]	66 [51-78]	58 [43-74]	0.005
Gender, male (%)	56.4	54.5	0.720
%TBSA, median [IQR]	21[10-35]	6 [3-10]	<0.001
Inhalation (%)	26.4	5.9	<0.001
Comorbidities (%)	78.0	52.4	<0.001
CCI, median [IQR]	2 [1-3]	1 [0-2]	<0.001

Age, %TBSA burned, CCI score, and the presence of inhalation injury (*Table VI*) were independently associated with prolonged LOS (30 days or more) among survivors.

Table VI - Factors influencing LOS (secondary outcome): multivariate analysis

	OR	p-value
Age	1.05	<0.001
%TBSA	1.23	<0.001
Inhalation	3.38	0.008
CCI	1.64	<0.001

Discussion

This is a retrospective study that aims to clarify the effect of preexisting medical comorbidities on mortality from burn injury and length of hospital stay among burn injury survivors. Comorbidities are a known outcome influencer in general intensive care patients.[12] Previous studies that examined mortality from burns have identified 3 major risk factors: age, percentage of TBSA burned and inhalation injury.[7,11] Smoke inhalation is commonly considered the strongest predictor of burn mortality[13] and our results support these data. Previous reports showed contradictory results on the effects of comorbidities on burn injury patients' outcome. Lionelli et al.[14] and Wibbenmeyer et al.[15] found no correlation between comorbidities and mortality in an elderly burn patient population. Likewise, Lundgren et al.[11] found no significant impact of baseline medical comorbidities on mortality and that the comorbidities, independent from hospital complications, were not associated with hospital length of stay.

On the other hand, Akhtar et al.[16] demonstrated a significant impact of various comorbid diseases, including cardiac, pulmonary, renal, hepatic and neurological disorders on the length of hospital stay and mortality. Knowlin et al.[7] found a linear increase in the likelihood of death with an increase in CCI. Thombs et al.[4] did a large study in 2007 that looked at the effect of various comorbidities on burn mortality based on the US National Burn Repository (NBR) report on 31338 burn records from 1995 to 2005. Using the Charlson comorbidity index and Elixhauser method of comorbidity measurement, they found that various pre-existing medical conditions affected burn mortality.

Nonetheless, our results showed that comorbidities and, consequently, CCI score, are highly and independently associated with inpatient mortality (OR=1.56 for each 1 point increase in CCI) and longer length of hospital stay in burn patients (OR=1.64 for each 1 point increase in CCI). Preexisting medical conditions were recorded in almost 58% of patients.

It was also shown that age, percentage of TBSA burned, CCI score and the diagnosis of inhalation injury were independently associated with inpatient mortality. BOBI's discriminative power was evaluated and compared to the new logistic regression model, that included CCI along with the variables used in BOBI's formula. Although BOBI score showed a good discriminative power for mortality prediction in our study population, the new mortality prediction model, which accounts for the presence of comorbidities, performed better than BOBI even though it did not reach statistical significance (p=0.054).

This study updates and reviews epidemiology of burn patients treated in a Portuguese major burn center and provides insights into factors associated with mortality and prolonged LOS over the past 5 years. There are some limitations to our study. This is a retrospective review from a single tertiary burn center, which may affect generalizability of the results. Data collection was dependent on chart documentation that may have been incomplete at times. Although the percentage of TBSA burned was reported as an index of burn severity, the study could have been strengthened had we had access to data regarding burn depth. The overall TBSA burned in our study population is relatively low and may not represent correctly large extensive burns. Also, we did not examine the impact of management decisions such as time of surgery. Finally, the Charlson comorbidity index was originally based on the predictive power to estimate mortality in medicine patients[10] and, to the authors' knowledge, it hasn't been validated to surgical or burn patients.

Conclusion

In conclusion, age, TBSA burned, inhalation injury and comorbidities are independently associated with burn patients' mortality and longer length of hospital stay. Regarding mortality prediction, the authors suggest that the inclusion of comorbidities (using, for example, the CCI score) should be considered in burn admission scores in an attempt to better predict burn mortality. Testing this new model in other burn centers (national and international) is the next step in order to validate the model.

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