

## Bronchoalveolar lavage analysis in victims of severe facial burns\*

Análise do lavado broncoalveolar em vítimas de queimaduras faciais graves

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### Abstract

**Objective:** To analyze bronchoalveolar lavage (BAL) specimens of burn victims who inhaled smoke, in order to identify alterations associated with mortality or survival. **Methods:** Eighteen victims of facial burns were submitted to BAL up to 24 h after the event. We investigated cell and protein content, including TNF- $\alpha$ , HLA-DR, CD14, CD68 and iNOS. **Results:** Of the 18 patients submitted to bronchoscopy, 8 (44.4%) died during the follow-up period. The mean age of patients who died was significantly higher (44.7 vs. 31.5 years). On average, the patients who died had burns covering 60.1% of the total body surface area, compared with 26.1% in the survivors ( $p < 0.0001$ ). Of the 18 patients submitted to bronchoscopy, 11 (61.1%) showed endoscopic signs of smoke inhalation injury, and 4 (36.4%) of those 11 died. Of the 7 patients with no signs of smoke inhalation injury, 4 (57.1%) died. The mean number of ciliated epithelial cells in the BAL fluid was significantly higher in the patients who died than in the survivors (6.6% vs. 1.4%;  $p = 0.03$ ). There were no significant differences between the groups in terms of any of the other parameters evaluated. **Conclusions:** The total body surface area burned was a predictive factor for mortality. Increased numbers of ciliated epithelial cells in the BAL fluid, denoting bronchial epithelial desquamation, were associated with higher mortality in patients with facial burns.

**Keywords:** Burns; Smoke inhalation injury; Bronchoalveolar lavage; Epithelial cells; Macrophages; Tumor necrosis factor- $\alpha$ .

### Resumo

**Objetivo:** Analisar o lavado broncoalveolar (LBA) de vítimas de queimaduras que inalaram fumaça a fim de identificar alterações que possam estar associadas à morte ou à sobrevivência. **Métodos:** Dezoito vítimas de queimaduras faciais foram submetidas a LBA até 24 h após o evento, sendo realizadas a análise do conteúdo celular e proteico, incluindo TNF- $\alpha$ , HLA-DR, CD14, CD68 e iNOS. **Resultados:** Dos 18 pacientes submetidos à broncoscopia, 8 (44,4%) morreram durante o seguimento. A média de idade dos pacientes que morreram foi significativamente maior (44,7 vs. 31,5 anos). A superfície corporal queimada foi em média de 60,1% nos pacientes que morreram e de 26,1% nos sobreviventes ( $p < 0,0001$ ). Entre os 18 pacientes submetidos à broncoscopia, 11 (61,1%) apresentaram sinais endoscópicos de lesão por inalação de fumaça, e 4 (36,4%) destes faleceram. Dos 7 pacientes sem sinais de lesão por inalação de fumaça, 4 (57,1%) faleceram. A média do número de células epiteliais ciliadas no LBA dos pacientes que morreram foi significativamente maior daquela dos sobreviventes (6,6% vs. 1,4%;  $p = 0,03$ ). Os demais parâmetros analisados não mostraram diferença entre os grupos. **Conclusões:** A superfície corporal queimada mostrou ser um fator preditivo de mortalidade. O aumento do número de células epiteliais ciliadas no LBA, denotando descamação epitelial brônquica, esteve associado à maior mortalidade de pacientes com queimaduras faciais.

**Descritores:** Queimaduras; Lesão por inalação de fumaça; Lavagem broncoalveolar; Células epiteliais brônquicas; Macrófagos; Fator de necrose tumoral alfa.

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## Introduction

In Brazil, approximately 100,000 patients/year seek hospital treatment due to burns suffered in accidents that occur, for the most part, in the home environment. The conditions in which such accidents occur can cause the resulting injuries to be severe or fatal. Flame burns are the most common, and alcohol is the fuel most often involved in such accidents.<sup>(1)</sup>

The total body surface area (TBSA) burned and the depth of the lesions are factors directly related to prognosis. In addition, factors such as age and airway obstruction caused by smoke inhalation injury (SSI) also affect prognosis.<sup>(1-4)</sup>

Not all signs and symptoms of SII are perceived by the examiner. Dyspnea, hypoxemia, cyanosis, abnormal respiratory sounds and chest X-ray abnormalities might not be present at the initial stage of the treatment of such patients.<sup>(5,6)</sup> In patients presenting symptoms consistent with upper airway injury, SII should be suspected.<sup>(7)</sup>

Determination of carboxyhemoglobin levels, chest X-ray, arterial blood gas analysis, scintigraphy with xenon-133 and pulmonary function tests are of limited value for the diagnosis of SII.<sup>(8)</sup>

In suspected cases of SII, the injury needs to be confirmed so that a prognosis can be determined and protective therapeutic measures, such as intubation and the use of inhaled heparin, can be instituted.<sup>(4,9,10)</sup>

Bronchoscopy is a method that has higher sensitivity and specificity for the diagnosis of SII than does the gold standard—histopathological analysis of a fragment of bronchial mucosa.<sup>(11)</sup> During bronchoscopy, it is possible to safely determine whether there was airway injury or not.<sup>(12)</sup> Mucosal hyperemia, edema, ulcerations or necrosis are endoscopic findings that confirm the diagnosis of SII.<sup>(12,13)</sup> In addition, bronchoscopy plays an important role in the diagnosis of contusion and pulmonary infection, as well as in the treatment of SII, allowing lavage of the tracheobronchial tree to remove soot, other carbonaceous materials and even membranes formed by fibrin, all of which are substances that adhere to the bronchial wall, causing obstruction of the lumen.<sup>(9,14)</sup>

It is believed that, in the presence of SII, there is a significant influx of neutrophils, as well as release of free radicals and production of inflammatory mediators. There seems to be a significant increase in the number of alveolar

macrophages and in the levels of TNF- $\alpha$ .<sup>(15,16)</sup> There is complete or partial desquamation of the tracheal, bronchial and bronchiolar epithelium. These alterations seem to be present in the initial phases of airway SII.<sup>(11)</sup>

The treatment of patients with SII should be initiated at the site of the accident, with the administration of pure oxygen.<sup>(4)</sup> The use of bronchodilators should be initiated whenever there is wheezing or signs of endobronchial secretion.<sup>(17)</sup> Orotracheal intubation should be performed when there is cyanosis or respiratory depression, secretion with laryngeal obstruction, significant thickening of the nasolabial region due to burn or a burn covering the entire neck circumference. If laryngoscopy shows significant mucosal edema, the possibility of using tracheostomy should be evaluated.<sup>(4)</sup> Humidification of the inhaled air and the use of continuous positive pressure are effective measures. The use of nebulized heparin and acetylcysteine reduces the need for reintubation, as well as the incidence of atelectasis and mortality.<sup>(9)</sup> Antibiotics are indicated whenever there are signs of infection. Corticosteroids are not routinely indicated and should be used only in cases of bronchospasm that is unresponsive to the initial measures.<sup>(4,18,19)</sup> Although the use of surfactant, deferoxamine and nitric oxide has proven efficacious in animal models,<sup>(20-22)</sup> clinical studies are needed.

Cytological, immunocytochemical and biochemical analyses performed in bronchoalveolar lavage (BAL) specimens can be useful for determining the pulmonary response to injury and predicting the clinical evolution of patients with SII. Early identification of SII can be the decisive factor in preventing acute respiratory failure and, consequently, in reducing patient mortality.<sup>(1-3,12)</sup> However, the information currently available on this matter comes predominantly from experimental studies in animal models. The objective of the present study was to promote better understanding of this matter by investigating cellular, biochemical and immunological factors in the lungs of victims of SII immediately after the accident (up to 24 h later) and establishing correlations with the prognosis of such individuals.

## Methods

This was a prospective cohort pilot study involving burn victims with initial evidence of

**Table 1** – Clinical description of the groups, with and without smoke inhalation injury, submitted to bronchoscopy.

Characteristic	With SII (n = 11)	Without SII (n = 7)	p	95% CI
Male/female, n/n	6/5	4/3	-	-
Age, years (SE)	34.55 (2.97)	41.86 (6.90)	0.28	-6.63-21.26
Flame burns, n (%)	8 (72.73)	3 (42.86)	0.51	-8.97-12.97
TBSA burned, % (SE)	32.19 (5.26)	56.50 (9.63)	0.028*	2.97-45.64
2nd and 3rd degree burns, %	100	100	-	-
IMV, n (%)	3 (27.27)	4 (57.14)	0.51	-8.97-12.97
Death, n (%)	4 (36.36)	4 (57.14)	0.33	-4.80-8.80

SII: smoke inhalation injury; SE: standard error; TBSA: total body surface area; and IMV: invasive mechanical ventilation.

\*p < 0.05 (Student's t-test).

SII. Patients were selected from among those treated between February 27, 2002 and June 24, 2004 at one of two specialized *Centros de Tratamento de Queimados* (CTQs, Burn Victim Treatment Centers), both located in the city of Rio de Janeiro, Brazil—one at the Galeão Air Force Hospital and another at the Andaraí Municipal Hospital. All burn victims were evaluated within the first 24 h after the accident. The experimental group included burn victims submitted to fiberoptic bronchoscopy with BAL, which was recommended by the clinical team in charge of the treatment of burn patients. Clinical data were collected, as were data regarding outcomes.

The inclusion criteria were as follows: having been burned in an enclosed space, having been found unconscious or presenting symptoms consistent with upper airway injury (nasopharyngeal irritation, hoarseness, stridor and cough); having suffered upper cervical burns, facial burns or burns accompanied by singed eyelashes and singed nasal vibrissae; presenting carbonaceous expectoration; and presenting respiratory sounds, wheezing, rales or cyanosis. Patients presenting hemodynamic instability or having eaten less than 4 h prior to the bronchoscopy were excluded.

All bronchoscopies with BAL were performed by the same professional, one of the authors of the study. The test was performed in order to confirm the diagnosis of SII and in accordance with the protocols previously established by the pulmonology departments involved, based on international standards.<sup>(2,3)</sup>

The material obtained was immediately sent, in sterile vials and packed in ice, to the Multidisciplinary Research Laboratory of the *Hospital Universitário Clementino Fraga Filho*

(HUCFF, Clementino Fraga Filho University Hospital) of the *Universidade Federal do Rio de Janeiro* (UFRJ, Federal University of Rio de Janeiro). The cell counts and the percentage of viable cells were determined using a hemocytometer (Neubauer chamber). The slides were stained by the May-Grünwald-Giemsa method, and differential counts of at least 400 nonsquamous cells were performed. The percentage of each cell type present in the BAL fluid was calculated. The remaining slides were fixed, packed and stored at -20°C for later use. In order to perform cell culture, the pellet was placed in sterile culture plates, which were incubated. After 1, 3 and 24 h, the culture plates were removed from the incubator. The supernatant was removed in duplicate from each plate, centrifuged and stored in identified test tubes at -80°C for later use. In order to perform the immunocytochemical study, the cytocentrifuged material, prepared from the BAL specimens and fixed, was removed from the refrigerator, allowed to reach room temperature (thermal balance), surrounded by a ring made of hydrophobic material and submitted to immunolocalization of molecules relevant to the present study: CD68, HLA-DR, CD14 and iNOS. The levels of TNF- $\alpha$  were determined using ELISA.

The Student's t-test was used for independent samples. Fisher's exact test was used for categorical variables and for sample values lower than five. The level of significance was set at p < 0.05.

The project was approved by the Ethics in Research Committee of the HUCFF/UFRJ School of Medicine, protocol no. 060/00 00, and all participants gave written informed consent.

**Table 2** – Clinical factors related to mortality in burn victims submitted to bronchoscopy.

Characteristic	Patients who died (n = 8)	Patients who survived (n = 10)	p	OR (95% CI)
Male, %	62.5	50	---	---
Age, years	44.75	31.50	0.0369*	(0.91-25.59)
TBSA burned, %	60.21	26.09	< 0.0001*	(26.59-41.64)
2nd and 3rd degree burns, %	100	100	---	---
IMV, yes/no	6/2	1/9	0.0128**	27.0 (1.98-368.6)

TBSA: total body surface area; and IMV: invasive mechanical ventilation. \*Student's t-test; \*\*Fisher's exact test.

## Results

Between February 27, 2002 and June 24, 2004, 78 burn victims with signs of facial burns and of possible SII were treated at the two CTQs that participated in this study. Of those, 18 were submitted to fiberoptic bronchoscopy with BAL, based on the clinical recommendation made by the team of attending physicians.

Of the 18 patients submitted to bronchoscopy, 7 (38.9%) were intubated and submitted to invasive mechanical ventilation. During the study period, 8 (44.4%) of the 18 patients died. Fatal outcomes were strongly related to three of the factors studied: percentage of TBSA burned; age; and development of acute respiratory failure, characterized by the institution of invasive mechanical ventilation. Gender had no influence on patient mortality.

Table 1 presents the clinical description of the group of 18 victims of facial burns, with or without SII, who were submitted to bronchoscopy with BAL. Among the 18 patients suspected of SII and submitted to bronchoscopy, the test

results were normal in 7 (38.9%), and the diagnosis of SII was confirmed in 11 (61.1%). The mean age was higher in the group without SII than in the group with SII ( $41.9 \pm 6.9$  years vs.  $34.6 \pm 3.0$  years;  $p = 0.28$ ). Most (72.7%) of the patients with SII had flame burns. The TBSA burned was significantly greater in patients with normal bronchoscopy results ( $p = 0.028$ ). Of the group of patients with SII, 3 (27.3%) were submitted to invasive mechanical ventilation, as were 4 (57.1%) of the 7 patients without SII. In the group with SII and in the group without SII, 4 patients (36.4% and 57.1%, respectively) died.

The factors related to death in this group of burn victims submitted to bronchoscopy were also evaluated (Table 2). Of the 18 such patients, 8 (44.4%) died. The mean age was significantly higher in the group of patients who died (44.8 years vs. 31.5 years;  $p = 0.0369$ ). The TBSA burned was significantly greater in the patients who died (60.2% vs. 26.09%;  $p < 0.0001$ ). Of the survivors, only 1 patient (14.3%) had been submitted to invasive mechanical ventilation,

**Table 3** – Bronchoalveolar lavage characteristics in burn patients with and without smoke inhalation injury.

Characteristic	With SII (n = 11)	Without SII (n = 7)	p*	95% CI
Volume, mL $\pm$ SE	49.91 $\pm$ 4.35	47.14 $\pm$ 3.3	0.6561	-15.69-10.16
Cells/mL $\times 10^5 \pm$ SE	19.29 $\pm$ 6.77	9.93 $\pm$ 2.59	0.3042	-28.06-9.335
Macrophages, % $\pm$ SE	80.34 $\pm$ 6.61	88.93 $\pm$ 2.71	0.3355	-9.751-26.94
Lymphocytes, % $\pm$ SE	1.34 $\pm$ 0.43	3.70 $\pm$ 1.31	0.0593	-0.1050-4.832
Eosinophils, % $\pm$ SE	0.21 $\pm$ 0.1	0.171 $\pm$ 0.171	0.8445	-0.4382-0.3629
Neutrophils, % $\pm$ SE	15.25 $\pm$ 5.9	2.11 $\pm$ 0.89	0.1002	-29.09-2.826
Epithelial cells, % $\pm$ SE	2.83 $\pm$ 1.33	5.1 $\pm$ 2.5	0.3940	-3.227-7.773
TNF- $\alpha$ in 24-h culture, pg/mL $\pm$ SE	333 $\pm$ 225	0.14 $\pm$ 0.02	0.2738	-970.5-303.6
CD14, % $\pm$ SE	23.5 $\pm$ 5.1	15.3 $\pm$ 6.3	0.3265	-25.37-8.975
CD68, % $\pm$ SE	28.6 $\pm$ 5.1	42.8 $\pm$ 10.3	0.1905	-7.804-36.14
HLA-DR, % $\pm$ SE	26.49 $\pm$ 8.42	29.04 $\pm$ 7.84	0.8385	-23.57-28.67
iNOS, % $\pm$ SE	31.29 $\pm$ 7.31	26.06 $\pm$ 9.91	0.6708	-30.86-20.40

SII: smoke inhalation injury; and SE: standard error. \*Student's t-test.

**Table 4** – Bronchoalveolar lavage characteristics in patients with facial burns, by outcome.

Characteristic	Patients who died (n = 8)	Patients who survived (n = 10)	p	95% CI
Volume, mL	44.38	52.40	0.1765	–20.06–4.006
N of cells, mL × 10 <sup>5</sup>	11.48	18.99	0.4033	–26.07–11.04
Macrophages, %	78.25	88.02	0.2618	–27.57–11.04
Lymphocytes, %	2.125	2.360	0.8566	–2.948–2.478
Eosinophils, %	0.05	0.31	0.1542	–0.6285–0.1085
Neutrophils, %	12.98	7.87	0.5301	–11.76–21.97
Epithelial cells, %	6.613	1.390	0.0341*	0.4423–10.0
TNF- $\alpha$ in 24-h culture, pg/mL	356.9	110.4	0.4246	–407.8–900.8
CD14, %	14.64	24.85	0.2084	–26.73–6.30
CD68, %	38.96	30.26	0.4204	–13.60–31.01
HLA-DR, %	26.26	28.46	0.8581	–27.83–23.44
iNOS, %*	30.09	28.59	0.9016	–23.78–26.78

\*p < 0.05 (Student's t-test).

compared with 6 (85.7%) of the 8 patients who died (p = 0.0128).

We investigated cell and protein content of the BAL specimens of burn victims with and without SII (Table 3). There were no significant differences between the groups of patients with facial burns with and without SII in terms of the several parameters evaluated in the BAL specimens. The only parameter for which the difference approached the level of significance was the percentage of lymphocytes, which was found to be reduced in victims of facial burns with confirmed SII (p = 0.059)

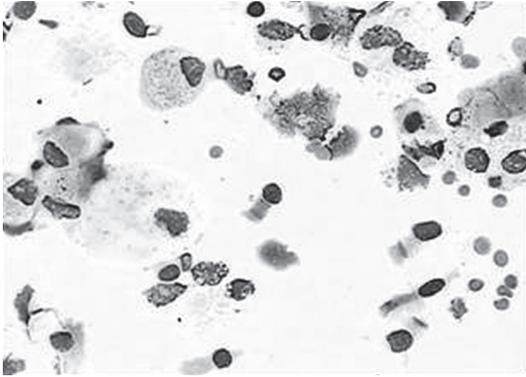
The BAL parameters of the victims of facial burns who survived or died are shown in Table 4. There were no differences between the victims who died and those who survived in terms of the parameters evaluated. There were, however, a greater proportion of epithelial cells in the patients who died (6.6% vs. 1.4%), and the difference was statistically significant (p = 0.03; Figure 1). In 4 patients, the 24-h culture was positive for TNF- $\alpha$ . Of those 4 patients, 3 survived and 1 died. Among the patients who survived, the mean TNF- $\alpha$  level in the 24-h culture was 110.4 pg/mL. In the patient who died, the TNF- $\alpha$  level in the 24-h culture was 356.9 pg/mL. The difference between the two groups was not significant (p = 0.42; 95% CI: 407.8–900.8). Although the BAL parameters were evaluated regarding the TBSA burned, there were no differences among the different parameters (data not shown). When a cut-off point of 30% of TBSA burned was established, only the number of cells obtained in the lavage was

different: > 30% ( $9.50 \pm 3.29 \times 10^5$  cells/mL) vs. < 30% ( $30.31 \pm 9.14 \times 10^5$  cells/mL; p = 0.033), suggesting that a greater TBSA burned translates to a smaller number of cells being found in the BAL fluid.

## Discussion

The presence of SII has been associated with higher mortality in burn patients and can result in an up to nine-fold increase in mortality.<sup>(24)</sup> Although one group of authors also observed an increase in mortality, the presence of SII provided little additional data for predicting mortality when the percentage of TBSA burned and age were used as prognostic factors.<sup>(25)</sup> Another group of authors used a formula to retrospectively predict fatal outcomes in 530 patients, concluding that patients who presented more than 40% TBSA burned, were older than 60 years of age and had SII were at a higher risk of death, mortality being as high as 95% when all three of these factors are present.<sup>(3)</sup> The accuracy of this model was tested in a study of 479 adult patients with a TBSA burned  $\geq$  20%, and the results were not encouraging.<sup>(26)</sup> In a study of 27 patients carried out at the Galeão Air Force Hospital, located in the state of Rio de Janeiro, the authors found the mortality rate to be 3.4% higher among patients who presented bronchoscopy findings consistent with SII.<sup>(13)</sup>

Our analysis of the results found in the 18 patients submitted to bronchoscopy revealed that TBSA burned and age are significant contributing factors to the increase in mortality,



**Figure 1** – Ciliated epithelial cells.

which is in accordance with the great majority of the studies found in the literature. In our study, the presence of SII in isolation did not contribute to the increase in mortality, and it is not a good predictive factor, as has also been observed by other authors.<sup>(25,26)</sup> There was also no relationship between TBSA burned and the presence of SII, since the patients with the highest mean TBSA burned presented no endoscopic findings indicative of SII.

Various authors have shown the need for recommending bronchoscopy in patients suspected of SII as a method for early detection of lung injury caused by smoke inhalation. Indirect observation has been used to diagnose this injury. Findings of facial burns, singed nasal vibrissae, respiratory tract secretion, wheezing and rhonchi, accompanied by a history of exposure to smoke in enclosed places or loss of consciousness at the site of the accident, are suggestive of SII and, therefore, confirm the recommendation for bronchoscopy. However, there is a high incidence of false-positive values for each finding. Although 70% of the patients with SII have facial burns, 70% of the patients with facial burns have no significant lower respiratory tract injury.<sup>(4)</sup>

Of the 18 patients submitted to bronchoscopy, all had facial burns. However, 7 (38%) had no endoscopic signs of SII. In addition, in the same period, the CTQ team of physicians failed to recommend bronchoscopy for 60 patients with facial burns. These data indicate the weakness of the use of indirect methods to determine SII. Facial burns were not a good predictive factor for SII, which underscores the importance of bronchoscopy in the initial evaluation of patients suspected of airway impairment.

<sup>(4,12)</sup> Hyperemia, edema, mucosal ulceration and presence of soot were the bronchoscopy findings that were diagnostic for SII.

The cytological analysis of BAL specimens has been the object of study in several animal models and in a few studies in humans. Two studies, one involving patients with burn-related acute respiratory distress syndrome (ARDS) and one involving rabbits submitted to smoke inhalation, revealed that both cohorts presented a great number of alveolar macrophages in the BAL fluid.<sup>(16,15)</sup>

The BAL fluid of the 18 burn patients evaluated in our study also showed a great proportion of alveolar macrophages, in those who died and those who survived ( $78.25 \pm 4.99\%$  vs.  $88.02 \pm 7.04\%$ ), and there was no statistically significant difference between the two groups. Our finding was similar to that described in a study on BAL specimens of smokers and nonsmokers ( $92.5 \pm 1.0\%$  vs.  $85.2 \pm 1.2\%$ ).<sup>(27)</sup> There were no significant differences between the patients who died and those who survived in terms of the proportions of lymphocytes, neutrophils and eosinophils. When compared with the BAL fluid of the smokers and nonsmokers described in the study mentioned above,<sup>(27)</sup> the BAL fluid of the SII victims evaluated in the present study contained fewer lymphocytes than did that of the nonsmokers ( $1.34 \pm 0.43$  vs.  $11.8 \pm 1.1$ ) and even fewer than did that of the smokers ( $1.34 \pm 0.43$  vs.  $5.2 \pm 0.9$ ). The proportion of eosinophils was similar to that described as the reference value ( $< 1\%$ ). In the patients with normal bronchoscopy results, the proportion of neutrophils ( $3.70 \pm 1.31\%$ ) was similar to the reference value (1-3%), although it was significantly greater in the patients with SII ( $15.25 \pm 5.91\%$ ). The proportion of epithelial cells was similar to that described as the reference value ( $< 5\%$ ). However, there was a statistically significant increase in the proportion of epithelial cells in the patients who died ( $6.61\%$  vs.  $1.39\%$ ), and this might be a marker of severity and of unfavorable outcome in patients admitted with burns. This finding is consistent with the description of alterations present in the initial phases of airway SII, when there is complete or partial desquamation of the tracheal, bronchial and bronchiolar epithelium.<sup>(11)</sup> The epithelium works as an important physical barrier of the mucosae in general, and its loss facilitates the onset of

infections. In addition, bronchial epithelial desquamation implies the loss of another important defense mechanism of the respiratory system: mucociliary clearance. These patients are highly vulnerable to infections. These injuries seem to depend on the dose and the duration of exposure to smoke.<sup>(28)</sup>

Despite the description of the increase in TNF- $\alpha$  in the presence of ARDS<sup>(16)</sup> and SII,<sup>(28)</sup> one group of authors did not find the same result in a sheep model.<sup>(29)</sup> The presence of TNF- $\alpha$  was detected in only 4 of the 18 patients submitted to bronchoscopy. There were no significant differences between patients with and without SII who survived or who died. The detection of TNF- $\alpha$  in the BAL fluid was not found to be useful to predict severity in burn patients.

One group of authors recently demonstrated the involvement of iNOS in the pathogenesis of acute lung injury in burn sheep with SII.<sup>(30)</sup> However, we found no significant differences in terms of iNOS values between the patients with and without SII who survived or who died.

In terms of the expression of CD14, CD64 and HLA-DR, there were no statistically significant differences between the patients with and without SII submitted to bronchoscopy or between those who survived and those who died.

The present study has some limitations, such as the number of cases included, since, although 78 patients were admitted to the two units participating in the study over 26 months, only 18 were referred for bronchoscopy by the clinical team. In addition, due to the great number of parameters that yielded negative results, as well as to the small number of cases recruited, an in-depth statistical analysis was not performed.

In conclusion, we observed that TBSA burned, age and the development of acute respiratory failure were factors related to mortality in victims of SII submitted to bronchoscopy with BAL. In the differential cytology of the BAL fluid of victims with SII, the increase in the number of ciliated epithelial cells in the BAL fluid seems to be a prognostic factor for mortality. The determination of the levels of TNF- $\alpha$  in 24-h BAL total cell culture presented no relationship with mortality. There were no differences between the patients with or without SII or between those who survived and those who died in terms of the phenotype of the alveolar macrophages obtained

through BAL, nor were there any differences in terms of the frequency of positive iNOS cells.

With the results achieved in our study, we hope to encourage the use of bronchoscopy in all burn patients with indirect signs of SII admitted to specialized centers. Obtaining BAL specimens and performing cell counts, an affordable and widely practiced method, can be useful as a prognostic marker and can contribute to a better understanding of the pathogenesis of SII.

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