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# Impact of diagnostic bronchoscopy in burned adults with suspected inhalation injury

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ABSTRACT

*Introduction:* Inhalation injury is a common complication of thermal trauma. Fiberoptic bronchoscopy (FOB) is regarded as current standard practice in diagnosing and grading inhalation injury. Nonetheless, its predictive value in terms of therapeutic decision-making and clinical outcome is controversial.

*Methods:* Adult burn patients with inhalation injury (InI) were selected from the National Burn Repository of the American Burn Association. Subjects were propensity score pair-matched based on injury severity and grouped based on whether or not FOB had been performed (FOB, CTR, respectively). Mortality, incidence of pneumonia, length of hospitalization, length of ICU stay and dependency on mechanical ventilation were compared between the two groups.

*Results:* 3014 patients were matched in two groups with a mean TBSA of 22.4%. There was no significant difference in carboxyhemoglobin fraction at admission. Patients, who underwent FOB on admission had a significantly increased incidence of pneumonia ($p < 0.001$), mortality ($p < 0.05$), length of hospitalization ($p = 0.002$), ICU stay ($p < 0.001$) and duration of mechanical ventilation ($p = 0.006$). In a subgroup analysis of patients with TBSA of at least 20%, incidence of pneumonia was significantly higher in the FOB group ($p < 0.001$) and longer mechanical ventilation was required ($p = 0.036$).

*Discussion:* Diagnosis and grading of InI through FOB is the current standard, although its predictive value regarding key outcome parameters and therapeutic decision-making, remains unclear. The potential procedural risk of FOB itself should be considered. This study demonstrates correlations of FOB with major clinical outcomes in both a general collective of burned adults as well as severely burned adults. Although these findings must be interpreted with caution, they may induce further research into potential harm of FOB and critical review of routine diagnostic FOB in suspected inhalation injury in thermally injured patients.



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## 1. Introduction

Inhalation injury (InI) is a comorbidity, that accompanies up to one-fifth of burn injuries and its prevalence increases proportionally with burn extent [1]. Acute chemical, or thermal damage to the lower airway is severely altering pulmonary integrity. Incomplete combustion of materials such as plastic, rubber, wood or cotton, which are commonly found in residential fires, causes the release of toxic fumes, which cause severe injury to the mucosa of distant segments of the respiratory tract upon involuntary inhalation. In contrast, inhalation of hot air characteristically causes harm to the upper airway while leaving the lower airway mostly unaffected [2]. The clinical importance of inhalation injury are grave: as opposed to thermal trauma alone, a near-doubling of mortality rates can be observed, when severe burn injury is accompanied by InI. Moreover, InI has been identified as the strongest predictor of mortality next to total body surface area (TBSA) burned and patient age [3]. Burn patients with InI require an increased volume of resuscitation fluid during the first 24 h of treatment [5], and require mechanical ventilation more frequently and for increased duration. Additionally, the risk for developing pneumonia quadruples in the presence of InI [4], encompassing an increase in mortality to up to 60 per cent [2]. While InI significantly affects the clinical course of burned patients, diagnosing it reliably and reproducibly, as well as objectively grading its severity remains challenging even for experienced burn physicians. Diagnosing criteria extend from physical exam findings [6], over fiberoptic bronchoscopy (FOB) [7] and virtual bronchoscopy [8] to xenon or 99m-technetium scanning [2]. Although FOB is widely accepted as the gold standard for diagnosing and grading InI [9], its predictive value as well as measurable impact on therapeutic decision-making have been discussed controversially [10–12]. Of note, FOB bears the risk of rare complications such as traumatic damage to the respiratory tract with hemorrhage, or pneumothorax [13]. Also, FOB might introduce an increased risk for bacterial contamination and subsequent pneumonia due to contamination of the injured airway [14–16]. The goal of this study is to gauge the clinical impact of FOB on admission of severely burned patients with InI.

## 2. Methods

Following approval by the American Burn Association (ABA), data from the National Burn Repository (NBR, in dataset version 8.0) containing anonymized data of patients treated from 2004 to 2011 were obtained from the ABA. Patients under the age of 16, as well as moribund patients treated palliatively, were excluded from the analysis. All remaining patients were screened and included in further analyses, if presence of InI on admission had been documented. Then, all included patients were either assigned to the intervention group (FOB, bronchoscopy performed on admission) or to the control group (CTR, no bronchoscopy performed on admission).

Individual patients of the FOB and CTR groups were then propensity-score-matched to one another based on the variables [age], [sex] and [TBSA burned]. Mean length of hospital stay, length of ICU stay, ventilation days as well as partial- and full thickness TBSA burned, area burned of head, neck and trunk, as well as serum carboxyhemoglobin (COHb) levels were compared between both groups using t-tests. Odds ratios were calculated for survival and incidence of pneumonia and compared using the McNemar-test. Subgroup analyses were performed accordingly including only severely burned patients with an affected TBSA of at least 20%. For all analyses, $p < 0.05$ was considered indicative of statistical significance. All results are presented as mean ± SD or absolute and relative frequencies unless otherwise noted.

## 3. Results

A total of 11,461 patients with InI were identified in the NBR dataset. After exclusion of patients under the age of 16 and moribund patients, 8179 patients were included for further analysis. Propensity score matching yielded 1507 patient pairs between the intervention (FOB) and the control group (CTR). Each group contained 492 (32.6%) female and 1015 (67.4%) male patients. Mean age was 47.5 ± 18.4 years in the FOB group and 47.1 ± 18.4 years in the CTR group. Mean TBSA (partial and full thickness burns) was 22.4 ± 24.00% (FOB) and 22.5 ± 24.56% (CTR; $p = 0.242$), respectively. TBSA of partial thickness burns was 10.6 ± 14.3% (FOB) and 9.5 ± 13.8% (CTR; $p = 0.012$), while mean TBSA of full thickness burns was 13.4 ± 22.1% in the FOB group and 14.4 ± 22.7% in the CTR group ($p = 0.205$). Burned surface area of the head averaged 2.7 ± 2.4% in the FOB group and 2.6 ± 2.3% in the CTR group, respectively ($p = 0.445$). On the neck 0.7 ± 0.8% TBSA (FOB) and 0.7 ± 0.81% TBSA (CTR; $p = 0.076$) were affected. On the anterior aspect of the trunk 3.8 ± 4.6% TBSA (FOB) and 3.3 ± 4.5% TBSA (CTR; $p = 0.357$) were burned, respectively.

The fraction of carboxyhemoglobin in serum was documented in 690 (FOB) and 693 (CTR) patients with a mean value of 10.5 ± 12.3% (FOB) and 8.6 ± 11.6% (CTR) without significant differences ($p = 0.1228$). Patient characteristics and further details are illustrated in Table 1.

In the FOB group the incidence of pneumonia was 169 (11.2%), compared to 64 (4.2%) in the CTR group ($p < 0.001$). The mortality rate was 22.7% ($n = 342$) in the FOB group and 19.6% ($n = 296$) in the CTR group ($p = 0.026$). The mean duration of hospital stay was 3.7 days shorter ($p = 0.002$) in the CTR group (24.1 ± 33.9 days; median 11 days, Q1–3 2–34 days) than in the FOB group (27.8 ± 35.2 days; median 18 days, Q1–3 5–37 days), the mean duration of intensive care was 4.7 days shorter ($p < 0.001$) in the CTR group (17.7 ± 29.2 days; median 5 days, Q1–3 1–24 days) than in the FOB group (22.4 ± 28.1 days; median 14 days, Q1–3 3–31 days). The duration of mechanical ventilation was 3.1 days shorter ($p = 0.006$) in the CTR group (13.9 ± 27.6 days; median 3 days, Q1–3 0–18 days) than in the FOB group (16.7 ± 27.58 days; median 9 days, Q1–3 2–22 days). Odds ratios and coefficients for clinical outcome parameters are shown in Table 2.

Propensity score matching for subgroup analysis of patients suffering from burns of ≥20% TBSA yielded 634 patients in each group; the subgroups were comparable in terms of age and sex distribution. Mean TBSA (partial and full thickness burns) was 45.0 ± 20.0.9% (FOB) and 44.1 ± 21.8%

**Table 1 – Patient characteristics after pair-matching by age, sex and TBSA.**

| | Group FOB – bronchoscopy performed | Group CTR – no bronchoscopy performed | Total | p-Value |
|---|---|---|---|---|
| Patients | 1507 | 1507 | 3014 | |
| Age (years) | | | | |
| Mean | 47.5 | 47.1 | 47.3 | 0.766 |
| SD | 18.44 | 18.45 | 18.44 | |
| Median | 46.2 | 46.8 | 46.3 | |
| Q1–Q3 | 32.8–60.0 | 31.8–59.6 | 32.1–60.0 | |
| Sex | | | | |
| Female | 492 (32.6%) | 492 (32.6%) | 984 (32.6%) | |
| Male | 1015 (67.4%) | 1015 (67.4%) | 2030 (67.4%) | |
| TBSA (%) | | | | |
| Mean | 22.4 | 22.5 | 22.4 | 0.242 |
| SD | 24.00 | 24.56 | 24.28 | |
| Median | 14.9 | 14 | 14 | |
| Q1–Q3 | 2–35.5 | 2–36 | 2–36 | |
| TBSA 2° (%) | | | | |
| Mean | 10.6 | 9.5 | 10.1 | 0.012 |
| SD | 14.38 | 13.83 | 14.12 | |
| Median | 5 | 4 | 4.5 | |
| Q1–Q3 | 0–15.5 | 0–13 | 0–14 | |
| TBSA 3° (%) | | | | |
| Mean | 13.4 | 14.4 | 13.9 | 0.205 |
| SD | 22.15 | 22.71 | 22.43 | |
| Median | 0 | 1 | 1 | |
| Q1–Q3 | 0–18 | 0–22 | 0–20 | |
| TBSA head (%) | | | | |
| Mean | 2.7 | 2.6 | 2.7 | 0.445 |
| SD | 2.43 | 2.36 | 2.40 | |
| Median | 2.4 | 2 | 2 | |
| Q1–Q3 | 0.3–4 | 0.3–4 | 0.3–4 | |
| TBSA head 2° (%) | | | | |
| Mean | 1.8 | 1.7 | 1.8 | 0.413 |
| SD | 2.08 | 2.02 | 2.05 | |
| Median | 1 | 1 | 1 | |
| Q1–Q3 | 0–3 | 0–3 | 0–3 | |
| TBSA head 3° (%) | | | | |
| Mean | 1.0 | 1.1 | 1.0 | 0.343 |
| SD | 2.07 | 2.16 | 2.12 | |
| Median | 0 | 0 | 0 | |
| Q1–Q3 | 0–0 | 0–0.9 | 0–0.2 | |
| TBSA neck (%) | | | | |
| Mean | 0.7 | 0.7 | 0.7 | 0.076 |
| SD | 0.79 | 0.81 | 0.80 | |
| Median | 0.5 | 0.5 | 0.5 | |
| Q1–Q3 | 0–1 | 0–1.5 | 0–1.1 | |
| TBSA neck 2° (%) | | | | |
| Mean | 0.4 | 0.4 | 0.4 | 0.812 |
| SD | 0.66 | 0.66 | 0.66 | |
| Median | 0 | 0 | 0 | |
| Q1–Q3 | 0–1 | 0–1 | 0–1 | |
| TBSA neck 3° (%) | | | | |
| Mean | 0.3 | 0.3 | 0.3 | 0.285 |
| SD | 0.63 | 0.68 | 0.65 | |
| Median | 0 | 0 | 0 | |
| Q1–Q3 | 0–0 | 0–0 | 0–0 | |
| TBSA anterior trunk (%) | | | | |
| Mean | 3.8 | 3.3 | 3.6 | 0.357 |
| SD | 4.67 | 4.52 | 4.60 | |
| Median | 1 | 0.5 | 1 | |
| Q1–Q3 | 0–7 | 0–6 | 0–6.7 | |
| TBSA anterior trunk 2° (%) | | | | |
| Mean | 1.6 | 1.5 | 1.6 | 0.135 |
| SD | 3.19 | 3.09 | 3.14 | |
| Median | 0 | 0 | 0 | |

*(continued on next page)*

**Table 1 (continued)**

| | Group FOB– bronchoscopy performed | Group CTR– no bronchoscopy performed | Total | p-Value |
|---|---|---|---|---|
| Q1-Q3 | 0-2 | 0-1 | 0-1.5 | |
| TBSA anterior trunk 3° (%) | | | | |
| Mean | 2.0 | 2.4 | 2.2 | 0.040 |
| SD | 3.87 | 4.19 | 4.04 | |
| Median | 0 | 0 | 0 | |
| Q1-Q3 | 0-2 | 0-3 | 0-3 | |
| Carboxyhemoglobin (%) | | | | |
| Missing | 817 | 814 | 1631 | |
| Mean | 10.5 | 8.6 | 9.5 | 0.123 |
| SD | 12.34 | 11.61 | 12.01 | |
| Median | 4.8 | 3.6 | 4.2 | |
| Q1-Q3 | 2.2-14.8 | 1.8-10.4 | 2-12.6 | |

**Table 2 – Odds ratio for pneumonia and survival comparing groups with or without bronchoscopy performed at admission and mean differences (MDiff) in hospital stay, ICU stay and ventilator days.**

| | OR/MDiff | 95%-CI | p-Value |
|---|---|---|---|
| Pneumonia | 2.721 | [2.029;3.649] | <0.001 |
| Mortality | 1.256 | [1,032;1.526] | 0.026 |
| Hospital stay | 3.703 | [1.392;6.014] | 0.002 |
| ICU stay | 4.390 | [2.073;6.707] | <0.001 |
| Ventilator days | 3.079 | [0.868;5.290] | 0.006 |

(CTR; p = 0.789), with an average partial thickness burn surface area of 19.4 ± 17.6% (FOB) and 17.6 ± 18.0% (CTR; p = 0.073) and an average full thickness burn surface area of 28.1 ± 26.1% (FOB) and 29.8 ± 25.8% (CTR), respectively (p = 0.183). Fraction of carboxyhemoglobin was documented in 252 (FOB) and 288 (CTR) cases with a mean fraction of 8.9 ± 10.6% (FOB) and 8.8 ± 12.6% (CTR; p = 0.477). Further patient details are listed in Table 3.

The incidence of pneumonia was 13.4% (n = 85) in the FOB group and 5.5% (n = 35) in the CTR group (p < 0.001); mortality rate was 37.4% (n = 237) in the FOB group and 38.3% (n = 243) in the CTR group (p = 0.741). The mean length of hospitalization was 36.8 ± 38.1 days (median 26 days, Q1–3 7–54 days) in the CTR group and 40.9 ± 45.5 days (median 32 days, Q1–3 7–56 days) in the FOB group (p = 0.067), the mean duration of intensive care was 28.9 ± 32.5 days (median 20 days, Q1–3 3–40 days) in the CTR group and 33 ± 35.8 days (median 24 days, Q1–3 6–45 days) in the FOB group (p = 0.095) and the duration of mechanical ventilation was 3.7 days shorter (p = 0.036) in the CTR group (21.5 ± 27.86 days; median 12 days, Q1–3 2–30 days) than in the FOB group (25.2 ± 37.2 days; median 16 days, Q1–3 4–35 days). Odds ratios and coefficients for clinical outcome parameters are shown in Table 4.

## 4. Discussion

In this registry study we assess the largest patient collective to date with regard to outcomes correlated to fiberoptic bronchoscopy during admission for burn injury in general and severe thermal trauma in particular with accompanying InI.

To date, numerous options for diagnosing suspected InI are available. Although FOB is used as gold standard in diagnosing and grading InI, its impact on clinical outcome and its importance for therapeutic decision-making remains unclear [1,17]. Initial clinical criteria for diagnosing InI include history of exposure to fire within an enclosed space and unconsciousness at site of accident, as well as clinical findings during physical examination such as singed nasal hair, carbonaceous sputum or facial burns. Even though this combination circumstantial evidence and clinical findings is frequently used in diagnosing and grading InI, a recent retrospective analysis illustrated a poor predictive value and weak correlation between diagnosis by clinical examination versus bronchoscopy [6]. While chest X-ray and pulmonary function testing have low relevance in diagnosing InI on admission, scintigraphy with either technetium-99m or Xenon133 showed promising results towards providing an objective diagnosis in the course of treatment beyond the initial, acute setting [18]. Due to limited availability, high cost and impractical implementation in an intensive care setting, scintigraphy is rarely used in burn care [2]. A more recent approach in radiologic imaging of InI is virtual bronchoscopy through computed tomography (CT): pilot studies have been conducted [19] and analyses comparing FOB to CT - bronchoscopy in animal studies may show more precise diagnostic results with the latter [8]. Granted its own unique risks, limited clinical experience beyond experimental settings and a certain degree of impracticability, this method is not yet of relevance.

Acknowledging the need for reliable diagnosis of InI, FOB has been established as standard practice in assessing the grade/severity of InI [4] and is routinely used in burn centers worldwide. The method allows for direct observation of the respiratory tract for soot, mucosal erythema or necrosis. To quantify InI, several grading systems have been proposed [7,20]. The abbreviated injury score (AIS) is used by most authors investigating bronchoscopy. It uses bronchoscopic findings of carbonaceous deposits and mucosal alterations to grade InI from 0 (no injury) to 4 (massive injury) [7]. The original authors were able to show a difference in mortality when comparing patients with AIS grade 0 and 1 with grades 2, 3 and

**Table 3 – Patient characteristics of subgroup analysis including only patients suffering from TBSA >= 20% after pair-matching by age, sex and TBSA.**

| | Group FOB– bronchoscopy performed | Group CTR– no bronchoscopy performed | Total | p-Value |
|---|---|---|---|---|
| Patients | 634 | 634 | 1268 | |
| Age (years) | | | | |
| Mean | 45.3 | 46.6 | 45.9 | |
| SD | 17.82 | 18.50 | 18.16 | |
| Median | 44.35 | 45.3 | 44.95 | |
| Q1–Q3 | 31.5–56.2 | 32.0–58.0 | 32.0–57.0 | |
| Sex | | | | |
| Female | 191 (30.1%) | 190 (30.0%) | 381 (30.0%) | |
| Male | 443 (69.9%) | 444 (70.0%) | 887 (70.0%) | |
| TBSA (%) | | | | |
| Mean | 45.0 | 44.1 | 44.6 | 0.789 |
| SD | 19.97 | 21.78 | 20.89 | |
| Median | 40 | 39.4 | 39.8 | |
| Q1–Q3 | 29–57.2 | 28–57.9 | 28.1–57.6 | |
| TBSA 2° (%) | | | | |
| Mean | 19.4 | 17.6 | 18.5 | 0.073 |
| SD | 17.69 | 18.06 | 17.89 | |
| Median | 18 | 13 | 15 | |
| Q1–Q3 | 4.5–29.6 | 2–27 | 3.1–28 | |
| TBSA 3° (%) | | | | |
| Mean | 28.1 | 29.8 | 29.0 | 0.183 |
| SD | 26.17 | 25.82 | 26.00 | |
| Median | 22 | 24.9 | 23.7 | |
| Q1–Q3 | 4–45.5 | 9.5–44 | 6–45 | |
| TBSA head (%) | | | | |
| Mean | 4.2 | 4.3 | 4.2 | 0.591 |
| SD | 2.32 | 2.33 | 2.33 | |
| Median | 4 | 4 | 4 | |
| Q1–Q3 | 2.5–7 | 2.9–7 | 2.75–7 | |
| TBSA head 2° (%) | | | | |
| Mean | 2.5 | 2.3 | 2.4 | 0.049 |
| SD | 2.32 | 2.31 | 2.32 | |
| Median | 2.4 | 2 | 2 | |
| Q1–Q3 | 0–4 | 0–4 | 0–4 | |
| TBSA head 3° (%) | | | | |
| Mean | 2.0 | 2.2 | 2.1 | 0.396 |
| SD | 2.67 | 2.74 | 2.70 | |
| Median | 0 | 0 | 0 | |
| Q1–Q3 | 0–4 | 0–4.5 | 0–4 | |
| TBSA neck (%) | | | | |
| Mean | 1.2 | 1.3 | 1.3 | 0.037 |
| SD | 0.78 | 0.72 | 0.76 | |
| Median | 1 | 1.5 | 1 | |
| Q1–Q3 | 0.5–2 | 1–2 | 1–2 | |
| TBSA neck 2° (%) | | | | |
| Mean | 0.7 | 0.6 | 0.7 | 0.414 |
| SD | 0.78 | 0.77 | 0.78 | |
| Median | 0.3 | 0 | 0 | |
| Q1–Q3 | 0–1 | 0–1 | 0–1 | |
| TBSA neck 3° (%) | | | | |
| Mean | 0.6 | 0.7 | 0.7 | 0.203 |
| SD | 0.82 | 0.86 | 0.84 | |
| Median | 0 | 0 | 0 | |
| Q1–Q3 | 0–1 | 0–2 | 0–1.5 | |
| TBSA anterior trunk (%) | | | | |
| Mean | 7.1 | 7.3 | 7.2 | 0.062 |
| SD | 4.56 | 4.56 | 4.56 | |
| Median | 7 | 8 | 7.8 | |
| Q1–Q3 | 3–11.5 | 3.8–11.4 | 3–11.5 | |
| TBSA anterior trunk 2° (%) | | | | |
| Mean | 3.1 | 3.0 | 3.0 | 0.734 |
| SD | 4.03 | 4.04 | 4.03 | |

*(continued on next page)*

**Table 3 (continued)**

| | Group FOB– bronchoscopy performed | Group CTR– no bronchoscopy performed | Total | p-Value |
|---|---|---|---|---|
| Median | 1 | 0.5 | 1 | |
| Q1–Q3 | 0–5.5 | 0–5 | 0–5 | |
| TBSA anterior trunk 3° (%) | | | | |
| Mean | 4.4 | 4.8 | 4.6 | 0.180 |
| SD | 4.77 | 4.89 | 4. | |
| Median | 3 | 4 | 3 | |
| Q1–Q3 | 0–9 | 0–9.8 | 0–9 | |
| Carboxyhemoglobin | | | | |
| Missing | 382 | 346 | 728 | |
| Mean | 8.9% | 8.8% | 8.8% | 0.477 |
| SD | 10.67% | 12.65% | 11.75% | |
| Median | 3.9% | 3.7% | 3.8% | |
| Q1–Q3 | 2.0–10.85% | 1.9–9.2% | 2.0–9.9% | |

**Table 4 – Subgroup analysis showing odds ratio for pneumonia and survival and mean differences (MDiff) in hospital stay, ICU stay and ventilator days between treatment groups with and without bronchoscopy performed.**

| | OR/MDiff | 95%-CI | p-Value |
|---|---|---|---|
| Pneumonia | 2.613 | [1.727;3.953] | <0.001 |
| Mortality | 0.949 | [0.732;1.230] | 0.741 |
| Hospital stay | 4.060 | [−0.282;8.402] | 0.067 |
| ICU stay | 3.540 | [−0.616;7.696] | 0.095 |
| Ventilator days | 4.363 | [0.281;8.446] | 0.036 |

4, but no significant difference in ventilator days [7]. Likewise, a recent retrospective analysis compared groups of AIS grade 0, grade 1 or 2 and grade 3 or 4 regarding their clinical outcomes. An increased rate of pneumonia, longer ventilator dependence, longer hospitalization and a higher rate of multiple organ disfunction was found but no difference in mortality [21]. Other studies found neither an impact of AIS grades on mortality, the development of acute respiratory distress syndrome, nor on ventilator dependence in general [10]. These inconsistencies of predictive value of bronchoscopically graded InI – perhaps attributable to interrater variability as well as difficult assessment of the distal airway– underline the method's risk for misinterpretation [4,10].

There have been few studies attempting to predict clinical decision making based on FOB findings: Bearing in mind an increased fluid demand during early resuscitation of thermal trauma with InI, Endorf and Gamelli were unable to predict resuscitation volumes of patients with no or mild InI (AIS grade 0 and 1) and moderate to severe InI (AIS grade 2–4) [7]. These findings were confirmed in a subsequent investigation which expanded the assessment time to 72 h [10,11,22].

While the prognostic value of FOB is not reliably validated, procedure-related complications of invasive FOB must be considered. Overall risk for severe complications is low; Marek et al. investigated complications of 261 patients undergoing FOB for suspected InI and found hypoxia during examination in 7.2%, bradyarrhythmia in 2.29%, thrombembolic incidents in 4.2%, bleeding of the digestive tract in 3.83%, bleeding of respiratory tract in 1.9% and pneumothorax in 1.14% of cases [13]. Bacterial contamination of the lower respiratory tract and consecutive infections have been described after performing bronchoscopy [15,16]. Although these studies investigated patient collectives, suffering neither from burns nor InI, the results might be transferable, especially given that an injured lower respiratory tract is more susceptible to bacterial invasion, and burn-induced immunosuppression might increase the risk of infectious systemic spread [23].

The goal of this study was to investigate the impact of a performed FOB in the presence of InI on treatment and outcome parameters. Our analysis of NBR data revealed a significantly increased incidence of pneumonia, when FOB was performed at admission. Similar results are shown in the subgroup analysis of patients with severe burns of more than 20% TBSA, where incidence of pneumonia was also higher. Subsequently, respirator dependence was longer after FOB both in the whole collective as well as in the subgroup of severe burns. These significant correlations, although explicitly incapable of conferring causation, do raise the question whether FOB may be currently underestimated in terms of its inherent risk, and overestimated regarding its clinical impact for therapeutic decision-making, beyond mere diagnosing and grading of InI.

Strengths of this analysis were the large sample size and robust modelling. Due to propensity score matching, group comparability in terms of injury severity (with comparable TBSA, burn depth and affection of head, neck and anterior trunk) was excellent; when patients with minor injuries were ruled out by subgroup analysis, the observed differences were particularly robust. In addition to the aforementioned potential direct negative effects of FOB, one could speculate, that an overestimation of FOB findings may have induced over-resuscitation instead of adherence to urine-output based monitored volume resuscitation, subsequent pulmonary edema and other clinical complications associated with over-infusion [24,25]. Perhaps a more restrictive use of FOB, especially in patients with less severe clinical symptoms, could be clinically beneficial.

When assessing the risk-benefit ratio of an invasive diagnostic tool, the therapeutic consequences have to be carefully considered. Specific therapies for inhalation injury

include nebulization of heparin [26] and/or epinephrine [27], which have been shown to be effective in ovine models and clinical studies in pediatric burn patients. Increased volume of intravenous fluid resuscitation is at the same time a specific treatment requirement for InI, as well as a known risk factor for clinical outcome itself.

The present study has several limitations which have to be taken into account. Primarily, the method of diagnosing InI is different between both study groups. While the diagnosis was apparently confirmed by FOB in the intervention group, it was derived from a combination of clinical findings, elevated carboxyhemoglobin and circumstantial findings in the CTR group. On the other hand, patients with clinically suspected InI, who might have been ruled out through FOB were not marked as InI in the register and therefore could not be included in the analysis. This could have introduced selection bias towards disproportionate false positive diagnoses for InI in the control group. Secondly, in burn centers, where not every patient admitted to the ICU undergoes FOB, the severity of symptoms might be the indication to undergo FOB and thereby patients with mild or less severe symptoms may not be assessed by FOB. This is especially important as some burn centers might perform FOB only in patients, that were already intubated on admission or were intubated during admission process due to ventilatory insufficiency or an overall insufficient condition. Unfortunately, information on intubation status on admission could not be derived from the available data. This may lead to an imbalance with more severe cases of InI in the FOB group. In order to control for this confounder, analysis of carboxyhemoglobin levels in both groups was performed, as carboxyhemoglobin levels correlate well with presence and even severity of InI. This comparison showed no significant discrepancy between the groups, but its value is limited due to a very low documentation rate of carboxyhemoglobin of 46% in the study collective and 41% in subgroup analysis allowing no information on severity of InI in more than half of the study population. Due to propensity matching and subgroup analysis of patients with severe trauma, key factors such as TBSA, burn depth and location are well comparable between groups; however, other differences such as comorbidities, other concomitant injuries and otherwise worse condition on admission could not be ruled out based on available data. Whether this effect alone can account for the observed differences remains questionable.

The present study warrants further prospective and controlled scientific investigation, particularly controlling for more and multifactorial influences on clinical outcome in relation to FOB and critically questioning its impact on therapeutic decision-making beyond diagnosing and grading InI.

## 5. Conclusion

Potentially negative clinical effects of performing FOB in assumption of inhalation injury should be considered, despite several limitations that require cautious interpretation of the presented results. Further research should address potential harm of FOB, review its predictive value and assess the need for the routine use of FOB in diagnosing Inhalation injury.

## Conflict of interest statement

All contributing authors confirm that there are no known conflicts of interest associated with this publication.

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