Prevalence and prognostic impact of inhalation injury among burn patients: A systematic review and meta-analysis

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Abstract

Background: The objective of our study was to perform a systematic review and meta-analysis aimed at assessing the prevalence of inhalation injury in burn patients and its prognostic value in relation to in-hospital mortality.

Methods: We searched the PubMed and EMBASE databases for noninterventional studies published between 1990 and 2018 investigating in-hospital mortality predictors among burn patients.The primary meta-analysis evaluated the association between inhalation injury and mortality. A secondary meta-analysis determined the global estimate of the prevalence of inhalation injury and the rate of mortality. Random effects models were used, and univariate meta-regressions were used to assess sources of heterogeneity. This study is registered in the PROSPERO database with code CRD42019127356.

Findings: Fifty-four studies including a total of 408,157 patients were selected for the analysis. A pooled inhalation prevalence of 15.7% (95% confidence interval, 13.4%-18.3%) was calculated.The summarized odds ratio of in-hospital mortality secondary to an inhalation injury

was 3.2 (95% confidence interval, 2.5-4.3). A significantly higher odd of mortality was found among the studies that included all hospitalized burn patients, those that included a lower proportion of male patients, those with a lower mean total body surface area, and those with a lower prevalence of inhalation injury.

Conclusion: Despite our study's limitations due to the high risk of bias and the interstudy heterogeneity of some of our analyses, our results revealed a wide range of prevalence rates of inhalation injury and a significant association between this entity and in-hospital mortality in burn patients. However, this association is not significant if adjusted for disease severity.

Level of evidence: Systematic review/meta-analysis, level III.

Key Words: Meta-analysis; mortality; burns; inhalation injury

The term “inhalation injury” describes the aspiration of hot gas and toxic products derived from incomplete combustion. Its pathophysiology includes varying degrees of airway edema caused by direct thermal action, bronchospasm secondary to aerosolized irritants, small airway obstruction, and alveolar flooding due to epithelial disruption. Its clinical consequences include airway obstruction and bronchospasm, usually appearing within the first 24 hours, pulmonary shunt associated with decreased compliance, and lung infection that often develops over the following days. The diagnosis of this entity is mostly clinical and supported by a series of indirect observations. Bronchoscopy procedures and, occasionally, xenon 133 (133-Xe), are often applied in clinical settings to identify subglottal damage.

Enormous differences in the prevalence of this entity were observed between the different series analyzed,[1–4] which the authors attribute to the arbitrariness of its definition in the absence of imaging studies,[5] to the incidence of the different injury mechanisms (flame injuries) and their relationship with the extent of the burn,[2,6,7] or to the demographic profile of the burn patients.[1,7]

The clinical literature of the last 25 years suggests that inhalation injury may play a role in mortality after thermal trauma. However, several models studying this indicator have obtained varying results, in such a way that inhalation injury is not identified as a predictor of mortality in certain series,[8–10] but is in others despite having a low incidence.[11] This could be due to the variety of definitions used by different authors, the difficulty of determining the severity of the injury or quantifying the affected parenchyma, its association with severe burns with a greater impact on prognosis, or to the improvements achieved in the care of patients with inhalation injury over time.

To the best of our knowledge, the role of inhalation injury in the prognosis of patients has not yet been systematically reviewed and meta-analyzed. Our aim, therefore, is to carry out a systematic review to assess the prevalence of inhalation injury in burn patients, as well as the available qualitative and quantitative evidence of its impact on in-hospital mortality.

METHODS

This review was carried out and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[12] and the guidelines of the Meta-Analyses of Observational Studies in Epidemiology group.[13]

Search Strategy

A comprehensive systematic bibliographic search of the medical literature published until June 2018 was performed to identify studies that explored prognostic variables in burn patients. To perform an updated literature review, articles published before January 1990 were excluded from the analysis. The literatura search for relevant publications included in the PubMed database and the Excerpta Medica Database (EMBASE) was carried out using combinations of keywords “burns”, “mortality”, and “adult” (Supplemental Digital Content, Table 1,

http://links.lww.com/TA/B489). With regard to the language of publication, the search was restricted to articles written in English and Spanish. The search strategy was supervised by the local medical librarian.

Study Eligibility

Studies were considered to be relevant to this review if they met the following inclusion criteria (Supplemental Digital Content, Table 2, http://links.lww.com/TA/B489):

(1) Studies analyzing predictors or risk factors of in-hospital mortality among burn patients and including variable “inhalation” in their analysis.
(2) Noninterventional observational studies, such as cohort studies, case-control studies, and cross-sectional studies in which case the mortality predictors had to have been identified by means of a multivariate analysis.
(3) Studies that included at least 100 patients.

The following exclusion criteria were considered:

(1) Interventional studies, animal studies, studies investigating inhalation with intermediate disease endpoints, reviews, case reports, letters, and meeting abstracts.
(2) Studies that exclusively included a population of pediatric patients.
(3) Studies that exclusively included injuries due to electrical or chemical damage.
(4) Studies involving fewer than 100 patients.
(5) Studies in which mortality was not the primary outcome or in which mortality was analyzed either prior to the patients' admission or after their discharge from the hospital.
(6) Studies carried out before January 1990.

Assessment of Study Eligibility

Two reviewers (L.S. .and R.G.) performed the study selection process independently. The reviewers first examined the study titles (530 citations) and excluded 149 duplicate studies. Abstracts (381 citations) of each article were then reviewed to identify those studies that could be included in the next step of the selection process. The full text of the studies that appeared to be eligible based on the results of the first screening was then read (148 publications) and compared against the inclusión criteria to confirm that they were eligible to be included in the final analysis. Disagreements regarding the selected studies were solved by reaching a consensus between the two reviewers. When the inclusion of a study continued to be ambiguous, a third reviewer (S.P.) was included in the process to solve the debate and reach a final consensus decision. If more than one report relating to the same cohort was identified, the report with the most relevant information for our analysis or that including the greater number of patients was used. A total of 54 studies were finally included in the systematic review. All articles included in the study provided mortality data, 51 also reported inhalation injury prevalence data, and 27 studies described an adjusted measure of the impact of inhalation injury on mortality.

An overview of the selection process is shown in Figure 1.

Data Collection Process

Two authors (L.S. and R.G.) independently extracted data from each eligible study. The extracted data were then managed using predesigned data collection forms.

The information extracted from the selected studies included the following data whenever they were available: the first author, the year and country of publication, the study design, the sample size, the sample characteristics, the prevalence of the inhalation injury, the health care setting,

the mortality rate, the risk estimates together with their 95% confidence intervals (CIs), and all factors that had been adjusted for the analysis.

When data were exclusively provided for derivation or validation sets, these figures were the ones considered. If a study did not include the quantitative data needed to perform a meta-analysis, the reported association was summarized. In those cases, in which the data could not be pooled, the consistency of the association between the pooled results and the studies was evaluated.

Quality Assessment of the Studies Included

To assess the risk of bias, we used the Methodological Index for Non-Randomized Studies (MINORS)[14] quality assessment tool as an instrument designed to assess the methodological quality of comparative or noncomparative nonrandomized studies.

Statistical Analysis

The primary meta-analysis evaluated the association between inhalation injury and mortality among burn patients. A secondary meta-analysis was then performed to calculate a global estimate of the prevalence of inhalation injury and the mortality rate among these patients.

The overall pooled estimates of the prevalence of inhalation injury and the incidence of hospital mortality were obtained together with their 95% CIs using random effects models and applying the inverse-variance random effects method. A logistic (logit) transformation was applied to the raw proportions, and the inhalation and mortality figures of the individual studies were finally represented together with their exact binomial 95% CIs.

The core meta-analysis was initially performed using data obtained exclusively from studies that reported multivariate adjusted risk estimates (n = 27). The results of each study were reported in terms of the most adjusted odds ratios (ORs), relative risks (RRs), or hazards ratios

(HRs) for mortality linked to patients with inhalation injury versus patients with no inhalation injury. The HRs were treated as RRs. Given that the event rates were not low enough, the RRs were not considered to be comparable to the ORs, and a separate meta-analysis was consequently performed for three studies that reported HRs or RRs.

For Kim et al.'s study,[15] individual OR estimates were reported separately in three groups (subjective, upper, and lower) according to the patients' inhalation status. An overall estimate was calculated for this study based on the available ORs using a fixed effects model and the inverse-variance method. The same strategy was used for Mosier et al.'s study,[16] for which an overall OR estimate was obtained based on the data published for patients with and without early-onset nonrenal organ failure.

To assess the impact of adjusting the data for relevant confounders and intermediate variables, the meta-analysis was repeated including all the studies that reported both adjusted and unadjusted effect estimates. Therefore, adjusted risk estimates were used whenever they were available, and the corresponding unadjusted association measure was used in the opposite case. Given that only significant variables are usually maintained in multivariate analyses, excluding the studies that did not report the adjusted risk measures could have led to an overestimation of the effect of inhalation injury on mortality. In our study, we decided to present both models to assess the impact on the reported association.

Overall estimates were presented as ORs (or RRs) together with their 95% CI values using the DerSimonian-Laird random effects models with the inverse-variance random effects method. Interstudy heterogeneity was evaluated using Cochran's Q test and quantified with the I^2 statistic (ranging from 0% to 100%), and was considered to be statistically significant at p values less than 0.05, with I^2 values of 25%, 50%, and 75% representing cutoff points for low, moderate, and high degrees of heterogeneity, respectively.

Sources of heterogeneity were explored in two ways: (1) results were compared by stratifying the studies according to the prespecified study-level and patient-level characteristics, and (2) univariate random effects meta-regressions with logtransformed ORs (RRs) were then used to assess potential sources of heterogeneity.

To assess the robustness and conclusiveness of our results, a sensitivity analysis was also carried out using the one-study-out method by excluding studies one at a time and repeating the meta-analysis based on the remaining data.

Finally, publication bias and small-study effects were explored by analyzing funnel plots and performing an Egger's test.

All statistical analyses were carried out using the *meta* package in R software version 3.5.1 (The R Project for Statistical Computing). Statistical tests were two-sided and applied a significance threshold of p less than 0.05.

RESULTS

Study Characteristics

Fifty-four studies including a total of 408,157 patients were selected for the analysis. The main characteristics of these studies are described in Table 1. Most of them were performed in North America (n = 24), Europe (n = 11), and Asia (n = 10), and included 37 single-center studies and 17 multicenter studies, all of which primarily used a retrospective (n = 48) cohort design. The mean MINORS score for all studies was 10.6.

The number of patients included in each study ranged from 128 to 73,140, with a median of 755 patients. Sixteen studies exclusively evaluated patients hospitalized in the intensive care unit (ICU). The mean age of the patients included in these studies ranged from 10 to 76.5 years (median age, 35.0 years), and the percentage of male patients ranged between 39.6% and 97.5% (median percentage, 72.0%). The median percentage of patients with flame burns was 58.3%

(range, 17.2%–90.4%), with a mean affected total body surface area (TBSA) ranging between 4% and 51.8% (median TBSA = 14.9%) (Table 1)

In most of the reviewed studies, the identification of inhalation injury was based on clinical findings and the results of ancillary tests (n = 25). In seven studies, inhalation injury was diagnosed based exclusively on clinical findings, whereas no definition of inhalation was specified in 22 articles (Supplemental Digital Content, Table 3, http://links.lww.com/TA/B489). The role of inhalation as a predictor of in-hospital mortality among burn patients was a determining factor in most of the studies after adjusting the analyses for a wide range of potential confounders, such as sociodemographic variables, the affected TBSA, and the presence of comorbidities or other traumas (Table 2).

Rates of Inhalation Injury and in-Hospital Mortality

The point prevalence of inhalation injury reported in the individual studies ranged between 1.2% and 74.6%. The meta-analytic pooling of the estimates of the prevalence of inhalation injury reported by 51 studies yielded a pooled inhalation prevalence of 15.7% (95% CI, 13.4%–18.3%), with significant evidence of considerable interstudy heterogeneity (I^2 = 99.6%, p < 0.001) (Supplemental Digital Content, Fig. 1, http://links.lww.com/TA/B489). The sensitivity analysis, in which case the meta-analysis was serially repeated after excluding each study individually, yielded prevalence figures that ranged between 15% and 16.50%. In this analysis, the studies carried out by Stylianou et al.,[11] Alp et al.,[27] and Kim et al.[15] contributed to the greatest difference in the pooled estimate (Supplemental Digital Content, Fig. 2, http://links.lww.com/TA/B489).

No statistically significant differences were observed in the prevalence estimates according to the criteria specified for the identification of an inhalation injury (Fig. 2A). In contrast, a statistically significant higher prevalence of inhalation injury was found in those studies that

only included burn patients admitted to the ICU in comparison with those that included all hospital admissions (34.8% vs. 10.8%) ($p < 0.001$) (Fig. 2B).

According to other study-level characteristics, no statistically significant differences were found between the inhalation injury rates reported in the studies carried out in Europe and those carried out in North America (14.5% vs. 14.3%, respectively); however, a higher prevalence was found in the studies performed in Asia (24.6%) ($p = 0.030$). Significantly higher prevalence estimates were reported in the studies with smaller sample sizes, in those that included older patients, flame burns, and patients with a greater affected TBSA (Table 3).

Concerning mortality, the death rates ranged between 1.3% and 58.2%. The overall pooled mortality estimate was 10.9% (95% CI, 9.2%–12.9%), the pooled mortality for the burn patients admitted to the ICU was 20.7% (95% CI, 16.1%–26.2%), and that of the studies including all hospital burn admissions was 8.3% (95% CI, 6.8%–9.9%) (Supplemental Digital Content, Figs. 3 and 4, http://links.lww.com/TA/B489).

Association of Inhalation Injury and In-Hospital Mortality

Of the 54 studies that were included in the systematic review, 27 provided an adjusted measure of the association between inhalation injury and mortality that was suitable for a meta-analysis, and eight provided a measure suitable for a univariate association. Among those that did not provide a suitable measure of quantitative effect for the meta-analysis, five concluded that there was no significant association between inhalation injury and mortality, seven reported a significant association between both parameters, and the other seven did not provide any conclusive information in relation to such association.

Twenty-four studies, which were included in the meta-analysis, provided adjusted OR values that allowed for analyzing the association between inhalation injury and mortality (Fig. 3). The summarized OR of in-hospital mortality secondary to inhalation injury was 3.2 (95% CI, 2.5–

4.3) and highly heterogeneous ($p < 0.001$, $I^2 = 94.0\%$). A similar trend was observed when combining the three studies[17,20,54] that provided a RR or a HR, although this association did not reach statistical significance, as the pooled RR was 2.0 (95% CI, 0.7–5.9) (Supplemental Digital Content, Fig. 5, http://links.lww.com/TA/B489).

The significant association found between inhalation injury and in-hospital mortality was stronger among the studies that included all hospital burn admissions (pooled OR, 3.9) compared with those that only included ICU patients (pooled OR, 2.0) ($p = 0.039$) (Fig. 3). A significantly higher likelihood of mortality was also observed among the patients with inhalation injury included in the studies with a lower proportion of male patients, a lower mean affected TBSA, and a lower prevalence of inhalation injury. A nonsignificant association between inhalation injury and mortality was found in the two studies in which the Acute Physiology and Chronic Health Evaluation (APACHE) score was adjusted at admission. Subgroup analyses revealed no differences in the pooled ORs based on other study parameters (geographical region, sample size, single-center vs. multicenter studies) or the patients' characteristics (mean age or percentage of flame burns) (Table 3).

These results were essentially the same when univariate ORs associated with the inhalation injury were considered in those studies that did not provide the adjusted figures (random effects pooled OR, 3.4; 95% CI, 2.6–4.4) (Supplemental Digital Content, Fig. 6 and Table 4, http://links.lww.com/TA/B489).

The sensitivity analyses showed no changes in the overall estimates when the fixed effects model was considered (OR, 3.3; 95% CI, 3.1–3.5), or when each of the individual studies were deleted from the meta-analysis (OR, 3.1–3.4) (Supplemental Digital Content, Tables 5 and 6, http://links.lww.com/TA/B489).

With regard to publication bias, no visual asymmetry was observed in the funnel plot.

Egger's test did not detect any significant evidence of publication bias either (p = 0.970) (Supplemental Digital Content, Fig. 7 and Figure 8, http://links.lww.com/TA/B489).

DISCUSSION

This systematic review and meta-analysis revealed the following: in the first place, that the relevant available clinical studies report a great variability in terms of the prevalence of inhalation injury (1.2%–74.6%). Our analysis showed that of the 408,157 patients studied, a mean of 19.8% had a concomitant inhalation injury.

After examining the factors that the available studies suggested could have an impact on the results of the prevalence of inhalation injury, we observed noticeable differences in the definitions provided by the authors with respect to the methodology used. Inhalation injury was defined as stated in each of the reviewed articles. The entity “inhalation injury” was not defined in 22 of the analyzed studies, was diagnosed based on clinical data in seven studies, and was identified based on clinical data and the results of ancillary tests in 25 cases. Only four publications admitted every patient with suspected inhalation injuries for further exploration studies to evaluate their lower airways (e.g., bronchoscopy/xenon analysis). Therefore, cases of both lower airway injury and upper airway edema may have been included. This variability proves that there is no standard definition that can be used to diagnose inhalation injury with certainty in all patients exposed to smoke. However, no differences were observed between the prevalence of inhalation injury reported in the studies in which only clinical data were used to define the entity and those in which the results of ancillary tests were also used. No significant differences were observed with respect to this variable either between the single-center and multicenter studies.

With regard to the factors related to the analyzed populations, no geographical differences were found in the prevalence of inhalation injury. The samples of patients that were analyzed belonged to two clinical settings (ICU admissions vs. Hospital admissions) that showed significant differences in terms of the prevalence of this entity. These differences were not related to the more homogeneous definition of inhalation injury among ICUs (no definition of the entity was provided in 7 of the 16 studies involving ICU patients)[8,16,17,29,31,33,36] nor to its increased documentation (only six studies based their identification on the results of ancillary tests).[10,15,25,34,42,52] However, these differences could be related to the association of this type of injury with more extensive burns and to the high percentage of flame burns (50%) reported in the studies analyzed in this setting.[8–10,16,23,25,31,36] Moreover, none of these studies included pediatric patients, in whom scald burns are more common. Although we found a higher prevalence of inhalation injury among older patients, this difference did not reach statistical significance, most likely because of the small number of studies that included patients with a mean age of 50 years or older.[8,31,37,40,56]

An analysis of the 51 studies that included this indicator demonstrated that the prevalence of inhalation injury has not decreased over the past three decades.

Second, based on the above, the fact that almost 2 of every 10 patients who survive hospital admission continue to have an inhalation injury has an impact on mortality rates. In this meta-analysis, the pooled overall mortality reported in the analyzed studies was 10.9% (95% CI, 9.2%–12.9%), with the greater rates being reported in the studies that were carried out in ICUs (20.7%; 95% CI, 16.1%–26.2%) in comparison with those that included all hospital admissions (8.3%; 95% CI, 6.8%–9.9%).

Thus, the pooled data suggest a significant effect of inhalation injury on in-hospital mortality (OR, 3.2) (OR, 3.9 when excluding studies carried out in ICUs). This figure falls within the significance range for studies carried out in ICUs and could be explained by a greater

contribution of the affected TBSA to the outcome of patients with extensive burns, considering that the impact of inhalation injuries did not appear to be significant in the studies that included patients with an affected total body surface area ≥ 20%, or by the introduction of variables in the model that reflected the risk associated with the severity of the inhalation injury. Thus, the studies that included APACHE scales in the analysis showed a nonsignificant association between the inhalation injury and in-hospital mortality.[16,17,25]

The APACHE scoring includes multiple components influenced by the respiratory system (respiratory rate, Pa02/Fi02 ratio, and pH). As such, the APACHE system can be strongly influenced, especially if the investigator chooses the worst APACHE score during the first 3 days of hospitalization. Thus, the injury/disease severity scoring already accounts for lung injury severity. The above was also true for those that did not offer a suitable measure of quantitative effect for the meta-analysis.[29,30,34,39] In this regard, the studies that considered the need for mechanical ventilation as a marker of a serious disease[10,15] and those that reported a significant association with other variables related to organ dysfunction (base deficit; acute kidney injury)[30,41,42] displaced inhalation damage in the final model. Models including an independent association with other variables that tend to appear throughout the clinical progress of this entity, such as infection,[5,43] could reduce the impact of the variables available at admission on the mortality rates.

Although inhalation injury has been analyzed as a predictor of clinical outcome, no standard definition or diagnostic guidelines for this entity are available for clinicians. We found no major effect of the inhalation injuries on in-hospital mortality in the studies in which the results of ancillary tests were used, given that no physical or clinical history finding is sufficiently sensitive or specific to reach a definitive diagnosis, and that fiber-optic bronchoscopy might overlook cases of inhalation injury if only the distal airway is involved. The fact that very few articles systematically studied the lower airways of every patient with suspected inhalation

damage may also explain why there were no differences in the impact of this variable between groups that did or did not receive supplementary tests. None analyzed severity groups based on the gravity of the injury identified in bronchoscopy studies. Because of the broad range of degrees of severity in this condition, we hypothesized that the studies that defined the entity in terms of its severity would show a greater effect of this variable; however, although the Stylianou et al.[11] and Belgian Outcome in Burn Injury Study Group[35] studies reported an OR of 6.39 and 6.8, respectively, Barber et al.[9] reported an OR of 1.66, and both Egozy et al.[21] and Ibarra et al.[23] stated that inhalation injury was not associated with an increased mortality in their final models.

A higher OR was observed in the studies carried out in Europe as compared with those performed in other geographical regions. Nevertheless, the definition terms, prevalence rates, mortality rates, and variables that made up these models were not homogeneous.

Despite the improvements achieved in the management of inhalation damage in recent decades, we found no reduction in the effect of this entity on mortality over time.

To our knowledge, this is the first systematic review and meta-analysis carried out to explore the prevalence of inhalation injury and its association with mortality. There were, however, certain inherent limitations to our research. As in the case of any systematic review and meta-analysis, we observed significant interstudy heterogeneity. Although we performed subgroup and sensitivity analyses to determine the potential causes of this heterogeneity, we were unable to find a variable that could clearly explain the differences. However, although most of the studies included in our analysis were adjusted for known potential causes of mortality, other confounding factors within each study could have modulated the risk of mortality. To maximize the inclusion of information published in the literature related to the subject of this review, some of the studies we analyzed also contained some pediatric patients (although not exclusively), even though this may have affected our results. Similarly, it was impossible to extract data

referring exclusively to patients who had not been admitted to the ICU from studies that had included “all hospital admissions.” We arbitrarily included only studies with cohorts of at least 100 patients and so this review did not analyze data from smaller series. Lastly, some studies lacked important information, which prevented us from performing a more extensive quantitative analysis.

Notwithstanding the above, this systematic review and meta-analysis provides the most accurate estimate to date of the prevalence of inhalation injury and its effect on mortality over the past three decades. Our results reflect a wide range of prevalence rates and a significant association between inhalation injury and in-hospital mortality. However, this association is not significant if adjusted for disease severity.

AUTHORSHIP

G.R. participated in literature search, study design, data interpretation, and drafting of this article. L.S.-Q. participated in literature search, data collection, data interpretation, and preparation of the tables. S.P.-D. participated in study design, data analysis, data interpretation, and drafting of this article.

DISCLOSURE

The authors declare no funding or conflicts of interest.

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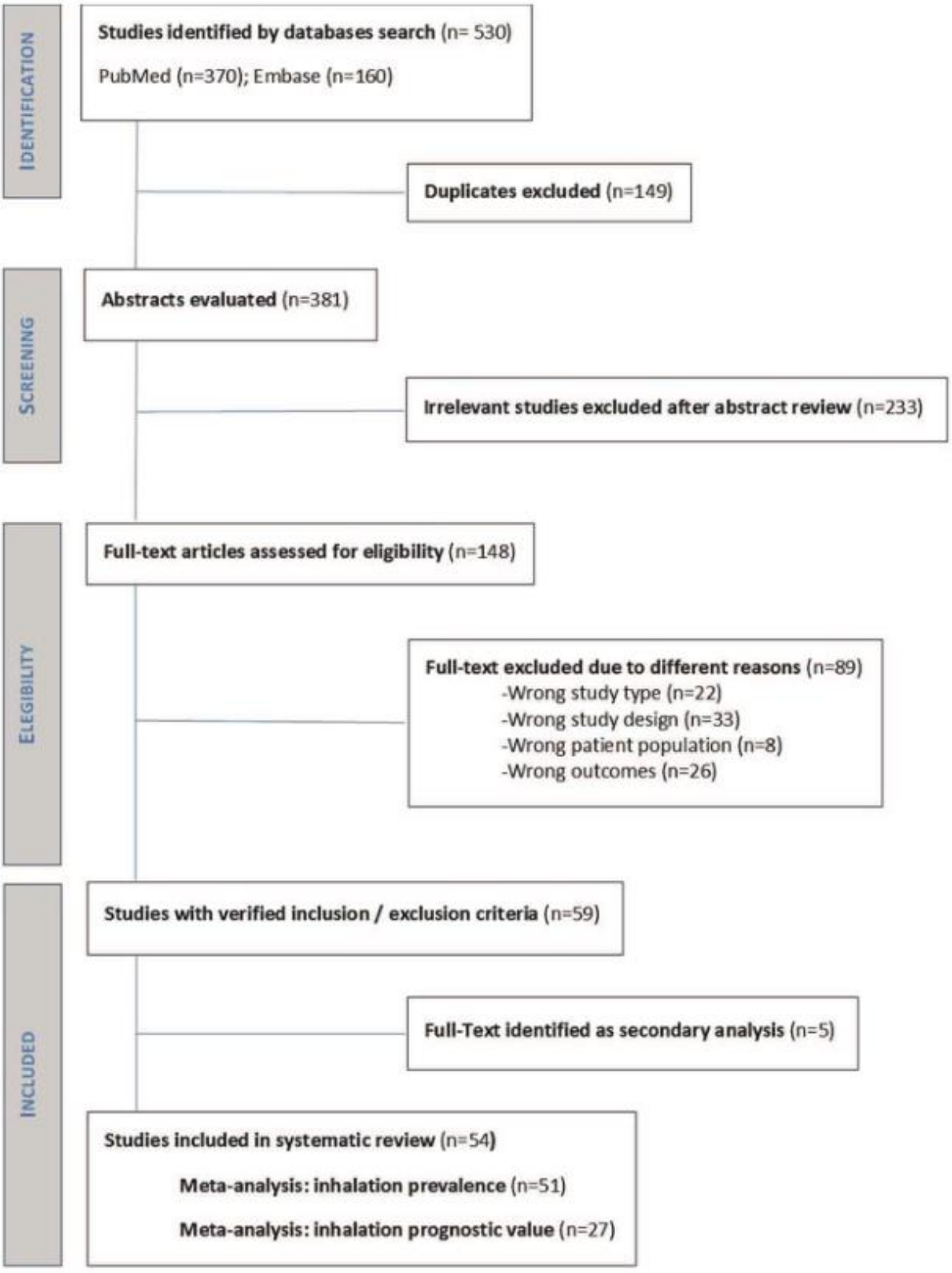

Figure 1. Study selection

TABLE 1. Selected Characteristics of the 54 Studies Included in the Systematic Review

First Author (Publication Year)	Setting	Study Design	*n*	Hospital vs. ICU Admissions	Age, y	Male (%)	Flame (%)	%TBSA	MINORS Score
Kuo (2018)[17]	Taiwan	Prospective single-center cohort	301	ICU admissions	Normal P: 45.0 ± 15.4 High P: 46.6 ± 19.5	78.4	68.1	Normal P: 43.4 ± 22.9 High P: 57.0 ± 30.7	11
Kim (2017)[15]	Korea	Retrospective single-center cohort	676	ICU admissions	48.9 ± 14.8	81.8	NA	36.8 ± 26.0	10
Knowlin (2016)[18]	USA	Retrospective single-center cohort	7640	Hospital admissions	32 ± 22.4	69.0	45.0	8.6 ± 12	10
Cassidy (2015)[19]	Australia/New Zealand	Retrospective multicenter cohort	2892	Hospital admissions	36 (24.5–51)	75.8	56.9	6 (3–12)	12
Duarte (2015)[20]	Brazil	Retrospective single-center cohort	1734	Hospital admissions	Accidental: 25.0(6.0–41.0); Self-inflicted 36.5 (29.0–45.0); Aggression: 30.0 (23.0–42.5)	69.9	58.5	Accidental: 10.8 (5.0–20.0); Self-inflicted: 27.0 (17.5–40.3; Aggression: 20.0 (10.0–36.0)	12
Egozi (2014)[21]	Israel	Retrospective single-center cohort	174	ICU admissions	42 ± 19	73.0	NA	34 ± 23	10
Harpole (2014)[22]	USA	Retrospective multicenter cohort	73140	Hospital admissions	GB: 36.8 ± 25.3; Non-GB: 34.7 ± 22.6	70.1	38.1	GB: 37.9 ± 28.4; Non-GB: 8.9 ± 13.9	10
Ibarra Estrada (2014)[23]	Mexico	Retrospective single-center cohort	146	ICU admissions	Mean: 35	80.8	82.2	Mean 51.8	10
Stylianou (2014)[11]	UK	Retrospective multicenter cohort	66611	Hospital admissions	25.5 ± 23.5	NA	17.2	3.96 ± 8.3	10
Bartosch (2013)[24]	Portugal	Retrospective single-center cohort	228	Hospital admissions	Mean: 48	64.5	68.0	Mean: 17.1	10
Moore (2013)[25]	Australia/New Zealand	Prospective and retrospective multicenter cohort	1715	ICU admissions	41.1 ± 18.0	79.7	68.3	17 (6–35)	13
Yanculovich (2013)[26]	Israel	Retrospective single-center cohort	558	Hospital admissions	15.4 (mean)	62.4	NA	NA	12

TABLE 1. Selected Characteristics of the 54 Studies Included in the Systematic Review

First Author (Publication Year)	Setting	Study Design	*n*	Hospital vs. ICU Admissions	Age, y	Male (%)	Flame (%)	%TBSA	MINORS Score
Alp (2012)[27]	Turkey	Retrospective single-center cohort	1190	Hospital admissions	median 10 (3–30)	66.8	26.0	median, 12 (7–20)	10
Chen (2012)[28]	Taiwan	Retrospective multicenter cohort	23147	Hospital admissions	31.05 ± 22.67	64.8	NA	NA	10
Guo (2012)[29]	China	Retrospective multicenter cohort	148	ICU admissions	NS: 41.16 ± 12.18; S: 41.58 ± 11.47	85.1	NA	NS: 91.15 ± 6.98; S: 80.43 ± 11.22	10
Stewart (2012)[30]	USA	Retrospective single-center cohort	692	Hospital admissions	25.5 ± 5.9	97.5	NA	9 (4–24)	12
Albornoz (2011)[8]	Chile	Single-center case-control	286	ICU admissions		70.6	58.2	≥65 y: 13 (1–76); <65 y: 22.5 (1–98)	20
Maldonado (2011)[31]	Germany	Retrospective single-center cohort	143	ICU admissions	52.03 ± 23.95	72.0	DS: 62.7	35 ± 22.15.	10
Othman (2011)[32]	Iraq	Retrospective single-center cohort	947	Hospital admissions	18 (4–29)	46.5	58.5	19 (10.5–44.0)	12
Huebinger (2010)[33]	USA	Retrospective single-center cohort	265	ICU admissions	35 (22–51)	75.0	NA	30 (20–45)	12
Moore (2010)[34]	Australia	Retrospective single-center cohort	228	ICU admissions	NS: 57 ± 20.0; S: 39.5 ± 16.7	81.0	57.9	NS: 44.2 ± 30.1; S: 25.0 ± 19.8	10
Mosier (2010)[16]	USA	Retrospective multicenter cohort	221	ICU admissions	AKI: 50.8 ± 18.3; No AKI: 39.1 ± 14.0	72.8	90.4	AKI: 42.5 ± 17.6; No AKI: 41.8 ± 19.4	10
BOBI Study Group (2009)[35]	Belgium	Retrospective multicenter cohort	6227	Hospital admissions	DS: 34 ± 23; VS: 35 ± 23	NA	NA	DS: 11.4 ± 15.7; VS: 11.0 ± 14.6	10
Galeiras (2009)[10]	Spain	Retrospective single-center cohort	851	ICU admissions	46.2 ± 20.6	70.4	86.6	20 (median)	10
Herruzo (2009)[36]	Spain	Prospective single-center cohort	1773	ICU admissions	NS: 1–10 d estancia: 54.9 ± 2.4. >10 d estancia: 54.9 ± 1.8. S: 1–10 d estancia: 39.9 ± 0.7.	63.5	60.5	NS: 1–10 d estancia: 42.8 ± 3.4; >10 d estancia: 37.3 ± 2 S: 1–10 d estancia: 11.1 ± 0.4;	10

TABLE 1. Selected Characteristics of the 54 Studies Included in the Systematic Review

First Author (Publication Year)	Setting	Study Design	*n*	Hospital vs. ICU Admissions	Age, y	Male (%)	Flame (%)	%TBSA	MINORS Score
					>10 d estancia: 43.4 ± 0.3.			>10 d estancia: 23.1 ± 0.7	
Lundgren (2009)[37]	USA	Retrospective single-center cohort	325	Hospital admissions	68.1 ± 10.2	63.7	58.2	14.9 ± 17.2	10
Taira (2009)[38]	USA	Retrospective multicenter cohort	25,572	Hospital admissions	35.6 ± 26	71.2	NA	NA	12
Gomez (2008)[39]	Canada	Retrospective single-center cohort	1343	Hospital admissions	DS 43.9 ± 17.9; VS: 45.6 ± 18.9	69.3	57.6	DS 18.5 ± 17.5; VS: 15.6 ± 16.1	10
Lumenta (2008)[40]	France	Retrospective single-center cohort	265	Hospital admissions	76.5 (65–100)	39.6	65.3	10.0 (5–20)	10
McGwin (2008)[5]	USA	Retrospective multicenter cohort	68,661	Hospital admissions	NS: 54.1 ± 25.6; S: 28.6 ± 21.9 (DS)	71.6	28.8	NS: 45.9 ± 28.0; S: 12.2 ± 13.2 (DS)	10
Barber (2007)[9]	USA	Prospective single-center cohort	233	ICU admissions	35 (21–48)	74.0	83	32 (23–48)	12
Coca (2007)[41]	USA	Retrospective single-center cohort	304	Hospital admissions	AKI: 45 ± 18; No AKI: 40 ± 16	78.0	NA	AKI: 34 ± 19; No AKI: 24 ± 18	10
Cochran (2007)[42]	USA	Retrospective single-center cohort	128	ICU admissions	35.2 ± 21.1	NA	NA	41.7 ± 17.9	10
Horvath (2007)[43]	USA	Retrospective single-center cohort	2651	Hospital admissions	28.8 (<1–101)	78.2	NA	10.3 (<1–99)	10
Macedo (2007)[44]	Brazil	Prospective single center cohort	278	Hospital admissions	24 (1–82)	60.1	54.7	14(1–100)	12
Thombs (2007)[45]	USA	Retrospective multicenter cohort	31338	Hospital admissions	43.33 ± 17.2	72.8	NA	13.1 ± 16.2	10
Albrecht (2006)[46]	USA	Retrospective single-center cohort	802	Hospital admissions	Infected 32.2 (19–81); Colonized 29.8 (17–79); Negative 35.9 (11–100)	NA	NA	Infected 29.1 (<1–80); Colonized 23.8 (2–81.5); Negative 14.2 (<1–97.9)	10

TABLE 1. Selected Characteristics of the 54 Studies Included in the Systematic Review

First Author (Publication Year)	Setting	Study Design	*n*	Hospital vs. ICU Admissions	Age, y	Male (%)	Flame (%)	%TBSA	MINORS Score
Fatusi (2006)[47]	Nigeria	Retrospective single-center cohort	139	Hospital admissions	With facial involvement 18.5 (median); without facial involvement: 22 (median)	62.6	66.9	With facial involvement: 19 (median); Without facial involvement: 25 (median)	10
Kerby (2006)[48]	USA	Retrospective multicenter cohort	49079	Hospital admissions	Male: 29.6 ± 21.4; Female 29.7 ± 26.5	70.2	45.4	Male: 13.6 ± 15.9; Female: 13.4 ± 16.4	10
George (2005)[49]	USA	Retrospective multicenter cohort	6236	Hospital admissions	Male 42.8 ± 15.81: Female 48.2 ± 18.95	77.4	30.5	Male: 13 (median); Female: 12 (median)	10
Lehnhardt (2005)[50]	Germany	Retrospective single-center cohort	464	Hospital admissions	With erythroblast: 48.6 ± 18.3; Without erythroblast: 42.1 ± 21.4	67.8	NA	With erythroblast 40.5 ± 18.5; Without erythroblast 18.7 ± 10.9	10
Suzuki (2005)[51]	Japan	Retrospective multicenter cohort	5560	Hospital admissions	40.1 ± 26.2	61.6	50.8	20.3 ± 23.0	10
Ho (2002)[52]	China	Retrospective single-center cohort	286	ICU admissions	23 (1 month to 93 y) 7	2.0	43.4	18 (10–95)	10
McGwin (2002)[53]	USA	Retrospective single-center cohort	1611	Hospital admissions	Male: 42.6 ± 15.9; Female: 48.4 ± 19.1	76.3	69.3	Male: 10 (median); Female: 10 (median)	10
Muller (2001)[54]	New Zealand	Retrospective single-center cohort	4094	Hospital admissions	29 (10–97)	75.0	43.8	NA	10
O'Keefe (2001)[55]	USA	Retrospective single-center cohort	4927	Hospital admissions	DS: 29 (8–43); VS: 28 (6–41)	74.5	NA	DS: 10 (5–18); VS: 9 (4–18)	10
Wibbenmeyer (2001)[56]	USA	Retrospective single-center cohort	308	Hospital admissions	71.5 ± 8.6	64.3	68.6	13.0 (6–29)	10
Attia (2000)[57]	Egypt	Retrospective single-center cohort	533	Hospital admissions	22.95 ± 16.71	49.9	66.8	NA	12
Ryan (1998)[58]	USA	Retrospective multicenter cohort	1665	Hospital admissions	21 ± 20	69.0	NA	14 ± 20	10

TABLE 1. Selected Characteristics of the 54 Studies Included in the Systematic Review

First Author (Publication Year)	Setting	Study Design	*n*	Hospital vs. ICU Admissions	Age, y	Male (%)	Flame (%)	%TBSA	MINORS Score
Germann (1997)[59]	Germany	Retrospective single-center cohort	498	Hospital admissions	NS: 49.9; S: 34.7	75.5	NA	NS: 49.9; S: 20.9	10
Coste (1996)[60]	France	Retrospective single-center cohort	708	Hospital admissions	NS: 61.1 ± 23.7; S: 40.0 ± 17.8	NA	NA	NS: 48 ± 27.6; S: 17.4 ± 16.7	10
Saffle (1995)[3]	USA	Retrospective multicenter cohort	6417	Hospital admissions	NA	73.1	50.3	14.1 ± 16.6	10
Wong (1995)[61]	Singapore	Retrospective single-center cohort	352	Hospital admissions	29 (8 months to 84 y)	70.7	NA	4 (0–91)	10
Smith (1994)[1]	USA	Retrospective single-center cohort	1447	Hospital admissions	30 (mean)	75.0	NA	18 (mean)	10

Data are shown as mean ± standard deviation or median (range) for quantitative variables.
BOBI, Belgian outcome in burn injury; DS, derivation set; VS, validation set; NS, nonsurvivor; S, survivor. GB, genital burn; non-GB, nongenital burns; AKI, acute kidney injury; no AKI, no acute kidney injury; P, phosphate level.

TABLE 2. Prevalence of Inhalation Injury and Adjusted Mortality ORs Reported in the Studies Included in the Systematic Review

First Author (Publication Year)	Definition of Inhalation Injury	Inhalation Injury (%)	Mortality (%)	Adjusted/Unadjusted* OR (95% CI)	Adjustments
Kuo (2018)[17]	No definition	37.9	24.2	HR, 0.61 (0.36–1.03)	Age, male sex, TBSA, p > 4.5 mg/dL, creatinine, urine output (L/d), AKI, APACHE II
Kim (2017)[15]	Clinical findings and complementary tests	44.0	25.6	Subjective: 0.47 (0.19–1.14); Upper: 1.91 (0.59–6.16); Lower: 0.77 (0.20–2.99)	Age, %TBSA, Mechanical ventilation, PF ratio, carboxyhemoglobin level
Knowlin (2016)[18]	Clinical findings and complementary tests	7.0	4.0	2.85 (1.99–4.08)	Age, TBSA, mechanism of injury, Charlson Comorbidity Index
Cassidy (2015)[19]	Clinical findings and complementary tests	12.5	2.4	5.74 (3.80–8.68)	Direct admission, TBSA, age, female gender, time to admission
Duarte (2015)[20]	Clinical findings and complementary tests	19.0	11.8	HR, 3.75 (2.53–5.56)	Age, sex, TBSA, Third-degree burn, injury intent, psychiatric disorders, comorbidities
Egozi (2014)[21]	Clinical findings	38.0	22	41.0 (11.6–144.8)*	Smoke, Age > 60 y, TBSA>40%, BSI
Harpole (2014)[22]	No definition	7.9	5.5	1.39 (1.22–1.59)	GB present, third degree burn, age, LOS, TBSA, Male, nonwhite ethnicity
Ibarra Estrada (2014)[23]	Clinical findings	50.7	58.2	0.7 (0.53–0.94)*	Male, age (>38 yrs.), third-degree burn, electric burn, ventilator-associated pneumonia, >49% TBSA
Stylianou (2014)[11]	Clinical findings	1.2	1.27	6.39 (4.87–8.38)	Age, TBSA, existing disorders, injury type
Bartosch (2013)[24]	No definition	12.0	11.0	4.70 (1.15–19.25)	Gender, age, %TBSA, surgery, etiology
Moore (2013)[25]	Clinical findings and complementary tests	36.2	10.9	1.42 (0.89–2.29)	Age, %FTSA, APACHE II (no age component), sex (female), % PTSA, deliberate self-harm
Yanculovich (2013)[26]	No definition	NA	3.2	2.30 (0.35–14.97)	TBSA, age, gender, ethnicity
Alp (2012)[27]	Clinical findings	1.3	7.0	NA	% TBSA, age, underlying disease
Chen (2012)[28]	No definition	7.8	2.08	3.08 (SE = 0.14)	Hospital admission status, flushing time, ICU admission, age, Head and neck burned, upper limbs burned, trunk burned, lower limbs burned, Burn Index, TBSA>20%, sex
Guo (2012)[29]	No definition	32.4	34.5	6.3 (2.9–13.4)*	FTSA%, total volume of fluid resuscitation, APACHE II, PPC ≥ 65% first 3 d, operation during first 3 d, PT, FDP
Stewart (2012)[30]	No definition	16.6	5.9	Inhalation injury not significantly associated with mortality	AKIN as AKI variable: age, ISS, %TBSA, AKIN-1, AKIN-2, AKIN-3 RIFLE as AKI variable: age, ISS, %TBSA, risk, injury, failure

TABLE 2. Prevalence of Inhalation Injury and Adjusted Mortality ORs Reported in the Studies Included in the Systematic Review

First Author (Publication Year)	Definition of Inhalation Injury	Inhalation Injury (%)	Mortality (%)	Adjusted/Unadjusted* OR (95% CI)	Adjustments
Albornoz (2011)[8]	No definition	39.5	29.5	2.59 (0.93–7.16)	Over 65 y, TBSA, proportion deep TBSA/TBSA
Maldonado (2011)[31]	No definition	DS: 74.6	DS: 34.7	DS 2.63 (0.98–7.11)*	Age, TBSA, pH value, magnesium
Othman (2011)[32]	Clinical findings	22.0	28 9.	78 (4.79–20.0)	Age, female sex, TBSA ≥40%
Huebinger (2010)[33]	No definition	19.0	15.0	4.35 (1.69–11.17)	Age, TBSA, sex (female), race/ethnicity, IL-10-592A/-819T
Moore (2010)[34]	Clinical findings and complementary tests	NA	11.8	Inhalation injury was not significantly associated with mortality	FTSA, APACHE III-j score
Mosier (2010)[16]	No definition	39.1	19.5	Without early-onset NROF factor: 1.07 (0.43–2.68). With early-onset NROF factor: 0.79 (0.29–2.13)	Without early-onset NROF factor: Early AKI, Age, %TBSA, nonrenal APACHE II > =20, presence of comorbidity. With early-onset NROF factor: early AKI, age, %TBSA, nonrenal APACHE II > =20, presence of comorbidity, early-onset NROF ≥2
BOBI Study Group (2009)[35]	Clinical findings and complementary tests	9.2	4.6	6.8 (4.6–10.1)	Age, % TBSA
Galeiras (2009)[10]	Clinical findings and complementary tests	43.6	17.6	3.83 (2.48–5.92)*	Age, female, early mechanical ventilation, TBSA, FTSA.
Herruzo (2009)[36]	No definition	7.3	12.2	7.85 (4.65–13.27)	Age, TBSA, period (1993 to 2001 and 1985 to 1992)
Lundgren (2009)[37]	Clinical findings and complementary tests	11.3	18.5	6.0 (2.0–17.5)	Age, sex (female), %TBSA, Charlson score
Taira (2009)[38]	Clinical findings and complementary tests	7.6	4.4	6.6 (5.72–7.68)	Off-hours admission, age, female, full-thickness injury, TBSA>30%, University hospital
Gomez (2008)[39]	Clinical findings	13.0	9.7	DS: 5.7 (2.6–12.9)*	Age, Day 1 APACHE II, %PTSA, % FTSA, sex
Lumenta (2008)[40]	Clinical findings and complementary tests	17.7	30.6	Inhalation injury correlated significantly with death	Deep TBSA, Baux score
McGwin (2008)[5]	Clinical findings and complementary tests	10.0	5.7	3.7 (3.37–4.14)	Age, female, TBSA, pneumonia, ≥1 medical condition, coexistent trauma
Barber (2007)[9]	Clinical findings	26.0	18	1.66 (0.68–4.05)	Age, FTSA, sex (female), ethnicity, CD14–159C, TLR4 + 896G, IL-1β-31C, IL-6-174C, TNF-α-308A
Coca (2007)[41]	No definition	20.4	13.2	3.37 (1.17–9.70)	Age, TBSA, RIFLE classification, sepsis

TABLE 2. Prevalence of Inhalation Injury and Adjusted Mortality ORs Reported in the Studies Included in the Systematic Review

First Author (Publication Year)	Definition of Inhalation Injury	Inhalation Injury (%)	Mortality (%)	Adjusted/Unadjusted* OR (95% CI)	Adjustments
Cochran (2007)[42]	Clinical findings and complementary tests	46.9	17.1	4.4 (1.5–12.9)*	Age, TBSA, serum lactate, base deficit
Horvath (2007)[43]	Clinical findings and complementary tests	14.3	7.8	2.18 (1.38–3.46)	TBSA, FTSA, age, FWI
Macedo (2007)[44]	Clinical findings and complementary tests	2.5	5.0	Inhalation injury was not associated with death	Age > 50 y, TBSA, Length of stay, multiresistant bacteria in wound, fungi in wound.
Thombs (2007)[45]	No definition	13.2	7.0	NA	Comorbidities
Albrecht (2006)[46]	No definition	12.7	8.7	Inhalation injury was not associated with death	Infection with Acb, Age, %TBSA, ISS, increasing length of stay in ICU, increasing time on the ventilator
Fatusi (2006)[47]	No definition	4.3	30.9	NA	Age, male, flame, TBSA, presentation at >24 h, wound infection
Kerby (2006)[48]	Clinical findings and complementary tests	10.5	5.3	NA	Sex, age, race, %TBSA, pneumonia
George (2005)[49]	No definition	7.3	8.6	NA	Sex, age, race, comorbidity, injury type, %TBSA
Lehnhardt (2005)[50]	Clinical findings and complementary tests	22.6	17.5	3.35 (1.93–3.89)	Sex, age, TBSA, Third-degree burn, white blood cell count, C-reactive protein, hemoglobin, erythroblasts
Suzuki (2005)[51]	Clinical findings and complementary tests	30.4	15.8	2.58 (2.03–3.29)	FTSA, PTSA, age
Ho (2002)[52]	Clinical findings and complementary tests	17.1	8.7	5.47 ($p < 0.001$)	Age, TBSA
McGwin (2002)[53]	No definition	9.6	8.7	NA	Sex, age, race, chronic medical conditions, %TBSA
Muller (2001)[54]	No definition	4.0	3.6	RR: 3.61 (2.39–5.47)	TBSA, age, sex, skin graft operation, upper limb burn
O'Keefe (2001)[55]	Clinical findings and complementary tests	7.5	5.3	3.4 (1.9–6.0)	TBSA, full-thickness burn, age, sex
Wibbenmeyer (2001)[56]	Clinical findings and complementary tests	15.6	30.2	5.2 (2.7–10.0)*	Age, TBSA
Attia (2000)[57]	No definition	8.6	33.0	0.08 ($p < 0.05$)	TBSA, depth of burn wound, degree of burn wound, age, sex, clothing ignition, intent
Ryan (1998)[58]	Clinical findings and complementary tests	15.0	4.0	NA	Age, % TBSA

TABLE 2. Prevalence of Inhalation Injury and Adjusted Mortality ORs Reported in the Studies Included in the Systematic Review

First Author (Publication Year)	Definition of Inhalation Injury	Inhalation Injury (%)	Mortality (%)	Adjusted/Unadjusted* OR (95% CI)	Adjustments
Germann (1997)[59]	Clinical findings and complementary tests	43.0	28.3	5.70 ($p < 0.05$)	Age, sex, TBSA, third-degree burn, lung, smoking, heart, alcohol
Coste (1996)[60]	No definition	NA	8.5	Inhalation injury was not associated with death	Age, TBSA
Saffle (1995)[3]	No definition	10.9	5.1	7.16 ($p < 0.001$)	Age, LOS, TBSA, days on ventilator support, FTSA, sex, surgical procedures
Wong (1995)[61]	Clinical findings and complementary tests	12.2	4.5	19.3 ($p < 0.05$)	TBSA
Smith (1994)[1]	Clinical findings and complementary tests	19.6	9.5	3.22 ($p < 0.05$)	Age, TBSA

PF, PO2/FIO2; BSI, bloodstream infection; LOS, total hospital length of stay; FTSA, full-thickness surface area; APACHE, acute physiology and chronic health evaluation; PTSA, partial-thickness surface area; PPC, percentage decline
platelet counts; PT, prothrombin time; FDP, fibrin degradation product; NROF, nonrenal organ failure; RIFLE, end-stage kidney disease; FWI, fungal wound infection; Acb, Acinetobacter baumannii complex; ISS, Injury Severity Score; AKIN,
Acute Kidney Injury Network; mCCI, Charlson Comorbidity Index excluding cardiovascular diseases; P, phosphate level; IRR, incidence rate ratio; SE, standard error.

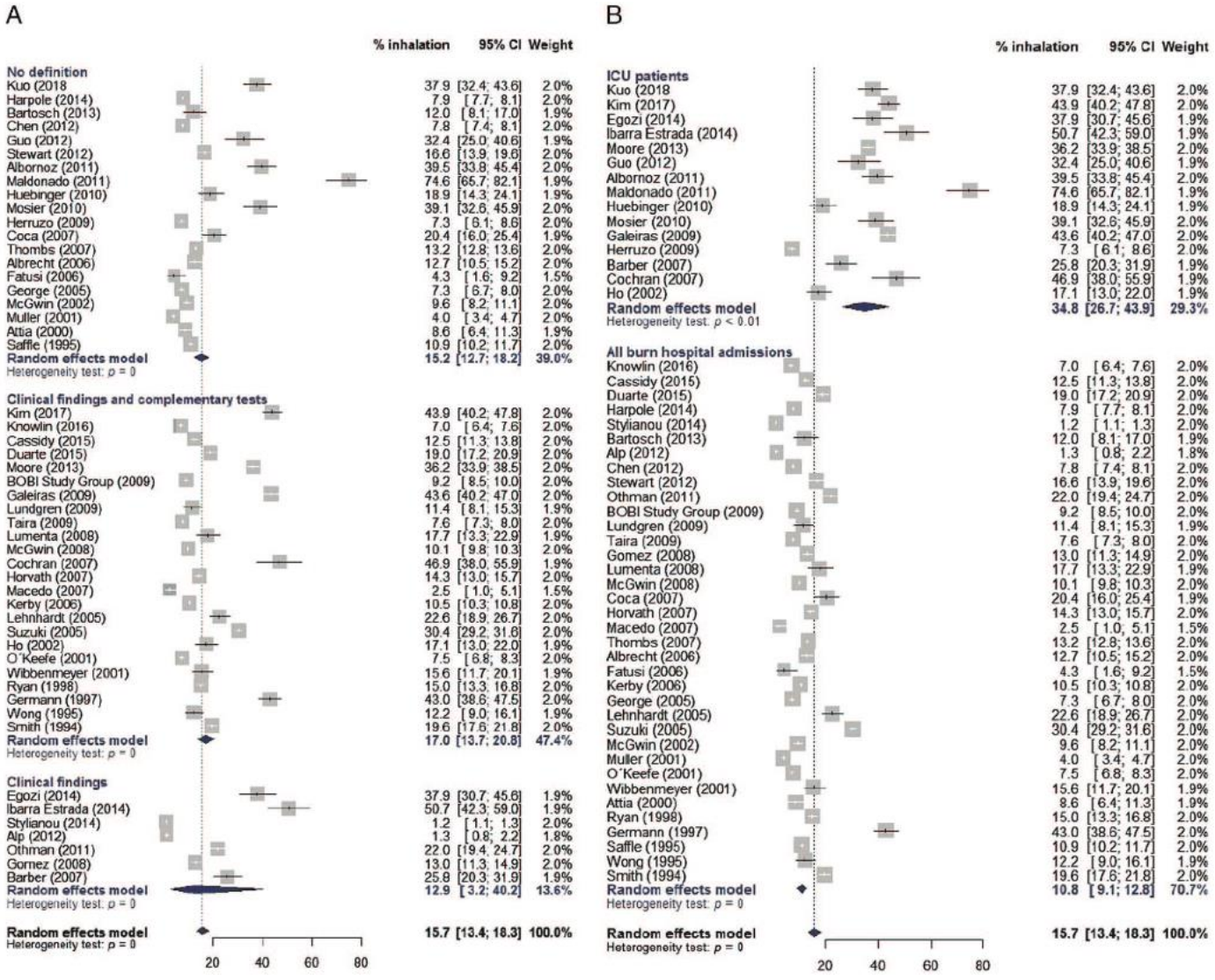

Figure 2. Forest plot of the pooled estimated prevalence of inhalation injuries among burn patients according to the definition used (A) and the type of patients included (B) in the studies.

TABLE 3. Results of the Meta-Analysis, and the Subgroup and Sensitivity Analyses

	*Inhalation Prevalence					Inhalation Prognostic Value**,†				
	No. Studies	Pooled Inhalation Prevalence	95% CI	Heterogeneity I^2 (%)	Meta-Regression, *p*	No. Studies	ORs	95% CI	Heterogeneity I^2 (%)	Meta-Regression, *p*
Overall	51	15.7%	13.4%–18.3%	99.6%		24	3.2	2.5–4.3	94.0%	
Sensitivity análisis										
Fixed-effects model	51	10.5%	10.4%–10.6%	99.6%		24	3.3	3.1–3.5	94.0%	
Random-effects model	51	15.7%	13.4%–18.3%	99.6%		24	3.2	2.4–4.3	94.0%	
Type of patients					<0.001					0.039
All burn admissions	36	10.8%	9.1–12.8%	99.6%		17	3.9	2.8–5.3	95.1%	
ICU patients	15	34.8%	26.7%–43.9%	97.9%		7	2.0	1.0–4.1	86.5%	
Inhalation injury definition										
Clinical findings	7	12.9%	3.2%–40.2%	99.8%	–	3	5.0	2.3–11.1	79.9%	–
Clinical findings and complementary tests	24	17.0%	13.7%–20.8%	99.6%	0.279	12	3.2	2.4–4.3	91.4%	0.223
No definition	20	15.2%	12.7%–18.2%	99.1%	0.520	9	2.8	1.6–4.7	88.7%	0.122
Geographical región										
Europe	10	14.5%	5.1%–34.9%	99.8%	–	5	6.0	4.6–7.8	33.0%	–
North America	24	14.3%	12.8%–16.0%	98.8%	0.929	11	2.8	1.8–4.3	96.5%	0.060
Asia	9	24.6%	13.9%–39.7%	99.7%	0.030	5	2.7	1.5–4.8	85.8%	0.099
Australia	3	13.1%	3.5%–38.1%	99.8%	0.777	2	2.9	0.7–11.3	94.8%	0.226
South America	3	14.8%	5.8%–32.8%	97.9%	0.848	1	2.6	0.7–7.2	–	0.365
Africa	2	6.7%	3.5%–12.7%	63.7%	0.094	0				
Sample size					<0.001					0.357
<1000 patients	27	23.8%	18.9%–29.5%	97.2%		11	2.8	1.6–4.8	76.1%	
≥1000 patients	24	9.7%	7.8%–11.9%	99.7%		13	3.6	2.5–5.0	96.5%	
Study design					0.165					0.939
Single-center studies	34	16.8%	12.9%–21.6%	98.9%		14	3.3	2.3–4.7	72.3%	
Multicenter studies	17	13.5%	10.5%–17.2%	99.8%		10	3.2	2.1–4.8	97.3%	
Participants' average age					0.074					0.203
<50 y	31	14.7%	10.9%–19.4%	99.7%		16	3.4	2.5–4.7	89.7%	
≥ 50 y	5	28.3%	13.2%–50.6%	97.8%		2	3.8	2.6–8.8	16.8%	

TABLE 3. Results of the Meta-Analysis, and the Subgroup and Sensitivity Analyses

	*Inhalation Prevalence					Inhalation Prognostic Value**,†				
	No. Studies	Pooled Inhalation Prevalence	95% CI	Heterogeneity I^2 (%)	Meta-Regression, *p*	No. Studies	ORs	95% CI	Heterogeneity I^2 (%)	Meta-Regression, *p*
% males					0.791					0.013
<50%	3	15.3%	8.6%–25.7%	95.0%		16	3.3	2.3–4.6	95.1%	
≥ 50%	44	16.5%	14.3%–18.9%	99.5%		6	2.4	1.2–4.5	86.1%	
% Flame					<0.001					0.149
<50%	9	5.7%	4.1%–8.1%	99.8%		4	3.1	1.6–5.9	98.3%	
≥ 50%	22	20.4%	15.8%–26.0%	98.7%		10	3.3	1.6–5.9	84.9%	
Participants' average TBSA					<0.001					0.007
<20%	22	10.8%	7.5%–15.2%	99.6%		10	4.2	2.8–6.1	84.1%	
≥ 20%	10	40.1%	33.2%–47.3%	96.0%		4	1.9	1.0–3.8	78.8%	
Inhalation injury prevalence										0.002
<20%	–	–	–	–		14	4.1	2.9–5.8	96.0%	
≥ 20%	–	–	–	–		9	2.2	1.4–3.4	80.7%	
Inhalation defined in terms of MV										0.310
No	–	–	–	–		21	3.1	2.3–4.1	94.2%	
Yes	–	–	–	–		3	5.0	2.9–8.5	76.6%	
Whether or not adjusted for APACHE score										0.022
No	–	–	–	–		22	3.6	2.7–4.7	94.1%	
Yes	–	–	–	–		2	1.2	0.8–1.8	0.8%	

V, mechanical ventilation.

*Meta-analysis of the prevalence of inhalation injury.

** Including data from studies reporting multivariable adjusted OR estimates.

† Meta-analysis of the association between inhalation injury and mortality

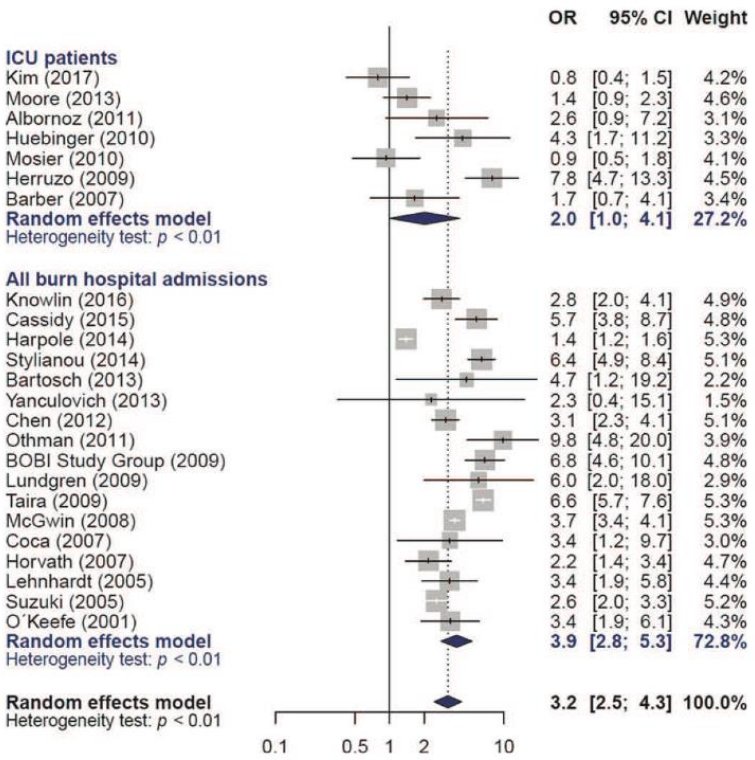

Figure 3. Forest plot of the summarized adjusted ORs of the association between inhalation injuries and mortality according to the type of patients included in the studies.