Egypt, J. Plast. Reconstr. Surg., Vol. 48, No. 4, October: 245-254, 2024

Guideline of Management of Acute Smoke Inhalation Injury: Systematic Review and Meta-Analysis of Last 10 Years

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Abstract

Background: Inhalation injury-based respiratory failure is the main cause of death in patients with severe burns. In general, damage from smoke inhalation results in airway edema, inflammation and, subsequently, cellular debris, mucus, fibrin clots and polymorphonuclear leukocytes PNL combine to form casts that lead to ventilation/perfusion mismatch and poor oxygenation.

Objective: This meta-analysis aims to review the Guideline of Management of Acute Smoke Inhalation Injury and discuss the different modalities and treatment.

Material and Methods: A comprehensive search of the literature to identify the Guideline of Management of Acute Smoke Inhalation Injury and discuss the different modalities and treatment. via electronic databases including OVID, Science Direct, Springer, Web of Science and Google Scholar. Initial search will carried out using keywords: “burns, “ARDS,” “adult respiratory distress syndrome”, “extracorporeal membrane oxygenation”, “ECMO,” “inhalation injury”, ”smoke inhalation injury”, and “heparinized oxygen mask”, ”ECMO”.

Results: All published articles were from 2013 to 2022 limited to human studies of different modalities will be analyzed and compared regarding the criteria of management.

Conclusion: The care of patients with burn related inhalation injury remains highly challenging. Key topics include airway management, nebulized heparin, NAC, chest physiotherapy and ECMO effect.

Early ambulation, nebulized Heparin in combination with NAC and albuterol was associated with a reduction in the duration of mechanical and decrease mortality rate.

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Key Words: *Acute Smoke Inhalation Injury – Burn Injuries – Nebulized Heparin – Chest Physiotherapy – ECMO Effect.*

Ethical Committee: Approved by ethical committee Ain Shams University MS 459/2023.

Disclosure: No conflict of interest.

Introduction

More than 120,000 people die from burn-related causes every year, making burn injuries a serious worldwide health concern [1]. One of the leading causes of mortality for burn patients is severe acute respiratory distress syndrome combined with refractory respiratory failure [2].

Inhalation injuries occur in 10% to 20% of patients admitted to burn centres, and the frequency rises with the extent of the burn. In burn patients, inhalation injury is a significant predictor of survival, prolonged ventilator use, length of hospital stays, and mortality, along with age and burn size [3].

Practically speaking, there are many etiological stages for inhalation injury: (1) Heat injury to the upper respiratory tract; (2) Toxic gas-related harm at the fire scene; and (3) Pulmonary parenchymal injury and systemic poisoning.

List of Abbreviations:

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta-Analyses
LOS : Length of hospital stays
DOMV : Length of mechanical ventilation
ARDS : Adult respiratory distress syndrome
ECMO : Extracorporeal membrane oxygenation

Inhalational injury divided into 4 degree of diagnostic values (1) Hyperaemia, (2) Patches of erosion, (3) Superficial ulcerative defect and fibrin clots, (4) Walls of the trachea and bronchi were covered with a dense greyish-black eschar [4].

The foundation of current treatment consists of vigorous airway toilet, humidification, mechanical ventilation, and supportive care for the airway. Heparin, N-acetylcysteine, and β2-agonist nebulization all play a part in treatment [5].

Aim of the work:

To review the Guideline of Management of Acute Smoke Inhalation Injury as a primary end point and discuss the different modalities of treatment.

Patients and Methods

Following the guidelines in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) statements, we conducted this systematic review and meta-analysis. Authors, editors, and reviewers conducting meta-analyses of interventional and observational research use the PRISMA and MOOSE reporting checklists. Reviewers are required by the International Committee of Medical Journal Editors (ICJME) to submit their conclusions according to each checklist element.

Criteria for considering studies for the review:

Types of studies:

In the present study, we included randomized comparative trials, prospective, and retrospective studies.

Types of participants:

We reviewed studies that include management of inhalation injuries with these different techniques between the years 2013 and 2022.

Types of outcome measures:

Impact on lung damage and lung function improvement in burn patients who have had an inhalation injury; length of hospital stays (LOS); length of mechanical ventilation (DOMV); complications; and death rate.

Inclusion criteria:

Studies from any geographical location in last 10 years (2013-2022), English language, study design: comparative (randomized), prospective or retrospective studies, population: Humans with inhalation smoke injuries, intervention: Supportive respiratory care with new medical treatment modalities (Nebulization of heparin, N-acetylcysteine and antibiotics), ECMO and chest physiotherapy.

Exclusion criteria:

Non-English language, studies with incomplete data or duplication, papers not published in a peer reviewed journal, published abstracts, case report, studies other than randomized controlled trials, opinion studies.

Methodology for finding research studies:

A thorough review of the literature to determine the Acute Smoke Inhalation Injury Guidelines and to address various treatment options. using online resources such as Google Scholar, OVID, Science Direct, Springer, and Web of Science. The terms "burns," "ARDS," "adult respiratory distress syndrome," "nebulized heparin," "extracorporeal membrane oxygenation," "ECMO," "inhalation injury," "smoke inhalation injury," and "ECMO" will be used in the initial search.

Every published paper from 2013 to 2022 that focused only on human research using various modalities will be examined and contrasted in terms of diagnosis and treatment standards.

Figure (1) illustrated the specifics of the research selection and search procedure. To recruit more instances, relevant publications cited in these original studies were also searched.

Locating and selecting studies:

Twenty publications make up the research included in the quantitative synthesis; a copy of each paper found will be acquired, and the first reviewer will abstract pertinent data for a quantitative summary. It will also determine the odds. When a study's information is ambiguous or there are inconsistencies, a second reviewer's abstraction will be attempted to settle the dispute.

Data extraction:

Extracting the following information independently from each study that satisfied the requirements for inclusion: study type, sample size, dates of inclusion, treatment plan, age, sex, nation, treatment regimen, presence of inhalation injury, settings for extracorporeal membrane oxygenation, follow-up time, mortality, and days spent on a mechanical ventilator. We will cross-check all retrieved data to ensure there are no inconsistencies.

Statistical analysis:

Review Manager version 5.3 software was used to do statistical analysis. In either a fixed-effect or random-effect model, the odds ratio (OR) with 95% confidence interval (CI) for dichotomous variables and the mean difference (MD) with 95% CI for continuous variables were calculated. The Chisquared test was used to justify the heterogeneity among the trials, and $p<0.1$ indicated statistical significance. I^2 was used to quantify the amount of heterogeneity, and an $I^2 >50\%$ suggested considerable heterogeneity. In cases where there was no proven substantial heterogeneity, a fixed effect model meta-analysis was conducted. The random-effect model was employed elsewhere.

Results

A total of 1513 articles were reviewed from Scopus, PubMed, web of science and google scholar. Thirty papers were duplicated, 1036 articles were excluded by title, 188 by Animal study, 20 by Bronchial asthma, 18 by infection, 20 by vaping & E-cigarette, 54 by case series & case report, 127 by review literature Finally, 20 studies (number of patients = 2261) were included in the study (Fig. 1).

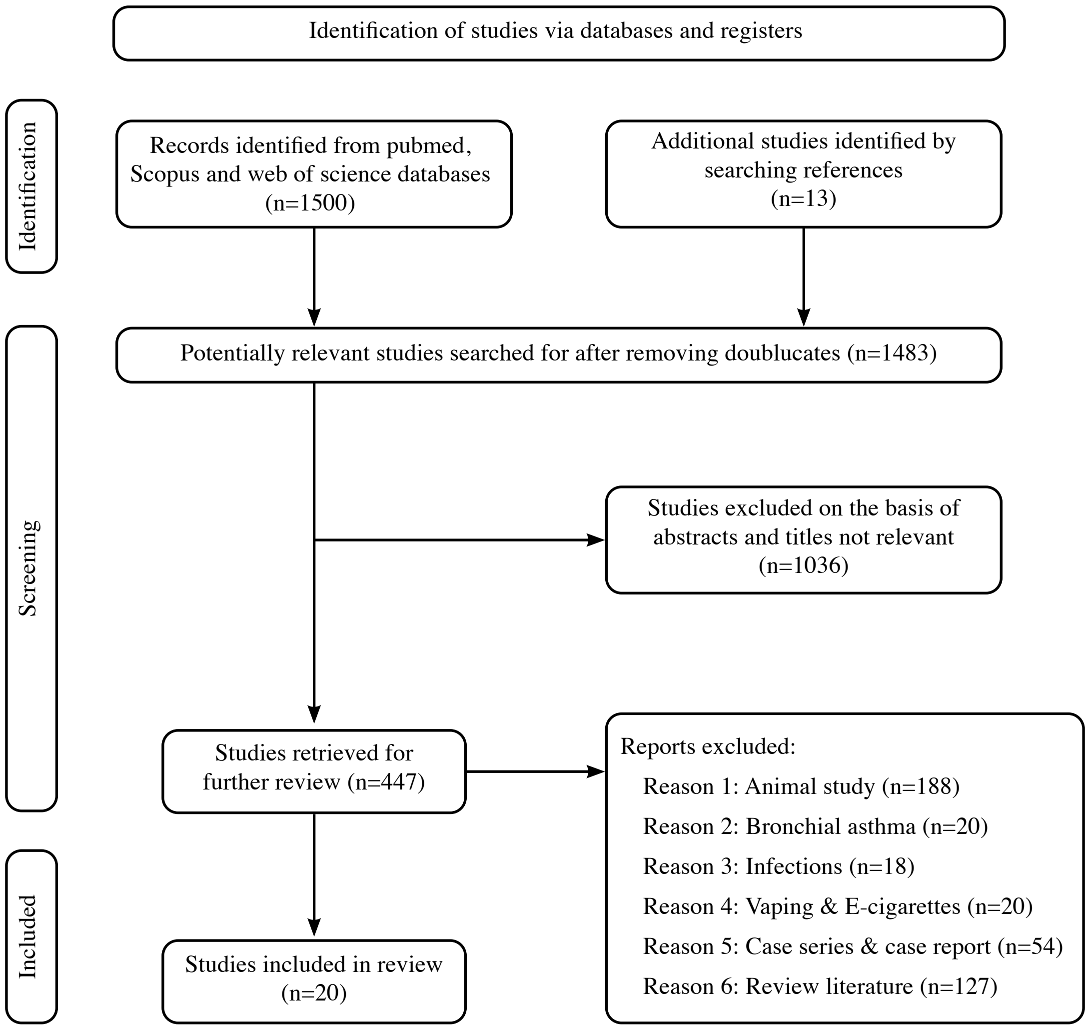


Fig. (1): Flow diagram of the literature search and study selection processes.

The present study included 20 studies published between 2014 and 2021. Seven studies were conducted in USA **[6-12]**, 3 in China **[13-15]**, two in Egypt **[16,17]**, two in UK **[18,19]**, two in German **[20,21]** one in Japan **[22]**, one in France **[23]**, one in Taiwan **[24]**, and one in india **[25]**.

Results in the current meta-analysis, twenty papers were included with total number of 2635 participants, 2135 with smoke inhalation injury, who participated in evaluation of different modalities in management of acute smoke inhalation injury as shown in Table (1).

Table (1): General characteristics of the included studies.

First author year	Site of study	Study design	TBSA	Total patients	Mean age (years)	Type of intervention	Follow-up period	Inhalation (n)	DOMV	Mortality
McIntire 2017	UK	Retrospective	10%	72	45	Nebulized heparin (10.000 iu,Q4h)+NAC+sulbtamol	June, 2014 - Feb, 2016	72	2 (2.8)	7.0±2.6
McGinn 2019	China	Retrospective study	5.25 (0.5-13.25)	48	N/A	Nebulized heparin (5.000 iu,Q4h)+NAC+sulbtamol	August 2014 -March 2016	48	3	3.0±1.8
Kashefi 2014	USA	Retrospective	22.5%	40	19	Nebulized heparin (5.000 iu,Q4h)+NAC+sulbtamol	January 2011 to July 2012	40	10	8.5±7.7
Elsharnouby 2014	Egypt	Prospective randomized	50%	53	34	Nebulized heparin (5.000 -10.000iu,Q4h)+NAC+	June 2006–May 2009	53	7	10±2
Sharma and Lunawat, 2015	India	Prospective randomized	35% - 75%	100	31.46±10.9	nebulized with heparin and n-acetylene cysteine	N/A	100	66	N/A
Ding2017	China	Prospective clinical	64±30.82	23	37.9±3.4	Intratracheal Instillation of Perfluorohexane	May 2012 to January 2013	23	N/A	N/A
Foncerrada 2017	USA	A prospective randomized study	58±14	16	12±4	Nebulized racemic epinephrine	September 2014-September 2016	16	N/A	7.5 (±5.5)
Kubo 2020	Japan	A Retrospective Study	N/A	271	53.5±15.11	Chest physiotherapy	2004-2014	271	50	11
Allam 2020	Egypt	A prospective randomized study	N/A	60	20-50	High frequency chest wall oscillation was administered by using the airway vest clearance device	N/A	60	N/A	N/A
Nosanov 2017	USA	A Retrospective Study	17	30	38.9	Extracorporeal membranous oxygenation (ECMO) VV (11), VA (17), mixed (8) Sarting Time (d) N/A	2002–2011	16	20	14.1
Li 2021	China	Retrospective	58.8	5	48.2	ECMO(VV)(5) ST:10.2	2014–2020	4	4	7.5
Szentgyorgyi 2018	UK	Retrospective	27.8	5	32.4	ECMO(VV)(5) ST:7.4	2011–2017	5	1	18
Dadras 2019	German	Retrospective study	37	8	48	VV ECMO (7), mixed (1) ST:9	2017–2019	7	3	16.1(±11.7)
Ainsworth 2018	USA	Retrospective study	27	36	36	VV ECMO (14) ST:N/A	2012–2017	4	6	11.5
Soussi 2016	France	Retrospective study	31	11	51	VV ECMO (8), VA ECMO (2), mixed (1) ST:4	2013–2016	6	8	3.75
Marcus 2019	USA	Retrospective study	30	20	32	VV ECMO (20) ST: N/A	2012–2018	2	8	10.3
Eldredge 2019	USA	Retrospective study	17	8	5.9	VV ECMO (8); ST:7.5	2006–2016	3	1	11
Behr 2020	Germany	Retrospective study	N/A	121	N/A	ECMO; ST: N/A	1989–2018	N/A	63	N/A
Burke 2016	USA	Retrospective	N/A	58	37	ECMO; ST:5	January 1999 and December 2015	58	33	N/A
Hsu 2016	Taiwan	Retrospective	50–99	6	30	ECMO; ST:1.	N/A	N/A	5	N/A

The primary endpoint of all enrolled trials is death. The studies showed no heterogeneity (p=0.51, I^2=0%), and the meta-analysis employed a fixed model. With an RR of 0.75 (95% CI 0.43 to 1.32, p=0.32), the pooled result showed that the mortality of the heparin-treated group was lower than that of the standard therapy group (Fig. 2).

The DOMV results were reported in six trials, yet there was variability across them (p<0.00001, I^2=84%). A random model meta-analysis revealed that patients treated with nebulized heparin had a lower DOMV than those treated with non-nebulized heparin (Fig. 3), with an MD of −5.67 (95% CI −8.47 to −2.87, p<0.0001).

The results of the length of hospital stay were published in five of the included studies. There was heterogeneity (p=0.09, I^2=51%) and the meta-analysis employed a random model. The findings demonstrated that patients in the heparin-treated group had shorter hospital stays than those in the group receiving standard care; the MD was −2.18 (95% CI −7.89 to 3.53, p=0.45) (Fig. 4).

Subgroup analysis with pooled in-hospital mortality data. In-hospital mortality was recorded in every study that was included. In-hospital mortality that was pooled was 49% (95% CI 34–64%).

Regarding outcome of nebulization by heparin and NAC

Mortality

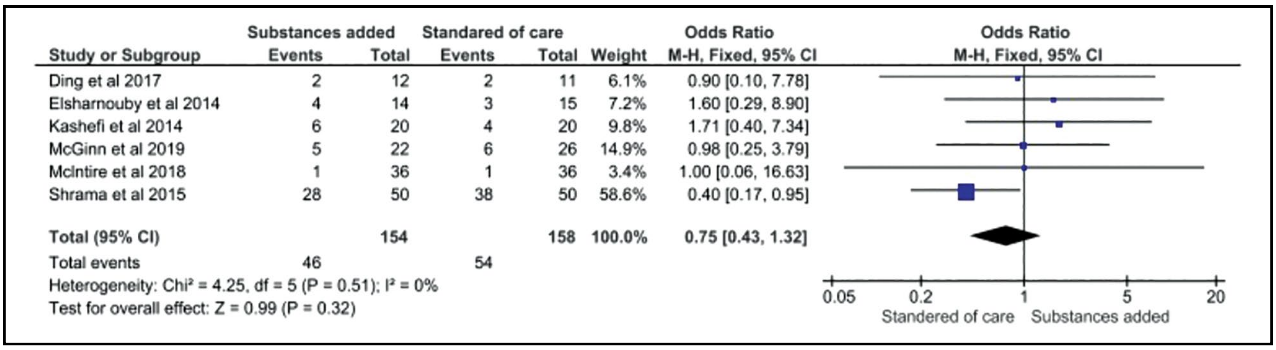


Fig. (2): Nebulized heparin's impact on mortality in burn patients who have suffered inhalation injuries is plotted as a forest. Relational risk (RR) and confidence interval (CI).

DOMV

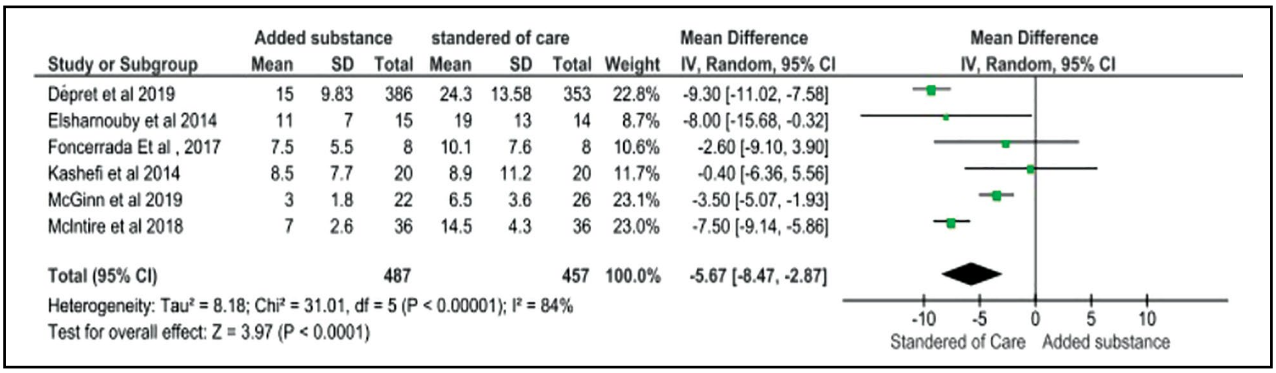


Fig. (3): A forest plot illustrating how long burn patients with inhalation injuries needed to be on mechanical ventilation in response to nebulized heparin. MD mean difference, CI confidence interval, and RR relative risk.

LOHS

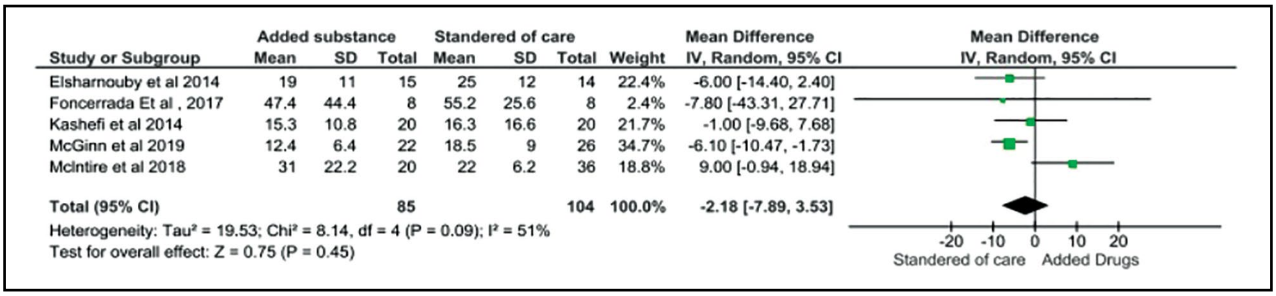


Fig. (4): Nebulized heparin's impact on the length of hospital stays for burn patients who have suffered an inhalation injury is shown in a forest plot. MD mean difference, CI confidence interval, and RR relative risk.

Regarding outcome of ECMO

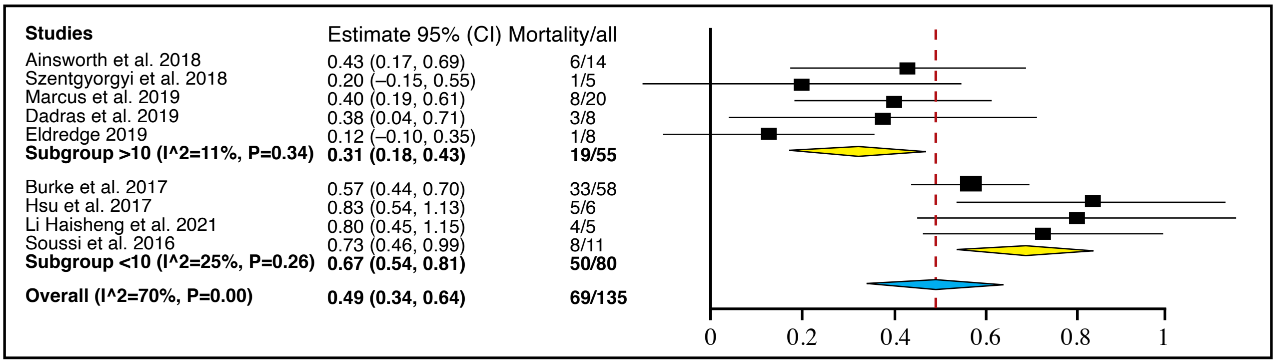


Fig. (5): Using a random-effect model, a forest plot of ECMO mortality for burn patients with varying burn severity.

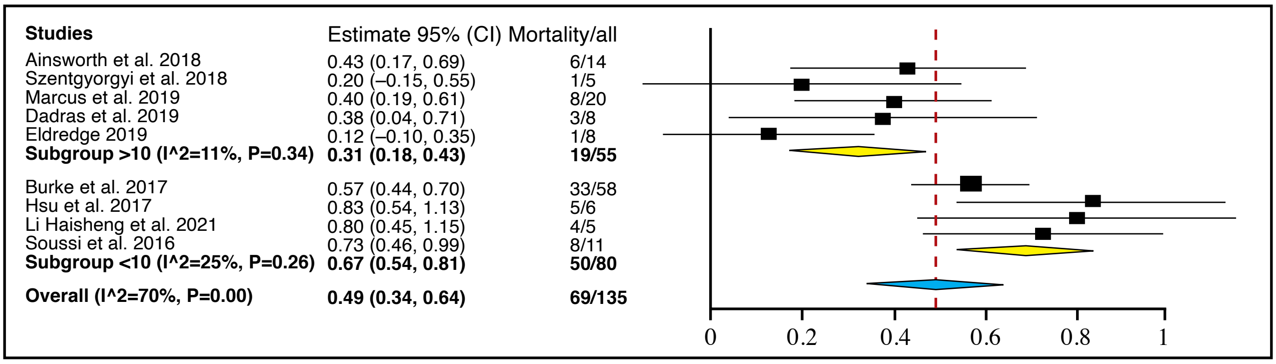
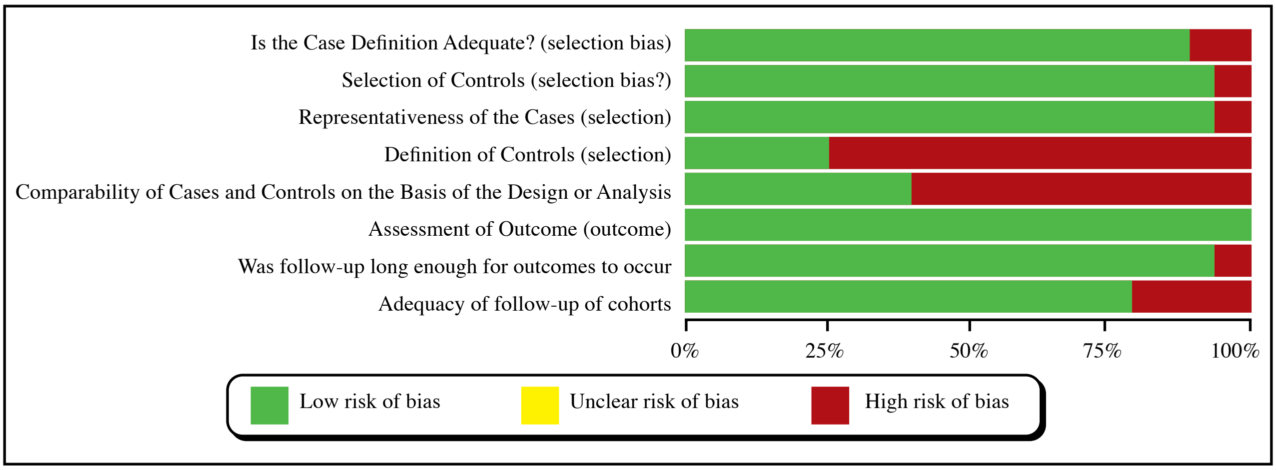


Fig. (6): A forest plot representing the death rate of burn victims receiving varying lengths of ECMO. In other investigations, the subgroup was divided based on the length of ECMO (≥10 vs <10 days). CI confidence interval, extracorporeal membrane oxygenation (ECMO).



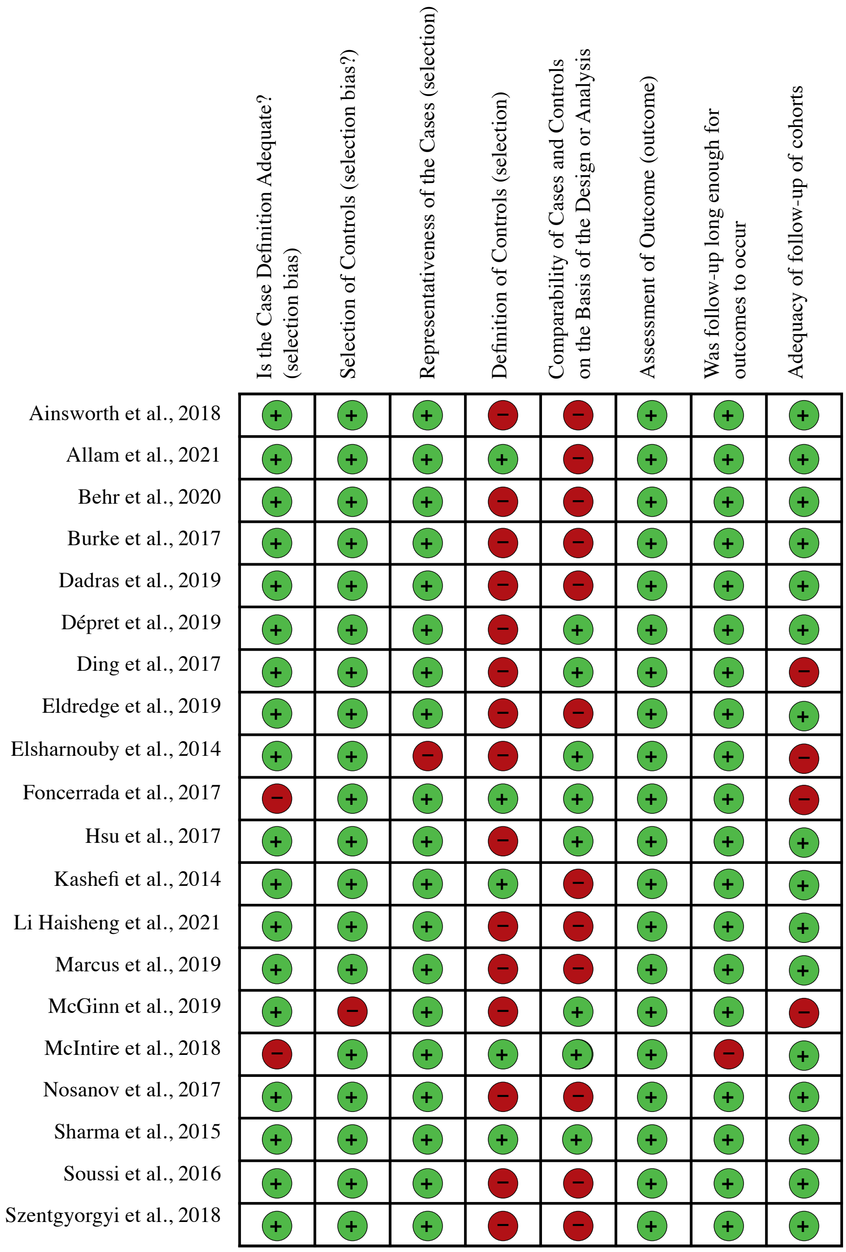


Fig. (7): Risk of bias summary for the included studies.

Discussion

To forecast the possibility and severity of inhalation damage, it is helpful to assess the patient's burn history and their overall clinical symptoms. Patients who were exposed to steam or fire in a small area had a higher risk of developing airway damage [26].

A patient's medical history and clinical symptoms, such as stridor, coughing, difficulty swallowing secretions, and hoarseness, might aid in the diagnosis of an inhalation injury; however, their absence does not rule it out [33]. When diagnosing inhalation injuries in burn patients, fiberoptic bronchoscopy is an incredibly helpful tool [27].

To treat severe burns with inhalation injury, the following steps are essential depending on the patient's condition: Prompt endotracheal intubation for mechanical ventilation, active management of excessive inflammation and other adverse reactions, prevention of secondary infection, and encouragement of lung tissue and airway healing [28].

We gave an evidence-based medical foundation for the use of inhalational heparin, N-acetylcysteine ECMO, nebulized epinephrine and chest physical therapy in the treatment of burn patients with inhalation injuries after conducting a thorough evaluation of various modalities.

Nebulized heparin can significantly lower the comprehensive scores of lung injury and does not cause coagulation disorders or changes in platelet count. According to [11,15,16,19], mortality was significantly lower in the heparin-treated group, and DOMV was significantly shortened.

But Kashefi et al., [11] discovered that burn patients' incidences of pneumonia significantly increased when they used heparin. They believed, as we do, that rather than being a direct result of the drugs themselves, the higher infection rates were caused by deficiencies in sterility during the nebulized medication's preparation and delivery.

The main conclusion of Foncerrada [7] was that racemic epinephrine nebulization was safe for patients who had suffered smoke inhalation injuries because no negative side effects were seen during or after the nebulization period, including an increase in heart rate or mean arterial blood pressure, arrhythmia, elevation of the ST segment, or death. The primary objective of this study was not to determine the efficacy of nebulized epinephrine due to the small number of patients in the control group. However, data extracted from this study indicate that patients treated with epinephrine had improved physical endurance, fewer days on mechanical ventilation (DOMV), and shorter lengths of hospital stays (LOS). However, there were differences in the groups with respect to age, weight, and burn size.

Regarding the impact of ECMO on the length of mechanical ventilation, studies with ECMO durations greater than 10 days had a lower pooled mortality (31%, 95% CI 18–43%) than studies with ECMO durations less than 10 days (67%, 95% CI 54–81%) (Fig. 6).

Two studies [17-22] on chest physiotherapy found that although high frequency chest wall oscillation (HFCWO) improves mucus clearance both centrally and peripherally and reduces the viscoelastic and cohesive properties of mucus, the CPT group experienced a lower incidence of pneumonia, fewer days of mechanical ventilation, and an earlier first day of bed edge sitting than the control group.

About the safety and effectiveness of ECMO in burn victims. The pooled mortality for burn patients was determined to be 49% by [8,9,18,20,21]. However, since there was never a control group in any of the investigations, it was impossible to determine how ECMO affected mortality. According to these findings, there was a 62% in-hospital death rate linked to VA ECMO. These results led us to conclude that ECMO may not be as clinically effective in circulatory support as in respiratory support [9,10].

According to a study by Nosanov et al., [6] most patients who died from burn injuries treated with ECMO had unclear causes of death, with multi-organ failure coming in second with 13.3% of cases. One suffered an intracerebral haemorrhage and passed away. Additionally, we observe that mortality declined with ECMO duration and beginning time and rose with age, burn area (TBSA), and inhalation injury.

Complications from the ECMO were still another crucial factor. Acute kidney damage is a common ECMO complication. It is a major cause of mortality for patients receiving ECMO, with a frequency of 70–85%. 30.8% was the pooled infection rate. Furthermore, Marcus (2019) [9] discovered that, due mostly to burn wounds and compromised skin barriers, the total infection incidence of burn patients receiving ECMO was almost three times higher than that of non-burn patients.

According to Ding et al. [14], the proportion of neutrophils and macrophages in bronchoalveolar lavage fluids (BAL) was reduced and increased, respectively, by perfluoro hexane PFC treatment. Numerous investigations have demonstrated that PFC reduced neutrophil aggregation in lung tissue.

Physical therapy was shown by Kubo et al. [22] to shorten hospital and ICU stays and the length of time patients needed mechanical breathing.

According to Allam et al. [17], the HFCWO vest lessens the cohesive and viscoelastic characteristics of mucus while improving central and peripheral mucus clearance. This meta-analysis has several shortcomings. A total of thirty-one studies were published in languages other than English.188 more through animal research. Much research was disregarded because it was outdated.

Not with standing these drawbacks, we offered the best evidence found in the literature to offer a reliable, consistent analysis of the outcomes reported using standardized measurement.

When it comes to diagnosing, treating, and forecasting the outcome of smoke inhalation lung damage, FOB may be quite valuable. In patients with SII, FOB acquired after a few hours of arrival was predictive of the overall number of ventilator days, ICU stay days, and the occurrence of pneumonia [29]. This analysis of the bronchoscopy results at admission revealed that they had early predictive value for the onset of pneumonia, the overall number of days spent on a ventilator, and the length of stay in the intensive care unit. A standardized bronchoscopy grading system for the severity of inhalation damage is the AIS criteria.

Bai et al., [27] reported that the flexible bronchoscope should be used in everyday clinical practice since it is very useful in diagnosing inhalation injuries without any problems. Flexible bronchoscopy must be used with the understanding that, given enough time, the airways will mend themselves.

Among fire victims, asphyxia due to CO toxicity is the primary cause of quick death. CO is produced mostly by incomplete combustion, which occurs when O_2 is consumed. With an avidity of 250:1, CO and O_2 fight for the O_2-binding sites on hemoglobin (Hb). The more successfully CO occupies the O_2-binding sites, the lower the partial pressure of O_2 (pO_2). The oxyhemoglobin (O_2) Hb dissociation curve is shifted to the left by the binding of CO, increasing the binding affinity of O2 to Hb and necessitating a higher level of tissue hypoxia before O_2 can be offloaded. Ultimately, CO attaches itself to intracellular cytochromes (a and a3), preventing the tissues from using oxidative energy sources. Overall, widespread asphyxia results, which is out of relation to the blood gas measurements of pO_2. The brain and heart, two organs with high rates of O_2 use, are most affected by the reduced O_2 supply [4].

The blood carboxyhemoglobin (COHb) content frequently affects the clinical signs of CO poisoning. Long-term emotional and neurological consequences damage the survivors. A history of CO exposure, a rise in COHb values, and ruling out other possible causes of symptoms or indications are the three main diagnostic criteria for CO poisoning. Early in the course of therapy, pulse oximetry and arterial blood gases may be otherwise normal since they are unable to distinguish between O_2 Hb and COHb.

The coexistence of inhalation damage with moderate (15% to 29% TBSA) to severe (30% to 69% TBSA) thermal burns resulted in the most negative impact on the outcome of burn patients. [30].

Conclusion:

It is still quite challenging to care for patients who have had respiratory impairments related to burns. Important topics include chest physical therapy, nebulized heparin, NAC, and the effects of ECMO. Heparin has been associated with a reduction in the amount of time critically ill patients with smoke inhalation injuries need to remain on mechanical support when paired with NAC and albuterol. Early ambulation and physical therapy reduced hospital stays and the length of time patients spend in the critical care unit and on mechanical ventilation. An evidence-based approach is to turn the patient side to side every two hours, administer chest physical therapy every four hours, and alternate aerosolizing 5000 units of heparin with 3 cc of normal saline + 20% acetylcysteine until such data are available. In cases of burn-associated ARDS and hypoxemic respiratory failure, prompt ECMO decision-making and careful patient selection can lead to excellent patient outcomes.

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