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Assessing the impact of pre-hospital airway management on severe traumatic Brain injury: A systematic review and Meta-analysis

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ABSTRACT

Objective: This study aimed to assess the impact of establishing a pre-hospital definitive airway on mortality and morbidity compared with no prehospital airway in cases of severe traumatic brain injury (TBI).
Background: Traumatic brain injury (TBI) is a global health concern that is associated with substantial morbidity and mortality. Prehospital intubation (PHI) has been proposed as a potential life-saving intervention for patients with severe TBI to mitigate secondary insults, such as hypoxemia and hypercapnia. However, their impact on patient outcomes remains controversial.
Methods: A systematic review and meta-analysis were conducted to assess the effects of prehospital intubation versus no prehospital intubation on morbidity and mortality in patients with severe TBI, adhering to the PRISMA guidelines.
Results: 24 studies, comprising 56,543 patients, indicated no significant difference in mortality between pre-hospital and In-hospital Intubation (OR 0.89, 95% CI 0.65–1.23, $p = 0.48$), although substantial heterogeneity was noted. Morbidity analysis also showed no significant difference (OR 0.83, 95% CI 0.43–1.63, $p = 0.59$). These findings underscore the need for cautious interpretation due to heterogeneity and the influence of specific studies on the results.
Conclusion: In summary, an initial assessment did not reveal any apparent disparity in mortality rates between individuals who received prehospital intubation and those who did not. However, subsequent analyses and randomized controlled trials (RCTs) demonstrated that patients who underwent prehospital intubation had a reduced risk of death and morbidity. The dependence on biased observational studies and the need for further replicated RCTs to validate these findings are evident. Despite the intricacy of the matter, it is crucial to intervene during severe airway impairment.

List of Abbreviations

Traumatic brain injury	TBI
Glasgow Coma Score	GCS
pre-hospital intubation	PHI
Advanced Trauma Life Support	ATLS
European Trauma Course	ETC
randomized controlled trials	RCTs
rapid sequence intubation	RSI
Injury severity score	ISS
Emergency department	ED

1. Introduction

Traumatic brain injury (TBI) is a leading cause of trauma-induced suffering and death worldwide [1-3]. This often results in a depressed level of consciousness and compromised airway reflexes, leading to apnea. Severe TBI has a substantial global impact, affecting approximately 939 per 100,000 individuals annually, causing morbidity and mortality and imposing a significant socioeconomic burden on families and societies [4,5].

Traumatic brain injuries are classified based on the Glasgow Coma Score (GCS), with a GCS score of <9 defining severe TBI. Such cases pose a considerable risk of aspiration or hypoxemia, which can worsen secondary brain damage [6]. Secondary systemic insults such as hypoxemia, hypotension, hyperthermia, and hypo/hypercapnia further

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worsen neuronal damage and have been associated with higher mortality rates in TBI cases [7,8]. Traditionally, prehospital intubation (PHI) has been used as a precautionary measure to manage these patients, offering several advantages such as reducing hypoxia, better ventilation control, and airway protection [9,10]. However, concerns have been raised about PHI potentially contributing to increased mortality rates due to factors such as delayed hospital admission and low success rates in performing the procedure [11,12].

Severe TBI is conventionally classified into primary and secondary phases, with primary injury resulting from initial mechanical forces causing shearing and compression of the neuronal, glial, and vascular tissues [13,14]. Secondary injury arises due to physiological disturbances such as ischemia, hypoxia, and reperfusion injuries. However, this classification oversimplifies the complex nature of TBI management, as the primary injury can be influenced by subsequent management, and secondary injury can begin from the initial insult. The management of severe TBI involves stabilizing hemodynamic parameters and securing a definitive airway following guidelines such as Advanced Trauma Life Support (ATLS) and the European Trauma Course (ETC) [15-17]. Despite conflicting opinions among experts such as the Brain Trauma Foundation and European Brain Injury Consortium, evolving knowledge and shifting approaches to TBI are contributing to the exclusion of this injury from trauma studies, resulting in ongoing discussions and updates to management guidelines [18,19].

To address these concerns, prehospital airway management should prioritize limiting secondary insults such as hypoxemia and hypercapnia. Prehospital intubation (PHI) has the potential to precisely manage these issues and positively affect patient outcomes. The primary objective of this systematic review and meta-analysis was to investigate the impact of prehospital intubation versus no prehospital intubation on both morbidity and mortality in severe TBI cases. The hypothesis under scrutiny suggests that early pre-hospital intubation may significantly affect patient outcomes in cases of severe TBI.

2. Method

The study undertaken was a systematic review and meta-analysis that adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two researchers conducted a comprehensive literature search of various databases including MEDLINE/PubMed, EMBASE, Google Scholar, and SCOPUS. The focus of the search was to identify relevant studies involving patients with severe Traumatic Brain Injury (TBI) who underwent prehospital airway management. The search was conducted until June 11, 2023. To ensure that no important publications were overlooked, a snowballing approach was used and manual searches of the reference lists of eligible articles were performed to avoid missing relevant sources. To eliminate duplicates, all retrieved articles were organized using Endnote X20 (Clarivate Analytics, PA, USA). The search strategy was independently developed by two investigators according to the specified criteria, and any discrepancies or misunderstandings were resolved by consensus with a third investigator.

2.1. Study selection

For the meta-analysis, we included studies that fulfilled the following criteria: [1] Examination of the efficacy or effectiveness of prehospital intubation versus no pre-hospital intubation in non-pediatric populations [2]. Comprised original research, including randomized controlled trials (RCTs), prospective or retrospective cohort studies, and case series [3]. Indications, goals, and relevant clinical outcomes were clearly described. Studies involving animal research, case reports, and editorials were excluded from analysis.

2.2. Outcome measures

The primary focus of this study was to analyze the impact of prehospital and in-hospital intubation on mortality and morbidity in patients with traumatic brain injury (TBI). The key finding was the association between intubation procedures and their effects on mortality and morbidity rates in this specific patient population.

2.3. Data extraction

MAS and AH acted as independent authors and extracted the essential information from the selected studies. In cases where disagreements or controversies arose, a third author, MSM, was involved in resolution. To ensure accuracy, extracted data were thoroughly reviewed to identify and remove duplicate studies. The extracted information included the author's name, publication year, sample size, population characteristics, type of intervention (prehospital vs. no pre-hospital intubation), and outcomes (mortality and morbidity).

2.4. Statistical analysis

Statistical analysis was conducted independently by the author MSM using Comprehensive Meta-Analysis Version 3.3. A random effects model was employed to combine the data and calculate the pooled effects between the control and intervention groups. Forest plots were generated to present major and secondary outcomes, including mortality and morbidity, using odds ratios (OR) with 95% confidence intervals. Heterogeneity was assessed using the I^2 statistic for sensitivity analysis of mortality. Heterogeneity was considered significant when I^2 was greater than a certain percentage, and was carefully evaluated in light of the study characteristics.

2.5. Quality assessment and risk of bias

Two different tools were used to assess the study quality. The Cochrane Collaboration tool for evaluating the risk of bias was used for two randomized controlled trials (RCTs). Studies were graded as high-risk, low-risk, and uncertain risk, whereas the Newcastle Ottawa Quality Assessment Scale was used for retrospective studies. Studies were considered acceptable if they were rated as fair or good in terms of quality, and demonstrated an overall low risk of bias. The leave-one-out strategy was used to conduct sensitivity analysis of the included studies. Funnel plots were used to explore the possibility of publication bias and the results are presented in Supplementary File 1.

3. Results

3.1. Literature search

A comprehensive search yielded 4651 papers from diverse sources, including PubMed, Scopus, Medline, Embase, and Google Scholar. After eliminating duplicates and excluding ineligible records, 1886 records remained eligible for further screening. Among these, 166 records underwent eligibility assessment, whereas others were excluded because of irrelevant outcomes or insufficient detail. Finally, we selected 24 studies suitable for the review. The PRISMA Flowchart (Fig. 1) summarizes the literature search results.

3.2. Study characteristics and quality assessment

Among the initially identified articles, 24 met the inclusion criteria and were included in this meta-analysis (Table 1). A total of 22 observational and two interventional studies comprising 56,543 patients were

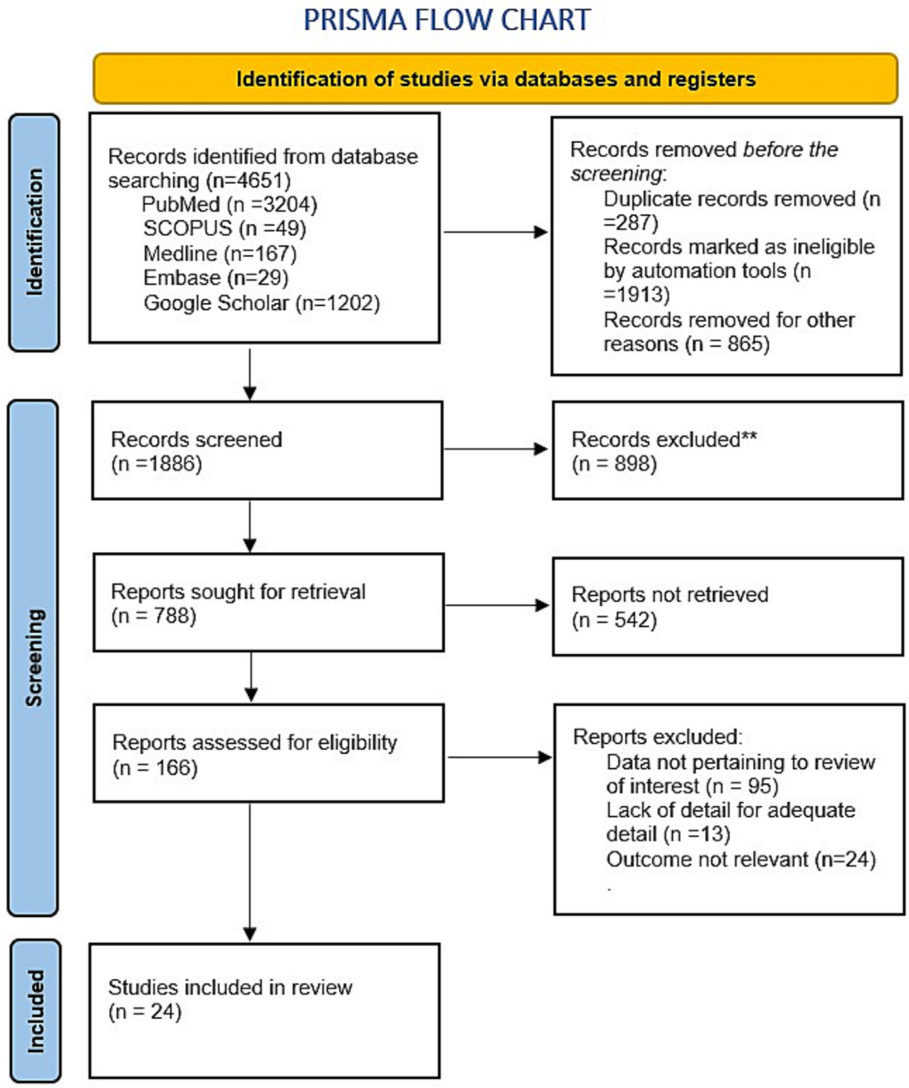


Fig. 1. PRISMA Flowchart depicting the selection process of studies for the meta-analysis.

included [20-43]. The quality of the included studies was assessed using the Newcastle–Ottawa scale, offering detailed insights. A funnel plot was generated to evaluate publication bias and is included in Supplementary File 1.

3.3. Mortality

The primary objective of this meta-analysis was to investigate the differences in mortality outcomes between patients who underwent Prehospital Intubation (PHI) and those managed with In-hospital Intubation. The combined analysis of the 24 relevant studies initially revealed an odds ratio (OR) of 0.89 [95% confidence interval (CI) 0.65, 1.23; $p = 0.48$, I^2 96%], suggesting no statistically significant difference in mortality between the two approaches (Fig. 2). Subsequent subgroup analyses revealed an overall odds ratio for Randomized Controlled Trials (RCT) of 0.67 (95% CI 0.23–1.94; $p = 0.46$; I^2 57.35%) and for Observational studies of 0.91 (95% CI 0.65–1.28; $p = 0.61$; I^2 96.44%). However, the considerable heterogeneity among the incorporated studies highlighted variations in effect sizes across studies, potentially impacting the overall reliability of the findings. To address this, a sensitivity analysis using the Leave-one-out method was conducted, and the corresponding forest plot is provided in supplementary file 1.

3.4. Morbidity

The meta-analysis also explored the differences in morbidity outcomes between prehospital and in-hospital intubation. Of the 24 studies, six were included in the analysis. The pooled analysis showed an odds ratio of 0.83 (95% CI 0.43, 1.63; $p = 0.59$; I2 93%). However, the limited number of studies and high level of heterogeneity observed among them may affect the precision of the findings, as shown in Fig. 3. Sensitivity analysis using Leave-one-out method was conducted, the forest plot of which has been included in the supplementary file 1.

3.5. Publication bias

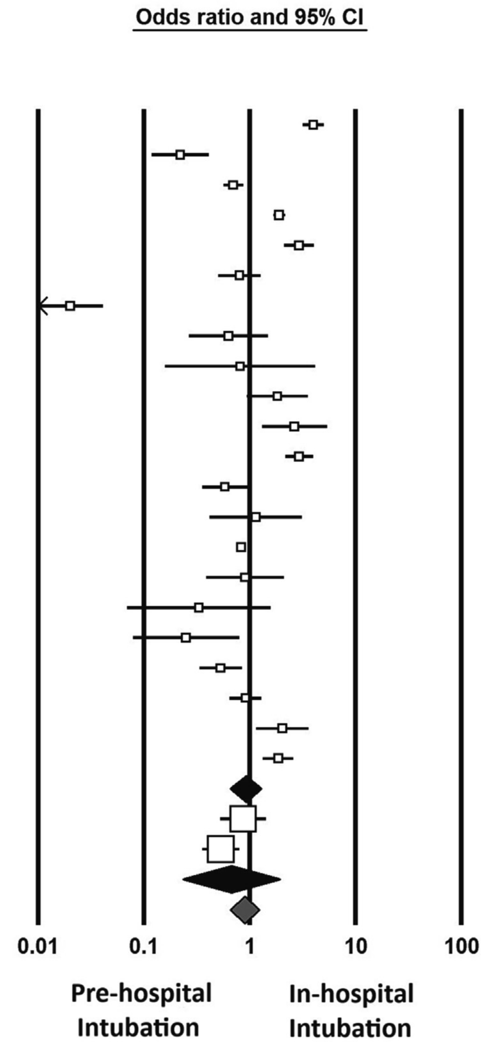
Examination of the funnel plot revealed some indications of publication bias. In addition to this potential bias, an Egger test was performed to further assess the reliability of the results, yielding an insignificant intercept value of -0.69 ($p = 0.32$). Notably, the outcomes of the trim-and-fill sensitivity analysis showed minimal impact on the findings. A slight attenuation in the pooled risk ratio was observed, suggesting that the potential exclusion of studies would not significantly alter the overall conclusion. These collective findings, coupled with the results

Table 1
Baseline Characteristics of Included Studies.

S. No.	Author	Year	Country	Design	Sample Size	Age	Inclusive Criteria	Exclusive Criteria	Outcome
1	Wang [20]	2004	USA	Retrospective	4098	≥18 years	Head/Neck AIS ≥3	Not treated by advanced life support, pediatric, transferred patients	Deaths, poor neurology, functional impairment
2	Davis [21]	2005	USA	Retrospective	4247	43.8(19.2) years	Head/Neck AIS ≥3	Neck injury-defined AIS value	Deaths
3	Bukur [22]	2011	USA	Retrospective	2366	>14 years	Isolated moderate to severe TBI (head AIS 3)	Non-survivable injuries, missing intubation data, <14 years	Deaths
4	Haltmeier [23]	2017	USA	Retrospective	16,278	42.0 (35.0) years	Severe blunt TBI, GCS ≤8	Field GCS score > 8	Total hospital LOS, ICU LOS, ventilator days, mortality
5	Sobuwa [24]	2013	South Africa	Observational	124	≥16 years	Confirmed TBI, GCS ≤8	Field GCS score > 8	N/A
6	Schwaiger [25]	2019	Austria	Retrospective	294	N/A	Severe TBI, ISSI ≥4, CPR requiring	N/A	Death
7	Lansom [26]	2016	Australia	Retrospective	296	41 [21] years	Suspected TBI, decreased GCS	<16 years, interhospital transfer, no clinical head injury	Deaths before CT, transport times
8	Bernard [27]	2010	Australia	RCT	312	>15 years	Head trauma, GCS < 9, age > 15 years	Within 10 min of the trauma hospital, no IV access, and allergies	Glasgow Outcome Scale, length of stay, survival
9	Davis [28]	2011	USA	Observational	1555	≥15 years	Systolic BP, GCS ≤8, airway management	No vital signs, unknown status, no resuscitative attempt	Death
10	Denninghoff [29]	2017	USA	RCT	882	35.5 years	Severe, moderate TBI, GCS 4–12	GCS 3, nonreactive pupils, prolonged hypotension/hypoxia	Death
11	Karamanos [30]	2013	USA	Retrospective	220	35.7 years	Isolated TBI, AIS ≥3, GCS ≤8	Extracranial AIS = 3, cardiac arrest, no immediate ABGs	Mortality, gas profile, ICU and hospital stay
12	Nordness [31]	2020	USA	Retrospective	1671	36 years	AIS Head ≥3, GCS ≤8	Pre-hospital cardiac arrest, interfacility transfers	FIM score, discharge facility, mortality
13	Pakkanen [42]	2019	Finland	Retrospective	651	50 years	GCS ≤8, isolated TBI	Non-Finnish, multiple injuries, surgical intervention	Mortality, neurological analysis
14	Rubenson-Wahlin [34]	2017	Sweden	Observational	458	47.1 (19.2) years	(≥15 years) with prehospital trauma charts and CT-verified traumatic brain injury.	Patients declared dead on scene, admitted >6 h post-trauma, or with unknown trauma time. Also, excluded transfers >24 h post-admission from other counties.	In-hospital mortality, long term GCS 1–3
15	Tuma [32]	2014	Qatar	Observational	160	31 (14) years	>14 years, intubation based on GCS, STBI	Died within 24 h, transferred, intubated in OR/ICU	Mortality
16	Vandromme [33]	2011	USA	Observational	334	38 years	Blunt injury, PH GCS ≤8	N/A	Mortality, GCS score < 8
17	Bossers [35]	2023	Netherlands	Retrospective	7041	63 years	Head AIS scores ≥4	N/A	Hospital mortality
18	Irvin [36]	2010	USA	Retrospective	10,948	37.5 years	Scene GCS 3	N/A	1st systolic BP, ISS, Penetrating Trauma, mortality
19	Bochicchio [37]	2003	Maryland	Prospective	191	37.5 (21) years	GCS ≤ 8, head AIS ≥ 3, intubated in the field or at hospital admission.	Died within 48 h, transferred, failed intubation	Hospital and ICU stay, ventilator days, mortality
20	Choffat [38]	2019	Switzerland	Prospective	832	54.3 years	Patients >16 years with severe TBI from blunt or penetrating trauma	Unclear brain trauma history or no signs of brain trauma. GCS not used due to high variability.	Mortality and GCS at 14 days
21	Evans [39]	2014	Canada	Retrospective	2229	>16 years	Eligible patients: >16 years, initial GCS <9, treated by ground-based paramedics.	N/A	Mortality
22	Schoeneberg [40]	2016	Germany	Retrospective	455	N/A	ISS >16, GCS < 9	N/A	Mortality, systolic BP, oxygen saturation
23	Franschman [43]	2011	Netherland	Retrospective	339	44-65 years	Patient with TBI, age > 16 years, admitted to two level 1 Trauma center ED	N/A	In contrast to slightly higher injury scores in intubated patients. Prehospital intubation was not predictive for patient outcome.
24	Jung [41]	2022	South Korea	Retrospective	562	18–65 years	Patients with TBI, age > 18 years, brought to CNUH by EMS.	Patients without airway management and mortality records.	Primary outcome: Survival to hospital discharge. Secondary outcome: Good neurological recovery and 6-month survival.

Abbreviations: AIS - Abbreviated Injury Scale, GCS - Glasgow Coma Scale, LOS - Length of Stay, ICU - Intensive Care Unit, PHI - Pre-hospital Information, ERI - Emergency Room Information, CPR - Cardiopulmonary Resuscitation, CT - Computed Tomography, EMS - Emergency Medical Services, RSI - Rapid Sequence Intubation, GOSe - Glasgow Outcome Scale extended, BP - Blood Pressure, ISS - Injury Severity Score, TBI - Traumatic Brain Injury, FIM - Functional Independence Measure, OR - Operating Room, N/A - Not Available.

Group by Study type	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Observational	Wang 2003	3.978	3.210	4.930	12.610	0.000
Observational	Bochicchio 2003	0.220	0.120	0.403	-4.895	0.000
Observational	Davis 2005	0.700	0.570	0.860	-3.404	0.001
Observational	Irvin 2010	1.900	1.700	2.123	11.321	0.000
Observational	Davis 2011	2.910	2.130	3.976	6.710	0.000
Observational	Vandromme 2011	0.800	0.510	1.255	-0.971	0.331
Observational	Bukur 2011	0.020	0.010	0.040	-11.060	0.000
Observational	Franschman 2012	0.630	0.270	1.470	-1.069	0.285
Observational	Sobuwa 2013	0.810	0.160	4.101	-0.255	0.799
Observational	Karamanos 2013	1.820	0.950	3.487	1.805	0.071
Observational	Tuma 2014	2.650	1.330	5.280	2.771	0.006
Observational	Evan 2014	2.941	2.190	3.950	7.168	0.000
Observational	Lansom 2016	0.580	0.360	0.934	-2.239	0.025
Observational	Schoeneberg 2016	1.137	0.420	3.080	0.253	0.800
Observational	Haltmeir 2017	0.830	0.770	0.895	-4.864	0.000
Observational	Wahlin 2018	0.900	0.390	2.077	-0.247	0.805
Observational	Schwaiger 2019	0.330	0.070	1.556	-1.401	0.161
Observational	Choffat 2019	0.250	0.080	0.781	-2.384	0.017
Observational	Pakkanen 2019	0.530	0.340	0.826	-2.803	0.005
Observational	Nordness 2020	0.910	0.650	1.274	-0.549	0.583
Observational	Jung 2022	2.029	1.160	3.550	2.481	0.013
Observational	Bossers 2023	1.860	1.350	2.563	3.796	0.000
Observational		0.916	0.655	1.281	-0.512	0.608
RCT	Bernard 2010	0.860	0.530	1.396	-0.611	0.542
RCT	Denninghoff 2017	0.530	0.360	0.780	-3.218	0.001
RCT		0.672	0.232	1.944	-0.733	0.463
Overall		0.891	0.647	1.226	-0.709	0.478



Mortality

Fig. 2. Forest plot illustrating the comparison of mortality outcomes between Prehospital Intubation and In-hospital Intubation.

of the Egger test, collectively indicate that the overall integrity of the analysis remains robust. The funnel plot, Egger test, and trim-and-fill results have been included in Supplementary File 1.

The meta-analysis found no significant difference in mortality rates between prehospital and in-hospital intubation. However, the sensitivity analysis suggested a possible increased risk of morbidity associated with prehospital intubation.

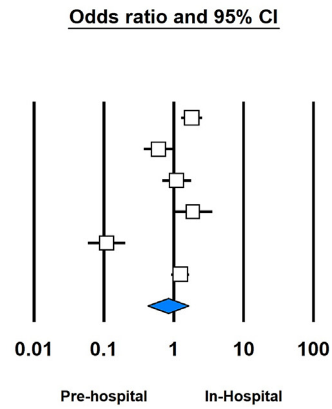
4. Discussion

Trauma is one of the most pertinent causes of death worldwide, especially in young individuals, and traumatic brain injury significantly contributes to this problem [44,45]. Traumatic brain injuries are the result of either penetrating injuries or blunt traumas, with motor vehicle collisions contributing to approximately 17% and falls contributing to as many as 35% of overall injuries [46,47]. In this study, we sought to determine the impact of endotracheal intubation in patients with TBI. Specifically, we sought to determine whether prehospital intubation is advantageous in patients with severe TBI compared to those without prehospital intubation.

In our meta-analysis, no statistically significant differences were found between prehospital and in-hospital intubation. However, after performing a sensitivity analysis, the results changed drastically, and prehospital intubation reduced mortality compared with in-hospital intubation. We found two clinical trials, which provided the highest level of evidence so far on this issue so far. These RCTs were conducted by Bernad et al. [27] and Denninghoff et al. [48]. Several factors, such as poor handling, hemodynamic instability, and poor sanitation, can contribute to poor outcomes while performing prehospital intubation, which will be managed in the hospital setting by trained staff and physicians.

Intubation poses inherent risks, especially in prehospital settings where individuals with insufficient airway training and experience may perform the procedure. Additionally, hemodynamic instability caused by medication administration can lead to unfavorable outcomes and an increased mortality risk. These two RCTs effectively addressed these confounding factors. The findings of these studies independently demonstrate that prehospital intubation can improve survival rates. These results emphasize the significance of proper airway training and experience in pre-hospital intubation procedures. Our presumption

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Wang 2003	1.799	1.290	2.510	3.460	0.001
Bernard 2010	0.604	0.380	0.960	-2.133	0.033
Denninghoff 2017	1.099	0.690	1.750	0.397	0.691
Wahlin 2018	1.869	0.990	3.530	1.929	0.054
Choffat 2019	0.110	0.060	0.200	-7.201	0.000
Nordness 2020	1.231	0.930	1.630	1.453	0.146
	0.833	0.426	1.629	-0.534	0.593



Morbidity

Fig. 3. Forest plot presenting the comparison of morbidity outcomes between Prehospital Intubation and In-hospital Intubation.

that prehospital intubation can be lifesaving is also supported by several cohort studies [27,48]. These studies mentioned that when several confounding factors are controlled, such as making patients vitally stable and following the ATLS protocol, identifying the deleterious effects of hypertension, maintaining oxygen saturation, and hypocapnia, the yield of the study can be increased.

In addition to mortality, our study aimed to determine the correlation between morbidity and pre-hospital intubation. Although the results were not statistically significant when comparing the link between morbidity and prehospital intubation or in-hospital intubation, there was also high heterogeneity present for which sensitivity analysis was performed. As in the case of mortality, the results showed that prehospital intubation could reduce morbidity to some extent, making the results significant and favoring prehospital intubation [27,34,49]. However, we did not find a direct link between the confounding factors that caused high heterogeneity in the original results; however, according to some studies, they are mainly attributed to hypoxia and hypotension. Meanwhile, other studies have found hypotension and the Injury Severity Score (ISS) as the culprits behind poor outcomes; the exact cause needs to be determined using more studies and larger sample sizes.

In our study of the literature, we also found, to our interest, that many studies did not induce anesthesia with RSI (rapid sequence intubation) [33,45,49,50] Since the induction of anesthesia without RSI is associated with many subsequent poor outcomes, which can vary from hemodynamic instability to aspiration pneumonia Since patients with severe TBI already have impaired vitals, these additional factors further exacerbate the preexisting morbidity and are a result of bias in study and analysis. Aspiration pneumonia alone has been shown to be a significant contributor to mortality, causing up to 50% of deaths in a study conducted in the UK [27].

Other parameters that were not addressed were the measurement of carbon dioxide levels, that is, hypocapnia or hypercapnia. David et al. [51] showed that hypocapnia with hyperventilation can result in increased mortality rates; this finding is supported by many other concurrent studies. We believe that the addition of a ventilator to capnography could have increased study yield by reducing mortality [27,49,52]. Along the same line, the above-mentioned measures also fall for the high ISS score, non-reactive pupillary response, and advanced age, since these factors cannot be controlled for and are a part of the study [50].

4.1. Strengths and limitations

In our meta-analysis, we aimed to include as many favorable articles as possible in order to assess efficacy and validity. We found two RCTs and retrospective cohort studies with significant differences in outcomes. This highlights the confounding factors in RCTs that affect the mortality and morbidity outcomes. Regarding morbidity, the number of studies reporting this was limited, thus impacting precision. Additionally, the chronic nature of TBI and the need for continuous follow-up complicates our analysis. Heterogeneity in functional outcomes was not accounted for, thus limiting the strength of this study. For a more thorough examination, Bayesian sensitivity analysis could be considered in addition to leave-one-out.

Another consideration is intubation intervention, with debates regarding who should perform it: paramedic staff or ED doctor. The included studies lacked information on potential bias. Finally, some studies used outdated intubation guidelines, making it challenging to keep up with the ever-evolving medical practices, which is a significant drawback of our review. However, our study differs from previous reviews by focusing on mortality and morbidity rather than secondary outcomes such as ventilation status and hemodynamic stability. By including both randomized controlled trials and observational studies, we offer a comprehensive data collection that considers confounding factors. This broader scope not only provides more insightful results but also aids future authors in addressing these factors, enhancing the robustness of their studies.

5. Conclusion

The initial investigation into the comparison of mortality rates between prehospital and in-hospital intubation did not reveal any significant differences. However, more recent high-quality trials have shown a slight preference for prehospital intubation, as it has been associated with a decrease in mortality and morbidity outcomes. The reliance on observational studies introduces biases, and while controlled randomized clinical trials (RCTs) have provided some clarity, further replication is necessary. Despite these complexities, the necessity for intervention during severe airway compromise is indisputable. Careful assessment is crucial when considering prehospital intubation, as it is important to weigh its potential advantages against the need for time-sensitive hospital transfers.

Ethical consideration

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Ethics declarations

Ethics approval and consent to participate.
Not applicable.

Consent for publication

Not applicable.

Compliance with Instructions to Authors

We hereby affirm that this manuscript has been meticulously prepared in strict accordance with all prescribed instructions provided to the authors.

Authorship Confirmation and Approval

We confirm that the authorship requirements have been diligently met, and the final version of the manuscript has been unanimously approved by all contributing authors.

Publication status

We certify that this manuscript is entirely original and has not been published previously, nor is it currently under consideration by any other journal.

Reporting checklist

We followed the PRISMA Guidelines for this systemic review and Meta-analysis and the checklist has been included in the files.

CRediT authorship contribution statement

Muhammad Ashir Shafique: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Abdul Haseeb:** Writing – original draft, Methodology. **Bushra Asghar:** Writing – original draft. **Aashish Kumar:** Writing – original draft. **Eymaan Riaz Chaudhry:** Writing – original draft. **Muhammad Saqlain Mustafa:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis.

Declaration of competing interest

The authors declare that they have no competing interests and there is no conflict of interest.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2024.01.030.

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