Prehospital intubation of patients with severe traumatic brain injury: a Dutch nationwide trauma registry analysis

Bossers, S.M.; Verheul, R.; Zwet, E.W. van; Bloemers, F.W.; Giannakopoulos, G.F.; Loer, S.A.; ... ; Schober, P.

PREHOSPITAL EMERGENCY CARE
2023, VOL. 27, NO. 5, 662–668
https://doi.org/10.1080/10903127.2022.2119494

Taylor & Francis
Taylor & Francis Group

ORIGINAL CONTRIBUTIONS

Prehospital Intubation of Patients with Severe Traumatic Brain Injury: A Dutch Nationwide Trauma Registry Analysis

Sebastiaan M. Bossers[a], Robert Verheul[a], Erik W. van Zwet[b], Frank W. Bloemers[c], Georgios F. Giannakopoulos[c,d], Stephan A. Loer[a], Lothar A. Schwarte[a,d], and Patrick Schober[a,d]

[a]Department of Anesthesiology, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [b]Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands; [c]Department of Surgery, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [d]Helicopter Emergency Medical Service Lifeliner 1, Amsterdam, The Netherlands

ABSTRACT

Objective: Patients with severe traumatic brain injury (TBI) are commonly intubated during prehospital treatment despite a lack of evidence that this is beneficial. Accumulating evidence even suggests that prehospital intubation may be hazardous, in particular when performed by inexperienced EMS clinicians. To expand the limited knowledge base, we studied the relationship between prehospital intubation and hospital mortality in patients with severe TBI in a large Dutch trauma database. We specifically hypothesized that the relationship differs depending on whether a physician-based emergency medical service (EMS) was involved in the treatment, as opposed to intubation by paramedics.

Methods: A retrospective analysis was performed using the Dutch Nationwide Trauma Registry that includes all trauma patients in the Netherlands who are admitted to any hospital with an emergency department. All patients treated for severe TBI (Head Abbreviated Injury Scale score $\geq$4) between January 2015 and December 2019 were selected. Multivariable logistic regression was used to assess the relationship between prehospital intubation and mortality while adjusting for potential confounders. An interaction term between prehospital intubation and the involvement of physician-based EMS was added to the model. Complete case analysis as well as multiple imputation were performed.

Results: 8946 patients (62% male, median age 63 years) were analyzed. The hospital mortality was 26.4%. Overall, a relationship between prehospital intubation and higher mortality was observed (complete case: OR 1.86, 95% CI 1.35–2.57, $p < 0.001$; multiple imputation: OR 1.92, 95% CI 1.56–2.36, $p < 0.001$). Adding the interaction revealed that the relationship of prehospital intubation may depend on whether physician-based EMS is involved in the treatment (complete case: $p = 0.044$; multiple imputation: $p = 0.062$). Physician-based EMS involvement attenuated but did not completely remove the detrimental association between prehospital intubation and mortality.

Conclusion: The data do not support the common practice of prehospital intubation. The effect of prehospital intubation on mortality might depend on EMS clinician experience, and it seems prudent to involve prehospital personnel well proficient in prehospital intubation whenever intubation is potentially required. The decision to perform prehospital intubation should not merely be based on the largely unsupported dogma that it is generally needed in severe TBI, but should rather individually weigh potential benefits and harms.

ARTICLE HISTORY
Received 12 May 2022
Revised 13 August 2022
Accepted 27 August 2022

Introduction

Severe traumatic brain injury (TBI) is associated with a high mortality (1). Patients are at risk of airway obstruction and pulmonary aspiration, and treatment protocols emphasize the need for early definitive airway protection in comatose patients to avoid secondary brain injury by hypoxia or hypercapnia (2–4).

Endotracheal intubation is considered the criterion standard in definitive airway protection, and patients with severe TBI are commonly intubated in the field by prehospital emergency medical personnel (5). However, evidence to support this common practice is scarce. While prehospital intubation should theoretically be beneficial to ensure airway protection and to prevent hypoxemia (6), the procedure also involves risks that may lead to adverse outcomes. This includes hypoxemia due to prolonged intubation attempts, increases in intracranial pressure during laryngoscopy, hemodynamic effects of anesthetic drugs, hypo- or hypercapnia due to inappropriate ventilation following endotracheal intubation, and delayed transport to definitive care (5,7,8).

Given potential benefits and risks, the net effect is still poorly understood and may depend on the experience of the EMS clinician who performs the intubation (7) and the

CONTACT Patrick Schober p.schober@amsterdamumc.nl

patient case mix (9,10). Therefore, to complement and expand the currently limited knowledge base, we studied the relationship between prehospital intubation and mortality in patients with severe TBI in the Netherlands, using a comprehensive national trauma database. We also specifically assessed whether the relationship differs depending on whether a physician-based emergency medical service (EMS) was involved in the treatment, as opposed to intubation by paramedics without involvement of a prehospital emergency physician.

Methods

Ethical Considerations and Informed Consent

The Medical Research Ethics Committee of the Amsterdam University Medical Center, location VUmc (reference number 2020.0639), reviewed the study protocol and concluded that the research is not subject to the Dutch Medical Research Involving Human Subjects Act; hence, formal approval was not required. Because all data are completely anonymous and cannot be traced back to individual patients, the requirement for informed consent was waived. Reporting of the study conforms with the STROBE guidelines (11).

Setting

The Netherlands is a densely populated country in Western Europe with approximately 17.5 million inhabitants in an area of about 41,500 km^2. The incidence rate of severe TBI in the Netherlands is 2.7 per 100,000 inhabitants per year (12). Prehospital trauma care is provided by 25 regional ambulance services. Two ambulance crews, each consisting of a prehospital emergency medical nurse and an ambulance driver trained to approximately the emergency medical technician level, are usually dispatched to major trauma cases. Additionally, four physician-staffed helicopter EMS (P-HEMS) are available 24/7 to respond to major emergencies. These crews include an anesthesiologist or surgeon well trained in prehospital emergency procedures, and a certified flight nurse (13).

The decision to perform endotracheal intubation as well as the intubation technique, including backup-procedures for failed attempts, is at the discretion of the treating clinician; typical indications include a (partially) obstructed or threatened airway, hypoxia, or the perceived need for mechanical ventilation. In the Netherlands, use of hypnotic agents other than midazolam and the use of neuromuscular blocking agents for rapid sequence intubation is limited to P-HEMS crews.

Data Registry, Patient and Data Selection

The Dutch Nationwide Trauma Registry (DNTR) collects data on all injured patients admitted to any hospital with an emergency department in the Netherlands, corresponding to about 80,000 included trauma cases annually. The registry contains information on prehospital treatment, treatment during hospital admission, and several outcome parameters according to the Utstein template for uniform reporting of data following major trauma (14). A detailed description of the dataset, data collection, and organization of the DNTR has been published previously (15).

To obtain a study population of patients with severe TBI, we selected all consecutive patients from the DNTR database with Head Abbreviated Injury Scale (AIS) scores of ≥ 4 who had been treated between January 2015 and December 2019, without any exclusion criteria. We restricted patient selection to the pre-COVID-19 period, as changes in patient case mix and operational characteristics of prehospital care during the COVID-19 pandemic may have biased the results.

Prehospital intubation status was the exposure of interest, and hospital mortality (i.e., dead versus alive at discharge) was selected as the primary outcome. Additional demographic (e.g., age and sex), injury-related (e.g., prehospital Glasgow Coma Scale score [GCS], abbreviated injury scale [AIS] scores, injury severity score [ISS]), and operational (e.g., interval to arrival on scene, transport interval to hospital, involvement of P-HEMS) data were selected from the database to descriptively characterize the study sample and to allow adjustments for potential confounders in the statistical analysis as described below.

Statistical Analyses

Descriptive statistics are presented as median [quartiles] for numeric data and as count (percentage) for categorical data (16). Multivariable logistic regression was used to assess the relationship between prehospital intubation and hospital mortality (17). The model was adjusted for potential confounders (18), namely demographic factors (age, sex), markers of injury severity (prehospital GCS score, ISS, individual AIS scores for injuries in eight body regions including head injury severity), and operational factors (involvement of P-HEMS, interval to arrival of first ambulance at the scene, transport interval to hospital). The continuous variables age and ISS were modeled as restricted cubic splines to relax the assumption of a linear relationship with the logit of mortality. To test the hypothesis that the relationship between prehospital intubation and mortality depends on the involvement of P-HEMS, we included the interaction between these variables in a separate model.

To account for missing data, complete case analysis as well as 10-fold multiple imputation was performed (19). Missing data were imputed using chained equations with the "mice" package in R (version 3.6.0) using default settings (20). All variables in the logistic regression model as well as auxiliary variables were considered for inclusion in the imputation model, and were included if the correlation with the missing variable was greater than 0.1. Analyses were performed with R version 4.0.5 (R foundation, Vienna, Austria) as well as Stata/BE 17.0 (StataCorp, College Station, TX).

Post-hoc subgroup analyses were performed in which patients were stratified according to the head-AIS, in which only patients with isolated TBI were considered (defined as patients with AIS scores ≤ 2 in all body regions except

Table 1. Patient characteristics.

	No intubation	Intubation	Unknown	*p*-value
N	5030	2011	1905	
Age (years)	67 [44, 80]	52 [26, 69]	66 [43, 79]	<0.001
Missing	1 (0.1%)	0 (0%)	0 (0%)	
Sex				<0.001
Male	3015 (59.9%)	1385 (68.9%)	1199 (62.9%)	
Female	2015 (40.1%)	626 (31.1%)	706 (37.1%)	
Missing	0 (0%)	0 (0%)	0 (0%)	
ISS				<0.001
16–24	2540 (50.5%)	407 (20.2%)	877 (46%)	
25–49	2434 (48.4%)	1423 (70.8%)	951 (49.9%)	
50–66	42 (0.8%)	133 (6.6%)	37 (1.9%)	
75	14 (0.3%)	48 (2.4%)	40 (2.1%)	
Missing	0 (0%)	0 (0%)	0 (0%)	
Head AIS				<0.001
4	2992 (59.5%)	742 (36.9%)	1064 (55.9%)	
5	2027 (40.3%)	1238 (61.6%)	803 (42.2%)	
6	11 (0.2%)	31 (1.5%)	38 (2%)	
Missing	0 (0%)	0 (0%)	0 (0%)	
Prehospital GCS				<0.001
3	178 (3.5%)	576 (28.6%)	80 (4.2%)	
4	48 (1.0%)	98 (4.9%)	14 (0.7%)	
5	51 (1.0%)	61 (3.0%)	8 (0.4%)	
6	62 (1.2%)	79 (3.9%)	23 (1.2%)	
7	79 (1.6%)	81 (4.3%)	21 (1.1%)	
8	80 (1.6%)	44 (2.2%)	21 (1.1%)	
>8	2164 (43.0%)	196 (9.7%)	264 (13.9%)	
Missing	2368 (47.1%)	876 (43.6%)	1474 (77.4%)	
Cause of trauma (n)				<0.001
Violence	141 (2.8%)	48 (2.4%)	29 (1.5%)	
Traffic	1689 (33.6%)	994 (49.4%)	621 (32.6%)	
Work related	165 (3.3%)	104 (5.2%)	48 (2.5%)	
Home accident	2825 (56.2%)	684 (34%)	856 (44.9%)	
Sport accident	108 (2.1%)	49 (2.4%)	27 (1.4%)	
Self-inflicted	38 (0.8%)	96 (4.8%)	23 (1.2%)	
Other	34 (0.7%)	16 (0.8%)	11 (0.6%)	
Missing	30 (0.6%)	20 (1%)	290 (15.2%)	
P-HEMS involved (n)				<0.001
No	4406 (87.6%)	602 (29.9%)	1600 (84%)	
Yes	570 (11.3%)	1402 (69.7%)	159 (8.3%)	
Missing	54 (1.1%)	7 (0.3%)	146 (7.7%)	
In-hospital mortality (n)				<0.001
Discharged alive	4095 (81.4%)	1020 (50.7%)	1467 (77%)	
Died during admission	933 (18.5%)	990 (49.2%)	436 (22.9%)	
Missing	2 (0%)	1 (0%)	2 (0.1%)	

Numbers are median [quartiles] for age or count (column percentage) for all other variables. P-values refer to the comparison between no intubation versus intubation, excluding missing values. Age was compared with the Mann-Whitney U test, all other variables with chi-square tests. AIS: Abbreviated Injury Scale; GCS: Glasgow Coma Scale; ISS: Injury Severity Score; P-HEMS: physician-based helicopter emergency medical service.

head), and in which only patients with P-HEMS involvement were considered.

Two-sided *p*-values < 0.05 were considered statistically significant. An a priori power calculation was not performed, and the sample size is based on the available number of patients meeting inclusion criteria in the study period.

Results

Between January 2015 and December 2019, a total of 8946 patients meeting inclusion criteria were identified and included for analysis. The median age was 63 [38, 78] years, and 5599 (62%) patients were male. Table 1 shows the patient and injury characteristics, stratified by exposure to prehospital intubation. Intubated patients (n = 2011) were on average younger (52 [26, 69] vs. 67 [44, 80] years, $p < 0.001$), more often male (68.9% vs. 59.9%, $p < 0.001$), more severely injured (see Table 1 for distribution of ISS and head-AIS, both $p < 0.001$), and were more often treated by P-HEMS (69.7% vs. 11.3%, $p < 0.001$).

Overall hospital mortality was 26.4% (2359 out of 8941 patients with non-missing mortality data, 95% CI 25.5 to 27.3%). In an unadjusted comparison between the groups, mortality was significantly higher when patients were prehospitally intubated as compared to non-intubated patients (49.2% vs. 18.5%, OR 4.26, 95% CI 3.81 to 4.77, $p < 0.001$). Adjusting for potential confounders in logistic regression analyses markedly shifted the effect size estimate toward the null hypothesis value as expected, but prehospital intubation was still significantly associated with an almost two-fold increase in the odds of mortality in the complete case analysis as well as after multiple imputation (OR 1.86, 95% CI 1.35 to 2.57, $p < 0.001$ and OR 1.92, 95% CI 1.56 to 2.36, $p < 0.001$, respectively, Table 2). Consistent results were observed across different subgroup analyses (Table 2).

Adding the interaction between prehospital intubation and P-HEMS to the model revealed that the relationship of prehospital intubation and mortality may depend on whether P-HEMS is involved in the treatment or not (*p*-value for the interaction 0.044 in complete case analysis and 0.062 after multiple imputation). Prehospital intubation performed by ambulance paramedics without P-HEMS physician involvement was associated with a markedly increased odds of mortality (complete case analysis: OR 2.75, 95% CI 1.68 to 4.50, $p < 0.001$; multiple imputation: OR 1.98, 95% CI 1.50 to 2.62, $p < 0.001$). P-HEMS involvement attenuated the detrimental association between prehospital intubation and mortality. However, the multiple imputation model provides evidence that prehospital intubation is still associated with increased mortality compared to no intubation, even when P-HEMS is involved (complete case analysis: OR 1.43, 95% CI 0.90 to 2.28, $p = 0.131$; multiple imputation: OR 1.43, 95% CI 1.07 to 1.91, $p = 0.017$).

Discussion

Securing the airway is generally considered a top priority according to the "ABCDE" (Airway, Breathing, Circulation, Disability, Exposure) principle during advanced trauma life support (21). As comatose patients have a considerable risk of hypoxia due to airway obstruction (22,23), hypoventilation/apnea (24), or pulmonary aspiration of gastric contents and blood due to impaired airway reflexes (25), early endotracheal intubation of patients with severe prehospital intubation has often been advocated (4,7,21). Even though prehospital intubation is common practice in many EMS systems, including in the Netherlands, there is a paucity of evidence to support this practice.

To our knowledge, only one randomized controlled trial has investigated the effects of prehospital endotracheal intubation in patients with severe TBI (26). Prehospital intubations were performed by intensive care paramedics who were well trained in endotracheal intubation with rapid sequence induction. While prehospital intubation improved the rate of favorable neurologic outcome at 6 months

Table 2. Logistic regression analysis results.

Analysis	Odds ratio	95% confidence interval	*p*-value
Overall main effect of prehospital intubation, no interaction			
Complete case analysis (CC)	1.86	1.35 to 2.57	<0.001
Multiple imputation (MI)	1.92	1.56 to 2.36	<0.001
Model with interaction between prehospital intubation and P-HEMS			
Interaction term, CC	NA	NA	0.044
Interaction term, MI	NA	NA	0.062
Effect of PHI without P-HEMS, CC	2.75	1.68 to 4.50	<0.001
Effect of PHI without P-HEMS, MI	1.98	1.50 to 2.62	<0.001
Effect of PHI with P-HEMS, CC	1.43	0.90 to 2.28	0.131
Effect of PHI with P-HEMS, MI	1.43	1.07 to 1.91	0.017
Stratified by severity			
Severe TBI (head AIS 4), CC	1.54	0.87 to 2.71	0.135
Severe TBI (head AIS 4), MI	1.51	1.05 to 2.18	0.027
Critical TBI (head AIS 5 and 6), CC	2.18	1.46 to 3.26	<0.001
Critical TBI (head AIS 5 and 6), MI	2.17	1.71 to 2.76	<0.001
Additional subgroup analyses			
Only isolated TBI, CC	1.58	1.05 to 2.37	0.028
Only isolated TBI, MI	1.99	1.55 to 2.55	<0.001
Only patients treated by P-HEMS, CC	2.10	1.25 to 3.53	0.005
Only patients treated by P-HEMS, MI	1.77	1.29 to 2.40	<0.001

Logistic regression analysis of the relationship between prehospital intubation and in-hospital mortality. All analyses are adjusted for sex, age, ISS, AIS scores for eight body regions (head, face, thorax, abdomen, spine, upper extremity, lower extremity, external), prehospital GCS, interval from call to arrival of the ambulance, transport interval to hospital, and presence of P-HEMS. AIS: Abbreviated Injury Scale; CC: complete case analysis; GCS: Glasgow Coma Scale; ISS: Injury Severity Score; MI: multiple imputation; NA: Not Applicable; P-HEMS: Physician-based helicopter emergency medical service; PHI: prehospital intubation; TBI: traumatic brain injury.

compared to in-hospital intubation, no difference in survival to hospital discharge was observed. All other evidence comes exclusively from observational studies. In 2015, we summarized the available evidence in a systematic review and meta-analysis, including the randomized trial and high-quality observational studies that adjusted their analyses for confounding, and observed a statistically significant 2.3-fold increase in the odds of mortality when prehospital intubation was performed by EMS clinicians with limited experience (7). When intubation was performed by experienced personnel, the odds of mortality were 25% lower, but this was not statistically significant and thus inconclusive. Since then, some further observational studies have been published with inconsistent results. These studies either reported improved outcomes after prehospital intubation (27), worse outcomes (28), no association with outcomes (29), or no overall association but observed that the association may depend on injury severity and injury pattern (9,10).

Given the remaining substantial uncertainty about the effects of prehospital intubation and the fact that effects may differ based on EMS clinician experience, case mix, and additional factors such as logistic or geographic factors (e.g., transport distances to trauma centers), we sought to investigate the relationship between prehospital intubation and mortality in the Dutch setting. As prehospital care in the Netherlands involves a mix of ambulance care with nurses who only infrequently perform endotracheal intubations and P-HEMS with emergency physicians well proficient in performing intubation, we had the unique opportunity to directly assess whether the relationship between prehospital intubation and mortality depends on involvement of EMS clinicians with specific prehospital intubation experience. While a previous meta-analysis provided evidence for a difference in the effect of prehospital intubation depending on EMS clinician experience when pooling data across studies (7), this hypothesis has to our knowledge never been tested before within the same patient population.

Overall, we observed a relationship between prehospital intubation and higher mortality, consistent with a number of previous observational studies (7,28). We are aware that the cohort of patients who received prehospital intubation systematically differs from patients without prehospital intubation, in particular, they were more severely injured. Therefore, it is not surprising that the mortality is higher in the prehospital intubation cohort in the unadjusted analysis, but a higher mortality – albeit less pronounced than in the unadjusted analysis – persisted after adjustment for differences in injury severity and other potential confounders. While this suggests that prehospital intubation might potentially be harmful, it is also well possible that the granularity of the information on injury severity in our database (AIS, ISS, GCS) was insufficient to completely account for the between-group differences in the analysis. Moreover, we were unable to account for factors in the prehospital phase that are known to influence outcomes, such as duration and depth of hypotension, hypoxia, or hypocapnia. Thus, the findings of increased mortality in patients after prehospital intubation might be explained by residual confounding. The data therefore do not demonstrate that prehospital intubation is harmful, and causal inference on the effects of prehospital intubation on outcomes is not possible with our observational study design. Importantly, however, our data clearly also do not show beneficial effects, and do not support the common practice of routine prehospital intubation in patients with severe TBI. Prehospital clinicians should therefore always individually weigh potential risks and benefits rather than making the default assumption that prehospital intubation is beneficial in severe TBI. Additional evidence, preferably from randomized controlled trials, is necessary to provide a definitive answer on the causal relationship between prehospital intubation and outcomes in patients with severe TBI.

We specifically tested the hypothesis that the relationship between prehospital intubation and mortality depends on the experience of the EMS clinician. In the Netherlands, P-HEMS crews are well trained and highly experienced with prehospital intubation, whereas ground ambulance crews generally less frequently perform prehospital intubation, such that we tested for the interaction between P-HEMS involvement and intubation. Note, however, that expertise in performing prehospital intubation does not necessarily depend on whether the clinician is a physician, nurse, or paramedic, and in other health care systems, nurses or paramedics might be specially trained and highly experienced in performing intubation. Therefore, P-HEMS can be read as a synonym for 'EMS clinician experienced in prehospital intubation' in the context of our study.

A significant interaction between prehospital intubation and EMS clinician experience was observed in the complete case analysis, whereas a P-value just above the significance threshold was found after multiple imputation. While the complete case analysis supports our hypothesis, the latter analysis apparently does not. Nonetheless, we still have good reason to believe that the interaction is a true rather than spurious finding. First, the significance threshold is arbitrary, and results with P-values just above the threshold and results with P-values just under the threshold should lead to very similar conclusions, not diametrically opposed ones (30). Second, given that it is very plausible that the risks of endotracheal intubation outlined above are more prevalent when performed by less experienced personnel, and given the empirical evidence from the previous meta-analysis (7), there is a high a priori chance that the effect of prehospital intubation on outcomes depends on user experience. While we have not used a Bayesian framework to formally incorporate a prior probability distribution in the analysis, we note that also within the frequentist approach used in our analysis, a high prior probability markedly increases the likelihood that the marginally significant interaction we observed is a true rather than spurious finding (31). Therefore, the analysis does provide support for the hypothesis that the effect of prehospital intubation depends on P-HEMS involvement.

Prehospital intubation was less strongly associated with mortality when P-HEMS is present than when performed by ambulance crews without P-HEMS involvement, suggesting that presence of P-HEMS might be beneficial when prehospital intubation is performed. Nonetheless, at least in the multiple imputation analysis, prehospital intubation was still significantly associated with increased mortality even when P-HEMS was present. While it is possible that prehospital intubation by prehospital emergency physicians is detrimental for outcomes, there are also alternative explanations. First, the results may be affected by residual confounding as noted above. Second, the database does not contain information on who actually performed the intubation, but only whether P-HEMS were involved in the prehospital treatment. It is likely that a proportion of the intubations in the P-HEMS cohort had already been performed by ambulance personnel before P-HEMS arrival, such that the data do not allow direct conclusions on the effects of prehospital intubation when performed by prehospital emergency physicians versus ambulance personnel. Third, experience in endotracheal intubation is not the only difference between P-HEMS and ambulance paramedics; for example, P-HEMS crews had access to hypnotic agents and neuromuscular blocking agents to perform rapid sequence intubation. Nonetheless, this suggests that our conclusion from the overall data – that there is no evidence for better outcomes with prehospital intubation – even hold true when a P-HEMS crew is involved in the treatment. Even then, there is no evident benefit of routine prehospital intubation, and this further supports our recommendation that an individual approach considering individual benefits and risks is always needed, rather than routine intubation of patients with severe TBI.

Limitations of our study include the inherent limitations of observational research, including the strong potential for residual confounding, as detailed above. In order to control confounding associated with different injury severities as well concomitant injuries, we performed subgroup analyses stratified by the severity of head injury, and only considering patients with isolated TBI. Results were consistent with those in the full patient cohort, and none of these analyses suggested benefit of prehospital intubation in any subgroup. Nonetheless, it is quite possible that residual confounding explains at least in part why prehospital intubation appears to increase mortality.

We avoided selection bias by including all patients with a Head AIS of $\geq$4 in the observation period, and information bias is minimized in the DNTR database by a dedicated data manager for each trauma center who takes responsibility for accurate data entry. Nonetheless, the possibility of errors in source data, such as occasional misclassification of intubation status or presence of P-HEMS in ambulance forms, cannot be excluded. Most variables had only a few missing values (Table 1), whereas in particular prehospital GCS was missing in a substantial proportion of cases as ambulance personnel often use the AVPU score (32) rather than GCS for initial neurologic assessment. To account for missing data, we performed complete case analysis as well as multiple imputation. Both analyses largely showed consistent results, suggesting that missing data did not affect the main conclusions of our study in a relevant way.

Strengths of the study include the use of a national database with comprehensive coverage of the entire population of acutely admitted Dutch trauma patients, and a large sample size of almost 9000 patients.

Conclusions

The data do not support the common practice of prehospital intubation of patients with severe TBI. Even though causal inference is not possible in this observational study, it seems that the effect of prehospital intubation might depend on EMS clinician experience, and it is therefore prudent to involve prehospital personnel well proficient in prehospital intubation in all cases where it is potentially required. The decision to perform prehospital intubation in severe TBI should not merely be based on the unsupported dogma that it is generally required, but should rather carefully weigh potential benefits and harms for each individual patient.

Acknowledgments

We thank the Dutch Nationwide Trauma Registry for supplying the data.

Disclosure Statement

The authors have no competing interests to declare.

Data Availability

The data are not publicly available. Please contact the Dutch Nationwide Trauma Registry (https://www.lnaz.nl/trauma/landelijke-traumaregistratie) for information and requests concerning the raw data.

ORCID

Sebastiaan M. Bossers http://orcid.org/0000-0002-2396-2777

References

1. Bossers SM, Loer SA, Bloemers FW, Den Hartog D, Van Lieshout EMM, Hoogerwerf N, van der Naalt J, Absalom AR, Peerdeman SM, Schwarte LA, BRAIN-PROTECT collaborators, et al. Association between prehospital tranexamic acid administration and outcomes of severe traumatic brain injury. JAMA Neurol. 2021;78(3):338–45. doi:10.1001/jamaneurol.2020.4596.
2. Badjatia N, Carney N, Crocco TJ, Fallat ME, Hennes HM, Jagoda AS, Jernigan S, Letarte PB, Lerner EB, Moriarty TM, BTF Center for Guidelines Management, et al. Guidelines for prehospital management of traumatic brain injury 2nd edition. Prehosp Emerg Care. 2008;12(Suppl 1):S1–S52. doi:10.1080/10903120701732052.
3. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kissoon N, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017;80(1):6–15. doi:10.1227/NEU.0000000000001432.
4. American College of Surgeons Committee on Trauma. Head Trauma. Advanced trauma life support (ATLS): student course manual. Chicago, IL: American College of Surgeons. 2018. 102–127.
5. Gravesteijn BY, Sewalt CA, Ercole A, Lecky F, Menon D, Steyerberg EW, Maas AIR, Lingsma HF, Klimek M, collaborators C-T, CENTER-TBI orators Variation in the practice of tracheal intubation in Europe after traumatic brain injury: a prospective cohort study. Anaesthesia. 2020;75(1):45–53. doi:10.1111/anae.14838.
6. Franschman G, Verburg N, Brens-Heldens V, Andriessen TM, Van der Naalt J, Peerdeman SM, Valk JP, Hoogerwerf N, Greuters S, Schober P, et al. Effects of physician-based emergency medical service dispatch in severe traumatic brain injury on prehospital run time. Injury. 2012;43(11):1838–42. doi:10.1016/j.injury.2012.05.020.
7. Bossers SM, Schwarte LA, Loer SA, Twisk JW, Boer C, Schober P. Experience in prehospital endotracheal intubation significantly influences mortality of patients with severe traumatic brain injury: a systematic review and meta-analysis. PLoS One. 2015;10(10):e0141034. doi:10.1371/journal.pone.0141034.
8. Lansom JD, Curtis K, Goldsmith H, Tzannes A. The effect of prehospital intubation on treatment times in patients with suspected traumatic brain injury. Air Med J. 2016;35(5):295–300. doi:10.1016/j.amj.2016.04.019.
9. Choffat C, Delhumeau C, Fournier N, Schoettker P. Effect of prehospital intubation in patients with severe traumatic brain injury on outcome: a prospective cohort study. J Clin Med. 2019;8(4):470.
10. Gravesteijn BY, Sewalt CA, Nieboer D, Menon DK, Maas A, Lecky F, Klimek M, Lingsma HF, collaborators C, Collaborators C-T. Tracheal intubation in traumatic brain injury: a multicentre prospective observational study. Br J Anaesth. 2020;125(4):505–17. doi:10.1016/j.bja.2020.05.067.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S, STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453–7. doi:10.1016/S0140-6736(07)61602-X.
12. Bossers SM, Boer C, Bloemers FW, Van Lieshout EMM, Den Hartog D, Hoogerwerf N, Innemee G, van der Naalt J, Absalom AR, Peerdeman SM, BRAIN-PROTECT Collaborators, et al. Epidemiology, prehospital characteristics and outcomes of severe traumatic brain injury in The Netherlands: the BRAIN-PROTECT study. Prehosp Emerg Care. 2021;25(5):644–55. doi:10.1080/10903127.2020.1824049.
13. Bossers SM, Boer C, Greuters S, Bloemers FW, Den Hartog D, Van Lieshout EMM, Hoogerwerf N, Innemee G, van der Naalt J, Absalom AR, BRAIN-PROTECT orators, et al. Dutch prospective observational study on prehospital treatment of severe traumatic brain injury: the BRAIN-PROTECT study protocol. Prehosp Emerg Care. 2019;23(6):820–7. doi:10.1080/10903127.2019.1587126.
14. Ringdal KG, Coats TJ, Lefering R, Di Bartolomeo S, Steen PA, Roise O, Handolin L, Lossius HM, Utstein TCDep, Utstein TCD expert panel The Utstein template for uniform reporting of data following major trauma: a joint revision by SCANTEM, TARN, DGU-TR and RITG. Scand J Trauma Resusc Emerg Med. 2008;16:7. doi:10.1186/1757-7241-16-7.
15. Driessen MLS, Sturms LM, Bloemers FW, Ten Duis HJ, Edwards MJR, den Hartog D, de Jongh MAC, Leenhouts PA, Poeze M, Schipper IB, et al. The Dutch nationwide trauma registry: the value of capturing all acute trauma admissions. Injury. 2020;51(11):2553–9. doi:10.1016/j.injury.2020.08.013.
16. Schober P, Vetter TR. Descriptive statistics in medical research. Anesth Analg. 2019;129(6):1445. doi:10.1213/ANE.0000000000004480.
17. Schober P, Vetter TR. Logistic regression in medical research. Anesth Analg. 2021;132(2):365–6. doi:10.1213/ANE.0000000000005247.
18. Schober P, Vetter TR. Confounding in observational research. Anesth Analg. 2020;130(3):635.
19. Schober P, Vetter TR. Missing data and imputation methods. Anesth Analg. 2020;131(5):1419–20. doi:10.1213/ANE.0000000000005068.
20. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J Stat Soft. 2011;45(3):1–67. doi:10.18637/jss.v045.i03.
21. American College of Surgeons Committee on Trauma. Airway and Ventilatory Management. Advanced trauma life support (ATLS): student course manual. Chicago, IL: American College of Surgeons. 2018. 22–41.
22. Boidin MP. Airway patency in the unconscious patient. Br J Anaesth. 1985;57(3):306–10. doi:10.1093/bja/57.3.306.
23. Safar P, Escarraga LA, Chang F. Upper airway obstruction in the unconscious patient. J Appl Physiol. 1959;14:760–4. doi:10.1152/jappl.1959.14.5.760.
24. Atkinson JL. The neglected prehospital phase of head injury: apnea and catecholamine surge. Mayo Clin Proc. 2000;75(1):37–47. doi:10.4065/75.1.37.
25. Lockey DJ, Coats T, Parr MJ. Aspiration in severe trauma: a prospective study. Anaesthesia. 1999;54(11):1097–8. doi:10.1046/j.1365-2044.1999.00754.x.
26. Bernard SA, Nguyen V, Cameron P, Masci K, Fitzgerald M, Cooper DJ, Walker T, Std BP, Myles P, Murray L, et al. Prehospital rapid sequence intubation improves functional outcome for patients with severe traumatic brain injury: a

randomized controlled trial. Ann Surg. 2010;252(6):959–65. doi: 10.1097/SLA.0b013e3181efc15f.

27. Denninghoff KR, Nuno T, Pauls Q, Yeatts SD, Silbergleit R, Palesch YY, Merck LH, Manley GT, Wright DW. Prehospital intubation is associated with favorable outcomes and lower mortality in ProTECT III. Prehosp Emerg Care. 2017;21(5):539–44. doi:10.1080/10903127.2017.1315201.

28. Haltmeier T, Benjamin E, Siboni S, Dilektasli E, Inaba K, Demetriades D. Prehospital intubation for isolated severe blunt traumatic brain injury: worse outcomes and higher mortality. Eur J Trauma Emerg Surg. 2017;43(6):731–9. doi:10.1007/s00068-016-0718-x.

29. Rubenson Wahlin R, Nelson DW, Bellander BM, Svensson M, Helmy A, Thelin EP. Prehospital intubation and outcome in traumatic brain injury-assessing intervention efficacy in a modern trauma cohort. Front Neurol. 2018;9:194.

30. Altman D. Principles of statistical analysis. Practical statistics for medical research. Boca Raton, FL: Chapman & Hall/CRC; 1999. p. 152–178.

31. Schmalz X, Biurrun Manresa J, Zhang L. What is a Bayes factor? Psychol Methods. 2021;

32. McNarry AF, Goldhill DR. Simple bedside assessment of level of consciousness: comparison of two simple assessment scales with the Glasgow Coma scale. Anaesthesia. 2004;59(1):34–7. doi:10.1111/j.1365-2044.2004.03526.x.