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The Impact of Prehospital Endotracheal Intubation on Outcome in Moderate to Severe Traumatic Brain Injury

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Background: Although early intubation to prevent the mortality that accompanies hypoxia is considered the standard of care for severe traumatic brain injury (TBI), the efficacy of this approach remains unproven.

Methods: Patients with moderate to severe TBI (Head/Neck Abbreviated Injury Scale [AIS] score 3+) were identified from our county trauma registry. Logistic regression was used to explore the impact of prehospital intubation on outcome, controlling for age, gender, mechanism, Glasgow Coma Scale score, Head/Neck AIS score, Injury Severity Score, and hypotension. Neural network analysis was performed to identify patients predicted to benefit from prehospital intubation.

Results: A total of 13,625 patients from five trauma centers were included; overall mortality was 22.9%, and 19.3% underwent prehospital intubation. Logistic regression revealed an increase in mortality with prehospital intubation (odds ratio, 0.36; 95% confidence interval, 0.32–0.42; $p < 0.001$). This was true for all patients, for those with severe TBI (Head/Neck AIS score 4+ and/or Glasgow Coma Scale score of 3–8), and with exclusion of patients transported by aeromedical crews. Patients intubated in the field versus the emergency department had worse outcomes. Neural network analysis identified a subgroup of patients with more significant injuries as potentially benefiting from prehospital intubation.

Conclusion: Prehospital intubation is associated with a decrease in survival among patients with moderate-to-severe TBI. More critically injured patients may benefit from prehospital intubation but may be difficult to identify prospectively.

Key Words: Prehospital intubation, Traumatic brain injury, Outcome, Mortality, Hypoxia.

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Multiple investigators have documented hypoxia in a substantial percentage of head-injured patients, with an associated increase in mortality.[1–9] This has resulted in aggressive field airway management protocols, including endotracheal intubation (ETI) performed by prehospital personnel.[10,11] Despite multiple studies exploring the relationship between invasive airway management and outcome, the efficacy of ETI remains unproven. The only prospective, pseudorandomized study addressing the issue of paramedic ETI enrolled pediatric patients requiring either bag-valve-mask ventilation (BVM) or ETI.[12] Intubation was successful in less than half of patients in the ETI cohort, and no difference in mortality was observed between the two groups. More recently, the San Diego Paramedic RSI Trial documented an increase in mortality after paramedic rapid-sequence intubation (RSI) of severely head-injured patients as compared with matched controls, possibly as a result of the high incidence of hypoxia and hyperventilation in the trial cohort.[13–17] Multiple retrospective studies documented an increase in mortality associated with paramedic ETI of head-injured patients but were limited by small numbers of intubated patients or the failure to include key variables in the analysis.[18–22]

One of the few studies to demonstrate improved outcomes with paramedic ETI was conducted by Winchell and Hoyt.[23] In a retrospective analysis, they demonstrated an absolute mortality benefit of 21% with field intubation in patients with isolated severe traumatic brain injury (TBI). Although patients were stratified by Glasgow Coma Scale (GCS) score, the analysis did not adjust for potentially important factors such as Head/Neck Abbreviated Injury Scale (AIS) score, hypotension, or Injury Severity Score (ISS). In this study, we used one of the largest databases of head-injured patients to further explore the relationship between paramedic ETI and outcome. Logistic regression was used to adjust for multiple variables that impact TBI outcomes. In addition, a neural network analysis was performed to identify patients who might benefit from paramedic ETI.

PATIENTS AND METHODS

Design

This was a retrospective, registry-based analysis using the San Diego TBI Database, which is a subset of the San Diego County Trauma Registry. Waiver of consent was granted by our institutional review board, and the study was supported by the San Diego Trauma Audit Committee.

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Subjects

The San Diego County Trauma Registry includes all patients meeting Major Trauma Outcome Study criteria admitted to San Diego County trauma centers since 1987. The San Diego TBI Database includes all patients in the registry with a Head/Neck AIS score of 3 or greater; patients in whom the Head/Neck AIS value is defined by a neck injury are excluded. The present analysis included all patients in the San Diego TBI Database treated between January 1, 1987, and December 31, 2003.

Setting and Prehospital System

San Diego County has a population of approximately 3 million in an area of over 4,200 square miles. Fifteen different paramedic agencies provide advanced life support; approximately 30% of all transports are for injury-related chief complaints. A minimum of two paramedics respond to all major trauma victims. Aeromedical crews respond from two bases at the discretion of ground paramedics; flight crews consist of a certified flight nurse (CFN) paired with either a specially trained flight paramedic, a second CFN, or an emergency medicine resident physician. Paramedics are trained in ETI and Combitube insertion (CTI), whereas CFNs and resident physicians are able to use nasotracheal intubation, cricothyrotomy, and RSI as appropriate.

Statistical Analysis

The primary goal of this analysis was to explore the impact of invasive prehospital airway management on outcome. Logistic regression was performed to identify the independent effect of prehospital intubation on mortality, controlling for the following variables that are known to affect outcome: age as a surrogate for comorbid disease, gender, mechanism of injury (assault, fall, found down, gunshot wound, motor vehicle crash, pedestrian versus automobile, stab wound, and other), level of consciousness as reflected by preadmission GCS score, head injury severity as reflected by Head/Neck AIS score, overall injury severity as reflected by ISS, and the presence of preadmission hypotension. The variable of interest was prehospital airway management strategy, which included ETI, CTI, cricothyrotomy, or none of these. Analysis was performed for all patients with complete data and for those with severe TBI, defined as either GCS score of 8 or less, Head/Neck AIS score 4 or greater, or both. Identical logistic regression analyses were performed after exclusion of patients transported by aeromedical crews and again using only those patients intubated in either the field or during the initial emergency department (ED) resuscitation. Statistical analysis was performed using StatsDirect (StatsDirect Software, Inc., Ashwell, UK). Odds ratios were used to quantify the relationship between paramedic intubation and outcome. Statistical significance was assumed for $p < 0.05$.

Neural network analysis was performed to identify a subgroup of patients who might benefit from paramedic ETI. All patients included in the San Diego TBI Database treated between January 1, 1987, and December 31, 2003, with complete data were used in the analysis. Half of the patients were randomly assigned to the training set to generate the neural network models, and the other half were used as the validation set. Fully connected feed-forward networks with a single layer of hidden units were used. Waikato Environment for Knowledge Analysis, Version 3.4 (University of Waikato, New Zealand) was used to generate the models, of which the three with the highest predictive ability were selected for further analysis. The predictive ability of these neural network models was compared with that for the logistic regression models described above.

The primary intent of the neural network analysis was to identify patients that might benefit from prehospital intubation. The three neural network models with the best predictive ability were each used to calculate a differential survival value (probability of survival with intubation minus probability of survival without intubation) for each patient. Two cohorts were then defined on the basis of a "vote" by the three neural network models. Patients were placed in the "increased survival with intubation" cohort if two or more of the three neural network models predicted an increase in survival with intubation (positive differential survival value); similarly, patients were placed in the "decreased survival with intubation" cohort if two or more of the three models predicted a decrease in survival (negative differential survival value). Patients with a predicted increase versus a decrease in survival with intubation were then compared with regard to age, gender, mechanism of injury, preadmission GCS score, Head/Neck AIS score, ISS, and the presence of preadmission hypotension. In addition, the relationship between mean differential survival value and age, gender, preadmission GCS score, Head/Neck AIS score, ISS, and the presence of preadmission hypotension were explored using linear regression, which was justified because of the normal distribution of mean differential survival values. The predictive ability of the neural network analysis was also compared with that for the logistic regression models as described above. Statistical calculations were performed using StatsDirect. Statistical significance was assumed for $p < 0.05$.

RESULTS

A total of 13,625 patients from five trauma centers were included in the analysis; overall mortality was 22.9%. Demographic and clinical data for all patients and each of the subgroups are displayed in Table 1. A total of 19.3% of all patients underwent prehospital intubation (18.1% endotracheal, 0.2% nasotracheal, 0.6% Combitube, and 0.4% cricothyrotomy). Mortality for patients undergoing prehospital ETI was 55% versus only 15% for those without invasive airway management (odds ratio [OR], 0.14; 95% confidence interval [CI], 0.13–0.16; $p < 0.001$). Even when adjusting for age, gender, mechanism of injury, preadmission GCS score, Head/Neck AIS score, ISS, and

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Table 1 The Relationship between Treatment Delay and Biceps Long Head Tendon Lesions

Symptom or Injury Time	Type 1 (n = 50)	Type 2 (n = 10)	Type 3 (n = 12)	Type 4 (n = 15)	Type 5 (n = 6)	Normal (n = 29)	Total
<3 mo							
Trauma	8	2	3	3	0	15	31
Nontrauma	6	1	1	2	2	14	26
3–6 mo							
Trauma	9	2	2	4	1	0	18
Nontrauma	13	2	1	2	1	0	19
>6 mo							
Trauma	8	1	3	3	1	0	16
Nontrauma	6	2	2	1	1	0	12

the presence of preadmission hypotension, invasive prehospital airway management was still associated with increased mortality (OR, 0.36; 95% CI, 0.32–0.42; $p < 0.001$). This was also true for patients with a GCS score of 8 or less, a Head/Neck AIS score of 4 or greater, and both (Table 2). Exclusion of patients transported by aeromedical crews did not alter these findings (Table 3).

A total of 4,885 patients underwent invasive airway management either in the field (n = 2,665) or in the ED during the initial resuscitation (n = 2,220). Mortality was increased among patients intubated in the field versus the ED for all patients and for those with a GCS score of 8 or less, a Head/Neck AIS score of 4 or greater, and both (Table 4).

A total of 13,084 patients with complete data were used for neural network analysis. The models were generated using 6,542 patients randomly assigned to the training set; their predictive ability was verified using the remaining 6,542 patients that constituted the validation set. Three models were selected on the basis of their predictive ability, which was similar to that of the logistic regression models described above (Table 5). Overall, the mean for all differential survival values predicted a 6.2% increase in mortality with intubation. A total of 1,787 patients were identified with a predicted increase in survival and 11,154 patients with a predicted decrease in survival with intubation. Comparisons between these two groups are displayed in Tables 6 and 7. Patients with a predicted increase in survival with prehospital intubation had higher Head/Neck AIS and ISS values, a higher rate of preresuscitation hypotension, and lower preresuscitation GCS scores. In addition, these patients had a substantially higher incidence of gunshot wounds and motor vehicle crashes. Despite the statistically significant differences between the groups, it is not clear that these differences were clinically significant enough to help guide prehospital personnel in selecting patients who might benefit from prehospital intubation. Similarly, statistically significant relationships were identified between each of the demographic/clinical variables and the mean differential survival value; however, the calculated values for slope were very close to zero and the correlation coefficient values (r) were relatively low.

Table 2 The Relationship between Torn Rotator Cuff Size and Biceps Long Head Tendon Lesions

Tear Size	Type 1 (n = 50)	Type 2 (n = 10)	Type 3 (n = 12)	Type 4 (n = 15)	Type 5 (n = 6)	Normal (n = 29)	Total
Massive (>5 cm)	3	4	6	7	4	1	25
Large (3–5 cm)	12	3	4	5	1	3	28
Medium (1–3 cm)	14	2	2	2	1	10	31
Small (<1 cm)	21	1	0	1	0	15	38
>5 cm^2	4	6	7	8	4	2	31
3–5 cm^2	22	3	4	5	2	9	45
<3 cm^2	24	1	1	2	0	18	46

Table 3 Correlation between Torn Rotator Cuff Tendon and Biceps Long Head Lesion

Torn Tendons	Type 1 (n = 50)	Type 2 (n = 10)	Type 3 (n = 12)	Type 4 (n = 15)	Type 5 (n = 6)	Normal (n = 29)	Total
Supraspinatus	34	1	0	5	0	23	63
Supraspinatus plus infraspinatus	12	1	2	5	3	5	28
Subscapularis	0	0	3	2	0	0	5
Supraspinatus plus subscapularis	4	4	3	3	1	1	16
Supraspinatus plus infraspinatus plus subscapularis	0	4	4	0	2	0	10

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Table 4 Comparison between patients intubated in the field versus the ED

Parameter	n	Mortality (%)	OR (95% CI)	Adjusted OR (95% CI)
All Patients	4247	1927 (45.4)	—	—
Prehospital intubation	2414	1390 (57.6)	0.31 (0.27, 0.35)*	0.47 (0.40, 0.55)*
ED intubation	1833	537 (29.3)		
GCS 3–8	3263	1747 (53.5)	—	—
Prehospital intubation	2221	1351 (60.8)	0.39 (0.34, 0.46)*	0.68 (0.56, 0.83)*
ED intubation	1042	396 (38.0)		
H/N AIS 4+	3428	1773 (51.7)	—	—
Prehospital intubation	2053	1284 (62.5)	0.33 (0.29, 0.38)*	0.69 (0.57, 0.83)*
ED intubation	1375	489 (35.6)		
GCS 3–8 & H/N AIS 4+	2813	1622 (57.7)	—	—
Prehospital intubation	1929	1250 (64.8)	0.39 (0.34, 0.46)*	0.70 (0.57, 0.86)*
ED intubation	884	372 (42.1)		

* $p < 0.001$.

DISCUSSION

Early intubation of severely head-injured patients is one of the most fundamental aspects of TBI care.[24] Although the association between head injury, hypoxia, and poor outcomes is undisputed, the efficacy of aggressive airway management remains unproven.[6–9] In this study, we documented an association between prehospital intubation and an increase in mortality despite controlling for multiple factors that affect outcome in TBI patients. This represents one of the largest databases of head-injured patients, with multiple factors collected systematically for analysis. In addition, a neural network analysis was performed to identify a subgroup of patients who might benefit from prehospital ETI. Despite good predictive ability for each of the models and multiple statistically significant differences between patients predicted to have increased versus decreased survival with prehospital intubation, it remains unclear whether prehospital personnel can prospectively identify patients who might benefit from prehospital ETI.

Table 5 Predictive ability of the neural network models. Sensitivity and specificity are reported at the "near" cutoff point that maximizes the area under the receiver-operator curve (ROC)

Parameter	Area under ROC	Sensitivity	Specificity	Correctly Classified
Model 1	0.93	85.0	86.4	85.2
Model 2	0.93	85.2	85.9	85.4
Model 3	0.93	85.4	85.8	85.5

Table 6 Demographic and clinical variables for all patients predicted to have an increase versus a decrease in survival with prehospital intubation by at least two out of the three neural network models

Parameter	Better with Intubation ($n = 1,787$)	Better without Intubation ($n = 11,229$)	P-value
Age (years)	31.3	40.3	<0.001
Gender (% male)	66.7	78.0	<0.001
Mechanism of Injury (%)			
Assault	3.1	5.9	<0.001
Fall	5.2	23.5	<0.001
Found down	1.4	0.7	0.001
GSW	26.6	2.5	<0.001
MVA	52.0	37.1	<0.001
Pedestrian vs. auto	9.5	9.3	0.848
Stab wound	0.2	0.9	0.003
GCS	6.2	10.4	<0.001
Hypotensive (%)	65.9	49.7	<0.001
Head/Neck AIS	4.11	3.93	<0.001
ISS	28.9	24.8	<0.001

Our findings are consistent with previous analyses exploring the impact of early intubation on outcome in patients with TBI. Murray et al. studied 852 patients with a Head AIS score of 3 or greater and a GCS score of 8 or less; only 81 of these underwent prehospital ETI.[18] They used logistic regression to document increased mortality with invasive airway management attempts, whether or not they were successful. They also stratified patients by ISS and GCS score but were unable to identify a subgroup with improved outcomes after prehospital ETI. Eckstein et al. compared 93 patients undergoing prehospital ETI with 403 patients undergoing BVM in the field followed by intubation on arrival at the trauma center.[19] They observed a 93% mortality rate among field-intubated patients versus only 67% with field BVM. This mortality increase with prehospital ETI persisted, even when adjusted for age, GCS score, Head AIS score, associated injuries, ISS, and mechanism of injury. Sloane et al. compared outcomes in 47 patients undergoing aeromedical RSI with 267 patients undergoing RSI in the trauma resuscitation suite and observed no differences in outcome.[20] Bochicchio et al. compared 78 severely head-injured patients (GCS score of 8 or less,[23] Head AIS score of 3 or greater) undergoing field intubation with 113 patients undergoing emergent intubation in the ED and observed a mortality increase among the field intubation patients despite no documented differences in injury severity. Gausche et al. observed no improvement in

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Table 7 **Correlation between various demographic/clinical variables and mean differential survival value generated from all three neural network models (predicted survival with intubation − predicted survival without intubation). A negative correlation coefficient (r) indicates a decrease in survival with an increase in the parameter value**

Parameter	Correlation Coefficient (95% CI)	Slope (95% CI)	P-value
Age	−0.43 (−0.45 to −0.42)	−0.0015 (−0.0015 to −0.0014)	<0.001
Gender	−0.02 (−0.04 to −0.01)	−0.0035 (−0.0065 to −0.0009)	0.010
GCS	−0.13 (−0.14 to −0.11)	−0.0018 (−0.0020 to −0.0016)	<0.001
Hypotensive	0.04 (0.02 to 0.06)	0.0055 (0.0031 to 0.0079)	<0.001
Head/Neck AIS	−0.15 (−0.16 to −0.13)	−0.0119 (−0.0132 to −0.0105)	<0.001
ISS	−0.08 (−0.10 to −0.06)	−0.0004 (−0.0005 to −0.0003)	<0.001

mortality with institution of an ETI protocol for pediatric patients requiring intubation for a variety of reasons.[12] It is difficult to determine the impact of intubation on outcome from their study, as the heterogeneity of diseases and low intubation success rate in the ETI cohort may have masked a true positive or negative effect of prehospital intubation on outcome. Stockinger and McSwain compared outcomes in 316 patients undergoing prehospital ETI and 217 patients undergoing prehospital BVM.[21] They used logistic regression, TRISS, and Revised Trauma Score predictions to document an association between early intubation and increased mortality. Only two thirds of patients had complete data available for analysis. Finally, Wang et al. recently presented data from 1,008 patients undergoing prehospital ETI and 1,223 patients undergoing ED ETI, documenting an increase in mortality and a decrease in good outcomes among patients undergoing prehospital ETI.[22] Of note, preadmission GCS scores were not available for use in their regression model.

The only evidence to support prehospital intubation in patients with severe TBI came from Winchell and Hoyt, using data from one of the trauma centers in our county.[23] Patients were stratified by GCS score (3 vs. 4–8) and by isolated severe TBI versus multiple trauma based on AIS scores for other body systems. An absolute mortality benefit of over 20% was observed with prehospital intubation among patients with isolated severe TBI. Logistic regression was not used to adjust for the influence of other variables on outcome. Interestingly, the rate of prehospital intubation was substantially higher among patients with GCS scores of 4 to 8 versus a GCS score of 3, suggesting some form of selection bias. Here, we incorporate data from all five trauma centers and adjust for multiple factors that affect outcome in TBI.

It is not clear whether the association between prehospital ETI and increased mortality represents a form of selection bias or a true detrimental effect of early intubation on outcome. It is likely that patients who are able to be intubated in the field have a decreased level of consciousness and more severe TBI than those who are unable to be intubated or require RSI medications, and even the most sophisticated regression models may not be able to account for these factors. Alternatively, a growing body of literature exists to provide an explanation for the potentially detrimental effects of ETI and positive-pressure ventilation on outcome. The propensity for emergency personnel to hyperventilate, the adverse hemodynamic effects of positive-pressure ventilation, and the apparent rise in cytokines and resultant detrimental effects on multiple organ systems as a result of injurious ventilation strategies may all combine to mask any potential benefits with regard to airway protection or improved oxygenation.[25–46] Furthermore, it is possible that the aspiration events associated with severe TBI occur before the arrival of prehospital personnel.[47,48] Similarly, the detrimental effects of TBI-associated hypoxia may not be reversible by aggressive airway management, and the strategy of hyperoxygenation by means of intubation may be unnecessary at best and detrimental at worst.[49–52]

It is interesting to note that the neural network analysis was able to identify a subgroup of patients who might benefit from prehospital intubation. These patients had slighter higher Head/Neck AIS and ISS values, a higher incidence of hypotension, and lower GCS scores. It is unclear, however, whether these differences were clinically significant enough to allow prehospital personnel to prospectively identify these patients in the field.

Despite the large sample size and relatively comprehensive data set available for each patient in this analysis, the limitations of this analysis must be considered when interpreting these results. As discussed above, logistic regression models may not be able to adjust for all of the factors that affect outcome, and the ability to perform ETI without RSI may ultimately represent a poor prognosis. In addition, this was a registry-based analysis, relying on data input by trauma center personnel. Although this was anticipated to result in a large percentage of patients with incomplete prehospital data, there were surprisingly few patients eliminated for this reason. Finally, the application of neural networks to clinical data, especially to explore the impact of a given variable on outcome, is not well described and necessitated a novel approach for this analysis.

CONCLUSION

Prehospital intubation is associated with a decrease in survival among patients with moderate to severe TBI, even after adjusting for multiple clinical variables that affect outcome. Neural network models were able to identify a subgroup of patients with more significant injuries who might

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benefit from field intubation; however, it is unclear whether these patients can be identified prospectively by prehospital personnel.

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