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Association between septic shock and tracheal injury score in intensive care unit patients with invasive ventilation: a prospective single-centre cohort study in China

Pei Zhang ,[1] Qilin Yang,[2] Chunhua Yin,[1] Zhigang Cai,[3] Huaihai Lu,[1] Haitao Li,[3] Liwen Li,[1] Ye Tian,[1] Long Bai,[1] Lining Huang[4]

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For numbered affiliations see end of article.

Correspondence to
Dr Lining Huang;
27701226@hebmu.edu.cn

ABSTRACT

Objectives There was no evidence regarding the relationship between septic shock and tracheal injury scores. Investigate whether septic shock was independently associated with tracheal injury scores in intensive care unit (ICU) patients with invasive ventilation.

Design Prospective observational cohort study.

Setting Our study was conducted in a Class III hospital in Hebei province, China.

Participants Patients over 18 years of age admitted to the ICU between 31 May 2020 and 3 May 2022 with a tracheal tube and expected to be on the tube for more than 24 hours.

Primary and secondary outcome measures Tracheal injuries were evaluated by examining hyperaemia, ischaemia, ulcers and tracheal perforation by fiberoptic bronchoscope. Depending on the number of lesions, the lesions were further classified as moderate, severe or confluent.

Results Among the 97 selected participants, the average age was 56.6±16.5 years, with approximately 64.9% being men. The results of adjusted linear regression showed that septic shock was associated with tracheal injury scores (β: 2.99; 95% CI 0.70 to 5.29). Subgroup analysis revealed a stronger association with a duration of intubation ≥8 days (p=0.013).

Conclusion Patients with septic shock exhibit significantly higher tracheal injury scores compared with those without septic shock, suggesting that septic shock may serve as an independent risk factor for tracheal injury.

Trial registration number ChiCTR2000037842, registered 03 September 2020. Retrospectively registered, https://www.chictr.org.cn/edit.aspx?pid=57011&htm=4.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study has incorporated a comprehensive range of confounding factors, encompassing laboratory indicators, treatment measures and aetiological outcomes.
⇒ We employed effect modification factor analysis and reached robust conclusions through subgroup analyses.
⇒ Due to the small sample size and the single-centre design, the results of the study may not be directly applicable or generalisable to a larger population.
⇒ Despite efforts to minimise variations among different respiratory therapists' assessments, the tracheal injury scores may still be influenced by this aspect.

INTRODUCTION

Sepsis is a critical syndrome that arises due to a disordered immune response to an infection, leading to organ dysfunction.[1] The most severe type of sepsis is known as septic shock, which manifests as low blood pressure that persists even after fluid resuscitation and the occurrence of tissue hypoperfusion.[2]

Tracheal lesions are a frequently encountered complication of endotracheal intubation in critically ill patients.[3 4] To avoid potential complications, such as tracheal stenosis or perforation, the tracheal tube cuff pressure (P_{cuff}) should be maintained at a level that is sufficiently low in comparison to the perfusion pressure.[5–8] To ensure patient safety, P_{cuff} should be regularly monitored at intervals and maintained within the range of 25–30 cmH2O.[9 10]

With the advent of high-volume, low-pressure endotracheal tubes, the severity of tracheal injuries and associated complications has decreased, leading to reduced clinical attention to airway injuries caused by this procedure.[11] However, as the COVID-19 virus continues to spread, concerns have resurfaced regarding tracheal damage and serious complications resulting from endotracheal intubation.[12–14] Previous studies have identified numerous risk factors for tracheal lesions, including high P_{cuff} (>30 cmH2O),[8 15] hypotension,[7] severe respiratory

failure,[3] inflammation,[3 16] continuous aspiration of subglottic secretions[17] and duration of mechanical ventilation.[18] Despite these findings, there remains a lack of comprehensive studies in this area, with most studies limited by small sample sizes or inadequate evaluation of tracheal injuries, except for the work by Lylia Touat *et al*.[18] Given the characteristic systemic tissue hypoperfusion in septic shock,[2] and the fact that over 70% of septic shock patients require intubation and invasive mechanical ventilation,[19] this population may be at a heightened risk of tracheal injury. However, previous studies have not specifically investigated the relationship between septic shock and tracheal injury scores. Therefore, this study aims to determine whether septic shock is independently associated with tracheal injury scores in intensive care unit (ICU) patients undergoing invasive ventilation.

MATERIALS AND METHODS

Study design and population

This prospective cohort study was conducted in the department of anaesthesiology within the ICU. Written consent was obtained from the patients or their proxies. The study enrolled participants between 31 May 2020 and the inclusion deadline was 5 March 2022. Inclusion criteria for this study were patients aged 18 or older who were intubated and expected to require mechanical ventilation for at least 24 hours. Patients already enrolled in another trial, those who had undergone mechanical ventilation for over 24 hours at the time of eligibility screening, those with a prior tracheostomy on ICU admission, or those with a history of two or more tracheal intubations were excluded from the study.

Treatment protocol

All patients enrolled in this study who required endotracheal intubation received routine intensive care. The diagnoses of septic shock were established at baseline according to the new Third International Consensus Definitions (Sepsis-3.0) criteria and recorded as categorical variables.[20] P_{cuff} was measured using a manual manometer every 4 hours, and P_{cuff} management was continued until the cessation of mechanical ventilation or death. The target P_{cuff} range was maintained between 25 and 30 cmH2O.

All patients included in the study underwent fiberoptic bronchoscopy at the time of extubation to assess for tracheal injuries. Prior to extubation, 3 mL of 2% lidocaine was atomised through the tracheal tube and oral topical anaesthesia with 2% lidocaine was administered. The fiberoptic bronchoscope was lubricated with tetracaine hydrochloride mucilage, and intravenous propofol (1–2 mg/kg) was administered to achieve sedation. After aligning the disinfected tip of the fiberoptic bronchoscope with the tip of the tracheal tube, ensuring they were at the same level, the tracheal tube securing device was removed. Following cuff deflation, the fiberoptic bronchoscope and tracheal tube were simultaneously withdrawn by two whole markings, equivalent to a length of 4 cm. Subsequently, the fiberoptic bronchoscope was inserted approximately 0.5 cm to inspect the tracheal mucosa within its field of view. The endotracheal tube and fiberoptic bronchoscope were then removed on completion of the evaluation. During the examination, the propofol dose was adjusted according to the patient's sedation state to ensure comfort and minimise coughing. Patients requiring percutaneous tracheotomies also underwent fiberoptic bronchoscopy. However, patients who died before extubation did not undergo fiberoptic bronchoscopy, and postmortem assessment of tracheal ischaemia was not conducted for these patients.

Definition of tracheal injured lesions

According to published research, the primary outcome measure was the tracheal injury score. Based on a review of clinical and histological studies, the most frequently reported intubation-related lesions included hyperaemia, ischaemia, ulcers and tracheal perforation. The specific method for scoring tracheal injury was entirely based on the study by Lylia Touat *et al*,[18] and the scoring method was as follows: tracheal injuries were evaluated by examining hyperaemia, ischaemia, ulcers and tracheal perforation, as outlined in online supplemental stable 1. Depending on the number of lesions, the lesions were further classified as moderate, severe or confluent. Fiberoptic tracheoscopy was performed by three respiratory therapists, Haitao Li (HTL), Chunhua Yin (CHY) and Liwen Li (LWL). HTL conducted the majority of fiberoptic tracheoscopy (85 out of 97 (87%)), and their observations were independent. Additionally, Zhigang Cai (ZGC) recorded and interpreted the examination when fiberoptic tracheoscopy was performed. ZGC was blinded to the study design.

Covariates

Patient characteristics at ICU admission were prospectively recorded and include the following: age, gender, medication history, alcohol and smoking status, body mass index (BMI), Charlson Comorbidity Index (CCI) and chronic diseases including hypertension, diabetes, immunosuppression, cardiovascular disease, heart failure, dyspnoea and chronic renal failure. The causes for ICU admission were also documented. During the ICU stay, data were collected on the tracheal tube size, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, temperature, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, white blood cell count, neutrophil percentage (NE%), platelet count, prothrombin time, international normalised ratio, activated partial thromboplastin time, fibrinogen, oxygenation index (OI), lactic acid, albumin, globulin, prealbumin, alanine aminotransferase, aspartate aminotransferase, urea nitrogen, creatinine, procalcitonin, microbiological examination, specimen origin for microbiological examination, the dosage of norepinephrine, the dosage of plasma, red blood cell transfusion, duration

of intubation, mechanical ventilation time, total norepinephrine, total epinephrine and length of ICU stay.

Follow-up procedure

We conducted follow-up through telephone inquiries, with a cut-off date of 5 March 2022 for participant follow-up. Telephone follow-ups were conducted 1 month after discharge, during which any difficulty breathing, shortness of breath or chest tightness experienced by participants were recorded as monitoring indicators.

Statistical analysis

We conducted a descriptive analysis for all participants, presenting categorical variables as percentages and numbers. Continuous variables were expressed as mean and SD for normal distributions or median and IQR for skewed distributions. We used various statistical tests including the χ^2 test, t-test and Mann-Whitney U test to compare categorical, normally distributed and non-normally distributed continuous variables, respectively. Because the percentage of missing data was small (0%–4%), no imputation was performed.

In Step 1, univariate linear regressions were employed to examine the associations between various factors and tracheal injury score. In Step 2, multivariable-adjusted linear regression was used to analyse the relationship between septic shock and the tracheal injury score. Covariates with a variance inflation factor of less than 2 were selected according to the literature to avoid multicollinearity problems. Five models were constructed. Model 1 had no adjustment. Model 2 adjusted for adjusted for age, gender, medication history, smoking, BMI, CCI, APACHE II score, tracheal tube size, septic shock, OI and duration of intubation. Model 3 adjusted for age, gender, BMI, CCI, APACHE II score, tracheal tube size, septic shock, OI, duration of intubation, total norepinephrine and total epinephrine. Additionally, because age, gender and duration of intubation were important confounding factors, stratified analysis were conducted to compare the relationship between septic shock and the tracheal injury score across different age groups, genders and duration of intubation groups. Age was categorised based on clinical cut-off points, while duration of intubation was categorised based on the median. An interaction test was then performed. All statistical analyses were conducted using R V.3.3.2 (http://www.R-project.org, The R Foundation) and Free Statistics software V.1.1. A two-tailed test was used, and statistical significance was set at $p<0.05$.

Patient and public involvement

Patients and the public were not involved in the design of the study or the dissemination of the findings.

RESULTS

Baseline characteristics of selected participants

Out of the 115 patients, 18 (16%) were excluded from the study. The final data analysis was performed on 97 participants, among whom 31 were diagnosed with septic shock. A flow chart illustrating the study's selection process is presented in figure 1. We presented the baseline characteristics of these selected participants in table 1, categorised based on the clinical diagnosis of septic shock. On average, the selected participants were 56.6±16.5 years old, with 64.9% of them being men. Patients in the septic shock group had more severe conditions, as evidenced by higher levels of heart rate, NE%, lactic acid and procalcitonin poorer coagulation indicators and renal function. Participants diagnosed with septic shock required higher doses of norepinephrine and plasma transfusions, and had more critical vital signs compared with those without septic shock. What makes sense was that in online supplemental stable 2, patients were divided into groups with tracheal injury score >6. In the group with tracheal injury score >6, 18 cases were septic shock, accounting for 43.9%. In the group with non-tracheal injury score >6, 13 cases were septic shock, accounting for 23.2%; 43 cases were non-septic shock, accounting for 76.8% and p=0.031.

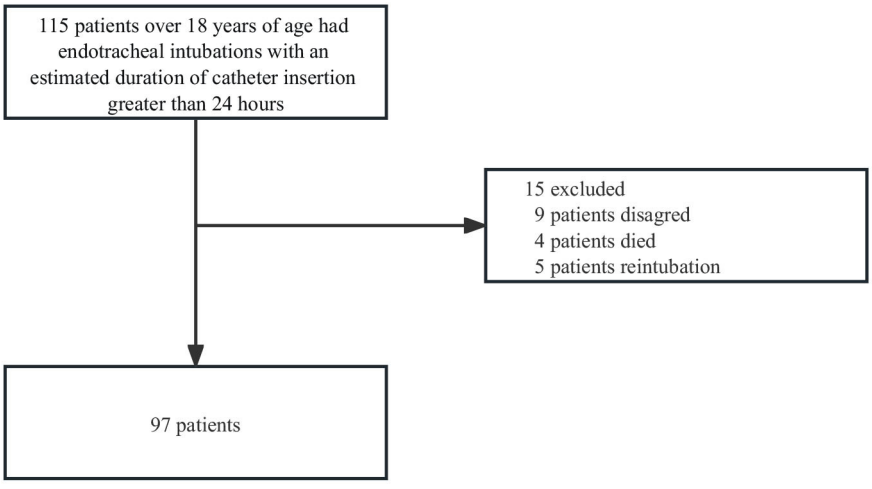

Figure 1 The flow chart of the study.

Table 1 Features in patients with and without septic shock

	Total (n=97)	Septic shock		P value
		Yes (n=31)	No (n=66)	
At admission				
Age, years	56.6±16.6	58.6±15.5	55.7±17.1	0.41
Male, n (%)	63 (64.9)	22 (71)	41 (62.1)	0.394
Medication history, n (%)				
Yes	39 (40.2)	9 (29)	30 (45.5)	0.124
β.blocker	11 (11.3)	2 (6.5)	9 (13.6)	0.494
CCB	19 (19.6)	0 (0)	19 (28.8)	< 0.001
ACEI	7 (7.2)	5 (16.1)	2 (3)	0.032
Aspirin	5 (5.2)	3 (9.7)	2 (3)	0.323
Glucose-lowering drugs	8 (8.2)	2 (6.5)	6 (9.1)	1
Alcohol involved, n (%)	21 (21.6)	7 (22.6)	14 (21.2)	0.879
Smoking, n (%)	8 (8.2)	3 (9.7)	5 (7.6)	0.708
BMI, kg/m^2	24.8±3.2	24.3±3.1	25.1±3.2	0.248
CCI	2.0 (1.0–4.0)	3.0 (1.0–4.0)	2.0 (0.2–3.8)	0.338
Chronic diseases, n (%)				
Hypertension	32 (33.0)	7 (22.6)	25 (37.9)	0.135
Diabetes mellitus	10 (10.3)	2 (6.5)	8 (12.1)	0.494
Immunosuppression	1 (1.0)	0 (0)	1 (1.5)	1
Cardiovascular disease	10 (10.3)	2 (6.5)	8 (12.1)	0.494
Heart failure	1 (1.0)	0 (0)	1 (1.5)	1
Dyspnoea	0 (0)	0 (0)	0 (0)	1
Chronic renal failure	4 (4.1)	1 (3.2)	3 (4.5)	1
Causes for ICU admission, n (%)				<0.001
Biliary tract infection septic shock	7 (7.2)	7 (22.6)	0 (0)	
Enterogenic septic shock	15 (15.5)	15 (48.4)	0 (0)	
Other causes of septic shock	9 (9.3)	9 (29)	0 (0)	
Diseases of digestive system	8 (8.2)	0 (0)	8 (12.1)	
Neurosurgery	47 (48.5)	0 (0)	47 (71.2)	
Pulmonary diseases	6 (6.2)	0 (0)	6 (9.1)	
Others	5 (5.2)	0 (0)	5 (7.6)	
In ICU				
Tracheal tube size				0.785
7.0	2 (2.1)	0 (0)	2 (3)	
7.5	93 (95.9)	3 (96.8)	63 (95.5)	
8.0	2 (2.1)	1 (3.2)	1 (1.5)	
APACHE II score	21.0±6.9	22.3±6.3	20.4±7.1	0.221
Temperature, °C	36.8±1.0	36.5±1.1	36.9±0.9	0.04
Heart rate, bpm	101.0±26.4	119.7±25.7	92.2±21.9	< 0.001
SBP, mm Hg	128.0±28.0	108.4±31.3	137.2±20.9	< 0.001
DBP, mm Hg	71.3±16.7	61.9±17.6	75.7±14.5	< 0.001
MAP, mm Hg	90.2±19.1	77.2±21.4	96.3±14.5	< 0.001
Laboratory examinations				
WBC, ×10^9/L	11.7±5.7	13.1±7.4	11.0±4.5	0.082
NE, %	84.8±9.3	89.3±5.1	82.7±10.2	0.001
Platelet, ×10^9/L	189.0 (132.0–243.0)	213.0 (142.5–284.0)	172.5 (130.5–234.8)	0.092

Continued

Table 1 Continued

	Total (n=97)	Septic shock		P value
		Yes (n=31)	No (n=66)	
Prothrombin time, s	13.1 (12.2–14.1)	14.1 (13.1–17.9)	12.7 (11.9–13.7)	< 0.001
INR	1.2 (1.1–1.3)	1.3 (1.2–1.6)	1.1 (1.1–1.2)	< 0.001
APTT, s	28.0 (26.1–32.0)	30.1 (28.4–36.7)	27.0 (25.1–29.5)	< 0.001
Fibrinogen, g/L	3.4 (2.5–4.5)	4.0 (2.4–4.5)	3.4 (2.6–4.4)	0.828
Oxygenation index,	204.2 (163.0–63.0)	202.0 (144.2–263.5)	205.1 (171.0–262.8)	0.313
Lactic acid, mmol/L	1.9 (1.2–3.1)	3.0 (1.6–4.8)	1.6 (1.1–2.5)	0.003
Albumin, g/L	32.5±6.5	29.5±6.7	33.9±5.9	0.001
Globulin, g/L	22.9±5.1	21.8±5.1	23.4±5.0	0.162
Prealbumin, g/L	0.2 (0.1–0.2)	0.1 (0.1–0.2)	0.2 (0.1–0.2)	0.001
ALT, U/L	21.3 (12.6–42.1)	30.0 (16.9–48.5)	19.3 (12.1–36.5)	0.067
AST, U/L	32.7 (18.3–58.4)	41.2 (23.4–83.2)	30.9 (16.5–51.7)	0.043
Urea nitrogen, mmol/L	5.7 (4.1–9.1)	7.8 (5.9–16.4)	4.8 (3.9–6.7)	<0.001
Creatinine, µmol/L	80.0 (57.0–114.0)	111.0 (89.0–155.5)	70.0 (52.2–87.5)	<0.001
Procalcitonin, ng/ml	0.6 (0.1–4.4)	4.7 (1.3–15.6)	0.3 (0.1–0.8)	<0.001
Microbiological examination, n (%)				0.121
Negative	28 (29.2)	5 (16.1)	23 (35.4)	
Acinetobacter baumannii	23 (24.0)	11 (35.5)	12 (18.5)	
Escherichia coli	6 (6.2)	4 (12.9)	2 (3.1)	
Klebsiella pneumoniae	25 (26.0)	7 (22.6)	18 (27.7)	
Staphylococcus aureus	3 (3.1)	1 (3.2)	2 (3.1)	
Burkholderia cepacia	2 (2.1)	0 (0)	2 (3.1)	
Others	9 (9.4)	3 (9.7)	6 (9.2)	
Specimen origin for microbiological examination, n (%)				0.032
Undone	1 (1.0)	0 (0)	1 (1.5)	
Sputum	85 (87.6)	24 (77.4)	61 (92.4)	
Body fluid	10 (10.3)	7 (22.6)	3 (4.5)	
Blood	1 (1.0)	0 (0)	1 (1.5)	
Dosage of norepinephrine, ug/kg.min	0.0 (0.0–0.0)	0.2 (0.0–0.5)	0.0 (0.0–0.0)	<0.001
Treatments				
Duration of intubation, days	8.0 (5.0–11.0)	8.0 (5.0–11.0)	7.5 (4.2–10.8)	0.499
Mechanical ventilation time, hours	227.0 (141.0–381.0)	201.0 (142.5–354.5)	245.0 (133.0–396.0)	0.637
Dosage of plasma, mL	400.0 (0.0–1000.0)	1000.0 (0.0–2900.0)	0.0 (0.0–450.0)	<0.001
Red blood cell transfusion, U	4.0 (0.0–10.0)	10.0 (0.0–12.0)	4.0 (0.0–8.0)	0.056
Norepinephrine, n (%)	67 (69.1)	31 (100)	36 (54.5)	<0.001
Epinephrine, n (%)	9 (9.3)	3 (9.7)	6 (9.1)	1
Total norepinephrine, ampoule	12.0 (0.0–33.0)	31.0 (17.5–74.0)	2.0 (0.0–21.5)	<0.001
Total epinephrine, ampoule	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.83
Tracheal injury score	4.0 (1.0–9.0)	7.0 (3.0–11.5)	2.0 (1.0–8.0)	0.001
ICU LOS, days	15.0 (9.0–23.0)	15.0 (10.0–25.0)	15.5 (9.0–21.8)	0.518

Data were mean±SD or median (IQR) for skewed variables or numbers (proportions) for categorical variables.
ACEI, angiotensin converting enzyme inhibitor; ALT, alanine aminotransferase; APACHE, Acute Physiology and Chronic Health Evaluation; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BMI, body mass index; bpm, beat per minute; CCB, calcium channel blocker; CCI, Charlson Comorbidity Index; DBP, diastolic blood pressure; ICU LOS, length of intensive care unit stay; INR, international normalised ratio; MAP, mean arterial pressure; NE%, neutrophil percentage; SBP, systolic blood pressure; WBC, white blood cell count.

Table 2 Linear multivariate regression analyses of tracheal injury score

		Model 1		Model 2		Model 3	
	n	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
Age, years	97	0.04 (–0.02~0.09)	0.244	0.01 (–0.08~0.11)	0.765	0.01 (–0.08~0.11)	0.771
Gender							
Male	63	Reference		Reference		Reference	
Female	34	1.27 (–0.77~3.31)	0.225	1.93 (–0.37~4.24)	0.104	1.72 (–0.57~4.02)	0.145
APACHE II score	97	–0.03 (–0.17~0.12)	0.707	–0.09 (–0.24~0.06)	0.25	–0.06 (–0.21~0.10)	0.467
OI	97	0 (–0.01~0.01)	0.676	0 (–0.01~0.01)	0.652	0 (–0.01~0.01)	0.684
Septic shock							
No	66	Reference		Reference		Reference	
Yes	31	3.07 (1.06~5.08)	0.004	3.29 (1.19~5.39)	0.003	2.99 (0.70~5.29)	0.012
Duration of intubation, days	97	0.31 (0.08~0.54)	0.01	0.29 (0.05~0.52)	0.021	0.3 (0.06~0.54)	0.016

Model 1 no adjusted.
Model 2 adjusted for age, gender, medication history, smoking, BMI, CCI, APACHE II score, tracheal tube size, septic shock, OI, duration of intubation, the model is not adjusted for the variable itself.
Model 3 adjusted for age, gender, BMI, CCI, APACHE II score, tracheal tube size, septic shock, OI, duration of intubation, total norepinephrine, total epinephrine, the model is not adjusted for the variable itself.
APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CCI, Charlson Comorbidity Index; OI, oxygenation index.

Linear regression analyses

Linear regression analysis was chosen based on the correlation matrix plots between different covariates and tracheal injury score (online supplemental figure 1). The results of univariate regression analysis (online supplemental stable 3) indicate that age, gender, smoking, BMI, tracheal tube size, APACHE II score, OI, dosage of norepinephrine, total norepinephrine and total epinephrine were not significantly associated with the tracheal injury score. However, concomitant septic shock and duration of intubation were found to be positively correlated with the tracheal injury score. To further investigate the independent effects of septic shock and duration of intubation on the tracheal injury score, we constructed five models using univariate and multivariate linear regression analysis. The effect sizes and their 95% CIs are reported in table 2. The results showed that in the crude analysis (Model 1), there was a statistically significant positive association between septic shock and the tracheal injury score (β: 3.07; 95% CI 1.06 to 5.08), suggesting that patients with septic shock had higher tracheal injury scores. This association remained significant in the multivariable analysis (Model 3) (β: 2.99; 95% CI 0.7 to 5.29), after adjusting for age, gender, BMI, CCI, APACHE II score, tracheal tube size, septic shock, OI, duration of intubation, total norepinephrine and total epinephrine. Furthermore, there was a statistically significant positive association between the duration of intubation and the tracheal injury score (β: 0.31; 95% CI 0.08 to 0.54) in table 2, suggesting that for each additional day of endotracheal intubation, the tracheal injury score increased by 0.31 points. This association was also significant in the multivariable analysis (Model 3) (β: 0.30; 95% CI 0.06 to 0.54). Considering the small sample size, we established a fully adjusted model (Model 6, online supplemental stable 4) and the results remained stable (β: 0.29; 95% CI 0.04 to 0.53).

Subgroup analysis

We used age, gender and duration of intubation as stratification variables to observe the trend in effect sizes for these variables (figure 2, table 3). Notably, interaction was only observed with the duration of intubation (P for interaction <0.05). Subgroup analysis results of this study suggested that in different age groups, there was no statistically significant difference in tracheal injury scores between patients with septic shock and those without septic shock. Similarly, in different gender groups, there was no statistically significant difference in tracheal injury scores between patients with septic shock and those without septic shock. However, when the duration of intubation exceeded 8 days, the tracheal injury scores were four points higher in patients with septic shock than in those without septic shock (β: 4.09; 95% CI 1.01 to 7.18). Furthermore, results from figure 3 indicated that when the duration of intubation was divided into four quartiles, there was no statistically significant difference in tracheal injury scores between the septic shock group and the non-shock group when the intubation time was less than 8 days (>5 days, p=0.3664; 5–8 days, p=0.8186). However, when the duration of intubation exceeded 8 days, the tracheal injury scores in the septic shock group were higher than those in the non-septic shock group (8–11 days, p=0.0194; >11 days, p=0.0087).

In the follow-up data, there was one patient diagnosed with pancreatic cancer who was admitted to the respiratory unit for treatment of severe tracheal stenosis on day 61 after extubation. This patient had a tracheal injury score of 12 and had been intubated for 14 days.

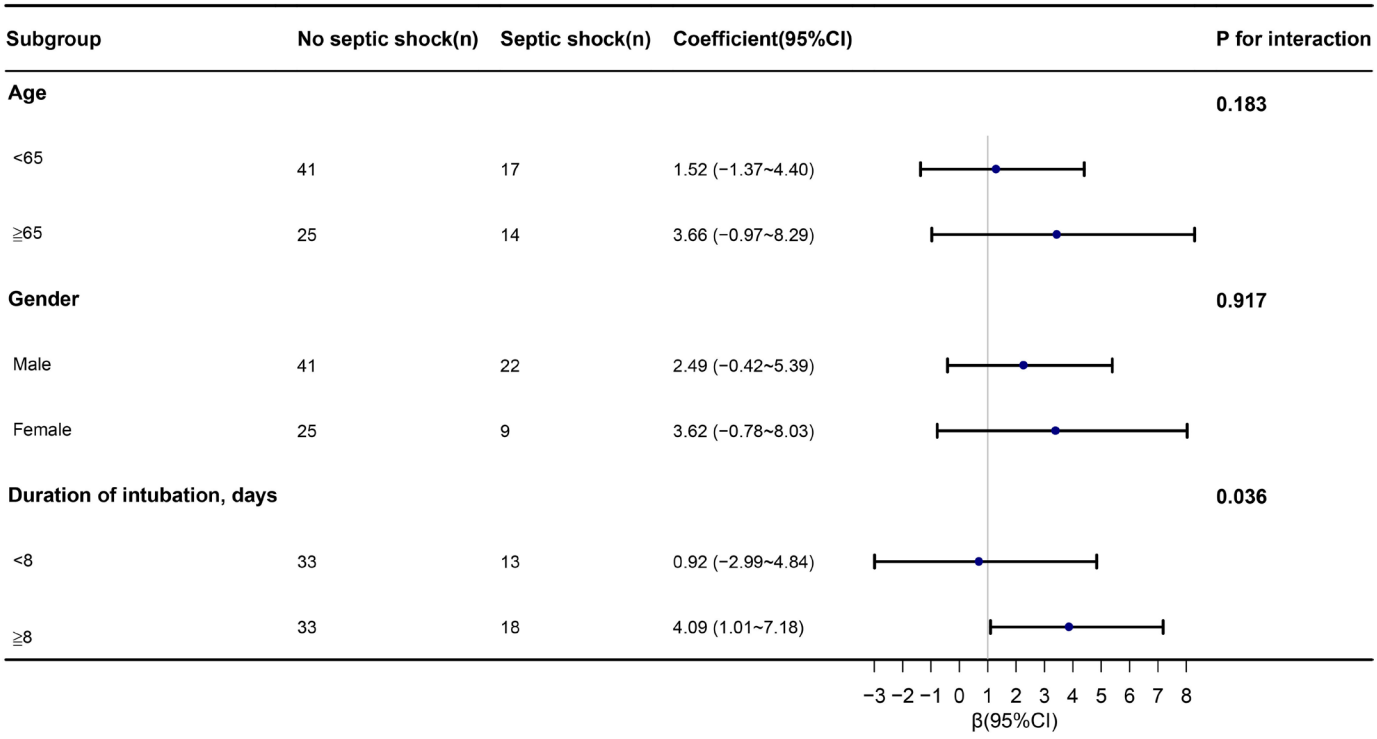

Figure 2 Forest plot shows tracheal injury score in septic shock group and non-septic shock group in subgroup analyses.

DISCUSSION

Our findings indicate that tracheal lesions are prevalent among critically ill patients who undergo intubation.[18] We observed a positive association between septic shock and the duration of intubation with the severity of tracheal injury scores, even after controlling for other variables. This indicates that septic shock is an independent risk factor for severe tracheal lesions. Interestingly, our study revealed that bacteriological findings from infection assessment did not influence the tracheal injury score, which is a novel finding in the literature.

Our study's findings align with those of Lylia Touat, who also observed tracheal injuries in the cuff contact area and reported a similar incidence of tracheal lesions (89% vs 83%). Additionally, Touat identified intubation time as an independent risk factor for severe tracheal lesions, which is consistent with our own results. However, our study differs in that we identified septic shock as an independent risk factor for tracheal injury, which was not highlighted in Lylia Touat's research regarding the influence of aetiology on tracheal injury scores. From a clinical perspective, our results could be explained

Table 3 The subgroup analyses of tracheal injury score in septic shock group and non-septic shock group

Subgroup	Septic shock (n)		β (95% CI)	P value	P for interaction
	No	Yes			
Age					0.183
<65	41	17	1.52 (–1.37~4.40)	0.309	
≥65	25	14	3.66 (–0.97~8.29)	0.133	
Gender					0.917
Male	41	22	2.49 (–0.42~5.39)	0.100	
Female	25	9	3.62 (–0.78~8.03)	0.120	
Duration of intubation, days					0.036
<8	33	13	0.92 (–2.99~4.84)	0.647	
≥8	33	18	4.09 (1.01~7.18)	0.013	

Adjusted for age, gender, BMI, CCI, APACHEIIscore, tracheal tube size, septic shock, OI, duration of intubation, total norepinephrine, total epinephrine, the model is not adjusted for the variable itself.
Age and duration of intubation as the continuous variables were added to the adjusted model as confounding factors.
APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CCI, Charlson Comorbidity Index; OI, Oxygenation index.

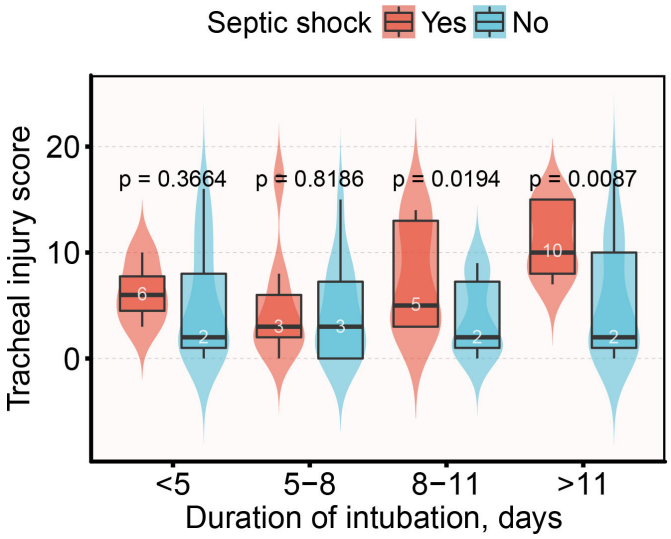

Figure 3 Comparison of tracheal injury score between septic shock group and non-septic shock group at different intubation times. The duration of intubation was divided into four quartiles.

by the association between tracheal mucosal damage and tracheal mucosal perfusion pressure.[21–26] Patients with septic shock are more likely to develop microcirculatory disorders,[1 2] leading to a sustained decrease in tissue perfusion pressure and resulting in more severe tracheal mucosal injury. We analysed Touat's study, which yielded inconsistent results compared with ours. We hypothesise that the differing outcomes may be attributed to various factors, including variation in study populations, different methods used to assess shock and failure to consider the effects of covariates on the relationship between septic shock and tracheal injury scores. Notably, our research results indicated that age, gender and hypoxaemia factors were not significantly associated with tracheal injury scores.[3 27 28] However, previous studies only conducted univariate analyses and did not adjust for potential confounding factors through multivariate analysis, leading to different research outcomes. Furthermore, our study presents novel findings indicating that bacteriological findings during infection assessment were not associated with tracheal injury based on univariate analysis. Interestingly, the results of the single-factor analysis did not find an association between tracheal injury scores and factors such as body temperature, white blood cell count, heart rate, low blood pressure, norepinephrine dose, epinephrine dose, lactate level and OI. One possible explanation for this is that the diagnosis of septic shock requires consideration of various factors, including clinical manifestations, laboratory tests and imaging, among others.[20 29 30]

The results of this study suggest that tracheal injury scores in ICU patients undergoing endotracheal intubation increase with prolonged intubation time. Tracheal injury scores remain relatively low when the intubation duration is less than 8 days. However, beyond this threshold, particularly in patients with septic shock, tracheal injury scores significantly escalate. This article introduces specific time frames for mitigating tracheal injury, emphasising the importance of controlling infection sources, administering appropriate antibiotics, managing systemic inflammation, stabilising circulation, adjusting ventilator settings and conducting timely assessments. These comprehensive measures aim to minimise intubation duration, thereby reducing the risk of severe tracheal injuries. Sudhoff's study highlights the endotracheal tube size as a risk factor for tracheal injury, particularly in shorter female patients.[31] The disparity in conclusions between our study and Sudhoff's may be attributed to the need for considering patient height and gender during endotracheal tube selection to mitigate tracheal injury risks. This oversight could have contributed to our study's negative results.

Our research provides the first independent association between septic shock and tracheal injury scores in patients receiving invasive ventilation in the ICU. It reminds us that for patients with septic shock, besides monitoring the functions of other organs, it is important to control the risk factors that may cause damage to the tracheal mucosa to avoid-related complications of tracheal ischaemic injury. We also report that bacteriological findings did not have an effect on tracheal injury scores, which has not been evaluated in previous studies. The insights gained from our study should aid in the development of future diagnostic or predictive models for tracheal injury scores. Although this was an observational study, making it susceptible to potential confounding factors, we employed a multiple linear regression model. By establishing a multifactorial correction model, we aimed to minimise the impact of residual confounding factors to the greatest extent possible. We conducted effect modification factor analysis, which allowed us to better use the data in our study and draw stable conclusions across different subgroups.

Due to the small sample size, the results may not be robust enough. However, considering the high mortality rate of septic shock and the associated high medical costs, and given that it was the first report of tracheal injury in such patients, the results had some interpretative value and we presented them. The study population was limited to invasively ventilated patients in the ICU, thus the generalisability of the findings may be limited. The collected data, however, are highly targeted and provide valuable insights for future randomised controlled studies focused on preventing tracheal ischaemic lesions. The use of certain classifications in subgroup analysis resulted in smaller sample sizes and limited the ability to draw definitive conclusions. The study did not specifically evaluate the effect of ventilator parameters on tracheal injury scores, but relevant clinical trials were considered. It was not possible to provide the number of suctionings performed during the tracheoscopy, which may affect the interpretation of the results. Although cuff pressure was measured every 6 hours and recorded within the control range, excessive pressure during the unmeasured

period cannot be ruled out. And due to the confusion of COVID-19 infections and the limitations of follow-up respiratory symptoms, it was difficult to detect the occurrence of mild tracheal stenosis and other complications. We did not assess the impact of sepsis cases on the study results, which is also one of the limitations of this study. In this research, the tracheal injury scores caused by other types of shock were not high. However, due to the small sample size, we cannot confirm whether the high risk of tracheal injury is specific to septic shock. The results of this study indicate that shock caused by sepsis is an independent risk factor for tracheal injury score, rather than sepsis or shock itself. According to the grouping criteria of this study, cases with combined sepsis may have been included in the non-septic shock group, which may affect the tracheal injury scores of the non-septic shock group. We will analyse the impact of sepsis on tracheal injury scores in subsequent studies.

However, it is important to note that the medical records of a patient with tracheal stenosis showed that they were not complicated by shock, and their intubation time and tracheal injury score were not the highest in our study. On further review of the case data, we discovered that the patient had received chemotherapy during hospitalisation. Therefore, it remains to be tested whether chemotherapy is a risk factor for tracheal stenosis in patients who have suffered from tracheal injury after intubation.[32]

CONCLUSIONS

According to our study, tracheal ischaemic lesions are common in critically ill patients who have been intubated. Septic shock appears to be an independent risk factor for severe tracheal ischaemic lesions. With the extension of intubation time, the tracheal injury score was higher and higher, especially in patients with septic shock. Our study provides valuable information that could be used to inform future research on the prevention and management of tracheal ischaemic lesions. We hope that our findings will help healthcare providers to identify and manage patients who are at high risk for tracheal injury, and ultimately improve patient outcomes in the ICU setting.

Author affiliations
[1]Department of Anesthesiology and Intensive Care, The Second Hospital of Hebei Medical University, Shijiazhuang, China
[2]Department of Critical Care, The Second Affiliated Hospital of Guangzhou Medical University, Guangzhou, China
[3]Department of Respiratory Medicine, The Second Hospital of Hebei Medical University, Shijiazhuang, China
[4]Department of Anesthesiology, The Second Hospital of Hebei Medical University, Shijiazhuang, China

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ORCID iD
Pei Zhang http://orcid.org/0000-0002-4776-6084

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