



doi: 10.4103/2221-6189.244166

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Comparison of risk factors associated with sepsis between road traffic injuries and non-road traffic injuries in ICU patients with severe trauma

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ARTICLE INFO

Article history:

Received 17 September 2018
Revision 25 September 2018
Accepted 6 October 2018
Available online 30 October 2018

Keywords:

Road traffic injuries
Non-road traffic injuries
Severe trauma
Sepsis
Risk factors

ABSTRACT

Objective: To estimate the incidence and related risk factors of sepsis between road traffic injuries (RTIs) and non-RTIs. **Methods:** Clinical data of 339 patients with severe trauma who were admitted into ICU in both Third Affiliated Hospital of Army Military Medical University and ChongGang General Hospital from January 2012 to December 2015 were retrospectively analyzed. Twenty items of potential risk factors affecting sepsis were evaluated by univariate and multivariate Logistic Analysis with the purpose of drawing a comparison between RTI patients and non-RTI patients. **Results:** There were 154 cases of RTI and 185 cases of non-RTI entering the study period. The significant independent risk factor of sepsis in RTIs was SOFA 11 ($OR=4.821$; 95% $CI=1.901-12.226$; $P=0.001$). The significant independent risk factors of sepsis in non-RTIs were SOFA 11 ($OR=12.410$; 95% $CI=2.559-60.185$; $P=0.002$), tracheal intubation ($OR=8.913$; 95% $CI=2.322-34.206$; $P=0.001$), APACHE II 15 ($OR=3.684$; 95% $CI=1.750-7.753$; $P=0.001$). **Conclusions:** The clinical medical personnel should not give equal treatment to RTI patients and non-RTI patients admitted in ICU in that factors predicting sepsis within above two groups are different. The sample volume should be increased and validated in further prospective research.

1. Introduction

According to the World Health Organization report, adverse outcomes following severe trauma will be the primary causes

threatening human health especially in developing countries by 2020[1]. The pattern of severe trauma patients admitted in Intensive Care Unit (ICU) mainly consist of road traffic injury (RTI), which are predominant over other injury causes, followed by high falling injury, blunt force injury, sharp injury and other types[2]. A disproportionate higher health burden of RTIs occurs in low

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Funding: This study was supported by the National Nature Science Foundation of China (NSFC, No. 81671906), National Natural Science Foundation of China (81860347), Hainan Provincial Natural Science Foundation of China (818MS140), Young Talents' Science and Technology Innovation Project of Hainan Association for Science and Technology (QXXM201816) and Hainan Provincial health and family planning commission project (18A200178).

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How to cite this article: Ma XY, Jin HJ, Cheng SW, Tang WQ, Ma W, Luo L, et al. Comparison of risk factors associated with sepsis between road traffic injuries and non-road traffic injuries in ICU patients with severe trauma. J Acute Dis 2018; 7(5): 191-196.

and middle income countries, while a lower rests on high income countries[3]. Nearly 1.2 million people die owing to road traffic accidents and additional 20-50 million people struggle for existence on non-fatal injuries from road trauma every year[4]. Most studies of risk factors after RTIs have been limited to some aspects associated with the severity and prevalence of road traffic injuries, such as the age of driver (>65 years old), drivers' road safety knowledge (primary), geographic location of residence, weather conditions, etc[5-9]. There are also some researches concentrated on risk factors of mortality in RTI patients with various poor outcomes, commonly seen in acute respiratory distress syndrome (ARDS), post-traumatic acute lung injury, etc[10,11]. Given that the incidence of wound infection/nosocomial infection and sepsis is higher in the post-traumatic pathologic process, however, determinants of infection or sepsis after RTIs among severe trauma patients are limited[12,13]. We, therefore, evaluated the independent risk factors related to sepsis in RTI patients admitted ICU and drew a comparison between RTIs and non-RTIs further. To such an extent, identification of distinctive risk factors among two groups that targeted prevention can be implemented in the subsequent process of clinical diagnosis and treatment.

2. Materials and methods

2.1. Sites and patients

Clinical data of 339 patients with severe trauma who were admitted into ICU in both Third Affiliated Hospital of Army Military Medical University and ChongGang General Hospital between January 2012 and December 2015 were retrospectively collected. There were 154 cases of RTI and 185 cases of non-RTI. The criteria of cases selection for these severe trauma patients had were as follows: age ≥ 16 years; the time of initial treatment achieved in hospital within 24 h; the length of ICU stay ≥ 48 h; Injury Severity Score ≥ 16 ; without coexisting illness. Patients who abandoned treatment or requested to transfer to another hospital were excluded. Patients were divided into two groups of RTIs including 57 infections cases of sepsis and 49 infections cases of non-sepsis. Patients were divided into two groups of non-RTIs including 71 infections cases of sepsis and 50 infections cases of non-sepsis. Non-RTI patients were comprised of 97 cases of high falling injuries, 37 cases of blunt instrument injuries, 29 cases of sharp instrument injuries and 22 cases of other types. Data of 339 patients' demographic characteristics, injury severity, common scoring systems in ICU, blood biochemical indices and identification of infectious bacteria were collected at the time of ICU admission. In addition, bacterial culture in sputum, blood, drainage liquid, cerebrospinal fluid, wound secretion, ascites, hydrothorax, urine and catheter were positive, which was identified as infection[14]. A suspicion of sepsis according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) was composed

of infection and Sequential Organ Failure Assessment (SOFA) ≥ 2 simultaneously[15]. The study was approved by the Third Affiliated Hospital of Third Military Medical University (Daping Hospital, Chongqing, China) Ethics and Research Committee (Clinical trial registration number of ChiCTR-TRC-14005119).

2.2. Risk factors

The following 20 potential risk factors associated with sepsis both in RTIs and non-RTIs were selected: (1) red blood count (RBC); (2) packed cell volume (PCV); (3) platelets (PLTs); (4) albumin; (5) carbamide; (6) international normalized ratio (INR); (7) blood FIO₂; (8) blood pH; (9) prothrombin time (PT); (10) thrombin time; (11) Glasgow Coma Scale (GCS); (12) Acute Physiology and Chronic Health Evaluation II (APACHE II), grouped as <15 or ≥ 15 ; (13) SOFA, grouped as <6, 6-10 or ≥ 11 ; (14) New Injury Severity Score (NISS), grouped as <16, 16-25 or ≥ 26 ; (15) gender; (16) tracheal intubation; (17) central vena catheterization (CVC); (18) shock on admission; (19) the number of injured area; (20) the degree of wound contamination (small wounds only involved in the epidermis or dermis, such as scratches, which were defined as 1; full-thickness wounds with raw surface or larger open wounds, such as fractures, which were defined as 1.5; severe penetrating wounds or compound wounds accompanied by obvious contaminants, such as dust or sediment, which were defined as 3). The first 14 items were measured and calculated during the first 24 hours after ICU admission.

2.3. Statistical analysis

Data within two groups was statistically compared by Student's *t* test for continuous variables and *chi*-square test for categorical variables. Variables presenting significant differences between above two groups in univariate comparison were entered in stepwise Logistic regression analysis. Entry and removal probabilities for the stepwise procedure are 0.15 and 0.05 respectively. Goodness of fit in the regression model was evaluated by the Hosmer-Lemeshow test ($P < 0.05$). Adjusted ORs with 95% CI were calculated. All analyses in this paper were performed by SAS 9.3. A two-side *P* value < 0.05 was considered to be statistically significant.

3. Results

There were 339 cases of severe trauma patients admitted in ICU in this retrospective study. Sepsis occurred in 57 infections cases in RTI group and 71 infections cases in non-RTI group, while non-sepsis occurred in 49 infections cases and 50 infections cases respectively in above two groups. There was also no significant difference in the incidence of sepsis between RTIs and non-RTIs (37.01% vs. 38.37%; $P = 0.882$). It did not show significant difference

Table 1

Demographic characteristics of 339 patients during ICU stay.

Variables	RTI (n=154)	Non-RTI (n=185)	t value	chi-square value	P value
Age (years)	48.53±17.50	50.06±16.80	0.820	—	0.410
Gender					
Male [n(%)]	98 (63.64%)	126 (68.11%)	—	3.750	0.037
Female [n(%)]	56 (36.36%)	59 (31.89%)			
Length of ICU stay (d)	18.00	15.43	1.184	—	0.237
Infection [n(%)]	106 (68.83%)	121 (65.41%)	—	1.891	0.504
Sepsis [n(%)]	77 (50.10%)	91 (49.19%)	—	0.056	0.882
MODS [n(%)]	124 (80.52%)	132 (71.35%)	—	3.120	0.051
ARDS [n(%)]	103 (66.88%)	115 (62.16%)	—	2.798	0.075
Hospital mortality [n(%)]	14 (9.10%)	20 (10.81%)	—	0.084	0.600
Death caused by sepsis [n(%)]	9 (11.69%)	19 (20.88%)	—	1.012	0.111

in demographic characteristics and baseline clinical data of patients between RTI group and non-RTI group (Table 1). A total of 37.01% (n=57) had developed sepsis in RTI group. Statistically significant unadjusted ORs among RTI patients in sepsis were associated with SOFA (OR=3.005; P=0.001), the degree of wound contamination (OR=2.151; P=0.038), INR (OR=3.437; P=0.031), PT (OR=3.369; P=0.039), PCV (OR=3.343; P=0.011), PLT (OR=1.121; P=0.025), RBC (OR=2.312; P=0.030), blood FIO₂ (OR=1.841; P=0.023) and blood pH (OR=3.431; P=0.007) (Table 2). The significant independent risk factor of sepsis in RTIs was SOFA 11 (OR=4.821; 95% CI=1.901-12.226; P=0.001). A total of 38.37% (n=71) had developed sepsis in non-RTIs. Statistically significant unadjusted ORs among non-RTI patients in sepsis were associated with albumin (OR=1.741; P=0.034), carbamide (OR=2.835; P=0.025), APACHE II (OR=2.313; P=0.018), SOFA (OR=3.228; P=0.001), tracheal intubation (OR=4.410; P<0.001), CVC (OR=3.230; P=0.027) and shock on admission (OR=3.382; P=0.014) (Table 3). The significant independent risk factors of sepsis in non-RTIs were SOFA 11 (β =2.519, OR=12.410; 95% CI=2.559-60.185; P=0.002), tracheal intubation (β =2.188, OR=8.913; 95% CI=2.322-34.206; P=0.001), APACHE II 15 (β =1.304, OR=3.684; 95% CI=1.750-7.753; P=0.001).

Table 2

Unadjusted odds ratios for potential risk factors associated with sepsis in RTIs (n=106).

Risk factors	β	Odds ratio	95% confidence interval	P value
SOFA	1.573	3.005	1.820-10.744	0.001
GCS	0.587	1.789	0.795-6.561	0.060
APACHE II	0.913	1.702	0.933-7.912	0.051
NISS	0.481	1.201	0.467-2.613	0.094
Contamination	0.756	2.151	0.908-8.933	0.038
Tracheal intubation	1.099	3.129	1.013-9.216	0.104
INR	1.273	3.437	1.458-9.674	0.031
PT	1.216	3.369	1.411-9.618	0.039
Albumin	0.512	1.909	0.703-6.561	0.065
Carbamide	1.913	2.608	1.960-9.121	0.071
PCV	1.205	3.343	1.200-9.413	0.011
PLT	0.523	1.121	0.439-2.517	0.025
RBC	0.983	2.312	0.906-6.768	0.030
Blood FIO ₂	0.530	1.841	0.667-8.212	0.023
Blood pH	1.267	3.431	1.376-9.607	0.007

4. Discussion

This retrospective case-control study revealed that several risk factors associated with sepsis were different between RTI patients

Table 3

Unadjusted odds ratios for potential risk factors associated with sepsis in non-RTIs (n=121).

Risk factors	β	Odds ratio	95% confidence interval	P value
RBC	0.693	1.899	0.906-6.701	0.106
PLT	0.333	1.005	0.304-2.452	0.121
Albumin	0.542	1.741	0.754-6.520	0.034
Carbamide	1.454	2.835	1.700-10.436	0.025
PT	1.128	3.214	1.305-9.457	0.085
Thrombin time	1.099	3.129	1.103-9.217	0.094
GCS	0.410	1.121	0.370-2.473	0.128
APACHE II	0.659	2.313	0.912-6.781	0.018
SOFA	1.196	3.228	1.207-9.318	0.001
NISS	0.561	1.763	0.774-6.549	0.133
Tracheal intubation	2.252	4.410	2.436-10.653	<0.001
CVC	1.198	3.230	1.210-9.321	0.027
Shock on admission	1.232	3.382	1.454-9.630	0.014
Number of injured area	0.566	2.006	0.823-9.677	0.060

and non-RTI patients in ICU.

The SOFA score was not so much called sepsis-related organ failure assessment score as under the title of Sequential Organ Failure Assessment when it was also applied to evaluate the prognosis of non-sepsis patients[16]. In Southern Europe, Mbongo *et al.* reported that the predictive effect of Simplified Acute Physiology Score 3 on hospital mortality was superior to SOFA (AUC: 0.916 *vs.* 0.846, $P > 0.05$) in adult patients admitted to ICU[17]. Nonetheless, value of SOFA in predicting ICU mortality is more satisfactory than Multiple Organ Dysfunction Score[18,19]. In the field of trauma surgery, SOFA score can dependably describe organ dysfunction/failure and mortality as well. It showed that the non-survivors had a higher SOFA score on admission than survivors which conformed to a longer length of ICU stay[20]. With respect to the critically ill patients with severe sepsis or sepsis shock, Macdonald *et al.* demonstrated that SOFA score had a positive correlation with mortality of patients with severe sepsis and septic shock from emergency department[21]. It should be noted that the new definition of sepsis (Sepsis 3.0) was put forward by Professor Craig Coopersmith, chairman of the Society of Critical Care Medicine, in 2016, which mainly concentrates on organ dysfunction[12,15]. We, therefore, evaluated the risk factors of sepsis on the basis of New Sepsis 3.0 within RTIs and non-RTIs. In the present study, as with non-RTIs (SOFA ≥ 11 , $OR = 12.41$), SOFA ≥ 11 ($OR = 4.821$) was also confirmed to be a significant factor for sepsis progression in RTIs.

The difference involving the incidence of infection, sepsis, MODS, ARDS, mortality caused by sepsis and all-cause mortality between RTIs and non-RTIs, though, were not statistically significant. However, there were 97 cases of high falling injuries, 37 cases of blunt instrument injuries, 29 cases of sharp instrument injuries and 22 cases of other types of injury embracing electrical injury and animal bites in non-RTIs group, indicating that more complicated kinds of trauma than that of singular RTIs group. This important factual characteristics are perhaps an explanation for three independent predictors of sepsis (SOFA ≥ 11 ; tracheal intubation; APACHE II ≥ 15) in non-RTIs compared with only one factor (SOFA ≥ 11) correlated with the risk of sepsis in RTIs in this setting. It is recognized that there are particular disciplines associated with airway management in critical care patients with severe trauma owing to exact cardinal rule of sufficient ventilation and oxygenation[22]. For that reason, the guidelines for emergency tracheal intubation among traumatic population were updated by the Eastern Association for Surgery of Trauma Practice Management Guidelines Committee, briefly covering a ketch of the determinants of oxygenation and ventilation, the severity and mechanism of trauma, the need of surgical operation and the complication following trauma *etc*[23]. The tracheal intubation is believed as a high risk factor of hospital infection which can wildly induce sepsis. In our research, patients who already had tracheal intubation in ICU admission had higher risk

of sepsis occurred in non-RTIs ($OR = 8.913$). Though tracheal intubation was not included in the stepwise Logistic regression analysis of RTIs, attention should be paid to the severe traumatic patients with submental tracheal intubation as before. Sirvent *et al.* reported patients with head trauma who had tracheal intubation within 24 hours had an closely correlation with colonization of *Staphylococcus aureus*, *Haemophilus influenzae* or *Streptococcus pneumoniae*, which was identified as a risk factor for developing early-onset ventilator-associated pneumonia[24]. In addition, tracheal injuries characterized by tracheal stenosis, trachemalacia, tracheoesophageal fistula, laryngotracheal ulceration, and vocal cord paralysis from endotracheal intubation are concerned with an increasing healthcare burden[25]. If these severe patients did not receive the treatment of endotracheal intubation, they would have their lives detrimentally imperiled.

APACHE II, one of the physiologic scoring systems widely used in critically ill patients in ICU, is composed of age score, acute physiology score and chronic health evaluation score[26]. Reports have revealed that APACHE II are positively correlated with sepsis and one-month mortality of ICU critical patients and injured patients[27-33]. In this setting, APACHE II ≥ 15 calculated during the first 24 hours after ICU admission among patients in non-RTIs was identified as an independent predictor for sepsis ($OR = 3.684$), which was complied with previous studies. It was a surprise that the risk factor of APACHE II ≥ 15 was found in non-RTI patients rather than in RTI patients in our report. Nevertheless, APACHE II ≥ 20 for RTI patients with ARDS acquired within 24 h in EICU stay had a definite relationship with mortality of surviving beyond 96 h ($OR = 2.534$), but was not a risk factor of mortality in duration of mechanical ventilation beyond 7 d[11]. Similarly, APACHE II ≥ 20 for RTI patients with acute lung injury acquired within 24 h in EICU stay was the essential risk factor for the outcome of acute lung injury among patients who survived > 24 h ($OR = 3.992$)[12]. The risk factor of APACHE II ≥ 15 emerging in non-RTI could be explained by the deficiency of clinical cases in this research. Therefore, it is needed to increase and validate the samples in further prospective study.

This study indicates that, in RTI population admitted in ICU, the SOFA score ranged from 6 to 10 might predict the outcome of sepsis in the early phase of treatment following trauma. SOFA score ≥ 11 , tracheal intubation and APACHE II score ≥ 15 are significantly correlated with sepsis following non-RTI population admitted in ICU.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Acknowledgments

The author thanks ICU in both Third Affiliated Hospital of Army Military Medical University and ChongGang General Hospital.

Funding

This study was supported by the National Nature Science Foundation of China (NSFC, No. 81671906), National Natural Science Foundation of China (81860347), Hainan Provincial Natural Science Foundation of China (818MS140), Young Talents' Science and Technology Innovation Project of Hainan Association for Science and Technology (QCXM201816) and Hainan Provincial health and family planning commission project (18A200178).

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