European Review for Medical and Pharmacological Sciences 2015; 19: 3693-3700

Risk factors for mortality in severe multiply injury patients with acute hypoxemic respiratory failure

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Abstract. – OBJECTIVE: To investigate the risk factors related to mortality in severe polytrauma patients with acute hypoxemic respiratory failure (AHRF).

PATIENTS AND METHODS: From December 2011 to December 2014, we identified and intubated 524 traumatic AHRF patients in a level 1 trauma centers. Amongst those, we enrolled seventy-six severe traumatic AHRF patients with an injury severity score (ISS) over 16 and need for over 24 hour intra-tracheal mechanical ventilation for our study. Patients were followed daily to collect data about demographics, injury characteristic, diagnostic, treatment, respiratory parameters, major complications, duration of mechanical ventilation, length of stay, prevalence of major complications and 28-days mortality.

RESULTS: Of the 76 patients in our study, 61 patients were male. Patients' ages were from 15 to 78 years old (43±17) and the predominant source of trauma was road traffic accidents. Before ventilation, patients had a mean PaO_2/FiO2 ratio of 108±63, pH of 7.1±0.3, $PaCO_2$ of 54±24 mmHg, respectively. The PaO2/$FiO2_2$ ratios were significantly improved by ventilation and the average duration of ventilation was 9.63±8.74 days. There were two peak dying times and the 28-days ICU mortality rate was 28.9%. Logistic regression analysis revealed the mortality rate to be significantly higher in patients with higher APACHE II scores (odds ratio: 1.60, p=0.002), shorter intervals between injury and admission (odds ratio: -0.91, p=0.03) and between admission and ventilation (odds ratio: -1.85, p=0.012), and lower pH (odds ratio: -0.692, p=0.044). The receiver operating characteristic (ROC) curves showed that best cut off points for mortality predictors were APACHE II scores greater than 25, time interval between injury and admission less than 2h, time interval between admission and ventilation less than 0.5h, and pH <7.16.

CONCLUSIONS: Traumatic AHRF patients requiring ventilation support show a high rate of early mortality. Greater vigilance for high APACHE II score, short time interval between injury and ventilation, low pH in traumatic AHRF patients is required.

Key Words:
Multiple injury, Mortality, Ventilation, Acute hypoxemic respiratory failure.

Abbreviations

MODS = Multiple Organ Dysfunction Syndrome; APACHE II = Acute Physiology And Chronic Health Evaluation score II; ECMO = Extracorporeal Membrane Oxygenation; GCS = Glasgow Coma Scale; SBP = Systolic Blood Pressure; IPPV = Intermittent Positive Pressure Ventilation; IQR = Inter Quartile Range.

Introduction

Despite of the recent improvements in ventilation methods, extracorporeal life support (ECLS) and resuscitation strategies for trauma[1-3], patients with severe multiple injuries in China still have a high mortality rate[4], which is approximately twice as high as in developed countries in Europe[5].

Chengdu is one of the biggest cities in southwest China with a population of just over 14 million. Considering Chengdu's demographic scale and the fast development it experienced in recent years, trauma related deaths have increased markedly in this city. In 1992, Sichuan Provincial People's Hospital of Sichuan Academy of Medical Sciences (SAMS) established its level 1 trau-

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ma center. In 2009, it established a trauma registry database for collecting information from all trauma patients admitted to the center. According to that database, a large proportion of trauma patients with acute hypoxemic respiratory failure (AHRF) often develop acute respiratory distress syndrome (ARDS) as well. The complexity of injuries in severe trauma cases often makes the ventilation very challenging. This challenge is due to the fact that medical staff should be able to provide an optimal oxygenation for the patients while protecting the lungs from further ventilator-induced injuries[6]. Prolonged mechanical ventilation (PMV) for more than 7 days, has been reported to result in a longer length of ICU stay and a higher mortality in severe multiple trauma patient[7]. However, a mortality benefit for PMV patients was also noted in regional trauma centre in New York, USA[8].

In this study we attempted to investigate the clinical characteristic and the mortality rates of severe traumatic AHRF patients needing ventilation support for more than one day. We also searched for possible correlation to the pattern of mechanical ventilation and outcomes of these patients.

Patients and Methods

Study Design and Patient Eligibility

From December 2011 to December 2014, we identified and intubated 524 traumatic AHRF patients in a 26-bed, surgeons-verified Emergency Intensive Care Units (EICU) in Sichuan Provincial People's Hospital. Patients' informations including gender, age, chronic disease, injury characteristic, emergency disposition (e.g. CT scan, blood test, cardiopulmonary resuscitation, intubation, ventilation, use of total parental nutrition, transfusion, use of H^2 blockers, steroids, and vasopressors/inotrope) were collected. As part of ICU routine, severity of the injury for each trauma victim was quantified using ISS on admission, APACHE II scores 24 hours after their admission[9]. Complications such as hypotension, renal dysfunction, MODS, gastrointestinal hemorrhage, aspiration of gastric contents, and infection were also recorded. These data were documented in the patients' charts and were accessible for further analysis.

The commonly accepted definition for severe multiply injury was consistent with both: several injury sites (from two or more anatomic sites) and at least one threatening life injury in one anatomic site[10-12]. Hypoxemia was defined as PaO_2/FIO_2 ratio of 300 or lower. The criteria used for intubation and ventilation were referred to Agle et al[13].

To investigate the pattern of admission and mortality rate of sever traumatic AHRF patients with prolonged mechanical ventilation, the following inclusion criteria and exclusion criteria were used. Inclusion criteria: (i) ISS over 16; (ii) Intubation and placement on mechanical ventilation within the first 24 h of injury; (iii) survival for more than 48h post-trauma. Exclusion criteria: Patients who were readmitted to EICU by virtue of non-traffic injuries or transferred to EICU from other hospitals after more than one day of treatment. No burn patients, ECMO patients or patients under 15 years old were included in this study. Mortality was calculated 28 day after the injury. Patients were divided into a survivors group and a non-survivor group and were statistically compared.

Statistical Analysis

For our statistical analyses we used the chi-square test for categorical variables and Student's *t*-test for continuous variables. Variables presenting significant differences between groups in multivariate analysis were entered in logistic regression analysis. All of the statistical analyses were performed using a statistical software package (SPSS for Windows, version 11.0, Chicago, IL, USA). A two-side p value of <0.05 was considered statistically significant.

Results

Traumatic AHRF Patient Characteristics

During the study period, 524 traumatic AHRF patients were intubated within the first day after injury in our EICU. Indications for initial intubation included airway (5%), breathing (48%), circulation (32%), and neurologic disability (15%). Among them, 127 patients with blood gas abnormality (PaO_2 < 60 mmHg/$PaCO_2$ > 60 mmHg and SaO_2 <90%) despite oxygen therapy, underwent ventilation within the first 24h ICU admission. Consequently, they were operated and resuscitated on an emergency bases, only patients who required ventilation for more than one day were included in this study. We excluded 24 patients who weaned within 1 day or changed to noninvasive ventilation, we also excluded 12 patients who gave up therapy or could not be contacted. Another 6 patients were excluded from analysis because they suffered from chronic lung diseases and another 4 patients for problems associated with drawing or gas poisoning, which might aggravate pulmonary failure (Figure 1).

Thus, we enrolled seventy-six traumatic AHRF patients (61 males) who required over 24 hour intra-tracheal mechanical ventilation. Patients' ages were from 15 to 78 years (average 43±17). The most common source of their injuries was road traffic collision (59.21%) followed by falls (21.05%). Penetrating trauma occurred in only 6 patients (8%). Overall, those seventy-six patients had 209 injured regions. The most common injured regions were the chest (30%), abdominal (23%), limbs (19%), head (12%), pelvic (10%) and spin (6%). The median ISS was 25 (16-43). The median GCS was 6 (3 to15). Duration of injured before admission was 11.5±6.2 hours in average.

Severity of Acute Hypoxemic Respiratory Failure

We encountered a variety of traumatic AHRF patients. Among them, 23 patients suffered from rib fractures, pneumothorax, tracheal bronchial rupture, hemothorax, flail chest and pulmonary contusion with respiratory insufficiency (respiratory rate over 29 per minute); Eighteen patients had abdominal trauma which lead to shallow breathing and aspiration of gastric contents; Twelve patients were unconsciousness due to head trauma or high thoracic spinal cord injuries with GCS < 9. The remaining 18 patients with SBP < 90 mmHg were accepted as shock patient, presenting with apnea or a gasping breathing pattern (respiratory rate under 6 per minute).

Duration of admission before commencement of ventilation was 8.5±1.9 hours. Before mechanical ventilation, the mean respiratory rate, arterial oxygen saturation (SaO_2), and PaO_2 were 23±17/min, 53±28%, and 83±47 mmHg, respectively. Patients had a mean PaO_2/FiO_2 ratio of 108±63, pH of 7.1±0.3, and $PaCO_2$ of 54±24 mmHg.

Details of Ventilation Support

IPPV was applied in all traumatic AHRF patients, including transient recruitment maneuvers in 8 patients, and prone positioning in 1 patient. The median (IQR) highest positive end expiratory pressure, tidal volume (per kg body weight), and peak airway pressure were 15±7 cmH_2O, 7.7±4.1 mL/kg, and 36±10 cmH_2O, respectively. The PaO_2/FiO_2 ratios were significantly improved by ventilation and the mean duration of ventilation was 9.3±6.4 days.

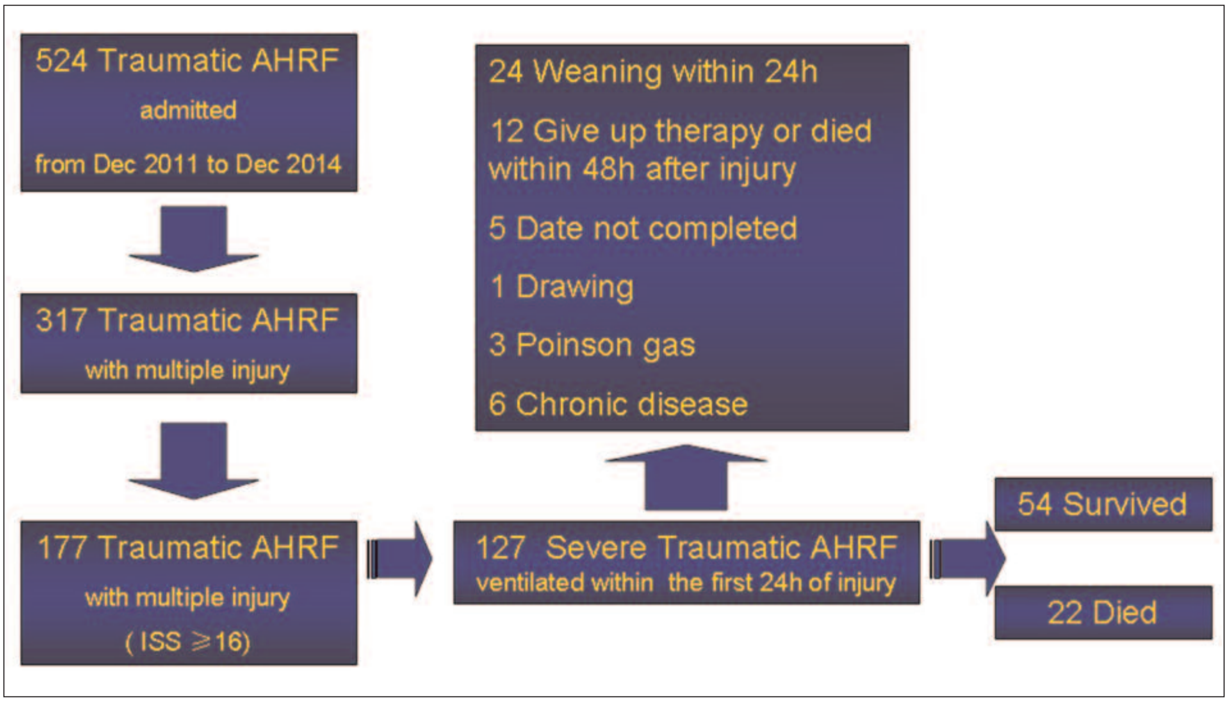

Figure 1. Flow diagram outlining the inclusion and exclusion criteria and study design.

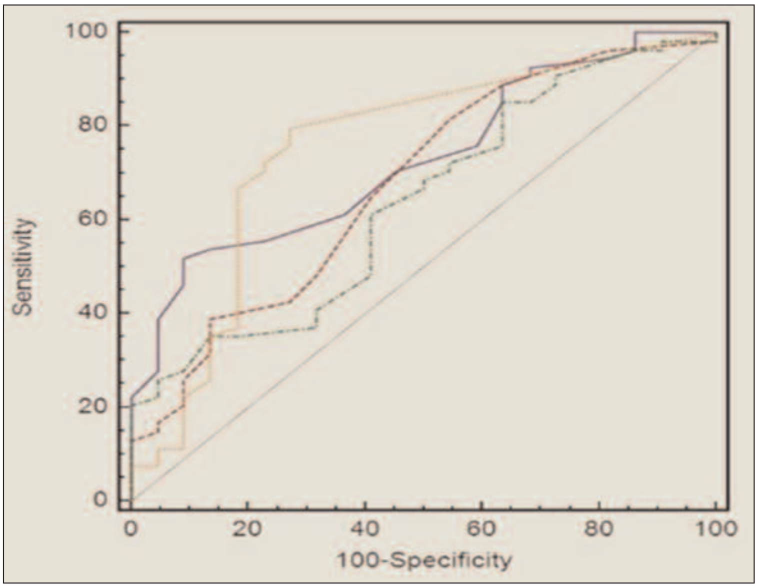

Figure 2. Receiver operating characteristic curves for the cutoff point of pH, APACHE II score, time interval between admission and ventilation, time interval between admission and injury that predicts mortality rate of traumatic AHRF patients. Green dotted line presented as pH; Red dotted line, time interval between admission and injury; Purple full line, APACHE II score; Yellow full line, time intervals between admission and ventilation.

Complications and Outcome

Coagulopathy, renal failure, MODS, hypotension and infection were the most prevalent post-trauma complications. Fifty-five traumatic AHRF patients required blood transfusion. The average amount of blood transfusion received by each patient was 1880±904 mL. Trauma-related coagulopathy was developed in 7 cases. Furthermore, 46 patients (60%) received vasopressor and 16 patients (24%) received renal replacement therapy. Infective complications occurred in 42 patients (52%) during ventilation on average 6.0±0.7 days after ventilation, with the most common sites being respiratory tract in 32 patients (40%), bloodstream in 14 patients (21%), and catheter-related infection in 13 patients (19%).

Twenty-two patients died (28.9%) 28 days after admission, with early death (less than 1 week) in 15 cases. Head traumatic AHRF patients had the highest mortality rate (9.6%). The cause of death was recorded as failed resuscitation (1%), MODS (5%), untreatable circulatory and renal (15%), respiratory (20%) or neurological failure (brain death or severe brain damage) (50%), infection (29%).

Multivariate Factor Analysis

By multivariate analysis, only the higher APACHE II score (32.86 ± 6.63 *vs.* 24.89 ± 7.72, *p*<0.001), shorter intervals between injury and admission (4.27 ± 3.94 *vs.* 7.81 ± 6.5, *p*=0.020), shorter intervals between admission and ventilation (2.77 ± 5.79 *vs.* 7.37 ± 6.50, *p*=0.006), lower pH (7.22 ± 0.13 *vs.* 7.28 ± 0.13, *p*=0.037), the proportion of vasopressor in use (81.82% *vs.* 37.04%, F<0.001), the presence of MODS (72.73% *vs.* 66.67%, F=0.005) were associated with higher mortality (Table I).

Logistic regression analysis revealed the mortality rate to be significantly higher in patients with higher APACHE II scores (odds ratio: 1.60, *p*=0.002), shorter intervals between injury and admission (odds ratio: -0.91, *p*=0.03) and between admission and ventilation (odds ratio: -1.85, *p*=0.012), and lower pH (odds ratio: -0.692, *p*=0.044) (Table II).

The receiver operating characteristic (ROC) curves showed that best cut off points for mortality predictors were APACHE II scores greater than 25, time interval between injury and admission less than 2h, time interval between admission and ventilation less than 0.5h, and pH <7.16 (Figure 2).

Discussion

To our knowledge this is the first report detailing the characteristics and clinical outcomes of traumatic AHRF patients treating with ventilation in West China. The basic findings of this study were as follows: i) The 28-day ICU mortality rates of traumatic AHRF patients were 28.9%; ii) APACHE II score, time interval between admission and ventilation, and pH were independent factors for mortality prediction in traumatic AHRF patients.

Table I. Univariaty analysis of risk factors for mortality rates of traumatic AHRF patients. Data presented as mean ± SD or numbers (%) as percentages of the overall number of patients (n =76). *p* values are the results of unpaired t-test or Mann Whitney U test for continuous variables, and $\chi 2$ test or Fisher's exact test for categorical variables. AHRF = Acute Hypoxemic Respiratory Failure. ISS = Injury Severity Scores. APACHE II scores = Acute Physiology and Chronic Health Evaluation II scores; NA = Not Analyzed; SD = Standard Deviation.

Variable	Survived (%) n = 54	Non-survivor (%) n = 22	*p*-value
Male/female, No	46/8	15/7	0.091
Age,years	41.32±13.33	46.91±17.19	0.132
Mechanism			
road traffic accident（%）	33 (61.11)	12 (54.55)	0.597
fall (%)	10 (18.52)	6 (27.27)	0.396
knife (%)	4 (7.41)	1 (4.55)	0.648
others (%)	7 (12.97)	3 (13.64)	0.692
Injured regions			
head (%)	14 (25.93)	12 (54.55)	0.004
chest (%)	43 (79.63)	19 (86.36)	0.492
abdominal (%)	39 (72.22)	9 (40.91)	0.010
spine (%)	8 (14.81)	5 (22.73)	0.406
pelvic（%）	16 (29.63)	5 (22.73)	0.542
others（%）	28 (51.85)	11 (50.00)	0.288
Primary chest injury（%）	43 (79.63)	19 (86.36)	0.435
Non-chest injury（%）	11 (16.67)	3 (4.55)	0.492
ISS	23.45±5.01	25.35±7.70	0.125
APACHE II scores	24.89±7.72	31.86±6.63	0.0000
Before ventilation			
Lowest pH	7.28±0.13	7.22±0.13	0.037
Highest PaO_2 (mmHg)	113.59±58.77	75±37.05	0.006
Lowest PaO_2/FiO_2 (mmHg)	191.47±80.22	128.19±68.90	0.002
The first 24h in EICU			
MAP (mmHg)	77.52±21.26	76.67±60.62	0.956
Vasopressor (%)	20 (37.04)	18 (81.82)	0.000
Glucose (mmol/L)	12.76±21.24	13.74±6.56	0.832
Hb (g/L)	89.93±35.70	89.27±29.92	0.940
Albumin (g/L)	21.04±9.39	19.85±9.26	0.614
Lactic acid (mmol/L)	5.55±3.17	6.75±3.00	0.135
Fluid resuscitation (ml)	5270±1600	3820±1524	0.188
Transfusion (ml)	800±400	1200±750	0.142
Time interval between admission and injury（h）	7.81±6.50	4.27±3.94	0.020
Time interval between admission and ventilation (h)	7.37±6.50	2.77±5.79	0.006
Ventilation parameters			
Highest FiO_2	1	1	NA
Highest PEEP, cmH_2O	10±7	9±7	0.681
Outcome			
Duration of ventilation(d)	10.02±9.52	8.68±6.53	0.549
Length of ICU (d)	13.80±12.01	8.93±6.55	0.078
Complications			
MODS (%)	36 (66.67)	16 (72.73)	0.005
Renal failure (%)	14 (25.93)	12 (54.55)	0.399
Infection (%)	36 (66.67)	18 (81.82)	0.04
28-days death	0	17 (77.27)	NA

Early Intubation and Ventilation of Traumatic AHRF Patients

AHRF is frequently encountered in multiple trauma patients, especially when the cause is an accident involving motor vehicles or a fall[6]. We found that chest and abdomen injuries were most commonly concomitant. For this reason, rapid assessment and intervention of AHRF in critical ill patients suffering from thoraco-abdominal injuries is very challenging. In a prior study[12] involving 2594 trauma mortality patients, researchers found that failure to ventilate the airway were the most common factors related to patient mortality, responsible for 16.7% of inpatient

Table II. Logistic regression analyses of risk factors for mortality rates of sever traumatic AHRF patients. OR = Odds ratio. AHRF = Acute Hypoxemic Respiratory Failure.

Variable	β	OR	*p*-value
APACHE II scores	1.601	4.959	0.002
Time interval between admission and injury (h)	-0.911	0.402	0.030
Time interval between admission and ventilation (h)	-1.852	0.157	0.012
pH	-0.692	0.501	0.044
PaO_2 (mmHg)	0.358	1.430	0.756
PaO_2/FiO_2 (mmHg)	-1.117	0.327	0.313
Vasopressor (%)	2.035	7.650	0.001
MODS	1.511	4.533	0.007

deaths. In our work, time intervals of admission and ventilation were 8.5±1.9 hours. Compare to the surviving-group, patients in the non-surviving group were admitted and ventilated much earlier, indicating their more intense need for being treated for respiratory insufficiency. In other words, early intubation and mechanical ventilation is of paramount importance in traumatic AHRF patients suffering from thoraco-abdominal injury.

Use of noninvasive ventilation (NIV) to prevent intubation in traumatic AHRF patients remains controversial because of the lack of good-quality data[10]. In one study[14], hypercapnia due to hypoventilation was demonstrated in patients arriving at a major Australian trauma center. In our study, traumatic AHRF patients were intubated and ventilated despite oxygen insufflations and after exclusion of tension pneumothorax. In severe cases, ECLS seems to be a valuable option to resuscitate patients with severe trauma when conventional ventilation therapies are insufficient[15].

Prolonged Mechanical Ventilation (PMV)

Although the early ventilation of AHRF patients considerably reduced the morbidity and the mortality, the prolonged mechanical ventilation (PMV), for situations such as traumatic brain injury (TBI) associated PMV, might lead to long ICU stays and even result in death[16]. To imitate PMV, traumatic AHRF patients who required more than 24-hour intra-tracheal mechanical ventilation were enrolled in our study. For the same reasons, only 48h post-trauma survivors were included in this study. As expected, PMV occurred in 81% of patients. The mean duration of ventilation (9.3±6.4 days) was comparable to published report on patients who underwent isolated valve surgery at Tehran Heart Center (PMV occurred in 6.6% of patients)[17]. However, no differences were observed in the length of ventilation, when the surviving and non-surviving groups were compared. Moreover, we found no differences in total fluid resuscitation, blood transfusion, facial trauma, age, and positive end-expiratory pressure equal or more than 10 mmHg on admission. Also, no differences were observed in arterial partial pressure of oxygen divided by the fraction of inspired oxygen ratio less than 300 at 24 hours between the two groups. Similar results revealed that mortality due to traumatic AHRF was declining in the last decade, which was attributed to an overall improvement of intensive care treatment and changes in ventilation and resuscitation strategies[18,19].

Predicition of Early Mortality or Delay Mortality for Traumatic AHRF Patients

Our results demonstrated a mortality rate equal to 28.9% among our 76 patients, which was higher compared to an earlier report which showed that polytrauma caused a mortality rate of 12.9%[20]. Several factors might have contributed to the higher mortality rates in our patients. First, long term observations were carried out in our patients (from one day to 28 days). Second, unavoidable intubation in the presence of critical injuries with high APACHE II score was not done at pre-hospital.

Noticeably, our data showed two peak dying times with the main peak time around 3 days after injure, the other two weeks after injury. Logistic regression revealed that pH, interval between injury and admission, intervals between admission and ventilation and APACHE II score on the first 24h, the prevalence of infection, the presence of MODS were the main factors that influenced outcomes of traumatic AHRF patients requiring ventilation support. Although studies on traumatic patients with AHRF failed to clearly define initial respiratory insufficient for outcome prediction[21], we found initial respiratory parameters (e.g. pH), and APACHE II score to be suitable parameters for prediction of early mortality for traumatic AHRF patients. Yet, it was noteworthy that respiratory failure might last up to weeks which may cause delayed deaths.

A substantial proportion of patients (19.4%) who survived for more than one week, died later. Meantime, infective complications occurred in 42 patients (52%) during ventilation on average 6.0±0.7 days after ventilation, with the most common sites being respiratory tract in 32 patients (40%). However, no differences in infection rates were observed between surviving group and non-surviving group. This was probably a product of the small number of traumatic AHRF patients used in this study. For the same reason, the number of outcome index for logistic regression analysis had to be limited. Considering the diversity of studied populations, more specific trials on less heterogeneous AHRF patient groups are needed to more focus on this aspect.

Conclusions

Traumatic AHRF patients requiring ventilation support had a high mortality rate (28.9%). APACHE II score, time interval before injury, interval between admission and ventilation, and pH were independent related factors for mortality prediction in traumatic AHRF patients in ICU.

Acknowledgements

The authors would like to thank for all the ICU clinicians for helping with data collection.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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