Title: The Risk Factors for Prolonged Mechanical Ventilation in Severe Multiple Injured Patients with Blunt Chest Trauma: A Single Center Retrospective Case-Control Study

A short running title: Prolonged Ventilation in Trauma Patients

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Abstract

Aim: Blunt chest trauma is common and associated with morbidity and mortality in multiple injured patients, frequently requiring invasive mechanical ventilation. The aim of this study was to elucidate risk factors for prolonged mechanical ventilation (PMV).

Methods: Consecutive adult multiple severe injured patients with blunt chest trauma treated in Chiba emergency medical center (Chiba city, Japan) between January 2008 and December 2015 were enrolled in this retrospective chart-review study. According to ventilatory time, the patients were divided into PMV (≥ 7 days) and shortened mechanical ventilation (SMV; < 7 days) groups. Thoracic Trauma Severity Score (TTSS) was calculated. To identify risk factors for PMV, univariate and multivariate logistic analyses, and receiver operating characteristic analysis (ROC) were performed.

Results: 84 and 49 patients were assigned to PMV and SMV groups, respectively. Compared with SMV group, PMV group had a significantly larger number of fractured ribs ($p<0.01$), higher rate of severe Glasgow Coma Scale (GCS ≤8) ($p<0.05$) and flail chest ($p<0.001$), higher TTSS ($p<0.001$), or longer ICU and hospital stay (both $p<0.001$). Logistic analysis showed that severe GCS (OR=4.6, $p<0.01$), flail chest (OR=3.0, $p<0.05$), or TTSS (OR=1.2; $p<0.01$) was an independent significant risk factor. ROC showed that area under curve (AUC) for TTSS, flail chest, and severe GCS was 0.74, 0.70, and 0.58, respectively. When the 3 factors were combined, AUC increased to 0.8.

Conclusion: Severe GCS (≤8), flail chest, or TTSS may be independent risk factors. Combining the 3 risk factors may provide high predictive performance for PMV. (250 words)

Keywords: Blunt chest trauma, rib fracture, Flail chest, Thoracic Trauma Severity Score, Mechanical ventilation.

Background

Blunt chest trauma was defined as blunt chest wall injury resulting in rib fractures, lung contusion, hemothorax, pneumothorax, and others with or without life-threatening lung injury [1]. According to the Japan Trauma Data Bank Report 2016, blunt chest trauma is the third most common injury followed by head and lower extremities injury [2].

Despite progress in intensive care for severe trauma, blunt chest trauma frequently requires some ventilatory assist and is associated with significant mortality and morbidity [3-7].

In multiple trauma patients, lung contusion, flail chest, and severe head injury are possible significant risk factors for mechanical ventilatory support [8-14]. However, to our knowledge, there have been no established risk factors for prolonged mechanical ventilation in patients with blunt chest trauma. In addition, early prediction for prolonged ventilatory support may provide useful information for planning the management of blunt chest trauma patients. The aim of the present study was to determine risk factors for prolonged mechanical ventilation in severe multiple injured patients with blunt chest trauma.

Methods

Participants and study design

Chiba emergency medical center is the sole tertiary acute critical care center in Chiba prefecture with a population of 6.25 million in Japan, and provides acute care to approximately 500 severe trauma patients per year.

After obtaining approval from the institutional ethical committee, this retrospective case-control study at the center was performed.

From January 2008 to December 2015, consecutive patients with blunt chest trauma treated in the Chiba emergency medical center were enrolled. Exclusion criteria were (1) died within 48 hours; (2) did not need invasive mechanical ventilation; (3) no rib fractures; (4) underwent surgical rib fixation; (5) injury severity score (ISS)<16; (6) < 2 injury regions; (7) age <15 years; (8) transferred to another hospital within 5 days; (9) mechanically ventilated for surgical procedures, not for respiratory dysfunction.

Length of mechanical ventilation was defined as the time elapsed from the initiation of ventilatory support to the accomplishment of weaning. Prolonged mechanical ventilatory support was defined as ≥7 days, based on a past report that the mean length of mechanical ventilation in blunt chest trauma was 7.3 days [15].

Thus, all patients were divided into the prolonged mechanical ventilation (PMV) group and the shortened mechanical ventilation (SMV) group.

In our institution, there are always licensed trauma surgeons, orthopedic surgeons, neurologists, and ICU physicians in the hospital 24 hours a day, 365 days a year, providing the same level of medical treatment. There are no residents or fellows in each shift. The initial management for all patients were done according to the Japan Advanced Trauma Evaluation and Care, then they received critical care in the intensive care unit [16].

Data collection

Clinical data such as sex, age, systolic blood pressure, respiratory rate, Glasgow Coma Scale (GCS), and P/F ratio on admission, as well as length of hospital stay, length of ICU stay, length of mechanical ventilation, insertion of chest tube, occurrence of pneumonia (within 7 days after admission), maximum amount of fentanyl daily administered, use of loxoprofen and/or acetaminophen, tracheostomy, performed emergency operation, and in-hospital death were extracted by medical chart review.

Radiographs and computed tomographic (CT) scan were obtained routinely for all patients. All injuries were diagnosed by two licensed trauma surgeons on admission and checked by diagnostic radiologists within 24 hours.

Severity of injury was assessed using the following scores that were coded and calculated by trained assistant and trauma surgeon: abbreviated injury scale (AIS) was coded by the AIS 90 update 98 [17] and then ISS and trauma and injury severity score (TRISS) was calculated.

Thoracic Trauma Severity Score (TTSS) was calculated by a licensed trauma surgeon, based on five physiologic and anatomical parameters: PaO_2/FiO_2, rib fracture, pulmonary contusion, pleural involvement, and age [9].

Flail chest was defined as three or more consecutive rib fractures, in $\geq$ 2 locations, consisting of a flail segment with/without paradoxical motion.

Statistical analysis

Categorical variables were described as number (percentage), and compared by Fisher's exact test or the Pearson's chi-square tests. Continuous variables were described as median and interquartile range (IQR), compared by Mann-Whitney U-test. Multivariate logistic analysis was performed to determine risk factors for PMV among significant variables by univariate analysis. In addition, the number of independent variables taken into logistic analysis was restricted to 4 (10 outcomes for each binary category = 49 patients in SMV group /10 = 4.9 categories). Multicollinearity was analyzed by calculating the variance inflation factor (VIF).

To evaluate the predictive performance of the risk factors determined by logistic analysis, receiver operating characteristic analysis (ROC) was performed and the area under curve (AUC) was computed. The Youden index was calculated to determine an optimal cut off value.

All statistical analyses were performed using SPSS Statistics version 22 (SPSS Japan, Tokyo, Japan), and a p value <0.05 was considered as significant.

Results

During the study period, a total of 4,317 injured patients were admitted to our hospital. According to the exclusion criteria, 4,184 patients were excluded; 3,626 patients did not have any rib fractures, 485 patients did not need mechanical ventilation, 31 patients died within 48 hours, 8 patients had ISS <16, 5 patients were transferred within 5 days, 29 patients were intubated for reasons other than respiratory failure, and no patients had fewer than 2 injury lesions (Fig. 1). Of the remaining 133 patients, 84 patients were assigned to the PMV group and 49 patients were assigned to the SMV group. Medical records and radiological data were obtained from all 133 patients. Emergency surgery was performed on 50/133 patients. All patients received invasive mechanical ventilatory support under sedation range (-2 to 1) of the Richmond Agitation Sedation Scale by a continuous infusion of dexmedetomidine or propofol with or without fentanyl. As adjunctive analgesics, loxoprofen and/or acetaminophen were given through a gastric tube at the ICU physician's discretion. Epidural analgesia was not provided for any patients.

The demographic and clinical characteristics of the patients are summarized in Table 1. The median of mechanical ventilation days in total, SMV group, and PMV group were 10 days, 4 days, and 20 days, respectively. There were no significant differences between the two groups in terms of sex, age, systolic blood pressure, P/F ratio on admission, rate of pulmonary contusion, pneumothorax, and hemothorax, ISS, AIS score in the head, the thorax, the abdomen, and the extremities, and maximum daily amount of fentanyl or total number of patients receiving loxoprofen and/or acetaminophen.

As compared with the SMV group, the PMV group had a significantly larger number of fractured ribs (p=0.001), higher rate of severe GCS (≤8) (p=0.047), higher rate of flail chest (p<0.001), and higher score of TTSS (p<0.001). The PMV group had a longer ICU stay (p<0.001), hospital stay (p<0.001), higher rate of tracheostomy (p<0.001), and mortality (p=0.011). All tracheostomies in both groups were performed on >7 days after ICU admission. In the SMV group, five patients could successfully wean from mechanical ventilation within 6 days and had a T-piece installed, but they finally underwent a tracheostomy due to severe head trauma after leaving the ICU.

Multivariate logistic regression analysis showed that severe GCS (≤8) (OR=4.6; 95% CI: 1.2-13; p=0.003), flail chest (OR=3.0; 95% CI: 1.1-8.2; p=0.029), or TTSS (OR=1.2; 95% CI: 1.1-1.4; p=0.008) were independent significant risk factors for PMV. VIF ranged from 1.0 to 1.6 for the risk factors, indicating no multicolliearities among the risk factors (Table 2).

The AUC for the TTSS, severe GCS (≤8), and flail chest were 0.74 (95% CI: 0.65-0.82), 0.58

(95% CI: 0.48-0.67), and 0.70 (95% CI: 0.61-0.79), respectively. The cut off value for TTSS was 11 points. When the three risk factors were combined, the AUC was increased to 0.80 (95% CI: 0.73-0.88) (Fig. 2).

Discussion

In the present study of severe multiple injured patients with blunt chest trauma, TTSS, severe GCS (≤8), or flail chest were determined to be independent risk factors for PMV. In addition, when the three factors were combined, ROC demonstrated a high predictive performance for PMV (AUC=0.8).

Blunt chest trauma such as rib fractures, lung contusion, pneumothorax, hemothorax, and others have been frequently associated with extra-thoracic injuries on the head, the abdomen, and the extremities [1, 8, 14-15, 18-20]. Of these injuries, it is reported that the four variables, i.e. flail chest, lung contusion, the number of rib fractures, and severe head injury, may cause PMV [8, 14]

Flail chest injury may be life-threatening resulting from deformity of the chest wall and volume loss of the lung [8, 21-23]. This severe injury of the chest wall may be demonstrated by inefficient breathing and respiratory suppression caused by chest pain and/or over dose of analgesics. Accordingly, the flail chest injury tends to require PMV. Actually, Dehghan et al. reported that 59% of flail chest patients needed ventilatory support [8]. Huber et al. reported a significant correlation between flail chest injury and mechanical ventilation. The present study also demonstrated that flail chest is an independent risk factor for PMV.

TTSS is a scoring system developed by Pape et al. combining the five physiologic and anatomical parameters; PaO_2/FiO_2, rib fracture, pulmonary contusion, pleural involvement and age. Each parameter is assigned to a score of 0 - 5 as the degrees of abnormality, and TTSS is calculated by summing the score of each parameter [9]. To our knowledge, the present study may be the first to show that TTSS can be a risk factor with good predictive performance for PMV in severe multiple injured patients with blunt chest trauma. TTSS seems to be reasonable because it includes an age parameter in addition to the physiologic and anatomical parameters. In fact, elderly patients with blunt chest trauma were reported to have a higher mortality and morbidity than younger patients [24].

The four variables for logistic regression analysis might be associated each other. For example, considering direct external forces to the whole body in severe trauma, patients with a larger number of rib fractures tend to also have flail chest, high TTSS, or head injury. Therefore, multicollinearity analysis among the variables was performed. The cut off value of VIF was determined according to the standard documented by Kutner et al. [25]. In the present study, a value of VIF <10 for the four variables strongly indicates no significant correlations among the factors.

Recently, the algorithm for the management of rib fractures have been published by the Western Trauma Association [26]. In the algorithm, they focused on adequate pain control, pulmonary hygiene, and ambulation. Surgical stabilization of rib fractures (SSRF) is indicated when patients should be free of other injuries prolonging intubation or immobility, the fixation should be performed early (ideally within 48 hours of admission), and the ribs can be fixed anytime during either a video-assisted thoracoscopy or thoracotomy. Actually SSRF is performed on only about 4 percent of rib fractured patients [27]. The results of the present study suggest that SSRF may be indicated for the patients who have flail chest, are free from severe GCS (≤8), and have a higher TTSS.

The present study has several important limitations. First, the single-center study design resulted in a small sample size. Second, our emergency medical center routinely conducts CT scans on all patients before entering the ICU, which would presumably result in over detection of clinically irrelevant lung contusion, pneumothorax, and head injury, as well as minor injuries not affecting the clinical course. Third, epidural analgesia considered as an effective method of pain control for rib fractures was not provided due to a shortage of anesthesiologists in our medical center.

Conclusions

Severe GCS (≤8), flail chest, or TTSS may be independent risk factors, and combining the 3 risk factors may provide high predictive performance for PMV.

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Disclosure

Approval of the research protocol: The present study was approved by the institutional ethical committee.

Informed Consent: N/A

Registry and the Registration No. of the study/Trial: N/A

Animal Studies: N/A

Conflict of interests: The author declares no conflict of interests.

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Figure Legends

Figure 1: Flow diagram of patients with blunt chest trauma

Figure 2: Comparison of receiver operating characteristic curve of TTSS, flail chest, and severe GCS (≤8), alone or in combination, for prediction of prolonged mechanical ventilation. GCS, Glasgow Coma Scale; TTSS, thoracic trauma severity score.

Table 1: Demographic and clinical characteristics of patients who needed mechanical ventilation

	SMV group n=49	PMV group n=84	*p* value
Sex (male), n (%)	41 (84%)	60 (71%)	0.082
Age(years), median (IQR)	57 (42-67)	60 (45-72)	0.27
sBP ≤80(mmHg), n (%)	9 (5.4%)	20 (28%)	0.31
GCS ≤8, n (%)	9 (5.4%)	28 (33%)	0.047
P/F ratio, median (IQR)	252 (141-368)	260 (143-323)	0.55
Hemothorax, n (%)	33 (67%)	65 (77%)	0.14
Pneumothorax, n (%)	36 (73%)	63 (75%)	0.50
Lung contusion, n (%)	42 (86%)	68 (81%)	0.33
Number of fractured ribs, median (IQR)	5 (3-8)	8 (4-11)	0.001
TTSS, median (IQR)	7 (9-12)	13 (11-15)	<0.001
Flail chest, n (%)	11 (22%)	52 (62%)	<0.001
Chest tube, n (%)	28 (57%)	58 (69%)	0.12
AIS (head) ≥3, n (%)	21 (43%)	45 (54%)	0.16
AIS (abdomen) ≥3, n (%)	15 (21%)	16 (19%)	0.10
AIS (chest) ≥3, n (%)	43 (88%)	79 (94%)	0.17
AIS (extremity) ≥3, n (%)	21 (43%)	44 (52%)	0.19
ISS, median (IQR)	29 (24-41)	34 (27-38)	0.30
TRISS, median (IQR)	0.88 (0.61-0.91)	0.79 (0.56-0.89)	0.10
Maximum amount of fentanyl (mg/day), median (IQR)	0.96 (0.72-1.2)	1.2 (0.96-1.4)	0.24
Total number of patients receiving loxoprofen and/or acetaminophen, n (%)	29 (59%)	54 (64%)	0.34
Pneumonia, n (%)	16 (33%)	38 (45%)	0.11
Emergency operation, n (%)	15 (31%)	35 (42%)	0.14

Tracheostomy, n (%)	6 (12%)	42 (50%)	<0.001
Ventilation time(days), median (IQR)	4 (3-5)	20 (12-25)	<0.001
ICU stay(days), median (IQR)	6 (4-8)	16 (10-22)	<0.001
Hospital stay(days), median (IQR)	35 (16-43)	45 (32-59)	<0.001
Mortality, n (%)	1 (2%)	13 (15%)	0.011

AIS, abbreviated injury scale; ICU, intensive care; ISS, injury severity score; sBP, systolic blood pressure; GCS, Glasgow Coma Scale; PMV, prolonged mechanical ventilation; SMV, shortened mechanical ventilation; TTSS, thoracic trauma severity score; TRISS, trauma and injury severity score; IQR, interquartile range;

Table 2: Multivariate logistic regression analysis of four variables for prolonged mechanical ventilation

	Odds ratio	95% CI	*p* value	VIF
GCS ≤8	4.6	1.2 - 13	0.003	1.0
Number of fractured ribs	1.0	0.90 - 1.1	0.69	1.5
Flail chest	3.0	1.1 - 8.2	0.029	1.6
TTSS	1.2	1.1 - 1.4	0.008	1.7

GCS, Glasgow Coma Scale ; TTSS, Thoracic Trauma Severity Score; CI, confidence intervals; VIF, variance inflation factor

Figure1

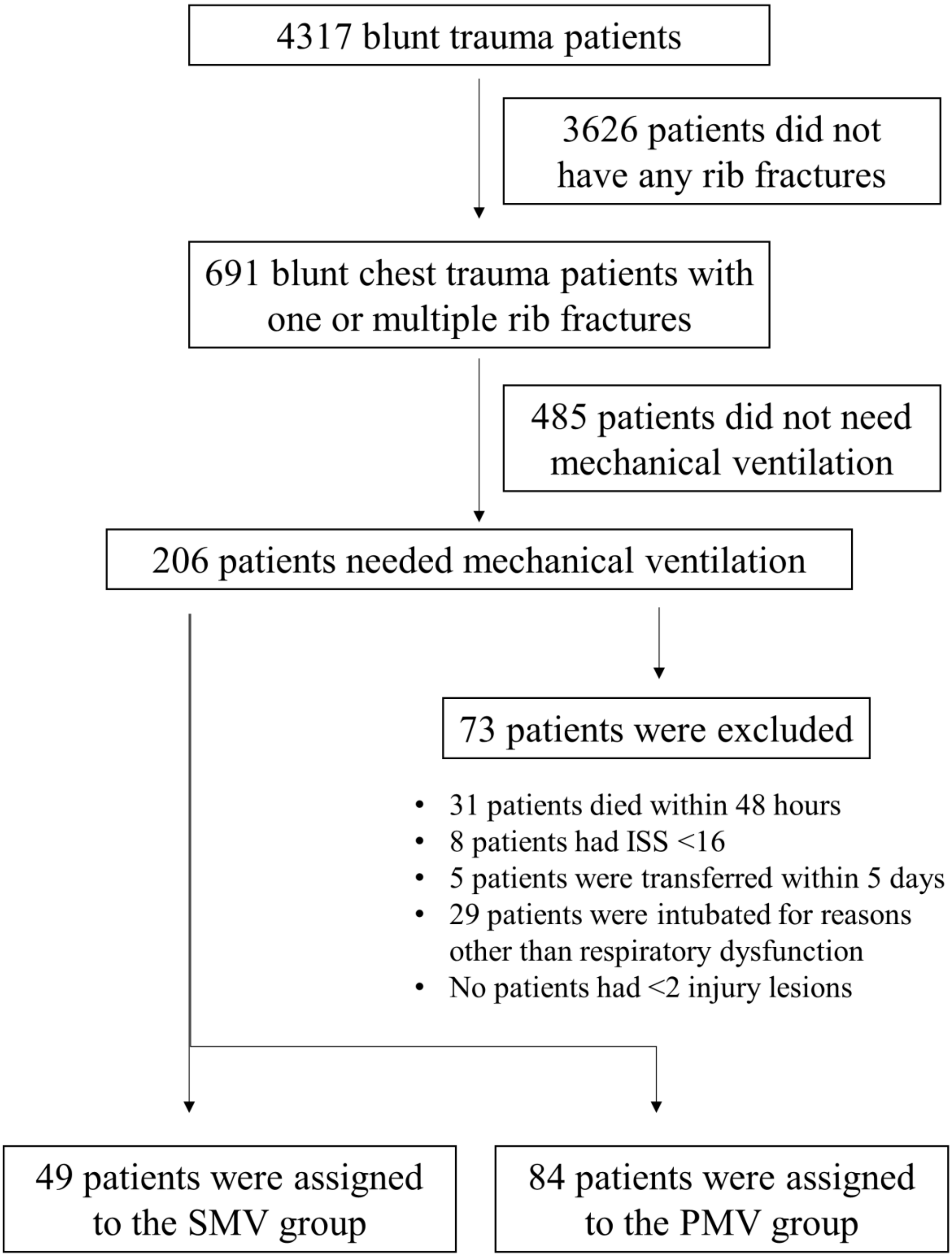
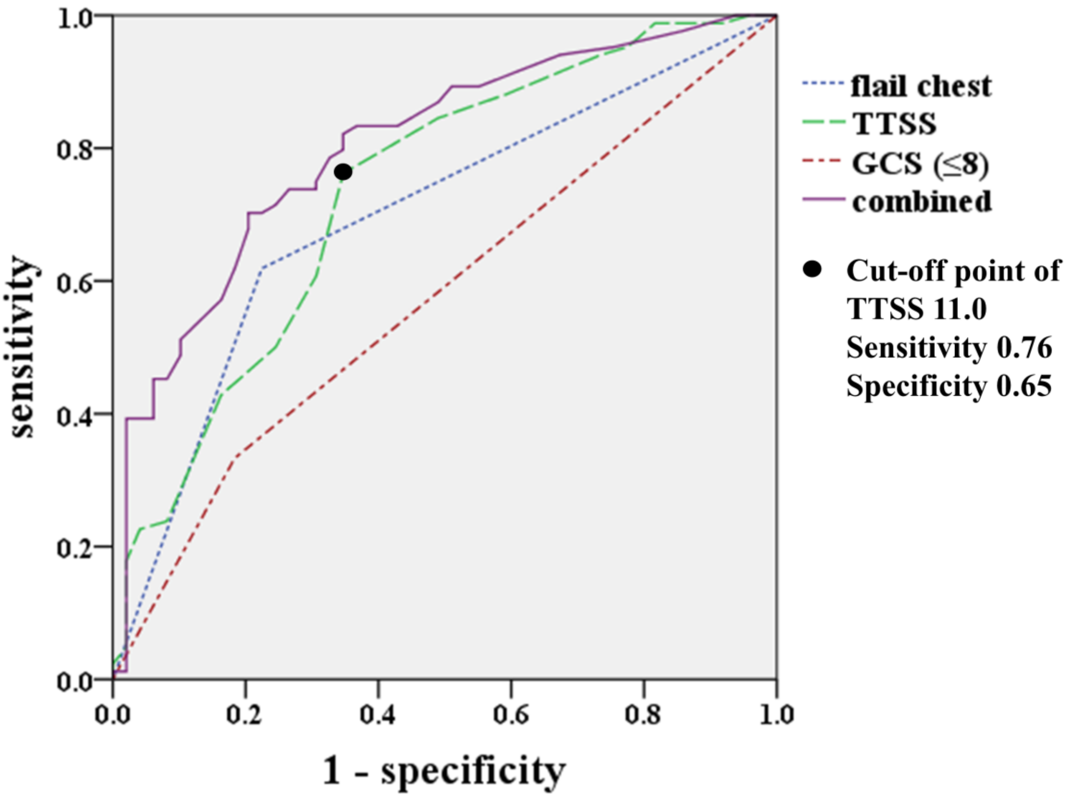

4317 blunt trauma patients
3626 patients did not have any rib fractures
691 blunt chest trauma patients with one or multiple rib fractures
485 patients did not need mechanical ventilation
206 patients needed mechanical ventilation
73 patients were excluded
• 31 patients died within 48 hours
• 8 patients had ISS <16
• 5 patients were transferred within 5 days
• 29 patients were intubated for reasons other than respiratory dysfunction
• No patients had <2 injury lesions
49 patients were assigned to the SMV group
84 patients were assigned to the PMV group

Figure2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sensitivity
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flail chest
TTSS
GCS (≤8)
combined
Cut-off point of
TTSS 11.0
Sensitivity 0.76
Specificity 0.65