The prognostic value of cardiac troponin T in different age groups of traumatic brain injury patients

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Abstract

Background The cardiac dysfunction has been confirmed as a common non-neurological complication and associated with increased mortality in traumatic brain injury (TBI) patients. As a biological marker of cardiac injury, the cardiac troponin T (TnT) has been verified correlated with the outcome of some non-traumatic brain injury patients. However, the prognostic value of TnT in TBI patients has not been clearly illustrated. We designed this study to explore the association between TnT and the outcome of TBI patients in different age subgroups.

Methods Patients diagnosed with TBI in a prospective critical care database were eligible for this study. Univariate logistic regression analysis was firstly performed to explore the relationship between included variables and mortality. Then, the real effect of TnT on the outcome of different age subgroups was analyzed by multivariate logistic regression analysis adjusting the confounding effects of other significant risk factors. Finally, we drew receiver operating characteristic (ROC) curves to evaluate the prognostic value of TnT in different age groups of TBI patients.

Results 520 patients were included in this study with a mortality rate of 20.2%. There were 112 (21.5%) non-elderly patients (age < 65) and 408 (78.5%) elderly patients (age ≥ 65). Non-survivors had a higher percentage of previous acute myocardial infarction ($p = 0.019$) and pupil no-reaction ($p = 0.028; p = 0.011$) than survivors. Survivors had higher GCS ($p < 0.001$) and lower TnT than non-survivors ($p < 0.001$). TnT was significantly associated with mortality in non-elderly patients ($p = 0.031$) but not in overall patients ($p = 0.143$) and elderly patients ($p = 0.456$) in multivariate logistic regression analysis. The AUC (area under the ROC curve) value of TnT in overall, non-elderly and elderly patients was 0.644, 0.693 and 0.632, respectively. Combining TnT with GCS increased the sensitivity of predicting the poor outcome in both non-elderly and elderly TBI patients.

Conclusion The prognostic value of TnT differed between elderly and non-elderly TBI patients. Level of TnT was associated with mortality of non-elderly TBI patients but not elderly patients. Combining the TnT with GCS could increase the sensitivity of prognosis evaluation.

Keywords Troponin T · Traumatic brain injury · Marker · Prognosis

Introduction

Estimated occurring nearly sixty-nine million times each year globally, traumatic brain injury (TBI) brings enormous burden to social economics and families of casualties [1]. The high mortality of TBI patients are attributable to complex injury pathophysiology caused by initial external mechanical forces and subsequent secondary brain injury [2]. In addition to intracranial injury, non-neurological organ dysfunction is also commonly observed and has been confirmed associated with the outcome of TBI patients [3, 4]. One study reported that 22.6% of TBI patients would develop at least one non-neurological complication during
hospitalization [5]. One of the most common non-neurological complications is cardiac injury, which was reported occurring in 22.3% of isolated severe TBI patients [6]. And it has been verified that cardiac dysfunction was positively correlated with brain injury severity and shorter in-hospital survival in moderate to severe TBI patients [7].

Some indicators of cardiac dysfunction such as cardiac troponin, abnormalities of echocardiography and electrocardiogram have been explored and utilized in various clinical settings. It has been discovered that elevation of serum TnI (Troponin I) level was not only observed in patients with myocardial infarction or acute coronary syndrome but also the patients diagnosed with sepsis, chronic renal failure, pulmonary embolism or non-traumatic brain injury [8–12]. Previous studies exploring the prognostic value of TnI have found that increased TnI was associated with injury severity and adverse outcome of TBI patients [13–15]. Compared with TnI negative group, TnI positive group had a longer length of hospital stay, higher Modified Rankin Scale and lower Glasgow Outcome Scale [16]. However, one of these studies concluded that TnI was an effective predictor of mortality in TBI patients under 65 years old but not in those over 65 years old [14]. Another two studies have indicated that Troponin T (TnT) was also valuable in predicting mortality of TBI patients even after adjusting confounders [17, 18]. However, the most of included participants in these two studies were young TBI patients. We suspected that age might also modify the effect of TnT on the outcome of TBI patients. Therefore, we designed this study to explore the prognostic value of TnT in different age subgroups including those younger than 65 and over 65 years old.

Methods

Patients included

This retrospective observational study was conducted utilizing data from the prospective Multiparameter Intelligent Monitoring in Intensive Care Database III (MIMIC-III database). Patients admitted to ICUs (Intensive Care Unit) of Beth Israel Deaconess Medical Center between 2001 and 2012 were included in this large critical care database. This freely available database was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology (MIT). Patients included in this public database were deidentified and anonymized for protecting their privacy. We got the certification to utilize data of MIMIC III after finishing the National Institutes of Health (NIH) Web-based training course and the Protecting Human Research Participants examination. In this study, patients diagnosed with TBI were eligible for this study. There were five exclusion criteria (Fig. 1): (1) head AIS < 3; (2) Chest AIS ≥ 3 (excluding the potential effect of blunt cardiac injury on TnT level); (3) Non-emergency admission; (4) lacking records of troponin T within 24 h after admission; (5) lacking records of Glasgow Coma Scale (GCS) and other relevant data. Finally, a total of 520 patients were included in this study.

Data included

All collected variables including age, sex, history of underlying disease, records of vital signs on admission, GCS, brain injury types, records of operation and blood transfusion, level of troponin T, length of hospital stay were extracted by us using Navicat Premium 12 (PremiumSoft, Hong Kong). The primary outcome of this study was in-hospital mortality.

Statistical analysis

The normality of included variables was validated by Kolmogorov–Smirnov tests. All included continuous variables were shown as median (interquartile range) because of the non-normality. Mann–Whitney U test was performed to compare differences between two groups of non-normally distributed continuous variables. And categorical variables were shown as numbers (percentage). The difference between two groups of categorical variables was analyzed by chi-square test. For subgroup analysis, overall patients were divided into two groups based on whether their age ≥ 65 years old. Univariate logistic regression was performed to find potential risk factors for in-hospital mortality in overall patients and two subgroups. Risk factors with \( p < 0.05 \) were eligible for subsequent multivariate logistic regression analysis. To analyze the real effect of troponin T on the outcome of overall patients and two subgroups, the confounding effect of aforementioned risk factors was adjusted by multivariate logistic regression analysis. And odds ratio (OR) and 95% confidence intervals (CI) of troponin T in overall patients and two subgroups were calculated and presented. Receiver operating characteristic (ROC) curves were drawn to evaluate the predictive value of troponin T and GCS. Z test was used to compare predictive value between single factors (troponin T or GCS) and a combination of factors (troponin T and GCS).

A \( P \) value < 0.05 was considered being of statistical significance. We used SPSS 22.0 Windows software (SPSS, Inc, Chicago, IL) for all statistical analyses and figures drawing.

Results

Baseline characteristics of included TBI patients

A total of 520 TBI patients was included in this study. There were 415 survivors and 105 non-survivors with mortality
rate of 20.2% (Table 1). The median age of overall patients was 80 years. There was no significant difference in the age between survivors and non-survivors (79 vs 81, \( p = 0.217 \)). The male ratio also did not differ between these two groups (54% vs 52.4%, \( p = 0.770 \)). The percentage of underlying disease including hypertension, coronary heart disease and diabetes mellitus did not differ between survivors and non-survivors. However, non-survivors were more likely to be complicated with previous acute myocardial infarction than survivors (11.4% vs 4.8%, \( p = 0.019 \)). Results of vital signs on admission showed no significant difference between survivors and non-survivors. And non-survivors had higher incidence of pupillary no-reaction whether one or both sides (9.5% vs 3.9%, \( p = 0.028 \); 6.7% vs 1.7%, \( p = 0.011 \)). Furthermore, the GCS of non-survivors was lower than survivors with statistical significance (6 vs 14, \( p < 0.001 \)). The occurrence rate of several injury patterns including epidural hematoma, subdural hematoma and intracerebral hematoma did not differ between survivors and non-survivors. Whereas non-survivors were more likely to suffer arrhythmia than survivors (48% vs 22.3%, \( p < 0.001 \)). A remarkable finding was that non-survivors had a significantly higher level of troponin T than survivors (0.02 vs 0, \( p < 0.001 \)). Compared with survivors, non-survivors had longer length of ICU stay (4 vs 2, \( p = 0.001 \)). Instead, the length of hospital stay was shorter in non-survivors than survivors (6 vs 8, \( p < 0.001 \)).

Compared with non-elderly TBI patients, elderly TBI patients were more commonly complicated with underlying diseases including hypertension (\( p < 0.001 \)), coronary heart disease (\( p < 0.001 \)) and diabetes mellitus (\( p = 0.038 \)) (Table 2). The systolic blood pressure (139 vs 135, \( p = 0.023 \)) was higher in elderly patients whereas diastolic blood pressure (62 vs 71, \( p < 0.001 \)), heart rate (80 vs 89, \( p < 0.001 \)) and body temperature (36.7 vs 36.9, \( p = 0.002 \)) were all lower in elderly patients. Elderly patients had significantly higher GCS than non-elderly patients (14 vs 10, \( p = 0.016 \)). And elderly patients were more likely to receive blood transfusion (41.9% vs 26.8%, \( p = 0.003 \)) and suffer arrhythmia (48% vs 22.3%, \( p < 0.001 \)) during hospitalization. Moreover, the serum level of TnT was higher in elderly patients than non-elderly (0.01 vs 0, \( p = 0.014 \)). While the in-hospital mortality did not significantly differ between elderly and non-elderly patients (20.3% vs 19.6%, \( p = 0.870 \)).

**Fig. 1** Flowchart of patients
Inclusion. MIMIC-III Multiparameter Intelligent Monitoring in Intensive Care Database III, TBI traumatic brain injury, AIS Abbreviated Injury Scale, GCS Glasgow Coma Scale
Univariate logistic regression analysis of risk factors for mortality

In overall included patients, history of acute myocardial infarction (OR = 2.548, \( p = 0.015 \)), pupil no-reaction (OR = 2.805, \( p < 0.001 \)), subarachnoid hemorrhage (OR = 1.601, \( p = 0.045 \)), intracerebral hematoma (OR = 1.799, \( p = 0.044 \)) and troponin T (OR = 2.541, \( p = 0.025 \)) were positively associated with poor outcome (Table 3). While body temperature (OR = 0.735, \( p = 0.011 \)) and GCS (OR = 0.770, \( p < 0.001 \)) were inversely correlated with poor outcome. In non-elderly patients, only pupil no-reaction (OR = 4.839, \( p < 0.001 \)) and GCS (OR = 0.723, \( p < 0.001 \)) were found related with in-hospital mortality (Table 4). And in elderly patients, coronary heart disease (OR = 1.869, \( p = 0.014 \)), body temperature (OR = 0.692, \( p = 0.012 \)), pupil no-reaction (OR = 2.398, \( p < 0.001 \)), GCS (OR = 0.772, \( p < 0.001 \)) and intracerebral hematoma (OR = 1.917, \( p = 0.048 \)) and arrhythmia (OR = 1.640, \( p = 0.047 \)) were significantly correlated with in-hospital mortality (Table 5).

Association between troponin T and outcome after adjusting confounders

To verify the independent association between troponin T and outcome, multivariate logistic regression analyses were performed in overall patients and two subgroups (age < 65, age ≥ 65). After adjusting the confounding effects of acute myocardial infarction, body temperature, pupil no-reaction, GCS, subarachnoid hemorrhage, intracerebral hematoma, the OR of troponin T was 1.909 without statistical significance (\( p = 0.143 \)) in overall included patients (Table 6). While in patients < 65 years old, the OR of troponin T was

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**Table 1** Baseline characteristics of overall patients and subgroups divided based on survival outcome

| Variables                        | Total patients (n = 520) | Survivors (n = 415, 79.8%) | Non-survivors (n = 105, 20.2%) | \( p \) |
|----------------------------------|--------------------------|-----------------------------|--------------------------------|-------|
| Age (years)                      | 80 (67–86)               | 79 (67–85)                  | 81 (67–88)                     | 0.217 |
| Male gender                      | 279 (53.7%)              | 224 (54%)                   | 55 (52.4%)                     | 0.770 |
| History of underlying disease    |                          |                             |                                |       |
| Hypertension                     | 328 (63.1%)              | 260 (62.7%)                 | 68 (64.8%)                     | 0.688 |
| Coronary heart disease           | 130 (25%)                | 96 (23.1%)                  | 34 (32.4%)                     | 0.056 |
| Acute myocardial infarction      | 32 (6.2%)                | 20 (4.8%)                   | 12 (11.4%)                     | 0.019 |
| Diabetes mellitus                | 131 (25.2%)              | 100 (24.1%)                 | 31 (29.5%)                     | 0.259 |
| Vital signs on admission         |                          |                             |                                |       |
| Systolic blood pressure (mmHg)   | 139 (127–148)            | 139 (128–147)               | 139 (124–153)                  | 0.713 |
| Diastolic blood pressure (mmHg)  | 62 (58–72)               | 62 (59–71)                  | 62 (52–73)                     | 0.411 |
| Heart rate (s\(^{-1}\))         | 81 (70–93)               | 81 (71–92)                  | 81 (70–94)                     | 0.840 |
| Respiratory rate (s\(^{-1}\))   | 18 (15–21)               | 18 (15–21)                  | 18 (15–21)                     | 0.659 |
| Body temperature (°C)            | 36.7 (36.2–37.3)         | 36.7 (36.2–37.3)            | 36.7 (35.9–37.3)               | 0.097 |
| SpO\(_2\) (%)                   | 98 (97–100)              | 98 (96.9–100)               | 99 (97.3–100)                  | 0.003 |
| Pupillary reactivity             |                          |                             |                                |       |
| No-reaction (one side)           | 26 (5%)                  | 16 (3.9%)                   | 10 (9.5%)                      | 0.028 |
| No-reaction (both sides)         | 14 (2.7%)                | 7 (1.7%)                    | 7 (6.7%)                       | 0.011 |
| GCS on admission                 | 13 (7–15)                | 14 (9–15)                   | 6 (4–10)                       | <0.001|
| Injury types                     |                          |                             |                                |       |
| Epidural hematoma                | 14 (2.7%)                | 11 (2.7%)                   | 3 (2.9%)                       | 1.000 |
| Subdural hematoma                | 273 (52.5%)              | 223 (53.7%)                 | 50 (47.6%)                     | 0.263 |
| Subarachnoid hemorrhage          | 138 (26.5%)              | 102 (24.6%)                 | 36 (34.3%)                     | 0.048 |
| Intracerebral hematoma           | 68 (13.1%)               | 48 (11.6%)                  | 20 (19%)                       | 0.051 |
| Surgical operation              | 133 (25.6%)              | 103 (24.8%)                 | 30 (28.6%)                     | 0.435 |
| Blood transfusion                | 201 (38.7%)              | 159 (38.3%)                 | 42 (40.0%)                     | 0.752 |
| Arrhythmia during hospitalization| 221 (42.5%)              | 169 (40.7%)                 | 52 (49.5%)                     | 0.105 |
| Troponin T (μg/L)                | 0.01 (0–0.03)            | 0 (0–0.03)                  | 0.02 (0–0.07)                  | <0.001|
| Length of ICU stay (days)        | 2 (1–5)                  | 2 (1–4)                     | 4 (12–7)                       | 0.001 |
| Length of hospital stay (days)   | 7 (4–13)                 | 8 (5–14)                    | 6 (3–11)                       | <0.001|

\( SpO_2 \) Pulse oxygen saturation, GCS Glasgow Coma Scale
3.178 with statistical significance ($p = 0.040$) after adjusting the confounding effects of pupil no-reaction, GCS. However, level of troponin T was not significantly associated with outcome in patients whose age ≥ 65 (OR = 1.839, $p = 0.456$), after considering the effects of confounders including coronary heart disease, body temperature, pupil no-reaction, GCS, intracerebral hematoma and arrhythmia.

**Prognostic value of troponin T in overall patients and subgroups**

The AUC value of troponin T and GCS for predicting mortality of overall patients was 0.644 and 0.794, respectively (Table 7) (Fig. 2A). GCS had a significantly higher AUC value than troponin T ($Z = 3.6939$, $p < 0.05$). Combining troponin T could not improve the predictive value of a single assessment of GCS (0.814 vs 0.794, $Z = 0.6006$, $p > 0.05$). For those age < 65, the AUC value of troponin T and GCS was 0.693 and 0.829, respectively (Fig. 2B). Troponin had comparable AUC value with GCS ($Z = 1.5804$, $p > 0.05$). The AUC value of combining troponin T with GCS was 0.862, which was higher than single GCS, though without statistical significance ($Z = 0.4568$, $p > 0.05$). However, the AUC value of combining troponin T with GCS was significantly higher than the single evaluation of troponin T ($Z = 2.0505$, $p < 0.05$). For those age ≥ 65, the AUC value of troponin T was 0.632 (Fig. 2C), which was significantly lower than 0.793 of GCS ($Z = 3.5778$, $p < 0.05$). Combining troponin T with GCS could not improve the predictive value of single GCS ($Z = 0.5260$, $p > 0.05$). A remarkable discovery was that combining troponin T could distinctly improve the sensitivity of predicting mortality.
Table 3 Univariate analysis of risk factors for mortality in overall TBI patients

| Variables                                | OR     | 95% CI   | p       |
|------------------------------------------|--------|----------|---------|
| Age                                      | 1.004  | 0.989–1.019 | 0.576  |
| Male gender                              | 0.938  | 0.611–1.440 | 0.770  |
| Hypertension                             | 1.096  | 0.701–1.713 | 0.689  |
| Coronary heart disease                   | 1.591  | 0.996–2.541 | 0.052  |
| Acute myocardial infarction              | 2.548  | 1.203–5.398 | 0.015  |
| Diabetes mellitus                        | 1.320  | 0.820–2.124 | 0.253  |
| Systolic blood pressure                  | 1.000  | 0.993–1.006 | 0.912  |
| Diastolic blood pressure                 | 0.996  | 0.984–1.008 | 0.491  |
| Heart rate                               | 0.998  | 0.986–1.010 | 0.769  |
| Respiratory rate                         | 0.992  | 0.950–1.035 | 0.703  |
| Body temperature                         | 0.735  | 0.581–0.931 | 0.011  |
| SpO2 (%)                                 | 0.987  | 0.935–1.041 | 0.623  |
| Pupil no-reaction                        | 2.805  | 2.052–3.836 | <0.001 |
| GCS                                      | 0.770  | 0.728–0.815 | <0.001 |
| Epidural hematoma                        | 1.080  | 0.996–1.086 | 0.066  |
| Subdural hematoma                        | 0.763  | 0.510–1.102 | 0.265  |
| Subarachnoid hemorrhage                  | 1.601  | 1.010–2.538 | 0.045  |
| Intracerebral hematoma                   | 1.799  | 1.015–3.189 | 0.044  |
| Surgical operation                      | 1.212  | 0.751–1.955 | 0.432  |
| Blood transfusion                        | 1.073  | 0.693–1.663 | 0.751  |
| Arrhythmia                               | 1.428  | 0.929–2.195 | 0.104  |
| Troponin T                               | 2.541  | 1.123–5.752 | 0.025  |

Bold values indicate statistically significant p values (p < 0.05)

Table 4 Univariate analysis of risk factors for mortality in non-elderly TBI patients

| Variables                                | OR     | 95% CI   | p       |
|------------------------------------------|--------|----------|---------|
| Age                                      | 0.986  | 0.949–1.025 | 0.487  |
| Male gender                              | 2.303  | 0.625–8.486 | 0.210  |
| Hypertension                             | 0.865  | 0.336–2.229 | 0.765  |
| Coronary heart disease                   | <0.001 | –        | 0.999  |
| Acute myocardial infarction              | 8.900  | 0.769–103.029 | 0.080 |
| Diabetes mellitus                        | 1.471  | 0.470–4.602 | 0.508  |
| Systolic blood pressure                  | 0.995  | 0.982–1.008 | 0.459  |
| Diastolic blood pressure                 | 0.993  | 0.970–1.015 | 0.519  |
| Heart rate                               | 0.999  | 0.976–1.023 | 0.948  |
| Respiratory rate                         | 1.005  | 0.923–1.094 | 0.909  |
| Body temperature                         | 0.834  | 0.547–1.272 | 0.400  |
| SpO2 (%)                                 | 1.108  | 0.860–1.427 | 0.428  |
| Pupil no-reaction                        | 4.839  | 2.429–9.641 | <0.001 |
| GCS                                      | 0.723  | 0.621–0.842 | <0.001 |
| Epidural hematoma                        | 4.400  | 0.584–33.142 | 0.150 |
| Subdural hematoma                        | 1.250  | 0.489–3.197 | 0.641  |
| Subarachnoid hemorrhage                  | 1.359  | 0.493–3.749 | 0.553  |
| Intracerebral hematoma                   | 1.444  | 0.417–5.003 | 0.562  |
| Surgical operation                      | 2.158  | 0.757–6.151 | 0.150  |
| Blood transfusion                        | 1.359  | 0.493–3.749 | 0.553  |
| Arrhythmia                               | 0.730  | 0.222–2.396 | 0.604  |
| Troponin T                               | 2.228  | 0.791–6.278 | 0.130  |

Bold values indicate statistically significant p values (p < 0.05)

Discussion

In our study, non-survivors had significantly higher serum TnT level than survivors. Results of univariate logistic regression showed TnT was only statistically significant in overall patients but not two age subgroups. However, the real effect of TnT on the outcome of TBI patients should be evaluated after adjusting potential confounders. Actually, we found that TnT was only statistically significant in a subgroup of patients younger than 65 by performing multivariate logistic regression analysis. And TnT was more effective in predicting in-hospital mortality of non-elderly TBI patients with a relatively high AUC value. This result was similar to the previous finding that TnI was an useful biological prognostic marker in isolated severe TBI patients whose age ≤ 65 but not patients whose age > 65 [14].

There are three isoforms of troponin complex: troponin C, I, and T [19]. The characteristic of troponin C isoform existing in both cardiac and skeletal muscle makes it could not be considered as a sensitive marker of cardiac injury. However, the myocardium-specific troponin I and T are useful biomarkers for myocardial necrosis and have been clinically used for early diagnosis and prognosis evaluation in patients with cardiopulmonary diseases such as acute coronary syndrome, acute myocardial infarction, heart failure and pulmonary embolism [20–27]. Whereas the clinical use of cardiac troponin could not only be limited in primary cardiopulmonary diseases. In fact, the serum cardiac troponin level could reflect the severity of developing cardiovascular complications involved in non-cardiovascular system-specific diseases such as sepsis and trauma [28–30]. The association between increased serum cardiac troponin level and poor outcome of these diseases has also been confirmed in previous studies [31–33]. In addition, the elevation of cardiac troponin was also discovered in non-traumatic brain injury patients including ischemic stroke, intracerebral hemorrhage and subarachnoid hemorrhage [34–37]. And the degree of increased cardiac troponin was positively correlated with the occurrence of cardiovascular dysfunction, brain injury severity and poor outcome of these brain-injured patients [11, 38–43].
neurogenic stunned myocardium, presenting with reversible left ventricular systolic dysfunction, pulmonary edema and cardiogenic shock, which was likely caused by sympathetic hyperactivity induced excessive release of catecholamines and acute inflammatory response [39, 44–47].

The development of cardiac dysfunction has been verified as a risk factor for in-hospital mortality of TBI patients [6].

### Table 5 Univariate analysis of risk factors for mortality in elderly TBI patients

| Variables                      | OR   | 95% CI          | p     |
|--------------------------------|------|-----------------|-------|
| Age                            | 1.027| 0.992–1.062     | 0.128 |
| Male gender                    | 0.81 | 0.498–1.316     | 0.394 |
| Hypertension                   | 1.173| 0.692–1.990     | 0.553 |
| Coronary heart disease         | 1.869| 1.132–3.085     | 0.014 |
| Acute myocardial infarction    | 2.206| 0.984–4.945     | 0.055 |
| Diabetes mellitus              | 1.288| 0.761–2.179     | 0.345 |
| Systolic blood pressure        | 1.001| 0.993–1.009     | 0.777 |
| Diastolic blood pressure       | 0.997| 0.983–1.011     | 0.708 |
| Heart rate                     | 0.998| 0.984–1.012     | 0.787 |
| Respiratory rate               | 0.987| 0.939–1.038     | 0.619 |
| Body temperature               | 0.692| 0.519–0.922     | **0.012** |
| \(\text{SpO}_2\) (%)           | 0.981| 0.929–1.036     | 0.488 |
| Pupil no-reaction              | 2.398| 1.673–3.437     | \(<0.001\) |
| GCS                            | 0.772| 0.725–0.823     | \(<0.001\) |
| Epidural hematoma              | 0.428| 0.053–3.428     | 0.424 |
| Subdural hematoma              | 0.686| 0.423–1.113     | 0.127 |
| Subarachnoid hemorrhage        | 1.672| 0.997–2.806     | 0.051 |
| Intracerebral hematoma         | 1.917| 1.005–3.658     | **0.048** |
| Operation                      | 1.049| 0.611–1.799     | 0.863 |
| Blood transfusion              | 1.013| 0.622–1.651     | 0.958 |
| Arrhythmia                     | 1.640| 1.008–2.670     | **0.047** |
| Troponin T                     | 3.168| 0.902–11.124    | 0.072 |

Bold values indicate statistically significant \(p\) values \((p < 0.05)\)

**OR** Odds ratio, **CI** confidence interval, **SpO\(_2\)** Pulse oxygen saturation, **GCS** Glasgow Coma Scale

### Table 6 Association between troponin T and mortality after adjusting confounders in overall TBI patients and subgroups

| Variables                      | OR   | 95% CI          | p     |
|--------------------------------|------|-----------------|-------|
| Overall patients\(^a\)         | 1.909| 0.803–4.536     | 0.143 |
| <65 years old\(^b\)           | 3.178| 1.057–9.562     | 0.040 |
| \(\geq 65\) years old\(^c\)   | 1.839| 0.371–9.113     | 0.456 |

**OR** Odds ratio, **CI** confidence interval

\(^a\) Adjusted for acute myocardial infarction, body temperature, pupil no-reaction, GCS, subarachnoid hemorrhage, intracerebral hematoma

\(^b\) Adjusted for pupil no-reaction, GCS

\(^c\) Adjusted for coronary heart disease, body temperature, pupil no-reaction, GCS, intracerebral hematoma, arrhythmia

It has been reported in previous studies that the incidence of cardiac dysfunction after TBI ranged from 13% to 22.3% [6, 48–50]. These studies usually evaluated the cardiac function according to the signs of echocardiogram such as reduced left ventricular ejection fraction and regional wall motion abnormalities. A novel neurogenic cardiac injury score (NCIS), which was calculated based on rising troponin I, abnormal echocardiography and hypotension, was recently designed and confirmed independently associated with in-hospital mortality of patients with severe head trauma after adjusting confounders [51]. Previous studies have investigated the prognostic value of troponin I in TBI patients and found that effect of troponin I on outcome could be modified by age [13–16]. The TnI was not as valuable in predicting outcome in elderly TBI patients as in non-elderly patients [14]. Another two studies discovered that high sensitive troponin T (HsTnT) was also an effective prognostic indicator in TBI patients [17, 18]. However, the patients included in these two studies were from the same trauma database and mostly were young injured patients with a median age of thirty. The homogeneous population of these studies limited the general applicability of TnT in TBI patients. Our study specially investigated the association between TnT and the outcome of TBI patients in different age subgroups. The TnT level was independently associated with in-hospital mortality of included non-elderly TBI patients but not elderly TBI patients. And single assessment of TnT performed well in predicting the outcome of non-elderly TBI patients with relatively high AUC. Instead, the low AUC, specificity and sensitivity of TnT in elderly TBI patients indicated that it could not be considered as an accurate indicator of prognosis in this age subgroup. This finding emphasized the conclusion that age could modify the effect of both TnI and TnT.
on the outcome of TBI patients. The limited effect of TnT on the outcome of elderly TBI patients were likely explained by the elevation of baseline TnT caused by natural aging and complicated chronic cardiovascular diseases. More detailed mechanisms involved in this finding should be explored in future studies. Meanwhile, more sensitive cardiac injury biomarkers in TBI patients should be developed to effectively detect potential cardiopulmonary complications and evaluate the prognosis of elderly TBI patients. One noteworthy finding in this study was that TnT combined with GCS significantly improved the sensitivity of predicting in-hospital mortality in both age subgroups, whether AUC was statistically improved or not. Based on this discovery, we concluded that assessment of TnT for evaluating cardiac injury was beneficial for physicians to screen patients with high probabilities of poor prognosis and give intensive care and therapies protecting cardiac function such as beta-blockers in the early stage.

There were several limitations in this study. First, we did not evaluate serial or peak level of TnT during hospitalization for included patients. This limitation could confound the effect of TnT on the outcome of TBI patients. Second, we could not compare the predictive value between TnI and TnT due to the incomplete records of TnI in included patients. Third, included patients mainly were elderly, with only 112 non-elderly patients. However, previous studies...
have analyzed the association between TnT and the outcome of TBI patients with younger age. Finally, some patients without records of TnT were excluded from this study, which could lead to selection bias. Therefore, our results should be verified in further prospective studies.

Conclusion

The prognostic value of TnT in elderly and non-elderly TBI patients is different. Higher level of TnT indicates increased mortality of non-elderly TBI patients. Evaluating the TnT is beneficial for physicians to predict the outcome of TBI patients with high sensitivity.

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Author contributions

RRW performed the statistical analysis and wrote the manuscript draft. MH collected clinical data. MH and JGX revised the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used of the current study are available upon reasonable request to the corresponding authors.

Declarations

Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

The study was performed using data from the public database MIMIC III. This freely available database was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology (MIT).

Informed consent

Patients included in this public database were de-identified and anonymized for protecting their privacy. And informed consent of each patient was signed once they admitted.

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