Predictive value of positive high-sensitivity troponin T in intubated traumatic brain injury patients

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OBJECTIVE The clinical relevance of high-sensitivity troponin T (HsTnT) in trauma patients is not well explored. In this study, the authors aimed to study the predictive value of serum HsTnT in intubated patients who had sustained traumatic brain injury (TBI).

METHODS A retrospective analysis was conducted for all intubated TBI patients between 2010 and 2014 at a national level 1 trauma center. Data were analyzed and compared based on the HsTnT status on admission (group 1, negative results; and group 2, positive results). Receiver operating characteristic curves were used to determine sensitivity, specificity, and cutoff level of HsTnT to predict mortality. Time to earlier discharge from hospital or death was modeled using Cox proportional hazard models to describe the relationship between HsTnT and in-hospital mortality.

RESULTS Of the 826 intubated TBI patients, 490 underwent HsTnT testing; 65.7% had positive HsTnT results. Patients in group 2 had a higher Injury Severity Score ($p = 0.001$) and head Abbreviated Injury Scale (AIS) score ($p = 0.004$) than those in group 1. In addition, group 2 patients were more likely to have lower Glasgow Coma Scale scores ($p = 0.001$) and more likely to experience intraventricular hemorrhage, brain edema, pneumonia, and sepsis ($p = 0.001$). HsTnT values positively correlated with head AIS score ($r = 0.19$, $p = 0.001$) and varied by the type of lesion and time to death. Ventilator days and length of hospital stay were more prolonged in group 2 patients ($p = 0.001$). Area under the curve (AUC) analysis showed that HsTnT ≥ 26.5 ng/L predicted all-cause mortality (AUC 0.75, 95% CI 0.699–0.801) with 80% sensitivity. Positive HsTnT was an independent predictor of mortality in multivariate models (adjusted OR 3.10, 95% CI 1.308–7.351) even after excluding chest injury (adjusted OR 4.18, 95% CI 1.320–13.231).

CONCLUSIONS Positive HsTnT results are associated with poor outcomes in intubated patients with TBI. In this subset of patients, measuring serum HsTnT on admission is a useful tool for early risk stratification and expedited care; however, further prospective studies are warranted.

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KEY WORDS cardiac troponin; high-sensitivity troponin T; traumatic brain injury; intubation; head; vascular disorders

MYOCARDIAL injury carries an increased risk of mortality in patients who are intubated in the acute period for noncardiac reasons.^{13,16,28,36} In trauma patients, diagnosis of myocardial injury could be easily overlooked, challengeable, and confusing, particularly in patients who are at low risk for acute cardiac events.¹³

Noncardiac surgery and traumatic injury are examples of potentially unexpected acute myocardial insults.^{13,16,28,36} The concept of the brain-heart interaction after trauma

is an interesting research field and needs further assessment.¹³ The neurocardiac axis theory and neurogenic stunned myocardium phenomenon could partly explain this link.⁶ Traumatic brain injury (TBI) is a serious public health issue worldwide, with high rates of mortality and morbidity.¹¹ Early recognition of clinical predictors in TBI patients is of utmost benefit for timely risk stratification and management.^{9,18} Following blunt TBI, the heart can be affected directly as a part of polytrauma or secondary to possible hypotension, coronary hypoperfusion, or exposure

ABBREVIATIONS AIS = Abbreviated Injury Scale; BB = beta blocker; DAI = diffuse axonal injury; GCS = Glasgow Coma Scale; HR = hazard ratio; HsTnT = high-sensitivity troponin T; IQR = interquartile range; ISS = Injury Severity Score; SBP = systolic blood pressure; TBI = traumatic brain injury; Tn = troponin.

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to excessive catecholamines and inflammatory markers released in response to the stressful effect of trauma.^{6,32}

Changes seen on electrocardiography and echocardiography after traumatic injury could be misconstrued as hemodynamic alterations or intracranial lesion effect rather than a direct or primary cardiac insult.¹² Serum troponins are well known biomarkers that are exclusively released from damaged myocardial cells, regardless of the underlying triggers.^{3,4,17,23,25,35,37,39} Elevated troponin levels have been reported in acute nontraumatic head disorders, such as stroke and subarachnoid hemorrhage.⁶ Recently, high-sensitivity troponin T (HsTnT) assay has been found to have the ability for early detection of a very low troponin concentration that might be missed by conventional troponin assays (TnT and TnI), even without the need for serial measurements.^{7,21,41} The precise mechanism, clinical relevance, and therapeutic implication of elevated troponins in TBI remain unclear.^{6,26,32,34} Moreover, the utility of HsTnT in TBI is rarely investigated. In this study, we aimed to assess the predictive role of serum HsTnT in TBI requiring endotracheal intubation.

Methods

This retrospective observational study was conducted in TBI patients who were admitted to the national level 1 trauma center, Hamad General Hospital, in Qatar, from January 2010 to December 2014. Patients were identified through a prospectively maintained trauma registry database. This registry actively participates in the National Trauma Data Bank and Trauma Quality Improvement Program of the American College of Surgeons Committee on Trauma. Patients with blunt TBI who required endotracheal intubation in the field or on arrival to the emergency department and were subjected to serum HsTnT testing during the initial 24 hours posttrauma, irrespective of age and sex, were included in the study.

Initial screening of HsTnT was performed at the discretion of the attending physician, as there was no specific institutional protocol (i.e., unexplained hypotension or electrocardiography changes or dysrhythmias). The troponin level and time from admission to testing were recorded. A positive HsTnT value was considered as one higher than 14 ng/L.⁴⁰ HsTnT was assayed using Elecsys (Roche Diagnostics International Ltd.) that fulfilled the guidelines of the American College of Cardiology/European Society of Cardiology in achieving a coefficient of variation less than 10% at the 99th percentile upper reference limit of a reference population.²¹

Collected data included patient demographics, mechanism of injury, vital signs, type of injury, Abbreviated Injury Scale (AIS) score, Glasgow Coma Scale (GCS) score, Injury Severity Score (ISS), neurosurgical interventions, pneumonia, sepsis and acute respiratory distress syndrome, ventilator days, and ICU/hospital length of stay. The primary clinical outcome was designated as all-cause in-hospital mortality.

TBI was diagnosed based on clinical and CT scanning examination results and was identified following the Centers for Disease Control and Prevention case definition (ICD-9-CM code 800.0–801.9, 803.0–804.9, 850.0–854.1,

950.1–950) and the Association for the Advancement of Automotive Medicine AIS 2005 updated in 2008.

Injuries were classified based on GCS scores as mild (13–15 points), moderate (9–12), and severe (3–8). The head AIS score was used to categorize injuries as mild to moderate (1–2 points), serious (3 points), severe (4 points), critical (5 points), and lethal (6 points).³³

Statistical Analysis

Data are presented as proportions, medians (interquartile range [IQR] or minimum–maximum range), or mean (SD). Patients were categorized into one of 2 groups based on their serum HsTnT status (negative vs positive results). To avoid selection bias, patients who did not undergo HsTnT screening were further subanalyzed and compared with the negative and positive HsTnT groups. Differences between categorical variables were analyzed using the chi-square or Fisher's exact test, and the Student t-test or 1-way ANOVA was performed to compare continuous variables. Multiple comparisons were performed with Bonferroni correction. For nonparametric analysis, the Kruskal-Wallis test was performed. The Pearson correlation coefficient was calculated between groups with respect to serum HsTnT values, head AIS score, ISS, and GCS score.

Multivariate logistic regression models were performed to identify predictors of mortality in the entire cohort and after excluding chest injury cases. All calculations were adjusted for potential covariates that showed relevant and significant association in univariate analysis. Data are expressed as odds ratios with the corresponding 95% confidence intervals. Receiver operating characteristic curves were used to determine the sensitivity, specificity, and cut-off level of serum HsTnT to predict mortality.

Time to the earlier discharge from hospital or death was modeled using Cox proportional hazard models to describe the relationship between HsTnT and in-hospital mortality. Hazard ratios (HRs) based on the diagnostic and prognostic cutoff levels of HsTnT were calculated. All hypothesis testing was 2-tailed, and any value of $p < 0.05$ was considered statistically significant. Data analysis was performed using SPSS version 18 (SPSS Inc.).

Results

Study Population

During the study period, 826 patients sustained TBI and required endotracheal intubation. Of these patients, 490 underwent serum HsTnT testing. Positive HsTnT results were found in 322 (65.7%) patients. The mean time from admission to the initial troponin test was 4.3 hours. When compared with patients who had negative HsTnT results, patients with positive test results were, on average, 3 years older and more frequently involved in motor vehicle crashes (50.3% vs 36.9%, $p = 0.001$) and ejections from the vehicle (19.2% vs 12.7%, $p = 0.01$).

Clinical Presentations

Table 1 lists the clinical presentation, type of TBI lesion, complications, and outcomes in patients with negative and positive HsTnT results. Patients with a positive HsTnT result were more likely to be intubated at the scene ($p =$

TABLE 1. Patient demographics, clinical characteristics, lesion type, complications, and outcomes in intubated TBI patients based on the serum HsTnT result

Variable	Overall (n = 490)	Negative (n = 168)	Positive (n = 322)	p Value
Age in yrs, mean (SD)	30.5 ± 13.3	28.4 ± 12.6	31.6 ± 13.5	0.01
Male, %	93.9	93.5	94.1	0.77
MVC, %	45.7	36.9	50.3	0.001
Fall from height, %	22.0	29.9	18.3	0.001
EMS time in mins, mean (SD)	66 ± 34	64 ± 40	67 ± 29	0.32
SBP at scene in mm Hg, mean (SD)	132 ± 31	132 ± 19	131 ± 36	0.77
GCS score at scene, mean (SD)	8.1 ± 3.9	9.97 ± 3.9	7.52 ± 3.8	0.001
SBP w/in 1 hr on ED arrival in mm Hg, mean (SD)	124 ± 29	132 ± 20	127 ± 27	0.02
GCS score in ED, mean (SD)	5.4 ± 3.8	7.7 ± 4.6	5.04 ± 3.6	0.001
Isolated TBI, %	20.5	65.7	51.5	0.03
ISS, mean (SD)	25.8 ± 9.8	20.8 ± 8.4	27.5 ± 10	0.001
Polytrauma, %	86	73.7	91	0.001
Chest injury, %	47.6	32.1	55.6	0.001
Head AIS score, mean (SD)	3.9 ± 1.1	3.7 ± 0.9	4.07 ± 1.1	0.004
Head AIS score >3, %	60	53	64	0.02
Chest AIS score, mean (SD)	2.8 ± 0.62	2.8 ± 0.63	2.8 ± 0.62	0.88
Pelvis AIS score, mean (SD)	2.18 ± 0.43	2.13 ± 0.35	2.19 ± 0.45	0.65
LVEF %, mean (SD)	53 ± 8	59 ± 5	53 ± 8	0.27
Intubated at scene, %	48.0	33.5	55.5	0.001
Ventilatory days, median (range)	5 (1–32)	3 (1–20)	6 (1–32)	0.001
ICU LOS in days, median (range)	10 (1–126)	7 (1–31)	11 (1–126)	0.001
Hospital LOS in days, median (range)	16 (1–304)	14.5 (1–223)	19 (1–304)	0.009
HsTnT in ng/L, median (range)	29 (10–111)	7 (4–10)	74 (30–241)	0.001
Skull fracture, %	61.8	57	64.3	0.12
Brain contusion, %	55.1	59.5	52.8	0.15
IVH, %	8.2	4.8	9.9	0.04
Brain edema, %	32.7	23.2	37.6	0.001
DAI, %	14.1	10.7	15.8	0.12
EDH, %	18.4	22	16.5	0.13
SDH, %	32	34	31	0.51
SAH, %	34.3	30.4	36.6	0.18
Surgical intervention, %	19.2	25.6	15.8	0.009
Pneumonia, %	36.5	28.6	40.7	0.008
Acute respiratory distress syndrome, %	4.1	3	4.7	0.37
Sepsis, %	13.3	8.9	15.5	0.04
In-hospital mortality, %	25.9	8.3	35.1	0.001

DAI = diffuse axonal injury; ED = emergency department; EDH = epidural hematoma; EMS = emergency medical services; IVH = intraventricular hemorrhage; LOS = length of stay; LVEF = left ventricular ejection fraction; MVC = motor vehicle crash; SAH = subarachnoid hemorrhage; SDH = subdural hematoma.

0.001) and to have chest injuries ($p = 0.001$), severe head injuries ($p = 0.02$), higher mean ISS ($p = 0.001$), greater head AIS score ($p = 0.004$), lower GCS score ($p = 0.001$), and lower systolic blood pressure (SBP) after hospital arrival ($p = 0.02$) than those with a negative test result. SBP at the scene and emergency medical services time (i.e., the time between arriving at the scene to admission), and chest AIS score, were comparable between the 2 groups. Transthoracic echocardiography examination data were captured in 48 cases, and the left ventricular ejection fraction was comparable between the 2 groups.

Hospital Course

Patients with positive HsTnT results remained mechanically ventilated for a longer duration than those with negative HsTnT results ($p = 0.001$). Also, patients with positive HsTnT results had a longer hospital stay ($p = 0.009$) and higher rates of pneumonia ($p = 0.008$) and sepsis ($p = 0.04$) while in the hospital.

HsTnT and Type of TBI Lesion

The group of patients with positive HsTnT results had

TABLE 2. Correlations between HsTnT, ISS, Head AIS score, and GCS score

Variable	HsTnT	GCS Score at Scene	Head AIS Score	ISS
HsTnT				
Pearson correlation	1	-0.231*	0.186*	0.147*
p value		0.001	0.001	0.001
No. of patients	490	418	486	488
ISS				
Pearson correlation	0.147*	-0.295*	0.611*	1
p value	0.001	0.001	0.001	
No. of patients	488	685	806	814
Head AIS				
Pearson correlation	0.186*	-0.289*	1	0.611*
p value	0.001	0.001		0.001
No. of patients	486	689	818	806
HsTnT w/ ISS <16				
Pearson correlation	1	-0.323†	0.757*	1
p value		0.016	0.001	
No. of patients		55	70	
HsTnT w/ ISS ≥16				
Pearson correlation	1	-0.216*	0.114†	1
p value		0.001	0.020	
No. of patients		361	414	

* Correlation is significant at the 0.01 level (2-tailed).

† Correlation is significant at the 0.05 level (2-tailed).

a higher proportion of brain edema ($p = 0.001$), intraventricular hemorrhage ($p = 0.04$), and neurosurgical interventions ($p = 0.009$). One-fifth of the cases had isolated TBI; of them, 51.5% had positive HsTnT findings.

HsTnT and Injury Severity

Table 2 demonstrates a positive correlation between HsTnT and head AIS score ($r = 0.19$, $p = 0.001$) and a negative correlation with GCS score ($r = -0.23$, $p = 0.001$). A significant correlation was shown between ISS and head AIS score ($r = 0.61$, $p = 0.001$). Further analysis was performed based on the ISS values. HsTnT correlated significantly with head AIS scores in patients with ISS less than 16 ($r = 0.76$, $p = 0.001$).

Based on the initial GCS categories (severe, moderate, and mild), the proportions of patients with positive HsTnT findings were 60.6%, 26.2% and 13.3%, respectively. Table 3 shows the median (IQR) of HsTnT values based on the GCS and head AIS categories and type of TBI lesion. According to the head AIS categories, the median (IQR) HsTnT level was directly proportional to injury severity. The presence of IVH, brain edema, or diffuse axonal injury (DAI) was associated with the highest HsTnT values ($p = 0.001$).

TBI Patients Without Troponin Testing

Serum HsTnT was not measured in 336 patients (Fig. 1). Patients who did not undergo troponin testing were, on average, 3 years younger and had significantly lower ISSs

TABLE 3. Summary of the HsTnT levels according to TBI severity, type of lesions, and outcome

Variable	HsTnT Value (ng/L)
GCS score	
13–15 (mild)	14 (9–33)
9–12 (moderate)	28 (9–85.5)
3–8 (severe)	48 (16–207)
p value	0.001
Head AIS score	
1–2 (mild-moderate)	16 (7–103)
3 (serious)	19 (9–83)
4 (severe)	28 (11.5–100)
5 (critical)	36 (12–185)
6 (lethal)	451 (162–1192)
p value	0.002
Multiplicity	
Isolated TBI	16.5 (7–49)
Polytrauma TBI	44 (13–147)
p value	0.001
TBI lesion	
IVH	54 (14–194)
Brain edema	48 (14–275)
DAI	36 (13–250)
SAH	28.5 (8–113)
SDH	25 (9–88)
Brain contusion	20 (9–94)
EDH	17.5 (9–57)
p value*	0.001
Outcome	
Alive	18 (9–63)
Deceased	121 (32–549)
p value	0.001
Day of death	
w/in 2 days	128 (47–219)
w/in 3–7 days	160 (41–659)
After 7 days	61 (25–476)
p value	0.013

Non-p values are presented as the median (IQR).

* Comparisons were performed by nonparametric tests.

and head AIS scores and higher GCS scores on admission than those who had positive HsTnT findings (Supplementary Tables 1 and 2). Also, a smaller proportion of these patients had chest injury, underwent surgical intervention, and died than those who had positive HsTnT findings.

All-Cause In-Hospital Mortality

Among patients who were screened for HsTnT, 127 died in the hospital. The in-hospital mortality rate was 4 times higher in patients with positive HsTnT results than those who had negative HsTnT results (35.1% vs 8.3%, $p = 0.001$). Positive HsTnT results were associated with an 8-fold increase in mortality in patients with isolated head injury, after adjusting for age and head AIS score (adjusted

FIG. 1. Flowchart of the study design. Figure is available in color online only.

OR 7.6, 95% CI 1.22–46.90; $p = 0.030$). In polytrauma patients, positive HsTnT results were associated with a 5-fold increase in mortality (adjusted OR 4.64, 95% CI 2.30–9.36; $p = 0.001$). HsTnT values were higher in the deceased patients than in the survivors ($p = 0.001$). Patients who died after the 1st week had lower HsTnT values than those who died within the first 7 days (Table 3).

Multivariate Logistic Regression Analysis

A positive HsTnT result was found to be an independent predictor of mortality after adjusting for age, ISS, SBP, GCS score, head AIS score, brain edema, intraventricular hemorrhage, neurosurgical interventions, and sepsis (adjusted OR 3.10, 95% CI 1.308–7.351; $p = 0.01$). A second regression analysis utilizing the same covariates showed that the effect of a positive HsTnT result on the in-hospital mortality persisted after excluding chest injury (adjusted OR 4.18, 95% CI 1.320–13.231; $p = 0.01$) (Fig. 2).

Area under the curve analysis showed the utility of serum HsTnT in the prediction of all-cause mortality (area under the curve 0.75, 95% CI 0.699–0.801, $p = 0.001$) with a cutoff level of 26.5 ng/L at 80% sensitivity and 60% specificity (Fig. 3).

FIG. 2. Multivariate logistic regression analysis for predictors of in-hospital all-cause mortality in intubated TBI patients with (left) and without chest injury (right). Hge = hemorrhage.

FIG. 3. Receiver operating characteristic and area under the curve analysis of the utility of serum HsTnT in the prediction of all-cause mortality. Area under the curve 0.75, 95% CI 0.699–0.801, $p = 0.001$, with HsTnT cutoff for mortality 26.5 ng/L at sensitivity 80% and specificity 60%. Figure is available in color online only.

Time to Discharge or Death Analysis

To explore the association of HsTnT levels with in-hospital mortality, HsTnT was categorized based on the diagnostic and prognostic cutoff points into 3 groups based on the ROC result as follows: negative results (< 14.00 ng/L), positive results (14–26.49 ng/L), and very highly positive results (≥ 26.50 ng/L). In these 3 groups, the mortality rates were 9%, 15%, and 40%, respectively ($p = 0.001$). Cox regression models for each HsTnT level group showed that only HsTnT values ≥ 26.5 ng/L had a significant association with time to hospital mortality, with an unadjusted HR of 4.67 (95% CI 2.67–8.18). Even after adjustment for

FIG. 4. Cox proportional hazard models of the relationship between HsTnT levels and in-hospital mortality with the unadjusted (left) and adjusted (right) hazard ratios. Figure is available in color online only.

age, GCS score and head AIS score, the HR remained significant at 2.44 (95% CI 1.35–4.42; Fig. 4).

Discussion

This is a unique study in which we have evaluated the predictive value of serum HsTnT in intubated TBI patients. In this study, positive HsTnT results were associated with a higher rate of hospital complications and a 3- to 4-fold increased risk of mortality regardless of the relevant covariates. Moreover, positive HsTnT results were found to correlate well with the severity of head injury, and this correlation was evident irrespective of the patient's ISS.

Salim et al.³² studied the conventional troponin I assay in 420 patients with severe blunt TBI. In that study, 125 (30%) patients had elevated serum troponin on admission; of these, 55 (44%) patients died. During the hospital course, serial troponin tests (up to 48 hours) revealed an additional 48 (11.4%) patients with elevated values; of these patients, 28 (58%) died. Moreover, the investigators found a positive correlation between troponin values and head AIS score. In contrast to the study by Salim et al., patients in the present study were 13 years younger, and positive HsTnT test results were found in two-thirds of these patients during initial testing. Our study showed that the median HsTnT values differed according to the type of brain lesion and the time to death, a finding that has not been previously addressed. The highest HsTnT levels were found in those who died during the 1st week after trauma and in those who had intraventricular hemorrhage, brain edema, and DAI. In our cohort, a serum HsTnT value of 26.50 ng/L or higher was an independent predictor of in-hospital mortality.

To avoid selection bias, a subanalysis including patients who did not undergo HsTnT testing had a hospital mortality rate of 28.6% in comparison with 8.3% in those who had negative results and 35% in those who had positive HsTnT results. This finding supports the need for early troponin testing in all TBI cases, whenever possible.

In our cohort, the severity of chest injury (mean chest AIS score) was comparable between the groups with negative and positive HsTnT findings. In the multivariate analysis, the impact of a positive HsTnT result on the overall mortality persisted, even after excluding cases with associated chest injuries.

Hays and Diringer¹⁷ found that positive troponin I results were associated with higher mortality in patients with spontaneous intracerebral hemorrhage. Notably, the investigators excluded patients with recent stroke or myocardial ischemia from their analysis. Moreover, in patients with intracerebral hemorrhage who underwent surgery, the troponin level on admission was a significant risk of in-hospital mortality, even after adjusting for age, sex, and the volume of hemorrhage.¹⁴ Miketic et al.²⁶ added that positive serum troponin findings in patients with aneurysmal subarachnoid hemorrhage were directly proportional to the severity of hemorrhage and independently predicted poor functional recovery.

Prior studies have shown that the prevalence of positive troponins (TnT or TnI) was similarly greater in critically ill patients, even in the absence of coronary artery disease (approximately 45% for each assay); however, it could reach 62% with the use of HsTnT assaying.^{1,24}

Serum HsTnT assaying is not only associated with higher sensitivity and specificity for myocardial injury than the

TABLE 4. Review of literature for brain injury, cardiac troponin with or without the usage of BBs

Authors & Year	Study Duration (yrs)	Study Design* & Population	Type of Troponin	BBs Used	Key Findings
Cai et al., 2016	6.5	580 TBI pts; 30.9% had detectable TnI w/in 24 hrs of admission	TnI	No	Pts w/ highest TnI (≥ 0.21 ng/ml) had significantly higher risk of in-hospital mortality (HR 1.39, 95% CI 1.04–1.88) compared w/ pts w/ undetectable TnI; mortality risk increased w/ higher troponin levels ($p < 0.0001$)
Hays & Diringier, 2006	4	235 pts w/ intracranial hemorrhage	TnI	No	Mortality was higher in the 18% w/ a peak TnI level >0.4 ng/ml (58 vs 34%, $p = 0.009$) & having elevated TnI was an independent predictor of in-hospital mortality ($p = 0.023$)
Ramappa et al., 2008		83 pts w/ SAH	TnI	No	Pts w/ abnormal TnI were more likely to die (55% vs 27%); on multivariate analysis, peak TnI ($p = 0.04$) & admission GCS score <12 ($p=0.02$) were independent predictors of death
Ko et al., 2016	2.5	440 pts w/ moderate/severe TBI; early BB administration to 109 pts	None	Yes	Early administration of propranolol was independently associated w/ lower mortality (aOR 0.25, $p = 0.012$)
Mohseni et al., 2015	5	874 isolated severe TBI pts; 33% were exposed to BB	None	Yes	Crude mortality was higher in pts w/o BBs (17% vs 11%, $p = 0.007$); after adjustment for significant confounders, pts not exposed to BB had a 5-fold increased risk of in-hospital mortality
Bukur et al., 2012	11.5	2446 pts w/ isolated blunt head injury	None	Yes	When stratified by race, only Asian & Hispanic descent demonstrated significantly improved outcomes associated w/ BB use
Cotton et al., 2007	1.25	420 pts w/ severe TBI; of these, 174 pts exposed to BB	None	Yes	Mortality was lower in BB group (5.1% vs 10.8%; $p = 0.036$); adjusted incidence rate ratio of mortality among pts exposed to BB was 0.29
Inaba et al., 2008	7.5	1156 pts with isolated head injury; of these, 18% received BB	None	Yes	BB use was an independent protective factor for mortality (aOR 0.54, 95% CI 0.33–0.91; $p = 0.01$); on subgroup analysis, elderly pts w/ severe TBI on BB had lower mortality (28% vs 60%)
Salim et al., 2008	7	420 severe blunt TBI pts who had serial TnI measurements during the 1st 24–48 hrs of admission	TnI	Yes	After adjusting for injury severity, elevated TnI was an independent predictor for mortality (OR 8.5, 95% CI 3.46–22.15; $p < 0.0001$); BB use was associated w/ a significant survival advantage (OR 0.38, 95% CI 0.15–0.87; $p = 0.03$) in TBI pts w/ any elevation of TnI
Lippi et al., 2013	NA	42 pts w/ mild TBI & tested for HsTnI w/in 1st 3 hrs†	HsTnI	No	Median HsTnI value was >2 -fold higher in pts w/ positive CT than in those w/ negative CT ($p = 0.003$)

aOR = adjusted OR; NA = not available; pts = patients.

* All studies were retrospective with the exception of the study by Lippi et al.

† Cross-sectional study.

conventional assaying, but also it allows injury detection in a shorter timespan (within 3 hours).^{3,21,31,41} The presence of low serum troponin concentration in healthy individuals has not yet been explained.^{10,15}

Detection of serum troponin at low concentrations is not necessarily indicative of myonecrosis; it may merely reflect increased cell wall permeability with stress as well as the production of membranous blebs containing troponins.³⁸ Moreover, positive HsTnI findings in noncoronary diseases were found to be associated with a 23% greater risk of death than negative test findings in the medical ICU.²⁹

In a small cohort of patients ($n = 42$) with only mild TBI, high-sensitivity troponin I (HsTnI) values were significantly greater in patients who had positive CT findings of TBI than in those with negative CT findings (63% vs 21%, $p = 0.001$).²² However, in that study, the authors did not report on the patients' hospital course or outcomes.

To understand the mechanism of myocardial injury after noncardiac trauma, it has been postulated that abrupt cerebral insults initiate a cascade of acute inflammatory responses and activation of the autonomic nervous system, resulting in an excessive release of catecholamines. This

catecholamines surge has deleterious effects on various body organs, including myocardial cells.^{3,6,23,25} Prior data showed that plasma and urinary catecholamine levels increased substantially after head injury.⁶

After traumatic injury, serum troponin positivity is multifactorial. It could be related to direct cardiac contusion, stress-induced high catecholamine effects, microthrombosis, stress-induced cardiomyopathy, vascular spasm, coagulopathy, myocardial ischemia, sepsis, or false interpretation.

From the therapeutic point of view, few studies have investigated the use of beta blockers (BBs) in patients with TBI, of which only one study retrospectively evaluated the use of BBs in a link with the troponin I assay result (Table 4).^{5,6,8,17,19,20,22,27,30,32} These studies showed favorable outcomes in those who received early BBs after TBI. Notably, BBs protect all end organs that are prone to damage caused by the TBI-induced catecholamine surge.² Salim et al. found an absolute risk reduction of 26% in patients with severe TBI who were on a regimen of BBs and particularly in those who had positive troponin findings.³² None of our cases were found to follow a BBs therapy protocol. How-

ever, our findings could be an initiative for further studies to adopt the use of BBs, if there are no contraindications, in TBI patients based on the result of the HsTnT test at the time of admission.

Limitations

The retrospective design of the present study could be a limitation to fill gaps and generalize the results. Although in this study a large number of patients had positive results for HsTnT, the exact clinical rationale in ordering these tests was not clearly given in the trauma database. Furthermore, the study could have a selection bias, as the troponin test was not performed in all patients. However, we analyzed the data of patients tested for HsTnT in comparison with those who were not tested, as shown in Fig. 1 and Supplementary Tables 1 and 2. We believe that trends of troponin levels within the initial postinjury days may give a better understanding. However, testing the HsTnT level could overcome this limitation, as it accurately identifies positive cases within the first 3 hours postinjury and can effectively rule out myocardial injury with a single blood draw in low-risk patients.^{2,7,41}

The role of inotropes was not addressed because the data were not fully available. Preexisting cardiac diseases and electrocardiographic findings were not captured in the registry database, which could be a confounder. However, the relatively young age of our cohort could preclude the likelihood of overt coronary artery disease. Moreover, abnormal findings on electrocardiography alone might not be considered as an indicator of cardiac cell injury in the absence of troponin release; it may merely reflect a transient neurogenic myocardial dysfunction. Furthermore, transthoracic echocardiography data were available for only 48 cases, and there were no coronary angiographic data. However, echocardiography is often not feasible in patients with moderate to severe TBI. Follow-up for long-term outcomes and disabilities were also lacking.

Conclusions

Positive results for serum HsTnT are associated with poor outcomes in intubated patients with TBI. The serum HsTnT level correlates with the severity of head injury and could be used for early risk stratification and to expedite care and prognosis in this subset of the TBI population. We recommend measuring serum HsTnT levels in patients with TBI for better patient triage, monitoring, and management. Further prospective studies are warranted to support our finding to accurately explain the cause of troponin release and to show whether this cardiac marker can be used as a predictor of clinical outcomes and type of lesion in patients with TBI.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: El-Menyar, Asim. Acquisition of data: El-Menyar, Asim, Al-Thani. Analysis and interpretation of data: El-Menyar, Bingdiwala. Drafting the article: all authors. Critically revising the article: El-Menyar, Latifi, Al-Thani. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: El-Menyar. Statistical analysis: Bingdiwala. Administrative/technical/material support: Asim. Study supervision: El-Menyar.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Tables 1 and 2. <https://thejns.org/doi/suppl/10.3171/2017.7.JNS17675>.

Previous Presentations

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