

Echocardiogram Utilization Patterns and Association With Mortality Following Severe Traumatic Brain Injury

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BACKGROUND: Severe traumatic brain injury (TBI) can result in left ventricular dysfunction, which can lead to hypotension and secondary brain injuries. Although echocardiography is often used to examine cardiovascular function in multiple clinical settings, its use and association with outcomes following severe TBI are not known. To address this gap, we used the National Trauma Data Bank (NTDB) to describe utilization patterns of echocardiography and examine its association with mortality following severe TBI.

METHODS: A retrospective cohort study was conducted using a large administrative trauma registry maintained by the NTDB from 2007 to 2014. Patients >18 years with isolated severe TBI, and without concurrent severe polytrauma, were included in the study. We examined echocardiogram utilization patterns (including overall utilization, factors associated with utilization, and variation in utilization) and the association of echocardiography utilization with hospital mortality, using multivariable logistic regression models.

RESULTS: Among 47,808 patients, echocardiogram was utilized as part of clinical care in 2548 patients (5.3%). Clinical factors including vascular comorbidities and hemodynamic instability were associated with increased use of echocardiograms. Nearly half (46.0%, 95% confidence interval [CI], 40.3%–51.7%) of the variation in echocardiogram utilization was explained at the individual hospital level, above and beyond patient and injury factors. Exposure to an echocardiogram was associated with decreased odds of in-hospital mortality following severe TBI (adjusted odds ratio [OR] = 0.77; 95% CI, 0.69–0.87; $P < .001$).

CONCLUSIONS: Echocardiogram utilization following severe TBI is relatively low, with wide variation in use at the hospital level. The association with decreased in-hospital mortality suggests that the information derived from echocardiography may be relevant to improving patient outcomes but will require confirmation in further prospective studies. (Anesth Analg XXX;XXX:00–00)

KEY POINTS

- **Question:** What is the rate of utilization of echocardiogram in patients with isolated severe traumatic brain injury (TBI) and are there any associations between echocardiogram utilization and clinical outcomes?
- **Findings:** The utilization of echocardiogram in patients with isolated TBI is 5.3% and is associated with decreased odds of in-hospital mortality.
- **Meaning:** The utilization rate of echocardiogram in patients with isolated TBI is low, and the association with decreased in-hospital mortality suggests that the use of echocardiography may be protective but will require confirmation in further studies.

GLOSSARY

AIAN = American Indian or Alaskan Native; **AIS** = abbreviated injury score; **APACHE** = Acute Physiology and Chronic Health Evaluation; **CAD** = coronary artery disease; **CEM** = coarsened exact matching; **CHF** = congestive heart failure; **CI** = confidence interval; **CPR** = cardiopulmonary resuscitation; **DAG** = directed acyclic graph; **ECG** = electrocardiogram; **GCS** = Glasgow Coma Scale; **HR** = heart rate; **ICC** = intraclass correlation coefficient; **ICD** = *International Classification of Disease*; **IRB** = institutional review board; **ISS** = injury severity score; **LV** = left ventricular; **MI** = myocardial infarction; **MVT** = motor vehicle trauma; **NTDB** = National Trauma Data Bank; **OR** = odds ratio; **PAD** = peripheral arterial disease; **POCUS** = point-of-care ultrasound; **PVD** = peripheral vascular disease; **RAM** = risk adjustment model; **SBP** = systolic blood pressure; **SD** = standard deviation; **SOFA** = sequential organ failure assessment; **STROBE** = Strengthening the Reporting of Observational Studies in Epidemiology; **TBI** = traumatic brain injury; **TTE** = transthoracic echocardiogram

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DOI: 10.1213/ANE.00000000000005110

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Traumatic brain injuries (TBI) occur in 1.7 million people annually in the United States, resulting in 275,000 hospitalizations and 52,000 deaths.¹ Initial traumatic injury in TBI is hypothesized to activate multiple catecholamine release pathways,² which results in a catecholamine excess that can affect multiple organ functions, including the cardiovascular system. These effects can result in left ventricular (LV) dysfunction, electrocardiogram (ECG) changes, and arrhythmia,³ as well as potential secondary brain injuries.⁴

One of the most common and readily available procedures to evaluate cardiovascular function is an echocardiogram, which can help diagnose early cardiac dysfunction resulting from severe TBI.^{5,6} While utilization of echocardiography in the care of severe TBI patients may theoretically help clinicians personalize hemodynamic management, improve cerebral perfusion, and possibly prevent secondary brain injuries, there is a gap in the literature regarding utilization characteristics of echocardiography and its association with clinical outcomes in patients with severe TBI. To address this gap, we examined the National Trauma Data Bank (NTDB) to describe utilization patterns of echocardiogram following severe TBI, as well as to examine the association of echocardiogram utilization with in-hospital mortality following isolated severe TBI.

METHODS

This study was exempt from institutional review board (IRB) review given the fully deidentified nature of the NTDB dataset, and the requirement for written informed consent was waived by IRB at Duke University. We conducted a retrospective cohort study using a large administrative trauma registry maintained by the NTDB from 2007 to 2014. Deidentified administrative data from the NTDB includes data about trauma patients and facility characteristics, including demographics, injury information, procedures, and outcomes. This manuscript adheres to the applicable Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Population

Patients >18 years with isolated severe TBI (Glasgow Coma Scale [GCS] ≤8 and head abbreviated injury score [AIS] ≥4) without concurrent severe polytrauma were included in the final analysis.⁷ We restricted our cohort to patients >18 years to examine echocardiogram utilization for the management of head trauma,

while also evaluating preexisting comorbid conditions, which are prevalent in the elderly TBI population.⁸ We also restricted our cohort to isolated severe TBI by excluding patients with severe polytrauma, defined as an AIS >2 in a nonhead body region; this was done to focus our analysis on echocardiogram utilization for the management of severe head trauma itself, rather than for confounding nonhead injuries.

Exposures, Outcomes, and Covariates

To ascertain possible factors associated with transthoracic echocardiogram (TTE) utilization, our exposures included a priori variables that could plausibly be associated with cardiac dysfunction and echocardiogram utilization based on prior literature and expert opinion.^{9–13} The primary outcome was echocardiogram utilization, as ascertained by *International Classification of Disease (ICD-9)* procedure code 88.72 (diagnostic ultrasound of the heart), which includes both transthoracic and transesophageal echocardiogram. For the analysis of clinical outcomes, echocardiogram utilization was the primary exposure and in-hospital mortality was the primary outcome; as a secondary outcome, we considered a composite of in-hospital mortality or discharge destination of “hospice.” Covariates considered in models examining factors associated with echocardiogram utilization and examination of hospital mortality included demographic characteristics (age, gender, race/ethnicity, insurance status), time (cohort year), clinical characteristics (admission GCS, admission AIS, injury severity score [ISS], admission systolic blood pressure [SBP], hypotension [admission SBP <90 mm Hg], admission heart rate), vascular comorbidities (history of myocardial infarction [MI], angina, diabetes, peripheral vascular disease, or prior stroke), prehospital cardiopulmonary resuscitation, need for mechanical ventilation, and facility characteristics (US census region, hospital bed size, hospital teaching status, trauma center designation). Time to echocardiogram was ascertained using time stamps provided in the NTDB procedure file.

Statistical Analysis

Descriptive statistics were used to examine demographic, clinical, and facility characteristics of the cohort, stratified by exposure versus lack of exposure to echocardiogram during the hospitalization. We examined factors associated with echocardiogram utilization using multilevel, mixed-effects logistic regression, with hospital as a random intercept, to account for clustering. The model’s intraclass correlation coefficient (ICC) was used to examine the percentage of variation in utilization at the level of the individual hospital—in other words, variation at individual hospitals, above and beyond patient-specific factors. The following factors were considered in the model: age,

Accepted for publication June 30, 2020.

Funding: National Institutes of Health (NIH) Grant no.: K23NS109274 (V.K.).

The authors declare no conflicts of interest.

Reprints will not be available from the authors.

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gender, race/ethnicity, GCS, ISS, injury year, admission blood pressure, admission heart rate, presence of vascular comorbidities, need for prehospital cardiopulmonary resuscitation (CPR), and facility characteristics (region, bed size, trauma designation, teaching status).

For examination of the association of exposure to echocardiogram with in-hospital mortality, we fit a multivariable logistic regression model. Analyses were controlled for a core list of risk adjustment variables needed for mortality studies using NTDB data as described previously¹⁴ and included age, GCS, ISS, hypotension, admission heart rate, and need for mechanical ventilation.

We performed an additional analysis that included these core variables with additional potentially relevant covariates selected through creating diagrams using directed acyclic graphs (DAG)¹⁵ to assist in selection of additional variables for the model including injury year, presence of vascular comorbidities, and exposure to prehospitalization CPR. An *E* value (the minimum strength of association of a possible unmeasured confounder to explain away the measured treatment-outcome association and reduce the odds ratio to 1.0) was calculated as a measure of residual confounding.^{16,17}

We performed sensitivity analyses to examine the robustness of our findings. First, we included terms for facility-level characteristics (level 1 trauma status, teaching status, and region) to the full DAG-driven model above. Second, since exposure to echocardiogram may potentially be at risk for confounding by indication (patients with more comorbidities may have been exposed to echocardiogram) and possibly biasing outcomes, we used a coarsened exact matching (CEM) technique¹⁸ to create matched cohorts of patients exposed and unexposed to early TTE and examined the association with in-hospital mortality. CEM was used to help to confirm the robustness of the findings of the multivariable models and aimed to provide improved balance between groups exposed and unexposed to echocardiography, through excluding patients without an appropriate match (based on covariate categories) between exposed and unexposed groups. CEM involved 4 steps: (1) the cohort was stratified by exposure to echo; (2) the cohort was matched within strata representing unique combinations of covariate categories from the risk adjustment model for hospital mortality,¹⁴ with any stratum being excluded (and the cohort pruned) if there were no patients exposed to echocardiogram; (3) available patients that were unexposed to echocardiogram were selected for matching, and weights were generated, so that covariate distributions of patients exposed and unexposed to echocardiogram was normalized; and (4) the matched cohort was used to fit a logistic regression model to examine the odds ratio

for in-hospital mortality. Finally, given that exposure to early TTE may theoretically offer the best opportunity to optimize hemodynamics and avoid secondary brain injuries following TBI, we reexamined outcomes but restricted the exposure to early (within 72 hours of hospitalization) echocardiogram. Based on a mortality prevalence of 0.30 in the control (unexposed) group and a clinically meaningful odds ratio of 0.9 for a mortality benefit of echocardiography, our sample size provided a power of >0.8 to examine this association. Given that additional models were performed as sensitivity analyses, no adjustments were made for multiple testing, and *P* values <.05 were considered significant. All analyses were performed using STATA 15.0 (StataCorp LLC, College Station, TX).

Table 1. Patient Demographic and Clinical Characteristics

Patient Factors	No Echocardiogram	Echocardiogram
No. of patients (N)	45,260	2548
Age (y)	50.2 ± 20.9	56.0 ± 20.1
Gender (N, %)		
Male	33,089 (73.2)	1732 (68.14)
Female	12,135 (26.83)	810 (31.86)
Race/ethnicity (N, %) ^a		
Caucasian	30,537 (67.5)	1847 (72.5)
AIAN	626 (1.4)	40 (1.6)
Asian	895 (2.0)	50 (2.0)
African American	4940 (10.9)	259 (10.2)
Hispanic	5120 (11.3)	169 (6.6)
Other	1888 (4.2)	113 (4.5)
Injury mechanism (%) ^a		
MVT (motorcyclist, cyclist, pedestrian, other)	11,608 (25.7)	591 (23.2)
Fall	20,533 (45.4)	1414 (55.5)
Firearm	2940 (6.5)	96 (3.8)
Pedal cyclist, pedestrian, other transport	2895 (6.4)	119 (4.7)
Struck	3741 (8.3)	128 (5.0)
Others	3543 (7.8)	200 (7.9)
Admission GCS (mean ± SD)	4.2 ± 1.75	4.2 ± 1.8
Head AIS score (mean ± SD)	4.2 ± 0.4	4.1 ± 0.4
Injury severity score (mean ± SD)	18.0 ± 8.8	17.5 ± 8.6
Mortality (%)	14,828 (32.8)	805 (31.6)
Payment (%) ^a		
Private/commercial	331 (0.73)	13 (0.5)
Medicare	4705 (10.4)	354 (13.9)
Medicaid	2310 (5.1)	109 (4.3)
Others	8332 (18.5)	409 (16.0)
Patient comorbidity (N, %)		
SBP (mean ± SD)	146.0 ± 33.8	145.4 ± 36
Admission HR	90.59 ± 26.4	92.7 ± 27.6
Vascular comorbidity (CHF, MI, CAD, PAD) (%)	3390 (7.5)	391 (15.4)
Prehospitalization CPR (%)	99 (0.2)	33 (1.5)

Abbreviations: AIAN, American Indian or Alaskan Native; AIS, abbreviated injury score; CAD, coronary artery disease; CHF, congestive heart failure; CPR, cardiopulmonary resuscitation; GCS, Glasgow Coma Scale; HR, heart rate; MI, myocardial infarction; MVT, motor vehicle trauma; NTDB, National Trauma Data Bank; PAD, peripheral arterial disease; SBP, systolic blood pressure; SD, standard deviation.

^aData reported in this table (for each variable) do not include patients with a missing value in the NTDB.

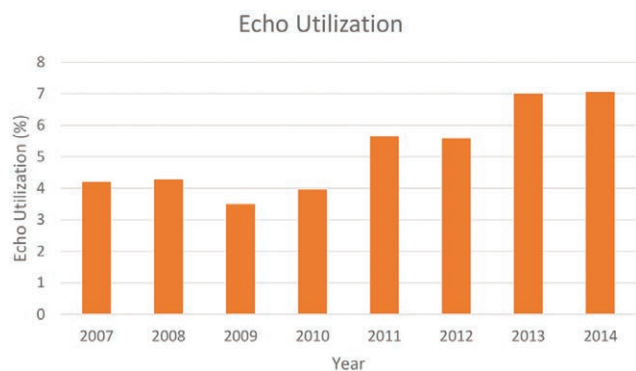


Figure. Echocardiogram utilization in severe TBI patients by year. TBI indicates traumatic brain injury.

RESULTS

Demographic, Clinical, and Facility Characteristics

Among a total of 47,808 patients included in the cohort, 2548 patients (5.3%) were exposed to an echocardiogram during their hospitalization. Demographic and clinical characteristics of the cohort are described and stratified by echocardiogram exposure status (Table 1). The distribution of patients across race/ethnicity was comparable between those who did and those who did not receive an echocardiogram. The average age of patients exposed and unexposed to echocardiogram was 56.0 ± 20.1 and 50.2 ± 20.9 years, respectively. Among patients who received an echocardiogram during the hospitalization, 68.1% were men and 31.9% were women; among patients who were unexposed to echocardiogram, 73.2% were men and 26.8% were women.

A higher percentage of patients exposed to echocardiogram had vascular comorbidities (15.4%) compared to patients unexposed to echocardiogram (7.5%). Among patients who were exposed to echocardiogram, 30% were treated in hospitals in the Northeast US census region, and only 10% were treated in hospitals in the West region. Among patients who were unexposed to echocardiogram, 15% were treated in the Northeast and 20% were treated in the West. Echocardiogram utilization was higher in 2014 (7.0%) compared to 2007 (4.2%; Figure). The distribution of both cohorts of patients across hospitals stratified by profit type and teaching status was comparable.

Factors Associated With Echocardiogram Utilization Following Severe TBI and Variation in Echocardiogram Utilization

We examined factors associated with echocardiogram utilization following severe TBI (Table 2). We found that age, time of injury (by year), presence of preexisting vascular comorbidities (MI, angina, diabetes, peripheral vascular disease, prior stroke), exposure to prehospital CPR, unstable admission vital signs (hypotension, tachycardia), and hospitalization at a level 1 trauma center

Table 2. Factors Associated With Echocardiogram Utilization in Severe TBI Patients^{a,b}

Factors	Odds Ratio (95% CI)	P
Age	1.01 (1.008–1.014)	<.001
Year ^c		
2011	1.64 (1.28–2.1)	<.001
2012	1.54 (1.29–2.11)	<.001
2013	2.22 (1.74–2.82)	<.001
2014	2.17 (1.71–2.77)	<.001
Hypotension	1.51 (1.19–1.92)	.001
Tachycardia	1.24 (1.12–1.38)	<.001
Vascular comorbidities	1.69 (1.46–1.95)	<.001
CPR	4.01 (2.39–6.74)	<.001
Region	Reference	
Northeast		
Midwest	0.39 (0.23–0.66)	<.001
West	0.32 (0.18–0.56)	<.001
South	0.34 (0.21–0.57)	<.001
Level 1	1.64 (1.22–2.21)	.001

Abbreviations: CHF, congestive heart failure; CI, confidence interval; CPR, cardiopulmonary resuscitation; GCS, Glasgow Coma Scale; HR, heart rate; ISS, injury severity score; MI, myocardial infarction; PVD, peripheral vascular disease; SBP systolic blood pressure; TBI, traumatic brain injury.

^aMultilevel, mixed-effects, logistic regression with the following covariates: age (years), gender, race/ethnicity, GCS, ISS, injury year (2007 as reference), admission hypotension (SBP <90 mm Hg), admission tachycardia (HR >100), presence of vascular comorbidities (CHF, MI/angina, diabetes, PVD, prior stroke), prehospital CPR, hospital region, bed size, level 1 trauma center designation, hospital teaching status.

^bOnly statistically significant associated factors are reported.

^c2007 is used as reference year for odds ratio.

Table 3. Association of Exposure to Echocardiogram and Hospital Mortality

	Odds Ratio (95% CI)	P
Primary model no. 1 ^a	0.77 (0.69–0.87)	<.001
Primary model no. 2 ^b	0.75 (0.67–0.85)	<.001
Sensitivity model no. 1 ^c	0.76 (0.67–0.85)	<.001
Sensitivity model no. 2 ^d	0.74 (0.67–0.85)	<.001
Sensitivity model no. 3 (CEM Pruned) ^e	0.81 (0.74–0.88)	<.001
Sensitivity model no. 4 (early echo [<72 h]) ^f	0.88 (0.78–0.99)	<.05
Sensitivity model no. 5 (early echo [<72 h]) ^g	0.86 (0.76–0.98)	<.05

Abbreviations: CEM, coarsened exact matching; CI, confidence interval; CPR, cardiopulmonary resuscitation; GCS, Glasgow Coma Scale; ISS, injury severity score; RAM, risk adjustment model.

^aPrimary model no. 1 (Haider et al,¹⁴ RAM) covariates: age, GCS, ISS hypotension, pulse, and need for mechanical ventilation.

^bPrimary model no. 2 covariates: all primary model covariates, with addition of injury year, vascular comorbidity, CPR.

^cSensitivity model no. 1: primary model no. 2 + facility covariates (level 1 status, teaching status, region).

^dSensitivity model no. 2 outcome: mortality as in-hospital deaths and all discharges to hospice.

^eCoarsened exact matching: weights generated for pruned cohort: total sample size of 31,271 patients (28,850 patients unexposed to echo and 2421 patients exposed to echo).

^fEarly echo model covariates (Haider et al,¹⁴ RAM): age, GCS, ISS hypotension, pulse, and need for mechanical ventilation.

^gEarly echo model outcome: mortality as in-hospital deaths and all discharges to hospice.

were associated with increased echocardiogram utilization. Relative to the Northeast, regions in the Midwest, West, and the South were associated with a decrease in echocardiogram utilization. Almost half of the variation in echocardiogram utilization was explained at

the hospital level, above and beyond patient factors (ICC = 46.0%, 95% confidence interval [CI], 40.3–51.7).

Association Between Exposure to Echocardiogram and Hospital Mortality

We examined the association between echocardiogram utilization and in-hospital mortality and found that exposure to echocardiogram was associated with decreased odds of in-hospital mortality among patients with isolated severe TBI (odds ratio [OR] = 0.77, 95% CI, 0.69–0.87, $P < .001$, E value 1.54; Table 3). We conducted multiple sensitivity analyses to analyze the robustness of this risk estimate. Using additional model covariates (OR = 0.75, 95% CI, 0.67–0.85; $P < .001$), CEM (OR = 0.81, 95% CI, 0.74–0.88; $P < .001$), and restricting to early (within 72 hours of admission) echocardiogram exposure (OR = 0.88, 95% CI, 0.78–0.99; $P < .05$), the finding of reduced odds of in-hospital mortality remained robust (Table 3).

DISCUSSION

Among patients with isolated severe TBI, we observed (1) overall echocardiogram utilization was low; (2) there was significant variation in echocardiogram utilization at the hospital level, above and beyond patient-level factors; and (3) exposure to echocardiogram was associated with reduced odds of in-hospital mortality following severe TBI. To our knowledge, this is the first study to examine utilization patterns of echocardiogram following severe TBI.

The echocardiogram utilization in patients following severe TBI from 2007 to 2014 was 5.3% (4.2% in 2007 and increasing to 7.0% in 2014). Current literature reports 15%–20% of patients develop systolic dysfunction or some hemodynamic instability following severe TBI,^{19,20} both of which can be indications for echocardiogram.²¹ An overall utilization rate of 5.3% is relatively low, given these common indications. This could be partially due to improved and more standardized shock management in the recent years,²¹ thus decreasing the practical need for early imaging and characterization of post-TBI cardiac dysfunction.

We examined factors associated with echocardiogram utilization and found that the presence of vascular comorbidities, unstable vitals on admission, treatment at a level 1 trauma center, and treatment in the Northeast region were associated with increased utilization of echocardiogram. Clinical factors such as vascular comorbidities and hemodynamic instability increase the probability of patients having indications for echocardiogram,¹³ leading to an expected rise in utilization in this group of patients. The increased rate of utilization associated with level 1 trauma centers and the Northeast region may be due to institutional, local practice, and regional cultural differences in hemodynamic management following TBI. Furthermore, we

found that nearly half (46.0%) of echocardiogram utilization variation was explained at the hospital level. This finding indicates that the admitting hospital itself plays an important role in determining whether a severe TBI patient will receive echocardiogram, above and beyond the patient's specific clinical factors. Currently, international severe TBI guidelines⁶ do not address the evaluation of cardiovascular function in severe TBI patients with shock; due to this lack of guidance, variation in echocardiogram utilization could be due to the differences in hospital culture and local practice guidelines.

We found that exposure to echocardiogram during the hospitalization was associated with decreased odds of in-hospital mortality following isolated severe TBI. No association between echocardiogram utilization and mortality has been previously reported in severe TBI patients, to the best of our knowledge. Although increased echocardiogram exposure was associated with patients who had more preexisting comorbidities, such patients still had improved outcomes after adjusting for additional clinical factors. This suggests that the information derived from an echocardiogram may possibly be protective, in that it was used to provide improved hemodynamic management to patients. Previous examination of echocardiogram utilization in broad settings revealed that about a third of echocardiogram examinations lead to a change in clinical management,²² with additional studies suggesting reduced mortality in specific clinical conditions (including acute MI, cardiac dysrhythmia, congestive heart failure [CHF], and sepsis).^{23,24} In the case of severe TBI, an echocardiogram may plausibly be obtained to diagnose and evaluate specific conditions such as systolic dysfunction and cardiogenic shock. In such cases, the use of echocardiogram could lead to change in vasopressor and fluids management, potentially leading to improved patient-level outcomes.²³ However, even given this biologically plausible rationale, our findings of reduced mortality in this observational study should be considered exploratory, interpreted with caution, and require confirmation in future studies.

There are several limitations to this study. First, because we relied on procedure codes for formal echocardiogram in this study of administrative data, we were unable to ascertain the use of bedside point-of-care ultrasound (POCUS) studies; therefore, it is possible that some patients in our cohort received a bedside-focused echocardiogram, without undergoing a full evaluation. There were also no further data available regarding the availability of POCUS studies and/or emergent echocardiogram at the institution level to help further understand the large amount of institutional-level variance. Second, the ICD-9 procedure code does not distinguish between transthoracic and transesophageal echocardiograms and therefore

both types were included in this study; however, in this critically ill setting, the majority of the echocardiograms conducted were likely transthoracic. Third, while our study hypothesis was that echocardiograms were ordered for hemodynamic evaluation in the setting of severe TBI, the reasons for echocardiogram were unknown in this administrative database; therefore, in some cases, imaging may have been ordered for reasons other than hemodynamic evaluation. Fourth, the NTDB does not provide data regarding findings of the echocardiograms performed, and therefore it was not possible to assess the impact on change in management due to these findings. Fifth, the NTDB does not provide data on ongoing hemodynamic monitoring and management such as inotrope and vasopressor utilization; therefore, it is not possible to determine how echocardiogram may have potentially mediated the association with reduced odds of in-hospital mortality. Sixth, in analyzing the association of exposure of echocardiogram with mortality, there may be a possibility of survivorship bias—certain patients who died may not have lived long enough to become exposed to echocardiogram. Finally, although this study utilized a comprehensive list of clinically relevant covariates and advanced matching techniques in sensitivity analyses, there is still the potential risk of residual confounding (eg, lack of detailed lab data, precluding calculation of sequential organ failure assessment [SOFA] or Acute Physiology and Chronic Health Evaluation [APACHE] scores), given the observational nature of our study and the limited granularity of the administrative data.

CONCLUSIONS

Echocardiogram utilization following severe TBI is relatively low, with wide variation in use at the hospital level. In exploratory analyses, exposure to echocardiogram was associated with reduced odds of mortality following severe TBI. Further studies are needed to confirm these findings, as well as to understand whether echocardiogram can contribute to enhanced hemodynamic management in severe TBI. ■■

DISCLOSURES

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