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# Use of Magnetic Resonance Imaging in Acute Traumatic Brain Injury Patients is Associated with Lower Inpatient Mortality

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### ABSTRACT

**Objectives:** While magnetic resonance imaging (MRI) has higher sensitivity than computed tomography for certain types of traumatic brain injury (TBI), it remains unknown whether the increased detection of intracranial injuries leads to improved clinical outcomes in acute TBI patients, especially given the resource requirements involved in performing MRI. We leveraged a large national patient database to examine associations between brain MRI utilization and inpatient clinical outcomes in hospitalized TBI patients.

**Material and Methods:** The National Inpatient Sample database was queried to find 3,075 and 340,090 hospitalized TBI patients with and without brain MRI, respectively, between 2012 and 2014 in the United States. Multivariate regression analysis was performed to independently evaluate the association between brain MRI utilization and inpatient mortality rate, complications, and resource requirements.

**Results:** The MRI group had a lower unadjusted mortality rate of 0.75% compared to 2.54% in the non-MRI group. On multivariate regression analysis, inpatient brain MRI was independently associated with lower mortality (adjusted OR 0.32, 95% CI 0.12–0.86), as well as higher rates of intracranial hemorrhage (adjusted OR 2.20, 95% CI 1.27–3.81) and non-home discharge (adjusted OR 1.33, 95% CI 1.07–1.67). Brain MRI was independently associated with 3.4 days (P < 0.001) and \$8,934 (P < 0.001) increase in the total length and cost of hospital stay, respectively.

**Conclusion:** We present the first evidence that inpatient brain MRI in TBI patients is associated with lower inpatient mortality, but with increased hospital resource utilization and likelihood of non-home discharge.

Keywords: Traumatic brain injury, Magnetic resonance imaging, Mortality, Outcome, Resource requirement

### INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death in the US, resulting in over 50,000 deaths annually among patients of all ages.<sup>[1]</sup> TBI also incurs high economic burden in the US, estimated at over \$10 billion for direct medical care and over \$60 billion for indirect expenditures annually.<sup>[2]</sup> While neuroimaging can be selectively utilized for patients with minor head injury,<sup>[3]</sup> it plays an essential role in acute moderate to severe TBI, providing assessment of the type, location, and severity of injury to guide medical and surgical treatment.

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Computed tomography (CT) is the primary imaging modality for evaluation of acute TBI, given its ability to detect clinically significant TBI with rapid scan time, wide availability, low cost, and few contraindications.<sup>[4]</sup> CT can show acute primary findings including hemorrhages, fractures, and foreign bodies, as well as secondary injuries such as cerebral edema, ischemia, and herniation.<sup>[5,6]</sup> In addition, CT-based scoring systems such as the Marshall Classification and Rotterdam Score can be used to predict mortality in acute TBI patients.<sup>[7]</sup> As a result, CT is widely implemented as the first-line screening study, obtained in over 80% of emergency department visits for head injury and in virtually all TBI patients requiring hospitalization.<sup>[8]</sup>

When magnetic resonance imaging (MRI) is used for evaluation of TBI, a recommended imaging protocol includes standard T1-weighted, T2-weighted, fluid-attenuated inversion recovery, and diffusion-weighted sequences, as well as a susceptibility-weighted or T2\*-weighted gradient echo sequence for detection of blood products.<sup>[9]</sup> The overall image acquisition takes approximately 20–25 min, and three-dimensional acquisitions are preferred for improved detection, localization, and characterization of small lesions.<sup>[10]</sup> Advanced MRI techniques such as perfusion imaging, diffusion tensor imaging, functional imaging, spectroscopy, and elastography are under active investigation but not in routine clinical use.<sup>[11]</sup>

The use of MRI is limited in acute TBI due to complex logistics, potential contraindications, and resource requirements.<sup>[4]</sup> A persistent neurological deficit not explained by CT is the main indication for MRI, as 30% of hospitalized TBI patients with normal CT can have abnormalities on MRI.<sup>[12]</sup> Specifically, MRI has higher sensitivity for certain types of traumatic injuries such as contusions, small hemorrhages, and axonal injuries.<sup>[4,6,7]</sup> MRI-based scoring methods such as the Firsching Score and Adams-Gentry Classification can also provide prognostic information in acute TBI patients.<sup>[13]</sup> Whether the additional information gained from MRI in acute TBI patients may lead to improved clinical outcomes, however, remains an important unanswered question given the cost and practical difficulties associated with performing MRI in hospitalized TBI patients.

To address this question, outcomes research is needed to determine the clinical benefits conferred by MRI and its resource requirements in acute TBI patients. Given the heterogeneity in patient management following TBI in hospitalized TBI patients across various practice settings,<sup>[14]</sup> a multi-institutional study design is preferred to gain generalizable insights into the clinical value of MRI. In this study, we leveraged a large national patient database to examine associations between brain MRI utilization and inpatient clinical outcomes in hospitalized TBI patients.

#### MATERIAL AND METHODS

#### **Study population**

The study was exempt from local Institutional Review Board approval due to the use of an anonymized public database. We conducted a retrospective cohort study using the National Inpatient Sample (NIS), a large database representing 20% of all inpatient admissions at non-federal hospitals in the United States.<sup>[15]</sup> Organized by the Agency for Healthcare Research and Quality, the NIS is based on International Classification of Diseases codes for both diagnoses and procedures. We used 3 years of data from 2012 to 2014, including over 21 million discharges from over 4,000 hospitals in 45 states.

We searched the NIS database to find a cohort of patients 18 years or older who were hospitalized with the principal diagnosis of TBI between 2012 and 2014. The patients were then stratified into those who underwent brain MRI during hospitalization and those without inpatient brain MRI. The baseline characteristics of the patients were obtained from the database with respect to gender, age, race, income, and insurance type, as well as hospital characteristics including hospital location, size, and teaching status. The presence of 15 different baseline comorbidities that may affect inpatient outcomes was also recorded.

#### Study outcomes

The primary outcome of the study was in-hospital mortality. The secondary outcomes were chosen to reflect two categories: inpatient complications and resource requirements. Inpatient complications included intracranial hemorrhage, tracheostomy, gastrostomy, and non-home discharge. Resource requirements were assessed based on the length of stay and total cost of hospitalization.

#### Statistical analysis

Stratification, clustering, and weighting were applied during analysis to accommodate the NIS design as described previously.<sup>[16]</sup> The baseline characteristics of the MRI and no MRI groups were compared using Chi-squared test for categorical variables and *t*-test for continuous variables. For each outcome, multivariable regression analysis was performed to isolate its association with brain MRI, using logistic regression for clinical outcomes and ordinary least squares linear regression for resource requirements. All statistical tests were performed using the weighted sample survey data analysis tool on Stata version 14 (StataCorp, College Station, TX).<sup>[17]</sup> Two-sided statistical tests with the alpha value of 0.05 were used throughout the study.

#### RESULTS

#### **Baseline characteristics**

A total of 3,075 patients in the MRI group and 340,090 patients in the no MRI group were included in the study [Table 1]. The patients in the MRI group were more likely to be women (P = 0.043), non-white (P = 0.005), earning higher income (P < 0.001), medically insured (P = 0.020), and admitted to a teaching hospital (P = 0.020) in the Northeast (P < 0.001). There was no significant difference in age between the two groups (P = 0.161). The baseline comorbidity profiles were overall similar between the two groups, except for higher rate of hypertension (P = 0.002) and lower rate of congestive heart failure (P = 0.004) in the MRI group.

#### **Clinical outcomes**

The MRI group had a lower unadjusted mortality rate of 0.75% compared to 2.54% in the non-MRI group [Table 2]. On multivariate regression analysis, inpatient brain MRI was independently associated with significantly lower mortality rate (adjusted OR 0.53, 95% CI 0.12–0.86, P = 0.024).

Regarding in-hospital complications, the unadjusted rate of intracranial hemorrhage was nearly twice in the MRI group (2.11%) compared to the no MRI group (1.14%). Slightly increased rate of non-home discharge was also observed in the MRI group (50.75% vs. 44.69%). On multivariate regression analysis, inpatient brain MRI was significantly associated with intracranial hemorrhage (adjusted OR 2.20, 95% CI 1.27–3.81, P = 0.005) and non-home discharge (adjusted OR 1.33, 95% CI 1.07–1.67, P = 0.012). There was no significant difference in the rates of gastrostomy (P = 0.093) or tracheostomy (P = 0.806) between the two groups.

#### **Resource utilization**

Unadjusted average length of stay was longer in the MRI group at 5.9 days compared to 3.9 days in the no MRI group [Table 3]. The average total cost of hospitalization was also higher at \$15,559 in the MRI group compared to \$10,633 in the non-MRI group. On multivariate regression analysis, brain MRI was independently associated with additional 3.4 days (95% CI 2.1 days-4.5 days, P < 0.001) and \$8,934 (95% CI \$5,031–\$12,848, P < 0.001) in the total length and cost of hospital stay, respectively.

#### DISCUSSION

In the present study, we used a large national dataset to show that brain MRI in hospitalized TBI patients is associated with lower in-hospital mortality. Since differences in baseline characteristics were found between the MRI and no MRI

Table 1: Baseline characteristics of the study cohorts.					
Variable	MRI n=3,075 (%)	No MRI n=340,090 (%)	P-value		
Women	47.6	43.6	0.043		
Race					
White	65.8	72.8	0.005		
Black	11.2	9.3			
Hispanic	12.4	9.3			
Asian or Pacific Islander	6.4	3.3			
Native American	0.0	3.3			
Other	4.2	3.1			
Median age, y	63.7	62.5	0.161		
Median annual income in					
patient's zip code, US\$					
\$1-\$38,999	20.5	26.3	< 0.001		
\$39,000-\$47,999	19.2	24.6			
\$48,000-\$62,999	23.3	24.7			
\$63,000 or more	37.0	24.5			
Insurance type	54.4	546	0.020		
Medicaid	56.6	54.6	0.020		
Drivata	10.6	9.1			
Private	27.0	26.5			
Hospital characteristics	5.8	9.0			
Hospital region					
Northeast	49 1	20.6	< 0.001		
Midwest	13.0	21.5	<0.001		
South	19.0	34.8			
West	18.5	23.1			
Hospital bed size	1010	2011			
Small	7.0	8.0	0.341		
Medium	20.5	23.4			
Large	72.5	68.6			
Location of hospital					
Rural hospital	4.2	4.1	0.907		
Urban hospital	95.8	95.9			
Teaching status of hospital					
Non-teaching hospital	23.9	30.2	0.020		
Teaching hospital	76.1	69.8			
Comorbidities					
Dementia	14.5	16.0	0.291		
History of myocardial	4.4	4.4	0.971		
infarction	•	•			
Malignancy	2.9	2.0	0.092		
Thrombocytopenia	4.1	4.2	0.852		
Chronic liver disease	6.3 0.5	4.9	0.125		
ruman immunodenciency	0.5	0.2	0.050		
Virus	EQ 1	51.4	0.002		
Diabatas mallitus	22.0	51.4 19.9	0.002		
Chronic obstructive lung	22.0 9 1	18.8	0.052		
disease	0.1	0.9	0.208		
Chronic kidney disease	10.9	Q 1	0 1 3 3		
Atrial fibrillation/flutter	11.9	13.8	0.133		
Coronary artery disease	16.9	17.9	0.560		
Peripheral artery disease	3.6	4.2	0.477		
Obesity	4.1	3.5	0.417		
Congestive heart failure	5.4	8.8	0.004		
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**Table 2:** In-hospital outcomes of TBI patients based on brain MRI utilization.

Outcome	Unadjusted Incidence (%)	Adjusted Odds Ratio (95% CI)	P-value
Mortality Intracranial	0.75 vs. 2.54 2.11 vs. 1.14	0.32 (0.12–0.86) 2.20 (1.27–3.81)	0.024 0.005
hemorrhage Gastrostomy	1.46 vs. 0.72	1.90 (0.90-4.01)	0.093
Tracheostomy Non-home discharge	0.33 vs. 0.22 50.75 vs. 44.69	1.28 (0.17–9.47) 1.33 (1.07–1.67)	0.806 0.012

\*Data are shown as MRI group versus No MRI group, MRI: Magnetic Resonance Imaging, TBI: Traumatic Brain Injury

**Table 3:** In-hospital resource requirements of TBI patients based

 on brain MRI utilization.

Resource	Unadjusted Mean	Regression Coefficient (95% CI)	P-value		
Length of stay Total cost	5.9 days vs. 3.9 days \$15,559 vs.	3.4 days (2.1 days-4.5 days) \$8,934 (\$5,031-\$12,838)	<0.001 <0.001		
\$10,633 *Data are shown as MRI group versus No MRI group, MRI: Magnetic					

Resonance Imaging, TBI: Traumatic Brain Injury

groups, especially with respect to income and insurance status, multivariable regression was an integral element of the analysis to independently examine the effects of brain MRI. Our study is the first to report the relationship between brain MRI utilization and change in outcome in TBI patients, in contrast to the rich body of literature focused on lesion detection and prognostication.

In the literature, the prognostic value of early brain MRI in TBI patients could be attributed to specific diagnostic information. In the multicenter TRACK-TBI study, detection of hemorrhagic axonal injury, brain contusion, and diffusion tensor imaging abnormality on early brain MRI predicted poor functional outcomes.<sup>[18,19]</sup> In a meta-analysis of 27 studies, detection of traumatic brainstem lesions on MRI predicted higher mortality and unfavorable functional outcomes, especially with involvement of more caudal structures.<sup>[13]</sup> While most prognostic studies focused on post-discharge outcomes, several studies showed that diffuse axonal injury and brainstem lesions on inpatient MRI were associated with increased duration and intensity of inpatient care as well as poor functional status at discharge.<sup>[20-23]</sup>

In contrast, the mechanisms by which diagnostic information obtained from MRI may alter patient management and improve the mortality rate in TBI patients remain unclear. Previously, Fiser *et al.* evaluated 40 hospitalized acute TBI patients to find that addition of MRI did not led lead to change in patient management despite detection of more injuries.<sup>[24]</sup> Similarly, Manolakaki et al. showed that the diagnostic value added by MRI did not lead to subsequent change in treatment in 123 acute TBI patients.<sup>[25]</sup> In a study involving 377 hospitalized TBI patients, Kin et al. found that finding a mismatch between CT and diffusion-weighted MRI had the potential to guide surgical management by predicting enlargement of hemorrhagic lesions.<sup>[26]</sup> Since mortality occurs in only a minority of hospitalized TBI patients, the single-center studies, each involving only few cases of mortality, were unlikely to be adequately powered to reveal the potential change in management leading to difference in mortality. The role of MRI imaging is a component of the ongoing analyses in the multi-national CENTER-TBI study (NCT02210221) involving 4,559 acute TBI patients, which may explain the findings of our study.

Regarding in-hospital complications, we found that brain MRI was associated with a higher rate of intracranial hemorrhage, which can be attributed to the higher sensitivity of MRI for detecting small hemorrhages.<sup>[7,12]</sup> Even after accounting for baseline characteristics such as insurance status that affect discharge disposition for TBI patients,<sup>[27]</sup> MRI was independently associated with non-home discharge. We speculate that the additional intracranial abnormalities found on MRI likely resulted in increased perceived severity of the patients' injuries, qualifying them for discharge to rehabilitation facilities more easily from medical and insurance perspectives. The higher rate of non-home discharge suggests that MRI is associated with additional resource requirements even beyond the period of acute hospitalization for TBI.

We found that MRI independently accounted for over 50% of the length and cost of hospitalization for acute TBI. Although the cost effectiveness of CT in acute TBI has been examined in several previous studies,<sup>[28]</sup> a counterpart analysis for MRI is lacking, likely due to the poor characterization of the clinical value of MRI in acute TBI. Since the adjusted OR of 0.32 for mortality in our study translates to approximately 68% relative risk reduction with rare outcome assumption,<sup>[29]</sup> further validation of the mortality benefit will likely support the cost effectiveness of MRI, especially given that the cost of direct medical care represents only a fraction of the total economic burden of TBI.<sup>[2]</sup>

The major limitation of the study is its observational design, which makes it difficult to directly attribute the mortality benefit to MRI utilization. Although many baseline characteristics were accounted for in our multivariable analysis, the NIS database does not contain information on the patients' clinical status at the time of imaging, such as the Glasgow Coma Scale, pupillary exam, and blood pressure which affect outcomes in acute TBI patients.<sup>[30]</sup> The unknown mechanism and severity of injury in our patient population

are potential additional confounders with influence on inpatient mortality rate and hospital resource requirements.<sup>[31]</sup> Controlling for the clinical confounders is essential to validate the results of our study, especially due to the introduction of selection bias when the decision to obtain MRI is made based on lack of abnormality on CT. Patient-level analysis with stratification based on CT findings would address this source of bias,<sup>[32]</sup> although it is beyond the capabilities of the NIS database. Furthermore, MRI studies are under-reported in the NIS database;<sup>[33]</sup> in a commercially insured US population, as high as 15% of patients obtain MRI within 2 days of diagnosis even for mild TBI.<sup>[34]</sup> Nevertheless, the large number of patients in our study offered sufficient statistical power for hypothesis testing. The MRI group exclusively contained patients who received brain MRI, and the statistical effect of contamination in the no MRI group was diluted by the low overall rate of MRI utilization in hospitalized TBI patients. Finally, we did not take into account the MRI techniques used for evaluation of TBI,<sup>[11]</sup> which may have different degrees of impact on inpatient outcomes.

Despite the limitations, the major significance of the study is the suggestion of a link between MRI utilization and lower inpatient mortality in acute TBI patients, which has not been examined previously. While it is neither judicious nor practical to recommend MRI in every patient admitted with TBI, the potential value of MRI in providing survival benefit beyond prognostication raises a possibility that merits further investigation. Identification of a subset of TBI patients who will likely derive survival benefit from MRI will justify integration of MRI into the clinical workflow for TBI evaluation, with the understanding that it may incur additional resource requirements and non-home discharge.

#### CONCLUSION

Inpatient brain MRI utilization in TBI patients is associated with lower inpatient mortality, as well as with increased hospital resource utilization and likelihood of non-home discharge. Further research is needed to clarify the nature of these associations and understand how MRI may be used to improve clinical outcomes in TBI patients. Since the initial hospitalization for acute TBI only marks the beginning of the medical care and rehabilitation process for TBI patients, the long-term benefits and costs associated with use of MRI in TBI patients remain to be investigated.

#### Declaration of patient consent

Not applicable given the use of an anonymized public database.

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No funding support was received for the study.

#### **Conflicts of interest**

There are no conflicts of interest.

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