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Craniotomy for Glioma Resection: A Predictive Model

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■ BACKGROUND: **Regulatory agencies are standardizing quality metrics on the basis of which surgical procedures will be evaluated. We attempted to create a predictive model of perioperative complications in patients undergoing craniotomies for glioma resection.**

■ METHODS: **We performed a retrospective cohort study involving patients who underwent craniotomies for glioma resection from 2005–2011 and were registered in the National Inpatient Sample (NIS) database. A predictive model for complications was developed and validated.**

■ RESULTS: **Overall, 21,384 patients underwent glioma resection. The respective inpatient postoperative risks were 1.6% for death, 25.8% for discharge to rehabilitation, 4.0% for treated hydrocephalus, 0.7% for cardiac complications, 0.5% for respiratory complications, 0.8% for deep wound infection, 0.6% for deep venous thrombosis (DVT), 3.1% for pulmonary embolus (PE), and 1.3% for acute renal failure (ARF). Predictive models for individual complications were developed on the basis of a logistic regression analysis and subsequently validated in a bootstrapped sample. The models demonstrated good discrimination with areas under the curve (AUC) of 0.71, 0.71, 0.69, 0.71, 0.74, 0.70, 0.73, 0.64, and 0.81 for postoperative risk of death, discharge to rehabilitation, hydrocephalus, cardiac complications, respiratory complications, deep wound infection, DVT, PE, and ARF, respectively. Additionally, the Hosmer-Lemeshow test was used to assess the calibration of all models.**

■ CONCLUSIONS: **The presented models can assist in the preoperative estimation of the complication risk for glioma patients and be used as an adjunct for outcome benchmarking in this population.**

INTRODUCTION

Several regulatory organizations are instituting quality metrics, on which surgeons will be held accountable in the near future (17). Although most of these efforts are targeting general medical conditions with high prevalence, they will likely be used without modification in subspecialty areas. Despite this drive, we lack data on how to predict or benchmark these complications in neurosurgery. Craniotomy for glioma resection is one of the most commonly performed cranial procedures (12). Assessing the risk of suboptimal performance on national quality metrics for this population is frequently arbitrary. The need to identify modifiable patient level risk factors for complications is obvious.

Several groups have demonstrated potential postoperative unfavorable outcomes in patients with brain tumors. The generalization of these findings is limited given their single institution, retrospective nature (6-8, 11, 13, 20, 22-24, 28, 30). Other regional analyses can be affected by selection bias (19, 25). Prior work on the National Surgical Quality Improvement Program (NSQIP) (4) has demonstrated the creation of an initial predictive model of complications for patients undergoing craniotomies for tumor resection. Although the benefits of using a validated registry are obvious, NSQIP does not focus on neurosurgical procedures and

Key words
- Craniotomy
- Glioma
- National Inpatient Sample
- Risk prediction

Abbreviations and Acronyms
ARF: Acute renal failure
CAD: Coronary artery disease
CHF: Congestive heart failure
CRF: Chronic renal failure
DM: Diabetes mellitus
DVT: Deep vein thrombosis
LOS: Length of stay
NIS: National Inpatient Sample
NSQIP: National Surgical Quality Improvement Program
PE: Pulmonary embolism
PVD: Peripheral vascular disease

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includes few craniotomies for brain tumors, from a limited sample of non−randomly selected institutions. This restricts the power to perform accurate subgroup analyses for specific brain tumor categories, such as gliomas.

The National Inpatient Sample (NIS) is a hospital discharge database that represents a random, validated sample of all inpatient admissions to nonfederal hospitals in the United States (26). It allows for the unrestricted study of the patient population in question. Using this database, preoperative comorbidities associated with postoperative death, discharge to rehabilitation, treated hydrocephalus, cardiac complications, respiratory complications, deep wound infection, deep vein thrombosis (DVT), pulmonary embolism (PE), and acute renal failure (ARF) in patients undergoing craniotomy for glioma resection were identified. On the basis of these data, a risk factor−based predictive model for negative outcomes in glioma surgery was developed.

METHODS

NIS Database

All patients undergoing craniotomy for glioma resection in the National Inpatient Sample (NIS) Database (26) (Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, Rockville, Maryland, USA) between 2005 and 2011 were included in the analysis. For these years, the NIS contains discharge data regarding 100% of discharges from a stratified random sample of nonfederal hospitals in several states to approximate a representative 20% subsample of all nonfederal U.S. hospital discharges. More information about the NIS is available at https://www.hcup-us.ahrq.gov/nisoverview.jsp.

Cohort Definition

In order to establish the cohort of patients, we used *International Classification of Diseases Codes-9-Current Modification* (ICD-9-CM) codes to identify patients in the database who underwent craniotomies (ICD-9-CM procedure code 01.51, 01.53, 0.59) for glioma resection (ICD-CM diagnostic code 191.0-191.9) between 2005 and 2011.

Outcome Variables

The primary outcome variables were inpatient postoperative mortality, cardiac complications, respiratory complications, treated hydrocephalus, DVT, PE, ARF, deep wound infection, and discharge to rehabilitation for patients registered in NIS, undergoing craniotomies for glioma resection. The coding definitions of our outcome and exposure variables can be found in **Table S1**.

Exposure Variables

The association of outcomes with the pertinent exposure variables was examined in a multivariable analysis. Age was a continuous variable. Gender and race (African American, Hispanic, Asian, or other, with Caucasian being the reference value) were categorical variables. The patient-level comorbidities (categorical variables) were diabetes mellitus (DM), hypertension, peripheral vascular disease (PVD), congestive heart failure (CHF), coronary artery disease (CAD), history of prior ischemic stroke, obesity, chronic renal failure (CRF), history of transient ischemic attack (TIA), hyponatremia, seizure disorder, and coagulopathy (any form of coagulation deficiency, medication induced, congenital, or otherwise).

The hospital characteristics used in the analysis as categorical variables included hospital region (West, South, Midwest, with Northeast being the reference value); hospital location (urban teaching, urban nonteaching, with rural being the reference value); and hospital bed size (medium, large, with small being the reference value). More information of the definitions of the various categories of hospital characteristics can be found at http://www.hcup-us.ahrq.gov/db/vars/nis_stratum/nisnote.jsp.

Statistical Analysis

Multivariable logistic regression was used to assess the ability of each patient characteristic to predict postoperative outcomes, and a parsimonious predictive model of each unfavorable outcome was developed. Models were created following a stepwise backwards elimination technique. Only significant variables at the 0.05 level were retained in the final predictive models. The discrimination of each of these models was assessed using the C-index (area under the receiver operating characteristic curve), which was corrected for overfitting bias using leave-out cross-validation (e.g., leave 10% out, repeated 1000 times). Our models were additionally validated using a bootstrapped sample, repeated 1000 times. The Hosmer-Lemeshow test was used to assess the calibration of each model.

Interactions were tested, but none were significant at the threshold (0.001) we set to correct for multiple testing ($20 * 19/2 = 190$ interactions in all) and none improved the C-index by more than 0.002. Departures from linearity were assessed with the use of restricted cubic splines for continuous variables. All hypotheses were tested at an alpha level of 0.05 and were based on two-sided tests. Statistical analyses were performed using the Stata version 13 (StataCorp, College Station, Texas, USA), SPSS statistical package version 20.0 (IBM, Armonk, New York, USA), and R version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient Characteristics

In the selected study period there were 21,384 patients undergoing glioma resection (mean age was 54.0 years, with 42.1% females) who were registered in NIS. The distribution of the patient and hospital characteristics can be seen in **Table 1**.

Clinical Outcomes

The respective inpatient postoperative outcomes (**Table 2**) were 1.6% for death, 25.8% for discharge to rehabilitation, 4.0% for treated hydrocephalus, 0.7% for cardiac complications, 0.5% for respiratory complications, 0.8% for deep wound infection, 0.6% DVT, 3.1% for PE, and 1.3% ARF. The low percentage of DVT is secondary to the fact that their detection depends on the aggressiveness of screening methods. However, PE is more frequently symptomatic and is therefore associated with a higher percentage in our data.

Regression Model Derivation

A multivariable analysis was performed investigating the effects of several risk factors on the risks of inpatient death, discharge to