A Predictive Model of Unfavorable Outcomes After Benign Intracranial Tumor Resection

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BACKGROUND: **Benchmarking of outcomes and individualized risk prediction are central in patient-oriented shared decision making. We attempted to create a predictive model of complications in patients undergoing benign intracranial tumor resection.**

METHODS: **We performed a retrospective cohort study involving patients who underwent craniotomies for benign intracranial tumor resection during the period 2005–2011 and were registered in the National (Nationwide) Inpatient Sample database. A model for outcome prediction based on individual patient characteristics was developed.**

RESULTS: **There were 19,894 patients who underwent benign tumor resection. The respective inpatient postoperative incidences were 1.3% for death, 22.7% for unfavorable discharge, 4.2% for treated hydrocephalus, 1.1% for cardiac complications, 0.9% for respiratory complications, 0.5% for wound infection, 0.5% for deep venous thrombosis, 2.3% for pulmonary embolus, and 1.5% for acute renal failure. Multivariable analysis identified risk factors independently associated with the above-mentioned outcomes. A model for outcome prediction based on patient and hospital characteristics was developed and subsequently validated in a bootstrap sample. The models demonstrated good discrimination with areas under the curve of 0.85, 0.76, 0.72, 0.74, 0.72, 0.74, 0.76, 0.68, and 0.86 for postoperative risk of death, unfavorable discharge, hydrocephalus, cardiac complications, respiratory complications, wound infection, deep venous thrombosis, pulmonary embolus, and acute renal failure. The models also had good calibration, as assessed by the Hosmer-Lemeshow test.**

CONCLUSIONS: **Our models can provide individualized estimates of the risks of postoperative complications based on preoperative conditions and potentially can be used as an adjunct for decision making in benign intracranial tumor surgery.**

INTRODUCTION

In the path to accountable care, benchmarking of outcomes will allow identification of quality and facilitate shared decision making (17). Craniotomy for brain tumor resection is one of the most commonly performed cranial neurosurgical procedures (12). Several efforts through the NeuroPoint Alliance are underway to create registries to monitor neurosurgical outcomes. However, this process has not started yet in the area of brain tumors. Although the possibility of unfavorable outcomes is estimated by practicing surgeons (12), the justification of the decision making on individual patient characteristics is frequently arbitrary. In this rapidly changing health care environment, the need to establish quality metrics and identify modifiable patient-level risk factors for complications is obvious.

Several studies investigating postoperative outcomes in patients with benign tumors have been published. Most of these have been retrospective analyses of single-institution experiences (6-8, 11, 13, 21,23-25, 29, 31), demonstrating results with limited generalization given their inherent selection bias. The interpretation of other multicenter studies is equally limited given their focus on regional data (20, 26). Bekelis et al. (4) developed a predictive model of complications after craniotomies for tumor resection based on a well-designed surgical registry. Although the benefits of using

Key words
- Benign intracranial tumors
- Craniotomy
- NIS
- Risk prediction

Abbreviations and Acronyms
ARF: Acute renal failure
CAD: Coronary artery disease
DVT: Deep vein thrombosis
NIS: National (Nationwide) Inpatient Sample
PE: Pulmonary edema
PVD: Peripheral vascular disease
TIA: Transient ischemic attack

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a validated registry are obvious, the National Surgical Quality Improvement Program is not specific to neurosurgery and includes only a small number of craniotomies for brain tumors from a limited sample of non−randomly selected institutions. The power to perform accurate subgroup analyses for specific brain tumor categories, such as benign tumors, is restricted.

The National (Nationwide) 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 (27). The NIS allows for the unrestricted study of the patient population in question. Using this database, we aimed to identify preoperative comorbidities associated with postoperative death, unfavorable discharge, treated hydrocephalus, cardiac complications, respiratory complications, wound infection, deep venous thrombosis (DVT), pulmonary embolus (PE), and acute renal failure (ARF) in patients undergoing craniotomy for benign intracranial tumor resection. Based on these data, we sought to develop a risk factor−based predictive model for negative outcomes in benign tumor surgery.

MATERIALS AND METHODS

NIS

All patients undergoing craniotomy for benign intracranial tumor resection in the NIS (Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, Rockville, Maryland, USA) (27) during the period 2005−2011 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 http://www.ahcpr.gov/data/hcup/nisintro.htm.

Cohort Definition

To establish the cohort of patients, we used *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes to identify patients in the database who underwent craniotomies (procedure codes 01.51, 01.53, 0.59) for benign intracranial tumor resection (diagnostic codes 225.0, 225.1, 225.2) during the period 2005−2011.

Outcome Variables

The primary outcome variables (Table S1) were inpatient postoperative mortality, cardiac complications, respiratory complications, treated hydrocephalus, DVT, PE, ARF, wound infection, and unfavorable discharge (transfer to short-term hospital, skilled nursing facility, intermediate care, or rehabilitation) for patients registered in NIS who were undergoing craniotomies for benign intracranial tumor resection.

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, other, with white being the reference value) were categorical variables. The patient-level (Table S1) comorbidities (categorical variables) were diabetes mellitus, hypertension, peripheral vascular disease (PVD), congestive heart failure, coronary artery disease (CAD), history of prior ischemic or hemorrhagic stroke, obesity, chronic renal failure, history of a transient ischemic attack, seizure disorder, and coagulopathy.

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 on 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. Based on this assessment, a parsimonious predictive model of each unfavorable outcome was developed. The probability (p) of a given postoperative complication was determined by the following relationship:

$$p = \frac{1}{1 + e^{-\left(\alpha + \sum_{i=1}^{n} (\beta_i X_i)\right)}}$$

where α is the model intercept; n is the number of variables; β is the model parameter, which is the natural logarithm of the odds ratio, ln(OR), for a given variable; and X is either 0 or 1 for qualitative variables, or the value of a quantitative variable.

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, and bootstrap validation, 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 >0.002. Other departures from linearity were assessed with the use of restricted cubic splines. All hypotheses were tested at an α level of 0.05 and were based on two-sided tests. Statistical analyses were performed using Stata version 13 (StataCorp LP, College Station, Texas, USA), IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, New York, USA), and R version 3.1.0 (R Foundation for Statistical Computing).

RESULTS

Patient Characteristics

In the selected study period, there were 19,894 patients who underwent benign intracranial tumor resection (mean age, 55.2 years; female patients, 66.6%) who were registered in the NIS.