Surgery for primary supratentorial brain tumors in the United States, 1988 to 2000: The effect of provider caseload and centralization of care

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Contemporary reports of patient outcomes after biopsy or resection of primary brain tumors typically reflect results at specialized centers. Such reports may not be representative of practices in nonspecialized settings. This analysis uses a nationwide hospital discharge database to examine trends in mortality and outcome at hospital discharge in 38,028 admissions for biopsy or resection of supratentorial primary brain tumors in adults between 1988 and 2000, particularly in relation to provider caseload. Multivariate analyses showed that large-volume centers had lower in-hospital postoperative mortality rates than centers with lighter caseloads, both for craniotomies (odds ratio [OR] 0.75 for a tenfold larger caseload) and for needle (closed) biopsies (OR 0.54). Adverse discharge disposition was also less likely at high-volume hospitals, both for craniotomies (OR 0.77) and for needle biopsies (OR 0.67). The annual number of surgical admissions increased by 53% during the 12-year study period, and in-hospital mortality rates decreased during this period, from 4.8% to 1.8%. Mortality rates decreased over time, both for craniotomies and for needle biopsies. Subgroup analyses showed larger relative mortality rate reductions at large-volume centers than at small-volume centers (73% vs. 43%, respectively). The number of U.S. hospitals performing one or more craniotomies annually for primary brain tumors decreased slightly, and the number performing needle biopsies increased. There was little change in median hospital annual craniotomy caseloads, but the largest centers had disproportionate growth in volume. The 100 highest-caseload U.S. hospitals accounted for an estimated 30% of the total U.S. surgical primary brain tumor caseload in 1988 and 41% in 2000. Our findings do not establish minimum volume thresholds for acceptable surgical care of primary brain tumors. However, they do suggest a trend toward progressive centralization of craniotomies for primary brain tumor toward large-volume U.S. centers during this interval.
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There is increasing evidence that patient mortality and morbidity are lower when complex medical or surgical procedures are performed at high-volume centers or by high-volume physician providers. For example, in-hospital mortality is lower when complex cancer operations (Begg et al., 1998; Hillner et al., 2000), cardiovascular operations (Birkmeyer et al., 2002), surgical repair of intracranial aneurysms (Bardach et al., 2002; Barker et al., 2003a; Johnston, 2000), carotid endarterectomy (Cronenwett and Birkmeyer, 2000), and transsphe-

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[2] Abbreviations used are as follows: AHRQ, Agency for Healthcare Research and Quality; CI, confidence interval; LOS, length of stay; NIS, Nationwide Inpatient Sample (NIS); OR, odds ratio.

noidal pituitary tumor surgery (Barker et al., 2003b) are performed at high-volume hospitals or by high-volume surgeons. Lower mortality and shorter length of hospital stay after craniotomy for brain tumor, broadly defined, in adult patients have also been shown to be characteristic of high-volume centers (Chernov, 2004; Cowan et al., 2003; Long et al., 2003; Tigliev et al., 1999). These investigations described the pooled results of craniotomies for many types of brain tumor, with little attempt to address temporal trends in practice patterns or results (Cowan et al., 2003; Long et al., 2003).

This analysis describes results of surgical treatment of adult primary brain tumors in the United States between 1988 and 2000. The mortality rates for both craniotomy and closed (needle) biopsy of primary brain tumors were examined for changes over time and for relation to provider volume. In addition, we examined national practice patterns for the possibility that progressive centralization of brain tumor surgery in specialized centers took place during this interval.

Subjects and Methods

The data source for this study was the Nationwide Inpatient Sample (NIS)[2] hospital discharge database for the years 1988 to 2000, obtained from the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (AHRQ), Rockville, Md. (Steiner et al., 2002). An overview of the NIS database is available on the Internet (http://www.ahcpr.gov/data/hcup/nisintro.htm). The NIS is a hospital discharge database that represents approximately 20% of all inpatient admissions to nonfederal hospitals in the United States. For the years 1988 to 2000, the NIS contains discharge data on 100% of discharges from a stratified random sample of nonfederal hospitals in 8 to 28 states to approximate a representative 20% subsample of all U.S. nonfederal hospital discharges. Because the NIS database contains data on all patients discharged from sampled hospitals during the year regardless of age or payer, it can be used to obtain the annual total volume of specified procedures at individual hospitals. For many states, the surgeon who performed the principal procedure during the admission is identified with a unique masked code.

Inclusion and Exclusion Criteria and Definition of End Points

An admission for surgical treatment of an adult primary brain tumor was defined by using a combination of patient age and ICD-9-CM (HHS, 1980) diagnosis and treatment codes. Admissions with patient age 19 or older; a diagnosis code of 191.0-5 or 191.8-9 (malignant brain tumor, excluding cerebellum or brain stem), 225.0 (benign brain tumor), or 237.5 (brain tumor of uncertain behavior); and primary procedure 01.13 (closed brain biopsy), 01.14 (open brain biopsy), 01.53 (lobectomy), or 01.59 (other brain resection) were included. Although most procedures coded as "closed needle biopsies" were probably performed by using stereotactic technique, the same ICD-9-CM procedure code is used for needle biopsies performed freehand without stereotactic targeting.

Two primary end points were examined: in-hospital mortality and disposition at hospital discharge. In-hospital mortality was coded directly in the NIS database and was analyzed by using logistic regression. Discharge disposition was coded on a 4-level scale and was analyzed with ordinal logistic regression, which allows use of the entire spectrum of outcomes rather than simplifying to a single cut point with resultant information loss (McCullagh and Nelder, 1989; Moses et al., 1992; Strömberg 1996). Discharge disposition was coded as death, discharge to a long-term facility, discharge to other facilities, or discharge home, as follows. NIS data distinguishes discharge to long-term facilities (such as skilled nursing facilities) from discharge to other (intermediate or short-term care) facilities for all states except California and Maryland; for these states, these discharges (1.0% of the total) were coded as discharge to "other facilities." Discharge home with home health care or i.v. therapy (7.8% of discharges) was counted as discharge home. Discharge to another acute care hospital (2.3% of discharges) was counted as discharge to an institution other than home, not as discharge to a long-term facility. Discharge against medical advice (0.1% of discharges) was counted as missing.

Length of stay (LOS) and total hospital charges were coded in NIS data. To avoid downward bias in LOS and hospital charges caused by early postoperative deaths, these analyses included only patients discharged from hospital alive. Hospital charges were converted to U.S. dollars, 2000 values, by using the all-cities Consumer Price Index (Bureau of Labor Statistics, 2004). LOS and hospital charge data were highly positively skewed and were analyzed as logarithmic transforms.

Patient Characteristics

Patient age, sex, race, the median household income in the patient's zip code of residence (specified by quartile with reference to U.S. national values), primary payer for care (Medicare, Medicaid, private insurance, self-pay, no charge, other), type of admission (emergency, urgent, elective), and admission source (emergency room, transfer from another hospital, transfer from long-term care, and routine) were coded in NIS data. Twenty-two patients (0.1%) with admission type of "other" were recoded as routine admissions. More than 5% of discharges had missing values for three variables used principally as stratification factors for other analyses, race (31% missing), admission type (13% missing), and whether the principal procedure was performed on the first hospital day (16% missing). When these variables were used as stratification factors, missing values for race and admission type were imputed as follows. Missing race was set to white. Missing admission type was set to "emergency" for admissions whose source was the emergency room, to "urgent" for admissions that were transfers from another hospital, and to "routine" for admissions from other sources. Whether the principal procedure was performed on the first hospital day was not imputed, and when race or admission type were the focus of the analysis, imputed values were not used.

To assess the effect of general medical comorbidity, several comorbidity markers and variables were considered. The set of 30 medical comorbidity markers described by Elixhauser et al. (1998), excluding the two specific neurological comorbidity variables ("paralysis" and "other neurological deficit"), were used, as well as three comorbidity variables likely to represent postoperative conditions ("fluid and electrolyte disorders," "blood loss anemia," and "deficiency anemias"). These markers and variables were calculated by using AHRQ comorbidity software (available at http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp) and summed to give a single comorbidity score ranging between 0 and 25.

Potential complications of brain tumor surgery were identified by using the following ICD codes: postoperative neurological complications, including those due to infarction or hemorrhage (997.00–997.09); hematoma complicating a procedure (998.1–998.13); hydrocephalus (331.3–331.4) or the performance of a ventriculostomy (02.2); mechanical ventilation (96.70–96.72); deep venous thrombosis, pulmonary embolism, or placement of an inferior vena cava filter (415, 415.11–19, 451.0–9, 453.0–9, 38.7); and transfusion of packed red blood cells (99.04).

Provider and Hospital Characteristics

Hospital region (Northeast, Midwest, South, or West), location (rural or urban), teaching status, and bed size (small, medium, large) were coded in NIS data. Hospital and surgeon volumes of brain tumor surgery cases were derived for each individual study year by counting the cases for each identified surgeon and hospital in the database. Because not all hospitals in a geographic region are included in the database, this method underestimates caseload for some surgeons who operate at multiple hospitals, because only a subset of the hospitals at which they operate are contained in the sample. This misclassification will bias estimates of the effect of surgeon caseload toward the null. However, we found that only 5% to 6% of identified surgeons in the database operated at more than one hospital. Surgeon identifier codes were missing for 54% of patients, mainly on a per-state basis. Patients whose surgeons were identified by masked codes underwent surgery at hospitals with annual tumor craniotomy caseloads of 15 per year, compared to 16 per year for patients without identified surgeons.

Because hospital and physician caseload distributions were positively skewed, the logarithmic transforms were used when volume measures were entered into regression models.

Statistical Methods

Statistical methods included the Fisher's exact and Wilcoxon rank tests; Spearman rank correlation; and log-linear least-squares, ordinary logistic, and proportional-odds ordinal logistic regression (Harrell, 2001; Hosmer and Lemeshow, 2000; McCullagh, 1980). To correct for possible clustering of similar outcomes within hospitals, which could cause falsely inflated estimates of the statistical significance of regression coefficients (Panageas et al., 2003), confidence intervals and statistical significance were calculated by using a sandwich variance-covariance matrix estimated by methods of Huber and White, with adjustment for clustering by hospital (Harrell, 2001). Multivariate models were constructed by step-down technique starting with the full (all-variables) model, with $P > 0.05$ as the threshold for removing variables. Stratification for tumor histology and location (for malignant tumors) and for geographic region was forced into all multivariate models. Testing for heterogeneity of the volume-outcome effect across diagnostic categories was done by using Cochran's Q statistic, with $P < 0.1$ considered evidence of significant heterogeneity (Costa-Bouzas et al., 2001). Length of stay and hospital charges were analyzed as logarithmic transforms by using least-squares regression corrected for clustering as described above.

Extrapolations to the entire U.S. population were adjusted for the NIS stratified survey method by using the SAS (version 8.2; SAS Institute, Cary, N.C.) PROC SURVEYMEANS procedure (AHRQ, 2002). Linear regressions on extrapolated population values (i.e., to test trends in annual number of admissions or mortality rates) were weighted by the inverse of the variance. Logistic and ordinal logistic regression analyses treated the sample as a simple random draw from an infinite possible population (i.e., without weighting or correction for a finite sampling fraction).

Calculations were performed by using SAS (version 8.2; SAS Institute, Cary, N.C.) and S-plus (version 3.3 for Windows; Insightful, Inc., Seattle, Wash.) with the Hmisc and Design modeling function software libraries of Harrell (Harrell 2000, 2001) and the Locfit local-likelihood regression library of Loader (Loader 1998, 1999). *P* values are two-tailed.

Results

There were 38,028 admissions for biopsy or resection of supratentorial primary brain tumors identified in the NIS database between 1988 and 2000. Clinical characteristics of the patients are shown in Table 1. Most patients were white, ages 40 to 70, with more men than women. One half of admissions were classified as routine, one quarter as urgent, and one quarter as emergencies. Admission from home was most common, although admissions through the emergency ward or as a transfer from another hospital were not unusual. Needle biopsies comprised 20% of the admissions in the database; open biopsies, 6%; lobectomies, 4%; and other resections, 70%. The in-hospital mortality rate for the cohort as a whole was 2.8% (95% confidence interval (CI), 2.7% to 3.0%). The mortality rate was 2.5% for needle biopsy (95% CI, 2.1% to 2.8%), 5.3% for open biopsy (95%

Table 1. Clinical characteristics of 38,028 patients who underwent surgical procedures for adult primary brain tumors, 1988 to 2000

Age	
Mean	55
Median	56
Interquartile range	42 to 68
Range	19 to 99
Female sex	44%
Race*	
White	86.6%
Black	4.6%
Hispanic	5.5%
Asian/Pacific Islands	1.3%
Native American	0.1%
Other	1.8%
Median household income for zip code of residence*	
Quartile 1 (lowest)	18%
Quartile 2	21%
Quartile 3	21%
Quartile 4 (highest)	39%
Primary payer*	
Medicare	33%
Medicaid	6%
Private insurance	53%
Self-pay	3%
No charge	0.2%
Other	4%
Admission type*	
Emergency	25%
Urgent	25%
Routine	50%
Admission source*	
Emergency ward	20%
Transfer from acute care hospital	7%
Transfer from long-term care	2%
Routine	70%
Year of treatment*	
1988–1990	18%
1991–1993	21%
1994–1996	24%
1997–2000	36%

* Percentages may not total 100 because of rounding.

CI, 4.4% to 6.2%), 3.2% for lobectomy (95% CI, 2.4% to 4.2%), and 2.7% for other resections (95% CI, 2.5% to 2.9%).

Patient Characteristics and Outcome

Age, sex, race, primary payer for care, median income in postal code of residence, admission type and source, timing of the surgical procedure, and medical comorbidity score were tested as predictors of mortality and discharge disposition (Tables 2 and 3). Age was an important predictor of death and discharge other than to home ($P < 0.001$, Fig. 1). Female patients had higher rates of discharge other than to home, but mortality did not differ from male patients. Black patients had higher mortality and worse discharge disposition. Private insurance was associated with lower mortality and more favorable discharge disposition. Patients with emergency or urgent admissions, admission other than routine (i.e., through the emergency room or as a transfer from another hospital), or whose procedure was not performed on the first hospital day had higher mortality and worse discharge disposition. Increasing medical comorbidity predicted higher mortality and worse discharge disposition. Nearly all of these variables were included in the multivariate analyses described below (Tables 2 and 3), in addition to stratification by hospital geographic region.

Hospital and Surgeon Characteristics and Outcome

Patients were treated at 955 of the 2671 hospitals included in the NIS database during the study period. Needle biopsies were performed at 65% of these 955 hospitals and craniotomies at 98%. Hospital characteristics predicting performance of one or more closed needle biopsies included urban location, teaching status, and larger bed size ($P < 0.001$ for all). The same hospital characteristics predicted performance of one or more craniotomies ($P < 0.001$ for all). For 46% of the admissions, 2149 treating surgeons were identified in the database. Of these, 46% performed needle biopsies and 92% performed craniotomies.

The annual procedure caseloads of the treating hospital and surgeon were examined as predictors of outcome separately for needle biopsy and for open procedures. Hospitals and surgeons varied widely in the volume of surgical procedures reported. For closed needle biopsies, the median annual hospital caseload (analyzed on a per-patient basis) was 6 admissions (range, 1–46 admissions; 25th percentile, 3 admissions; 75th percentile, 10 admissions). For craniotomies, on a per-patient basis, the median annual hospital caseload was 16 admissions (range, 1–218 admissions; 25th percentile, 8 admissions; 75th percentile, 35 admissions). For needle biopsies, 27% were the only needle biopsy reported by that surgeon that year, and 8% were the only needle biopsy reported by that hospital that year. For craniotomies, 12% were the only craniotomy reported by that surgeon that year, and 2% were the only craniotomy reported by that hospital that year.

Hospital caseload and surgeon caseload were strong predictors of mortality after surgical procedures for primary brain tumors. Odds ratios for the importance of hospital and surgeon caseload are reported for a tenfold difference in caseload, because this approximates the difference between 25th and 75th percentiles for caseload. Mortality was lower at high-volume hospitals, both for needle biopsies (OR, 0.54; 95% CI, 0.35–0.83; $P = 0.006$) and for craniotomies (OR, 0.75; 95% CI, 0.62–0.90; $P = 0.003$; Fig. 2, Table 2). For needle biopsy, mortality at lowest-volume-quintile hospitals (1 or 2 admissions per year) was 3.6%, compared to 1.7% at highest-volume-quintile hospitals (12 or more admis-

Table 2. Effect (odds ratios with 95% confidence interval) of patient characteristics and hospital caseload on in-hospital mortality rates after craniotomy for primary brain tumor

	Odds Ratio (CI)	
	Univariate	**Multivariate**
Age (per decade)	1.33 (1.27–1.39) $P < 0.001$	1.26 (1.18–1.34) $P < 0.001$
Female gender	0.96 (1.85–1.07) $P = 0.4$	
Race		
White vs. non-white	0.83 (0.67–1.05) $P = 0.12$	
Black vs. non-black	1.74 (1.27–2.38) $P < 0.001$	1.57 (1.09–2.25) $P = 0.02$
Primary payer (private insurance vs. other)	0.50 (0.44–0.57) $P < 0.001$	0.82 (0.68–0.99) $P = 0.04$
Median income in postal code of residence (by quartile)*	0.96 (0.90–1.03) $P = 0.3$	
Admission type (emergency vs. urgent vs. routine)	1.73 (1.58–1.90) $P < 0.001$	1.31 (1.14–1.51) $P < 0.001$
Admission source (any other vs. routine)	2.39 (2.02–2.82) $P < 0.001$	1.35 (1.09–1.67) $P = 0.005$
Surgery not done on day of admission to hospital	2.93 (2.46–3.50) $P < 0.001$	1.28 (1.02–1.60) $P = 0.03$
Medical comorbidity score	1.29 (1.21–1.38) $P < 0.001$	1.11 (1.01–1.21) $P = 0.02$
Later surgery (per year)	0.91 (0.89–0.93) $P < 0.001$	0.93 (0.91–0.95) $P < 0.001$
Hospital caseload (for tenfold increase)	0.49 (0.40–0.59) $P < 0.001$	0.75 (0.62–0.90) $P = 0.003$

*Univariate analysis stratified by year of surgery

sions per year). For craniotomy, mortality at lowest-volume-quintile hospitals (5 or fewer admissions per year) was 4.5%, compared to 1.5% at highest-volume-quintile hospitals (42 or more admissions per year). The effect of hospital volume on mortality after craniotomy was similar for all types of primary brain tumors: there was no heterogeneity in the volume-mortality relationship for all diagnostic categories (benign vs. malignant, and location within brain for malignant tumors; $P = 0.2$). Exploratory subgroup analyses showed no clear differences in the volume-mortality relationship with respect to several prognostic factors, with the possible exception of a weaker relationship between volume and mortality in patients with multiple medical comorbidities (Table 4).

Adverse discharge disposition was also less likely at high-volume hospitals, both for needle biopsies (OR, 0.67; 95% CI, 0.56–0.80; $P < 0.001$) and for craniotomies (OR, 0.77; 95% CI, 0.70–0.85; $P < 0.001$; Fig. 2, Table 3). For needle biopsy, discharge not directly home was 24.3% at lowest-volume-quintile hospitals (1 or 2 admissions per year), compared to 13.1% at highest-volume-quintile hospitals (12 or more admissions per year). For craniotomy, discharge not directly home was 30.2% at lowest-volume-quintile hospitals (5 or fewer admissions per year), compared to 17.3% at highest-volume-quintile hospitals (42 or more admissions per year). Exploratory subgroup analyses showed no clear difference in the volume-outcome relationship with respect to several prognostic factors (Table 4).

Table 3. Effect (odds ratios with 95% confidence interval) of patient characteristics and hospital caseload on adverse outcome at hospital discharge (4-level scale) after craniotomy for primary brain tumor

	Odds Ratio (CI)	
	Univariate	**Multivariate**
Age (per decade)	1.58 (1.54–1.61) $P < 0.001$	1.47 (1.42–1.51) $P < 0.001$
Female gender	1.24 (1.19–1.30) $P < 0.001$	1.12 (1.05–1.20) $P < 0.001$
Race		
White vs. non-white	1.01 (0.91–1.12) $P = 0.8$	
Black vs. non-black	1.21 (1.06–1.39) $P = 0.006$	1.33 (1.13–1.57) $P < 0.001$
Primary payer (private insurance vs. other)	0.38 (0.35–0.41) $P < 0.001$	0.77 (0.70–0.83) $P < 0.001$
Median income in postal code of residence (by quartile)*	0.92 (0.90–0.96) $P < 0.001$	
Admission type (emergency vs. urgent vs. routine)	1.53 (1.46–1.60) $P < 0.001$	1.11 (1.04–1.18) $P = 0.001$
Admission source (any other vs. routine)	2.10 (1.89–2.33) $P < 0.001$	1.37 (1.24–1.51) $P < 0.001$
Surgery not done on day of admission to hospital	2.15 (1.97–2.34) $P < 0.001$	1.34 (1.23–1.47) $P < 0.001$
Medical comorbidity score	1.53 (1.49–1.58) $P < 0.001$	1.14 (1.11–1.18) $P < 0.001$
Later surgery (per year)	1.01 (1.00–1.03) $P = 0.1$	1.03 (1.02–1.05) $P < 0.001$
Hospital caseload (for tenfold increase)	0.58 (0.53–0.64) $P < 0.001$	0.77 (0.70–0.85) $P < 0.001$

*Univariate analysis stratified by year of surgery

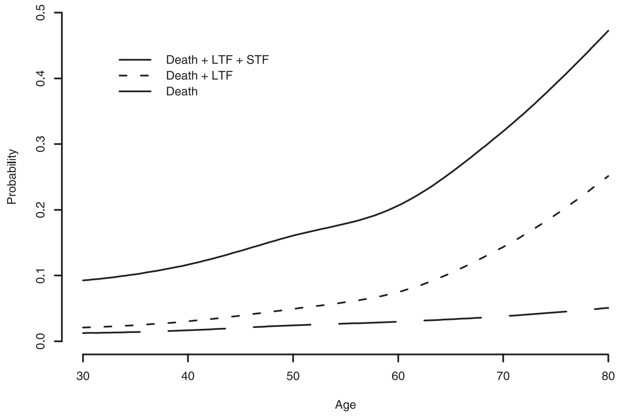

Fig. 1. Effect of age on probability of death or discharge other than to home after surgery (craniotomy or needle biopsy) for primary brain tumor, plotted using local-likelihood fitting. Dashed line, mortality; dotted line, death or discharge to long-term care facility (LTF); solid line, death or discharge to long-term or short-term facility (STF).

After adjustment for hospital caseload, the urban location, teaching status, and bed size were not significantly related to mortality or discharge disposition for either needle biopsies or craniotomies.

When craniotomies were performed by high-volume surgeons, mortality (OR, 0.60; 95% CI, 0.45–0.79; $P < 0.001$) and adverse discharge disposition (OR, 0.79; 95% CI, 0.70–0.89; $P < 0.001$) were significantly less frequent. After needle biopsies performed by high-volume surgeons, there were trends toward lower mortality (OR, 0.53; 95% CI, 0.24–1.12; $P = 0.1$) and less frequent adverse discharge disposition (OR, 0.77; 95% CI, 0.56–1.06; $P = 0.1$).

The difference in outcome between patients treated by high- and low-volume hospitals was present at all patient ages. Figure 3 shows the probability of death and of discharge other than to home as a function of age for highest- and lowest-volume-quintile hospitals.

Patient characteristics were tested as potential predictors of provider (hospital or surgeon) volume for patients who received a craniotomy (Table 5). Older patients were less likely to have a high-volume hospital or surgeon ($P < 0.001$ for both). Race was a significant predictor of both

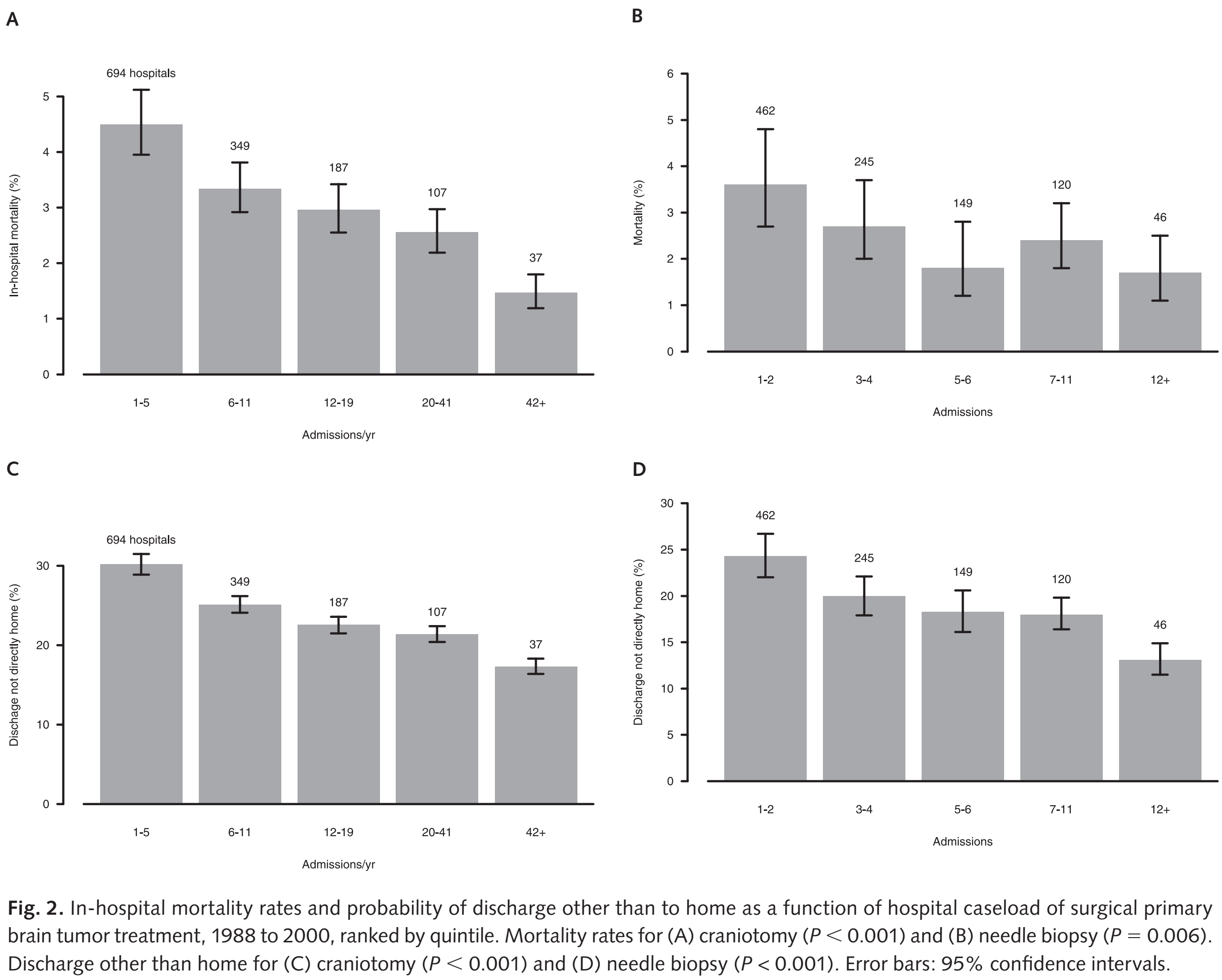

Fig. 2. In-hospital mortality rates and probability of discharge other than to home as a function of hospital caseload of surgical primary brain tumor treatment, 1988 to 2000, ranked by quintile. Mortality rates for (A) craniotomy ($P < 0.001$) and (B) needle biopsy ($P = 0.006$). Discharge other than home for (C) craniotomy ($P < 0.001$) and (D) needle biopsy ($P < 0.001$). Error bars: 95% confidence intervals.

Table 4. Effect of hospital caseload (odds ratio, 95% confidence intervals per tenfold increase in caseload) on patient outcome in patient subgroups (multivariate models)

	Odds Ratio (CI)	
	Mortality	Adverse discharge outcome (4-level scale)
Race		
White	0.73 (0.58–0.91)	0.75 (0.67–0.84)
Black	0.59 (0.21–1.6)	0.84 (0.62–1.15)
Other / unknown	0.85 (0.59–1.2)	0.83 (0.71–0.97)
Primary payer		
Private insurance	0.64 (0.47–0.89)	0.74 (0.66–0.85)
Other insurance	0.83 (0.67–1.02)	0.79 (0.70–0.88)
Admission type		
Emergency	0.80 (0.58–1.11)	0.83 (0.72–0.97)
Urgent	0.71 (0.47–1.05)	0.71 (0.62–0.80)
Routine	0.74 (0.55–1.005)	0.77 (0.64–0.93)
Medical comorbidities		
None	0.56 (0.43 – 0.72)	0.73 (0.65–0.82)
One	0.81 (0.600–1.11)	0.84 (0.73–0.96)
Two or more	1.07 (0.78–1.5)	0.76 (0.67–0.88)

hospital and surgeon caseload ($P < 0.001$ for both), with higher hospital and surgeon caseloads for white patients than for black patients. Primary payer for care was a significant predictor of both hospital and surgeon caseload ($P < 0.001$ for both), with highest provider volumes for those who had private insurance. Patients from higher-income areas of residence had higher-volume hospitals and surgeons ($P < 0.001$ for both). Emergency or urgent admissions were more common to lower-volume hospitals and surgeons ($P < 0.001$ for both). Patients with more medical comorbidity tended to have lower-volume hospitals and surgeons ($P < 0.001$ for both).

Trends over Time

Projected to the U.S. population, the total annual number of admissions increased from 12,000 in 1988 to 18,400 in 2000—a 53% increase, or 350 additional admissions for surgical treatment of primary brain tumors per year ($P < 0.001$). The increasing number of annual admissions was seen both for needle biopsies ($P = 0.01$) and for open procedures ($P = 0.003$; Fig. 4).

There were shifts in clinical characteristics of the patient population undergoing surgery for primary brain tumors during the study period. Median patient age decreased, from 58 in 1988 to 52 in 2000 ($P <$

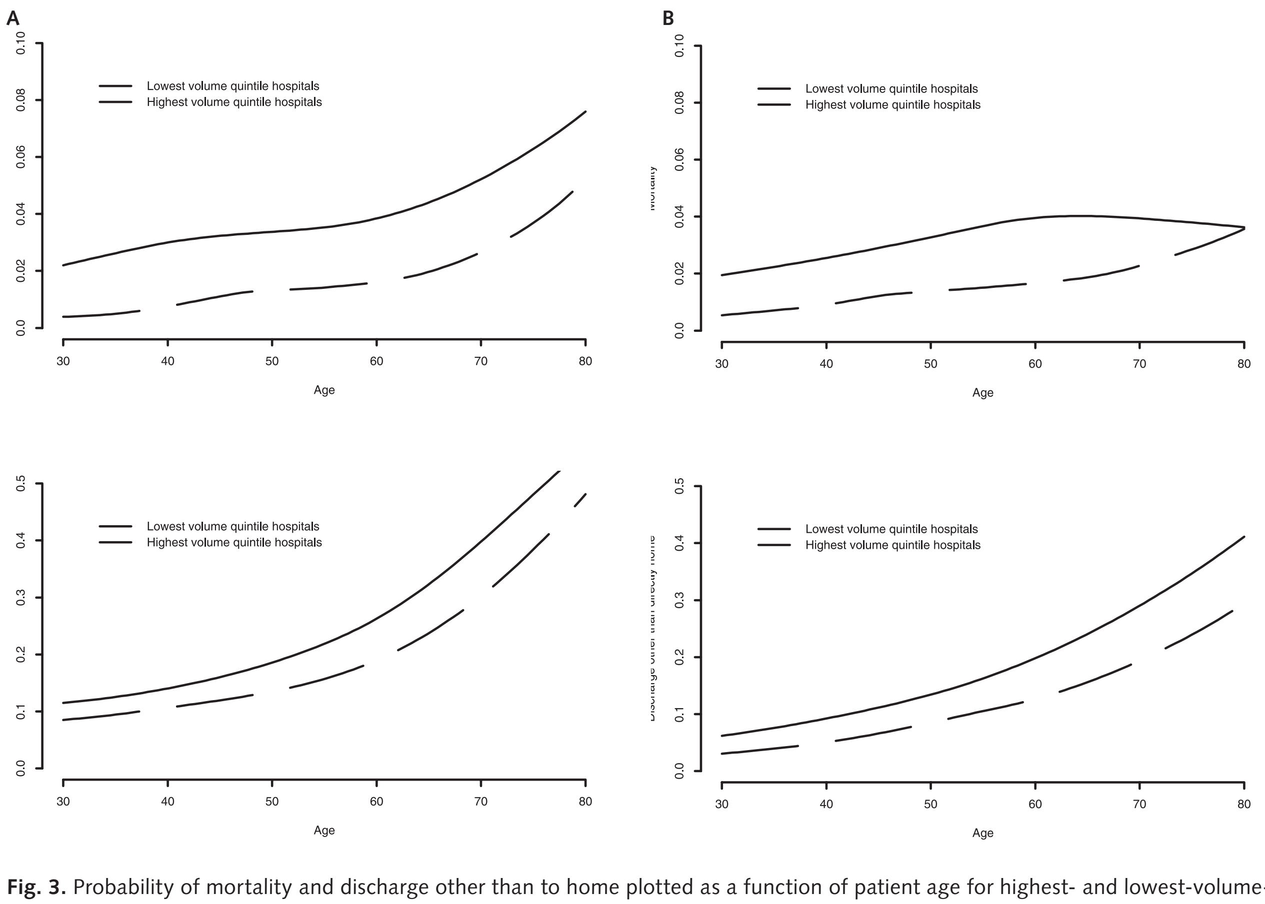

Fig. 3. Probability of mortality and discharge other than to home plotted as a function of patient age for highest- and lowest-volume-quintile hospitals. A, upper and lower panels. Craniotomy. B, upper and lower panels. Closed needle biopsy. Plots use local-likelihood fitting. The differences in mortality rates and hospital discharge disposition are present at all patient ages.

Table 5. Patient characteristics in highest- and lowest-volume quintile hospitals

	Lowest-volume quintile (1–5/year) (N = 5025)	Highest-volume quintile (42+/year) (N = 6184)
Age (median)	61	50
Female	46%	43%
Race		
White	85%	84%
Black	7%	4%
Primary payer		
Medicare	40%	22%
Medicaid	7%	6%
Private insurance	46%	66%
Median income in zip code of residence		
Quartile 1 (lowest)	19%	1%
Quartile 2	23%	17%
Quartile 3	21%	19%
Quartile 4 (highest)	37%	53%
Admission type		
Emergency	32%	18%
Urgent	29%	19%
Routine	39%	62%
Medical comorbidities		
None	49%	63%
One	30%	25%
Two or more	21%	12%

0.001). Patients who underwent more recent surgery were slightly less likely to be female (46% in 1988 vs. 43% in 2000, $P < 0.001$). Nonwhite patients were more common in later years (11% in 1988 vs. 16% in 2000, $P < 0.001$). Elective admissions became more common (45% in 1988 vs. 57% in 2000, $P < 0.001$). Benign tumors represented 7% of the patient population both in 1988 and in 2000 ($P = 0.4$).

The mortality rate for surgical treatment of primary brain tumors decreased during the study period: in-hospital mortality was 4.8% in 1988 (95% CI, 3.9%–5.9%) and 1.8% in 2000 (95% CI, 1.4%–2.3%), a reduction of 63%. In multivariate analyses that adjusted for age, sex, race, primary payer, admission type and source, procedure timing, comorbidity score, geographic region, diagnosis, type of procedure, and hospital caseload, mortality rates decreased both for craniotomies ($P < 0.001$; Fig. 5A) and for closed needle biopsies ($P = 0.003$; Fig. 5B).

There were changes in some practice patterns for surgical treatment of brain tumors during the study period. Projected to the U.S. nonfederal hospital universe of about 5000 hospitals, 1500 hospitals performed craniotomies for primary brain tumor in 1988 and 1332 in 2000, a significant decrease in number ($P < 0.001$). For hospitals in the NIS database that performed craniotomies for primary brain tumor, the median caseload increased little, from 4 admissions in 1988 to 5.5 in 2000. However, there was a disproportionate increase in caseload at the highest-volume centers during this period (Fig. 6). The 95th percentile for hospital tumor craniotomy caseload increased from 20 admissions in 1988 to 41 in 2000, and the estimated number of U.S. nonfederal hospitals performing more than 50 craniotomies annually for primary brain tumor increased from 11 in 1988 to 54 in 2000.

Annual provider caseloads increased during the study period for craniotomy, but not for needle biopsy. Analyzed per-patient, the median annual hospital craniotomy caseload increased from 11 (1988) to 22 (2000) and the median surgeon caseload from 4 to 6. In contrast,

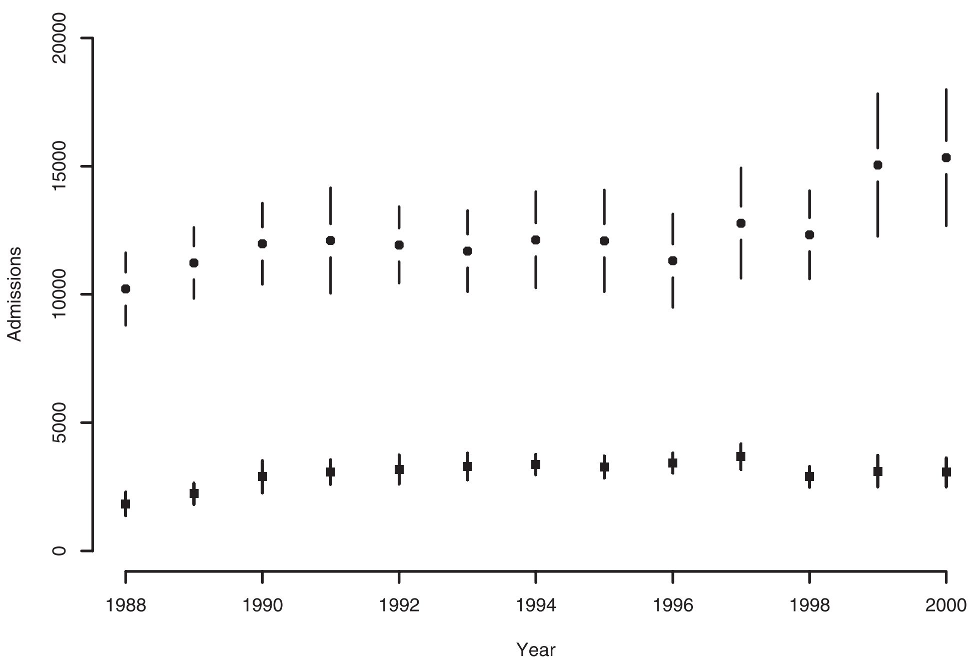

Fig. 4. Annual number of admissions for surgical treatment of primary brain tumors in nonfederal U.S. hospitals, 1988-2000. Circles, craniotomy; squares, needle biopsy; error bars, 95% confidence intervals.

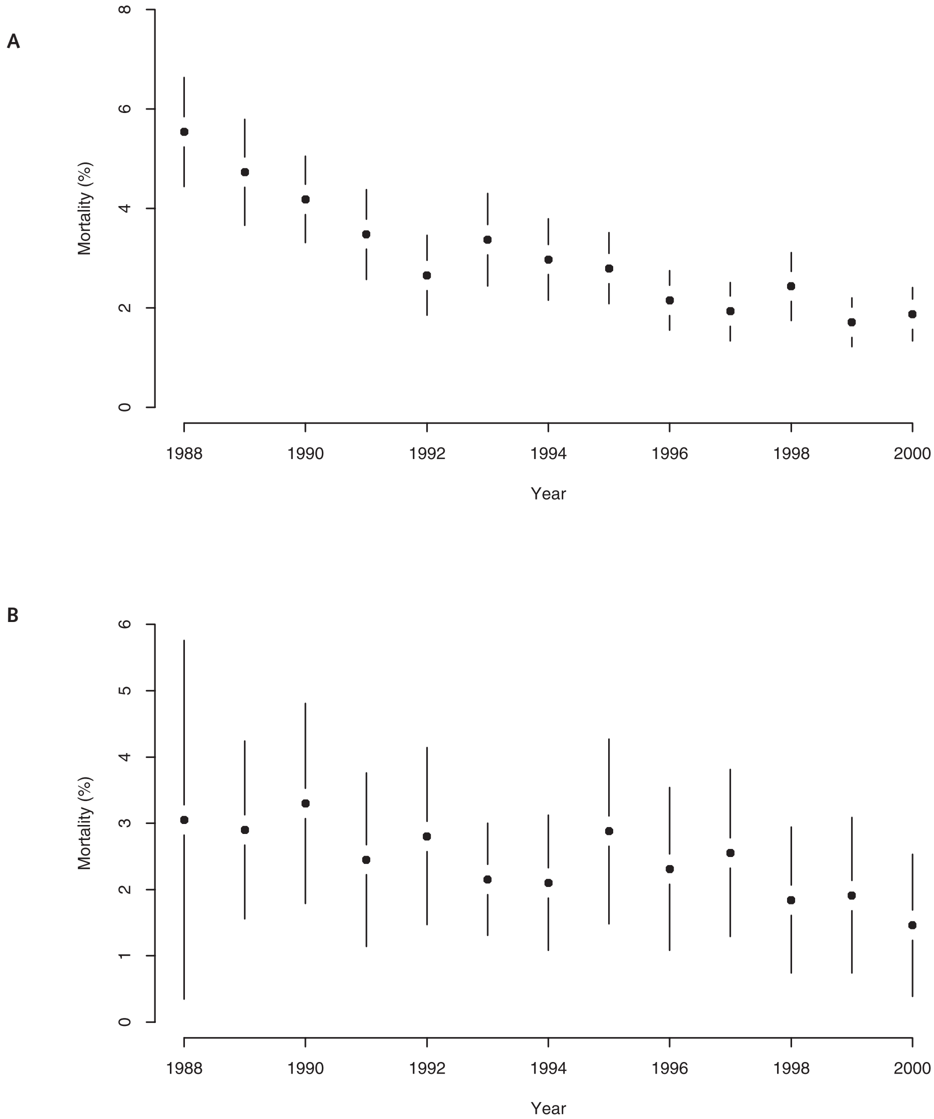

Fig. 5. In-hospital mortality rates for surgical treatment of primary brain tumors in nonfederal U.S. hospitals, 1988 to 2000. A. Craniotomy. B. Needle biopsy. The decrease in mortality was significant in multivariate analysis both for craniotomy ($P < 0.001$) and for closed needle biopsy ($P = 0.003$). Error bars, 95% confidence intervals.

the per-patient median annual hospital needle biopsy caseload decreased from 6 (1988) to 5 (2000) during the study period, and the median surgeon caseload remained unchanged at 2 per year.

As a consequence of these trends, the percentage of craniotomies performed at centers where caseload met or exceeded any specified threshold increased during the study period. For example, the largest-volume 5% of U.S. hospitals in 1988–1990 performed 25 or more craniotomies annually; these hospitals performed 23% of all craniotomies during these years. In 1997–2000, 44% of craniotomies in the U.S. were performed at hospitals where annual craniotomy caseload was 25 or more.

There was no tendency toward increased concentration of admissions for needle biopsies in specialized centers during the study period. The number of U.S. nonfederal hospitals performing needle biopsy increased significantly, from 501 (9%) in 1988 to 784 (16%) in 2000 ($P = 0.009$). The median number of needle biopsies performed at hospitals that performed at least one was 2 admissions both in 1988 and in 2000. The 95th percentile value for hospital needle biopsy caseload was 10 in 1988 and 12 in 2000.

We analyzed the share of total U.S. surgical primary brain tumor caseload treated at the 100 largest U.S. hospitals during the study period. Cut points identifying the 100 largest-caseload hospitals in the U.S. hospital universe were 22 admissions or more in 1988 and 37 admissions or more in 2000. In 1988, the 100 largest-caseload U.S. hospitals accounted for an estimated 30% of all U.S. primary brain tumor surgical admissions, a share which increased to 41% of admissions by 2000. These hospitals accounted for an estimated 7.6% of all U.S. medical and surgical admissions for any diagnosis in 1988 and 8.1% of all admissions in 2000. This suggests that the increased brain tumor caseload at the largest hospitals was the result of active concentration of caseload, rather than a passive change resulting from

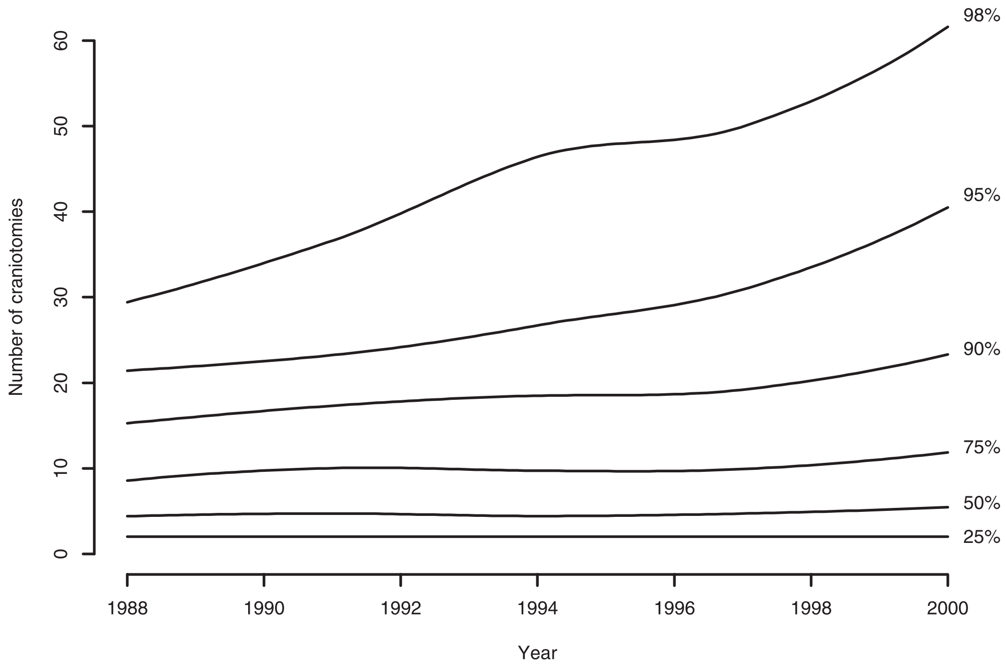

Fig. 6. Selected caseload percentiles for hospitals that performed at least one annual craniotomy. For example, the 90th percentile caseload for hospitals in 1988 was 16, increasing to 22 in 2000. Caseload at the largest centers increased disproportionately during the study period.

population shifts or selective enlargement of bed size at the largest hospitals.

Although these analyses suggested some tendency toward centralization of primary brain tumor procedures in specialized centers, at least for craniotomies, much of the reduction in mortality was not due to this cause. (This is shown by the multivariate analysis above: mortality decreased during the study period even after adjustment for hospital caseload.) The relative reduction in mortality was greatest at large-volume hospitals for craniotomies, but not for needle biopsies. Unadjusted mortality rates for craniotomies at the lowest-volume-quintile hospitals (5 or fewer cases per year) were 6.3% for 1988 to 1990 and 3.6% for 1997 to 2000, a relative reduction of 43%. For highest-volume-quintile hospitals (42 or more cases per year), unadjusted mortality rates were 3.3% in 1998 to 1990 and 0.9% in 1997 to 2000, a relative reduction of 73%. For needle biopsies, at the lowest-volume-quintile hospitals (1 or 2 cases per year), mortality was 5.7% for 1988 to 1990 and 2.4% for 1997 to 2000, a relative reduction of 58%. For highest-volume-quintile hospitals (12 or more cases per year), mortality was 3.2% in 1988 to 1990 and 1.1% in 1997 to 2000, a relative reduction of 66%.

Complications and Provider Volume

Several complications of surgery or perioperative care were examined. The types of complications (and the frequency of reported occurrences) are as follows: postoperative neurological complications, including those due to infarction or hemorrhage (reported in 2.6% of craniotomy patients and 0.7% of needle biopsy patients), hematoma complicating a procedure (2.2% of craniotomy patients and 1.4% of needle biopsy patients), mechanical ventilation (2.7% of craniotomy patients and 1.1% of needle biopsy patients), postoperative thrombotic disorders (deep venous thrombosis, pulmonary embolism, or placement of an inferior vena cava filter; 2.1% of craniotomy patients and 0.7% of needle biopsy patients), and transfusion of packed red blood cells (1.6% of craniotomy patients and 0.1% of needle biopsy patients).

The likelihood of coded complications after tumor craniotomies was analyzed in relation to hospital caseload by using multivariate logistic regression. Neurological complications were recorded more frequently at high-volume hospitals (OR for tenfold larger caseload, 1.67; 95% CI, 1.13–2.45; $P = 0.009$). However, adverse discharge disposition and death were less common among patients with coded neurological complications of surgery at high-volume hospitals: 19% of patients with coded neurological complications at lowest-quintile-volume hospitals died, as compared with 5% at highest-volume-quintile hospitals, and 59% of patients with coded neurological complications at lowest-volume quintile hospitals were not discharged directly home, compared with 43% at highest-volume-quintile hospitals. There was a trend toward less frequent occurrence of postoperative hematomas at high-volume hospitals (OR, 0.86; 95% CI, 0.69–1.06; $P = 0.15$). Mechanical ventilation was marginally less frequent at high-volume hospitals (OR, 0.73; 95% CI, 0.53–1.00; $P = 0.05$). Thromboembolic complications were more common at high-volume hospitals (OR, 1.46; 95% CI, 1.11–1.91; $P = 0.007$), a finding that was not affected by adjustments for hemiplegia or hydrocephalus. There was no significant relation between hospital caseload and the likelihood of a red cell transfusion.

Length of Stay and Hospital Charges

Median LOS decreased significantly during the study period, from 12 days (1988) to 5 days (2000) for craniotomy, and from 6 days (1988) to 3 days (2000) for needle biopsy. After multivariate adjustment for the patient covariates described above and stratification by treatment year, LOS was significantly shorter at higher-volume hospitals for needle biopsies (19% shorter for tenfold higher caseload; $P < 0.001$). There was a trend toward shorter LOS at higher-volume hospitals for craniotomies (4% shorter for tenfold higher caseload; $P = 0.07$).

Indexed to year 2000 U.S. dollars, median total hospital charges increased significantly during the study period, from $21,400 (1988) to $33,200 (2000) for craniotomies and from $9,800 (1988) to $15,910 (2000) for needle biopsies. After multivariate adjustment for the patient covariates described above and stratification by treatment year, charges were slightly higher at higher-volume hospitals (8% higher for tenfold larger caseload, $P = 0.03$). There was a trend toward lower charges at higher-volume hospitals for closed needle biopsies (8% lower for tenfold higher caseload, $P = 0.09$).

Discussion

This analysis included 38,028 admissions for biopsy or resection of supratentorial primary adult brain tumors, performed at U.S. nonfederal hospitals between 1988 and 2000. In-hospital mortality was 2.8% (2.5% for needle biopsy and 2.9% for craniotomies), and 22% of patients were not discharged directly home (19% of needle biopsy patients and 23% of craniotomy patients). Care provided by higher-volume hospitals and surgeons was followed by lower mortality and better outcome at hospital discharge, with similar lengths of hospital stay and total hospital charges. The benefits of high-volume care were more commonly enjoyed by patients who were younger, healthier, and white; who had private insurance; and who resided in wealthier areas. In-hospital mortality decreased substantially for both closed and open procedures during the study period. There was a tendency toward centralization of brain tumor surgery at high-volume centers, although much of the U.S. patient population continued to receive surgical care for brain tumors at low-volume hospitals throughout the study period.

Outcomes of patients who require complex medical care have been shown to be dependent on characteristics of health care providers, as well as on patient- and disease-specific risk factors. Outcomes after surgical procedures are commonly studied in this context because the treatment choice (procedure performed) can be narrowly defined. Provider characteristics that have been shown to predict patient outcomes after surgical procedures include current hospital or surgeon caseload, the surgeon's accumulated prior experience with similar procedures, and subspecialization at the physician or institutional level (Halm et al., 2002; Hewitt, 2000; Hewitt and Petitti, 2001; Luft et al., 1990). The tendency toward superior outcomes after care provided by physicians or hospitals with large current caseloads is called the volume-outcome effect.

The volume-outcome effect has been demonstrated previously for other intracranial procedures, such as clipping of intracranial aneurysms (Barker et al., 2003a; Johnston et al., 2001; Solomon et al., 1996), as well as for the surgical treatment of brain tumors in both pediatric patients (Smith et al., 2004a) and adult patients (Cowan et al., 2003; Long et al., 2003). Cowan et al. studied mortality in 7547 patients from the NIS database, 1996 to 1997, after craniotomy for malignant primary and metastatic intracranial tumors (Cowan et al., 2003). Mortality was lower with high-volume hospitals and surgeons, but a subgroup analysis suggested that the difference in mortality was only statistically significant for parietal lobe primary tumors and for metastases. Long et al. (2003) studied 4723 patients who underwent craniotomy in the state of Maryland, 1990 to 1996, for primary benign or malignant intracranial tumors, including meningiomas, metastases, pineal and pituitary tumors, hemangiomas, and cavernous angiomas. Mortality was lower for the two high-volume centers studied than for 31 low-volume hospitals. Tigliev et al. and Chernov reported lower mortality after brain tumor resections performed at higher-volume hospitals among a small cohort in Saint Petersburg, Russia (Tigliev et al. 1999; Chernov 2004). Latif et al. (1998) studied mortality, morbidity, and long-term survival after operations for malignant gliomas performed by a single specialist neurosurgeon compared to results achieved by nonspecialist colleagues at a single institution. Although the findings favored the specialist surgeon, statistical significance was not reached, and few conclusions were drawn.

The present study confirms and extends the volume-outcome relationship demonstrated previously. Mortality in this study was lower for high-volume hospitals and surgeons, with no evidence for concentration of the volume-outcome effect in subgroups based on histology or location (for malignant tumors, which comprised most of the study group). Another important measure of patient outcome, disposition at hospital discharge, was also more favorable in patients of higher-volume hospitals and surgeons in this study. Postoperative neurological complications, however, were more frequent at higher-volume centers. This could reflect a more challenging case mix at larger centers, with lesions more frequently located in speech or motor areas, or the effect of more aggressive resections of lesions adjacent to eloquent areas. It could also reflect systematically different thresholds for diagnosing new neurological deficits at high- and low-volume centers. The much more frequent association of a coded neurological complication with death or discharge to an institution at low-volume centers argues that this is at least a partial explanation for this finding. A similar association of less frequent death after certain coded postoperative complications at high-volume hospitals has also been interpreted as "failure to rescue" at low-volume centers by some authors (AHRQ, 2003; Zhan and Miller, 2003).

The mortality benefit of larger caseload was also present for needle biopsy of primary brain tumors. Although most of these procedures were probably performed by using either stereotactic frames or frameless stereotactic guidance techniques (Dorward et al., 2002), the same ICD-9-CM code is used for needle biopsies performed without stereotactic guidance. More frequent performance of such procedures at low-volume centers could explain poorer outcome, if such procedures are associated with higher mortality or morbidity (Lee et al., 1991). The volume-outcome effect is usually considered to be most characteristic of complex, risky surgical procedures such as esophagectomy or pneumonectomy (Begg, 1998; Birkmeyer et al., 2001, 2002). However, lower mortality when another "simple" neurosurgical procedure, ventriculoperitoneal shunt surgery, is performed at high-volume institutions has previously been demonstrated (Cochrane et al., 1995; Smith et al., 2004b). The present study indicates that the low rates of mortality and morbidity for stereotactic biopsy reported from specialized centers (Field et al., 2001; Hall, 1998; Kim et al., 2003; Kreth et al., 2001; Sawin et al., 1998) may not accurately describe the risks of needle biopsies performed at low-volume institutions.

The demonstration that better outcomes follow when complex surgical procedures are performed at higher-volume centers often leads to a call for concentration of care in the hands of a limited number of providers, as by regionalizing care at specialized centers or by requiring specialized certification for surgeons who perform the procedure. The limitations of a study such as this one should be carefully considered before its conclusions are accepted as supporting regionalization of brain tumor surgery. Because a hospital discharge database in which patient identities are masked was used as the data source, long-term outcomes such as functional status at 30 days or 6 months, or survival after discharge, were not available for study. Because some patients discharged to short-term rehabilitation centers return to normal functional levels when recovery is complete, using short-term outcomes is likely to magnify any difference between long-term functional outcomes for patients treated at high-volume hospitals and those for patients treated at low-volume hospitals. In addition, volume-outcome studies, for which randomization is difficult or impossible, are observational studies of competing treatments (i.e., treatment at high- or low-volume centers) and are hence liable to selection bias. This study showed some evidence for a lower risk population at high-caseload centers (such as younger patient age, less severe medical comorbidity, and less frequent emergency or urgent admission) and some evidence for higher risk patients at such centers (such as more frequent neurological complications). The multivariate adjustment for case mix used here is not capable of eliminating all effects of selection bias, and a data source with more detailed clinical patient and tumor information would be valuable in confirming the results of this analysis.

Preferential use of less aggressive (and hence lower risk) tumor resection at high-volume centers could also contribute to the effects observed in this study, although such a bias is not currently known to exist, and specialist surgeons typically advocate the most complete tumor resection possible. Disease-specific end points such as extent of resection are not contained in the NIS database. Albright et al. used data from patients entered into three Children's Cancer Group studies, combined with information on referring surgeons, to classify surgeons into three groups based on pediatric certification and experience. Pediatric tumor patients treated by more experienced or subspecialized surgeons had more complete resections (Albright et al., 2000). A similar study on extent of resection in adult primary brain tumor surgery would be a useful adjunct to studies such as the present one. Alternatively, a population-based data source containing both survival and information on the institution where surgery was performed could be used to study a survival end point. However, because subtle pathologic differences in primary brain tumors carry significant implications for prognosis, such a study might be biased in unpredictable ways by the lack of central review of surgical pathology (Aldape et al., 2000; Pollack et al., 2003; Scott et al., 1995).

Trends over Time

The analysis provided some novel insights into trends in brain tumor surgery practice patterns and outcomes during the 13-year study period. There was a modest decrease in median patient age, perhaps a consequence of more frequent detection of low-grade tumors because of more frequent use of screening imaging tests for minor or unrelated symptoms (Centers for Medicare & Medicaid Services, 2004; Maitino et al. 2003), because of increased willingness to submit such patients to operation, or both. The most important trend was the substantial decrease in mortality rates, from 4.8% (1988) to 1.8% (2000). Given the relationship between higher provider caseloads and lower mortality rates, one possible explanation for this finding would be a shift of patients from low-volume to high-volume centers. There was only modest evidence for such a trend, with median provider caseloads nearly unchanged during the study period. However, there was an increase in very-high-volume centers (informally defined as more than 50 admissions per year), from an estimate of 11 in the United States in 1988 to 54 in 2000. Of the 37 hospitals in the NIS database with annual caseloads of greater than 50, all but 2 were classified as teaching hospitals. This implies an increase in annual primary brain tumor surgery caseloads for many academic centers in the United States during this time period.

However, most patients undergoing surgical treatment for primary brain tumors in the United States are still treated at relatively low-volume centers (less than 6 craniotomies per year in 2000). Although mortality rates for craniotomy decreased in both low- and high-volume hospitals during the study period, the relative decrease in mortality was 43% for lowest-volume-quintile hospitals between the earliest and latest years in the series, compared to a relative mortality decrease of 73% at the highest-volume-quintile hospitals. The relatively larger reduction in mortality rates at highest-volume centers could be due to selective availability of high-technology equipment used during or after brain tumor surgery, to the progressive emergence of neuro-oncology services as recognized subspecialty providers at these centers during this time period, or to other factors such as anesthesia, nursing, or intensive care expertise. The availability of multicenter brain tumor treatment protocols and consortiums at highest-volume centers may also be drawing relatively healthy, well-educated, low-risk patients from the community. These trends are difficult to study in the absence of more detailed clinical and socioeconomic information than is contained in the NIS database.

Length of Stay and Hospital Charges

There was little difference between high- and low-volume centers in either LOS or hospital charges during this period. LOS was lower at high-volume centers, but not significantly so, and charges were slightly higher at high-volume centers (for craniotomies, 8% higher for a tenfold increase in hospital caseload). These trends are similar to results seen for other neurosurgical procedures (Barker et al., 2003a; Eskandar et al., 2003; Hoh et al., 2003; Kalkanis et al., 2003; Long et al. 2003) and may indicate that the benefits of high-volume neurosurgical care are typically achieved with little or no increased use of health care resources.

Conclusions

This study included a large representative sample of patients who underwent surgical treatment of primary brain tumors in the United States between 1988 and 2000. After adjustment for risk factors such as age, medical comorbidity, and tumor histology and location (for malignant tumors), both in-hospital mortality and adverse hospital discharge disposition were less frequent after surgery at high-volume centers or by high-volume surgeons, both for needle biopsy and for craniotomy. A bias toward concentration of low-risk patients at high-volume centers probably affected this study's results despite multivariate adjustment for observed risk factors. The study did not establish an annual caseload threshold below which mortality or morbidity abruptly worsened for either procedure.

Some trends in national practice patterns for the two procedures were also observed. During the study interval the aggregate U.S. annual caseload increased significantly. There was a substantial decline in mortality rates at centers of all sizes, but especially at larger centers. A trend toward progressive concentration of craniotomy admissions at the highest-volume centers was also seen. The reasons for the observed shifts in practice patterns are unclear, and will be an important topic for further research.

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