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Transsphenoidal Surgery for Pituitary Tumors in the United States, 1996–2000: Mortality, Morbidity, and the Effects of Hospital and Surgeon Volume

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Larger surgical caseload is associated with better patient outcome for many complex procedures. We examined the volume-outcome relationship for transsphenoidal pituitary tumor surgery using the Nationwide Inpatient Sample, 1996–2000. Multivariate regression adjusted for patient demographics, acuity measures, medical comorbidities, and endocrine status.

A total of 5497 operations were performed at 538 hospitals by 825 surgeons. Outcome measured at hospital discharge was: death (0.6%), discharge to long-term care (0.9%), to short-term rehabilitation (2.1%), or directly home (96.2%). Outcomes were better after surgery at higher-volume hospitals (OR 0.74 for 5-fold-larger caseload, *P* = 0.007) or by higher-volume surgeons (OR 0.62, *P* = 0.02). A total of 5.4% of patients were not discharged directly home from lowest-volume-quartile hospitals, compared with 2.6% at highest-volume-quartile hospitals. In-hospital mortality was lower with higher-volume hospitals (*P* = 0.03) and surgeons (*P* = 0.09). Mortality rates were 0.9% at lowest-caseload-quartile hospitals and 0.4% at highest-volume-quartile hospitals. Postoperative complications (26.5% of admissions) were less frequent with higher-volume hospitals (*P* = 0.03) or surgeons (*P* = 0.005). Length of stay was shorter with high-volume hospitals (*P* = 0.02) and surgeons (*P* < 0.001). Hospital charges were lower for high-volume hospitals, but not significantly.

This analysis suggests that higher-volume hospitals and surgeons provide superior short-term outcomes after transsphenoidal pituitary tumor surgery with shorter lengths of stay and a trend toward lower charges. (*J Clin Endocrinol Metab* 88: 4709–4719, 2003)

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 (1, 2) or cardiovascular operations (3) are performed at high-volume hospitals. Within endocrine surgery, studies have shown less frequent complications when thyroidectomies (4, 5) or parathyroidectomies (6) are performed by more experienced surgeons.

Surgical excision is the initial treatment for most pituitary tumors, excluding prolactinomas, for which surgery is often indicated when medical therapy is unsuccessful. Although reports of outcomes after transsphenoidal surgery for pituitary tumors usually originate in centers that specialize in such surgery, the extent to which transsphenoidal surgery is currently performed at low-volume centers and the results achieved in nonspecialized settings are relatively unknown.

We studied the volume-outcome relationship for transsphenoidal surgery for pituitary tumors performed in a representative sample of U.S. hospitals between 1996 and 2000. Specifically, we related the chance of adverse outcomes [in-hospital mortality, outcome at hospital discharge, complications of surgery, length of stay (LOS), and hospital charges] to the annual hospital and surgeon caseload of transsphenoidal surgery, as well as to other patient and provider characteristics.

Abbreviations: CI, Confidence interval; DI, diabetes insipidus; LOS, length of stay; NIS, Nationwide Inpatient Sample; OR, odds ratio; RBC, red blood cell.

Subjects and Methods

We obtained the Nationwide Inpatient Sample (NIS) hospital discharge database for the years 1996–2000 from the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (Rockville, MD) (7). The NIS is a hospital discharge database that approximates a 20% sample of all inpatient admissions to nonfederal hospitals in the United States. For these years, the NIS contains discharge data on 100% of discharges from a stratified random sample of nonfederal hospitals in 19–28 states to produce a representative 20% subsample of all U.S. nonfederal hospital discharges. Because the NIS 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, a code identifying the primary surgeon for the principal procedure during the admission is also included. An overview of the NIS is available at http://www.ahcpr.gov/data/hcup/nisintro.htm.

Inclusion and exclusion criteria and definition of endpoints

We defined an admission for transsphenoidal surgery for pituitary tumor by using a combination of ICD-9-CM diagnosis and primary procedure codes. We required a primary procedure code of 07.14, 07.62, or 07.65 (biopsy, partial resection, or total resection of pituitary gland using transsphenoidal approach, respectively) and one or more of the following diagnosis codes: 227.3 (benign neoplasm of pituitary), 194.3 (malignant neoplasm of pituitary), 237.0 (pituitary neoplasm of uncertain behavior), 239.7 (endocrine neoplasm of uncertain nature), 253.0 (acromegaly), or 255.0 (Cushing's syndrome). Other intrasellar lesions, such as craniopharyngiomas and Rathke's cleft cysts, were excluded.

Two primary endpoints were examined: in-hospital mortality and discharge to institutions other than home. In-hospital mortality was coded directly in the NIS database and was analyzed using logistic regression. Discharge to institutions other than home was coded on a four-level scale and was analyzed using ordinal logistic regression, which allows use of the entire spectrum of outcomes rather than simplifying to a single cutpoint with resultant information loss (8–10). Discharge 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, we coded these discharges (0.3% of the total) as discharge to other facilities. We counted discharge home with home health care or iv therapy (4.5% of discharges) and discharge against medical advice (0.05% of discharges) as discharge home. Discharge to another acute care hospital (0.2% of discharges) was counted as discharge to an institution other than home, not as discharge to a long-term facility.

LOS and total hospital charges were coded in NIS data. Four patients with LOS of zero were recoded as missing (all were discharged alive). LOS and hospital charge analyses included only patients discharged from hospital alive. LOS and hospital charge data were highly positively skewed and were analyzed as the logarithmic transforms.

Patient characteristics

Patient age, sex, race, median household income for ZIP code of residence (11), primary payer (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. Eleven patients (0.2%) with admission type listed as other were recoded as routine admissions. Five patients (0.1%) with admission source of court/law enforcement were recoded as admissions from home. More than 5% of discharges had missing values for three variables used principally as stratification factors for other analyses, race (22% missing), admission type (21% missing), and whether the principal procedure was performed on the first hospital day (12% 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, the set of 30 medical comorbidity markers described by Elixhauser *et al.* (12), excluding the two specific neurological comorbidity variables (paralysis and other neurological deficit) and three comorbidity variables likely to represent postoperative conditions (fluid and electrolyte disorders, blood loss anemia, and deficiency anemias), were calculated using Agency for Healthcare Research and Quality software (www.ahcpr.gov/data/hcup/comorbid.htm) and summed to give a single comorbidity score ranging between 0 and 25.

Endocrine diagnoses were defined as follows: Cushing's disease (ICD-9-CM 255.0), acromegaly (253.0), and noniatrogenic panhypopituitarism (253.2). Visual loss likely to be due to pituitary tumors was defined as visual field defects (368.40–49), optic atrophy (377.10), compression of optic nerve(s) (377.49), disorders of the optic chiasm associated with pituitary neoplasm (377.51), or disorders of other visual pathways due to neoplasm (377.61). We identified potential complications of transsphenoidal surgery using the following codes: postoperative neurological complications, including those due to infarction or hemorrhage (997.00–997.09); hematoma complicating a procedure (998.1–998.13); any intracerebral hemorrhagic event (430–432 or 998.1–998.13); fluid and electrolyte abnormalities (276.0-.9); diabetes insipidus (DI, 253.5); iatrogenic panhypopituitarism (253.7); diplopia, ptosis, or deficits of cranial nerves 3, 4, or 6 (368.2, 374.30–31, 378.50–59); cerebrospinal fluid rhinorrhea (349.81); performance of a cerebral arteriogram (88.41); mechanical ventilation (96.70–96.72); deep venous thrombosis, pulmonary embolism, or placement of an inferior vena cava filter (415, 415.11–19, 453.8–9, 38.7), and transfusion of packed red blood cells (RBCs) (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. We derived hospital and surgeon volumes of transsphenoidal surgery by counting the cases for each identified surgeon and hospital in the database. Because hospital and physician volumes 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 loglinear least-squares, ordinary logistic, and proportional-odds ordinal logistic regression (13–15). To correct for possible clustering of similar outcomes within hospitals, which could cause falsely inflated estimates of the statistical significance of regression coefficients, a sandwich variance-covariance matrix was estimated from the data using methods due to Huber and White, with adjustment for clustering by hospital or surgeon (15). LOS and hospital charges were analyzed as logarithmic transforms using least-squares regression corrected for clustering as described above. Calculations were performed using SAS (version 8.2; SAS Institute, Cary, NC) and S-plus (Version 3.3 for Windows; Insightful, Inc., Seattle, WA) with the Hmisc and Design modeling function software libraries due to Harrell [15; Hmisc and Design libraries for S-Plus for Windows (2000)—software and electronic documentation available from http://hesweb1.med.virginia.edu/biostat/s/splus.html] and the LOCFIT local-likelihood regression library due to Loader (16, 17). Extrapolations to the entire U.S. population were adjusted for the NIS stratified survey method using SAS PROC SURVEYMEANS (18). All *P* values are two-tailed.

Results

There were 5497 admissions for transsphenoidal surgery for pituitary tumors, performed at 538 hospitals by 825 identified surgeons. After adjustment for NIS weighting and stratified sampling, the calculated annual caseload for all U.S. nonfederal hospitals between 1996 and 2000 was 5410 cases per year. Our data therefore included about 20% of the U.S. nonfederal hospital caseload during this 5-yr period. Clinical characteristics of the patients are shown in Table 1. Most patients were white, age 35–65 yr, with slightly more women than men. Cushing's disease was coded in 7% of patients and acromegaly in 6%. Most admissions were classified as routine and admission through the emergency ward or as a transfer from another hospital was uncommon. There was no upward or downward trend in the annual number of cases during the study period and no trend in patient age, mortality, or outcome at hospital discharge over time. Thirty-two patients died (0.6%), 52 (0.9%) were discharged to long-term care facilities such as skilled nursing facilities, 118 (2.1%) were discharged to other facilities such as rehabilitation hospitals, and 5290 patients were discharged home (96.3%).

Patient characteristics and outcome

We tested five demographic variables as potential outcome predictors: age, sex, race, income in the ZIP code of the patient's residence (a surrogate for patient's income), and primary payer for care. In univariate analyses, age was a significant predictor both of mortality [odds ratio (OR) 1.6 per decade, 95% confidence interval (CI) 1.2–2.1, $P < 0.001$] and of worse outcome at hospital discharge (OR 1.8, 95% CI 1.6–2.0, $P < 0.001$; Fig. 1). Patient gender and race (coded as white *vs.* nonwhite or black *vs.* nonblack) had no significant

TABLE 1. Clinical characteristics of 5497 patients who underwent transphenoidal surgery for pituitary tumors

Age	
Mean	50 yr
Median	49 yr
Interquartile range	37–64 yr
Range	0–91 yr
Female sex (N = 5491)	2935 (53%)
Race (N = 4281)	
White	2901 (68%)
Black	636 (15%)
Hispanic	452 (11%)
Asian/Pacific islands	141 (3%)
Native American	14 (0.3%)
Other	137 (3%)
Median household income for ZIP code of residence (N = 5090)	
<$25,000	678 (13%)
$25,000–$34,999	1498 (29%)
$35,000–$44,999	1384 (27%)
>$45,000	1530 (30%)
Primary payer (N = 5483)	
Medicare	1254 (23%)
Medicaid	361 (7%)
Private insurance	3453 (63%)
Self-pay	188 (3%)
No charge	19 (0.3%)
Other	208 (4%)
Admission type (N = 4318)	
Emergency	366 (8%)
Urgent	420 (10%)
Routine	3520 (82%)
Admission source (N = 5339)	
Emergency ward	270 (5%)
Transfer from acute care hospital	98 (2%)
Transfer from long-term care	107 (2%)
Routine	4859 (91%)
Year of treatment	
1996	965 (18%)
1997	1150 (22%)
1998	843 (16%)
1999	1260 (24%)
2000	1279 (24%)
Procedure	
Biopsy	45 (0.8%)
Partial hypophysectomy	4091 (74%)
Total hypophysectomy	1361 (25%)
Cushing's disease	383 (7%)
Acromegaly	312 (6%)
Panhypopituiterism (excluding iatrogenic)	319 (6%)

relationship with mortality or outcome. Median income in the patient's ZIP code of residence was significantly related to outcome (better outcome in higher income areas, OR 0.86 95% CI 0.75–0.98, $P = 0.02$), but was not significantly related to mortality ($P = 0.3$). Primary payer for care was also significantly related both to mortality and to outcome at hospital discharge, findings that persisted after adjustment for patient age. Private insurance status predicted lower mortality (OR 0.32, 95% CI 0.12–0.80, $P = 0.01$) and better outcome at discharge (OR 0.19, 95% CI 0.09–0.44, $P < 0.001$). Age, sex, median income in ZIP code of residence, and stratification by race, primary payer, and geographic region were included in all models described below.

Four variables related to acuity of care and general comorbidity were examined: admission type (emergency, urgent, elective); admission source (emergency room, transfer from another hospital, routine); whether surgery was performed on the day of admission; and a general medical comorbidity score. Each of these variables was significantly related to outcome at hospital discharge ($P < 0.001$ for all) and all but the medical comorbidity score were significant predictors of mortality as well ($P < 0.02$ for all). All four acuity/comorbidity variables were included in subsequent multivariate models.

We tested coded diagnoses of Cushing's disease (coded in 7% of the cohort), acromegaly (6%), noniatrogenic panhypopituitarism (6%), and visual loss (6%) as outcome predictors. Cushing's disease was associated with trends toward higher mortality (OR 3.5, 95% CI 0.95–13, $P = 0.06$) and worse outcome at hospital discharge (OR 1.8, 95% CI 0.9–3.5, $P = 0.1$). Acromegaly, noniatrogenic panhypopituitarism, and visual loss were not significant predictors of mortality or outcome at discharge. Presence or absence of Cushing's disease was included in all subsequent models.

Hospital and surgeon characteristics and outcome

Patients were treated at 538 hospitals. For 2727 patients (50% of the total), 825 treating surgeons were identified in the database. Between 95 and 98% of surgeons operated at one hospital, and 2–5% operated at two or three hospitals. (Because not all hospitals per state are sampled, this represents a minimum estimate.) Hospitals and surgeons varied widely in the volume of transsphenoidal pituitary tumor surgery reported. Analyzed on a per-patient basis, the median annual number of transsphenoidal pituitary tumor operations was 10 per hospital (range, 1–126 admissions; 25th percentile, five admissions; 75th percentile, 25 admissions) or three per surgeon (range, 1–33 admissions; 25th percentile, two admissions; 75th percentile, seven admissions). For 251 patients (5%), no other transsphenoidal pituitary tumor operation was reported during that year at their hospital, and for 627 patients (23%) no other transsphenoidal pituitary tumor operation was reported that year by their surgeon. Table 2 shows clinical characteristics of patients treated at hospitals in the lowest- and highest-volume quartiles for transsphenoidal pituitary tumor surgery caseload (one to four admissions per year and 25 or more admissions per year, respectively).

We tested both hospital and surgeon annual caseload of transsphenoidal pituitary tumor surgery as outcome predictors. Both measures were highly significant outcome predictors, with larger annual caseload associated with better outcome for each. We report odds ratios for the importance of hospital and surgeon caseload for a 5-fold difference in caseload, because this approximates the difference between 25th and 75th percentiles for caseload. In multivariate analysis adjusted for the variables described above, a 5-fold larger hospital caseload was associated with significantly better outcome (OR 0.74, 95% CI 0.59–0.92, $P = 0.007$), as was a 5-fold larger surgeon caseload (OR 0.62, 95% CI 0.41–0.94, $P = 0.02$). Figure 2 shows the probability of discharge other than to home for operations at hospitals grouped by caseload into four quartiles and for surgeons similarly grouped. Discharge other than to home occurred after 5.4% (71/1312) of admissions for transsphenoidal pituitary tumor surgery at hospitals with annual caseload of one to four admissions

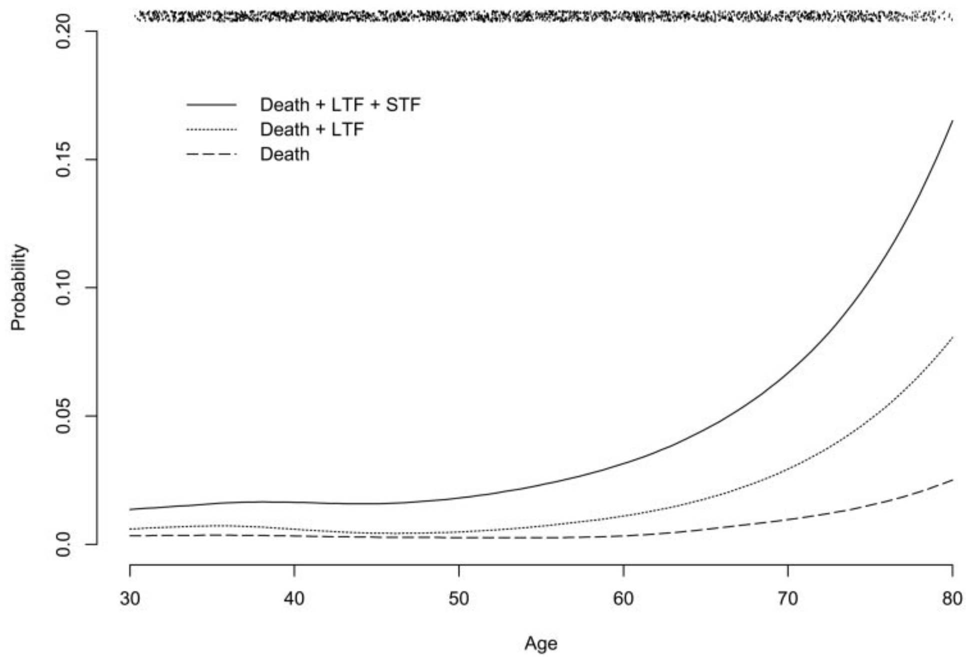

FIG. 1. Effect of age on probability of death or discharge other than to home after transsphenoidal surgery for pituitary tumors, plotted using local-likelihood fitting. *Dashed line*, Mortality; *dotted line*, death or discharge to long-term care facility (LTF); *solid line*, death or discharge to long-term or short-term facility (STF). *Bar* along top of graph: scatterplot showing the age distribution of the sample; each *dot* represents one patient admission.

TABLE 2. Patient characteristics in high- and low-volume hospitals

	Low-volume (1–4/yr)	High-volume (25+/yr)
Age (median)	52	47
Female	656/1313 (50%)	607/1389 (44%)
Race		
White	691/1015 (68%)	845/1210 (70%)
Black	165/1015 (16%)	123/1210 (10%)
Primary payer		
Medicare	376/1310 (29%)	261/1391 (19%)
Medicaid	74/1310 (6%)	80/1391 (6%)
Private insurance	759/1310 (58%)	981/1391 (71%)
Median income in ZIP code of residence		
<$25,000	190/1234 (15%)	126/1303 (10%)
$25,000–$34,999	395/1234 (32%)	320/1303 (25%)
$35,000–$44,999	339/1234 (27%)	363/1303 (28%)
>$45,000	310/1234 (25%)	494/1303 (38%)
Rural *vs.* urban (hospital location used as proxy)		
Rural	65/1302 (5%)	0/1392 (0%)
Admission type		
Emergency	90/1117 (8%)	38/729 (5%)
Urgent	124/1117 (11%)	64/729 (9%)
Routine	899/1117 (80%)	627/729 (86%)
Procedure		
Biopsy	13/1313 (1%)	13/1392 (1%)
Partial hypophysectomy	963/1313 (73%)	1165/1392 (84%)
Total hypophysectomy	337/1313 (26%)	214/1392 (15%)
Cushing's disease	36/1313 (2.7%)	173/1392 (12.4%)
Acromegaly	70/1313 (5.3%)	97/1392 (7.0%)
Panhypopituitarism (excluding iatrogenic)	102/1313 (7.8%)	51/1392 (3.7%)

compared with 2.6% (36/1390) of admissions at hospitals with annual caseload of 25 admissions or more. The corresponding rates for surgeon caseload were 6.2% (39/627) for admissions to surgeons with annual caseload of one case and 2.7% (18/657) for admissions to surgeons with annual caseload of eight or more.

The difference in outcome between high- and low-volume hospitals and surgeons varied according to patient age. Figure 3 shows the probability of discharge other than to home as a function of age for highest- and lowest-volume quartile hospitals. Older patients had a much greater difference between highest- and lowest-volume-quartile hospitals in probability of discharge other than to home.

In-hospital mortality was also lower at high-volume hospitals (OR for 5-fold higher caseload 0.54, 95% CI 0.31–0.95, $P = 0.03$). There was a trend toward lower mortality after surgery performed by high-caseload surgeons (OR 0.47, 95% CI 0.20–1.1, $P = 0.09$). Figure 4 shows mortality by hospital and surgeon caseload quartile. 0.9% of patients operated at lowest-caseload-quartile hospitals died, compared with 0.4%

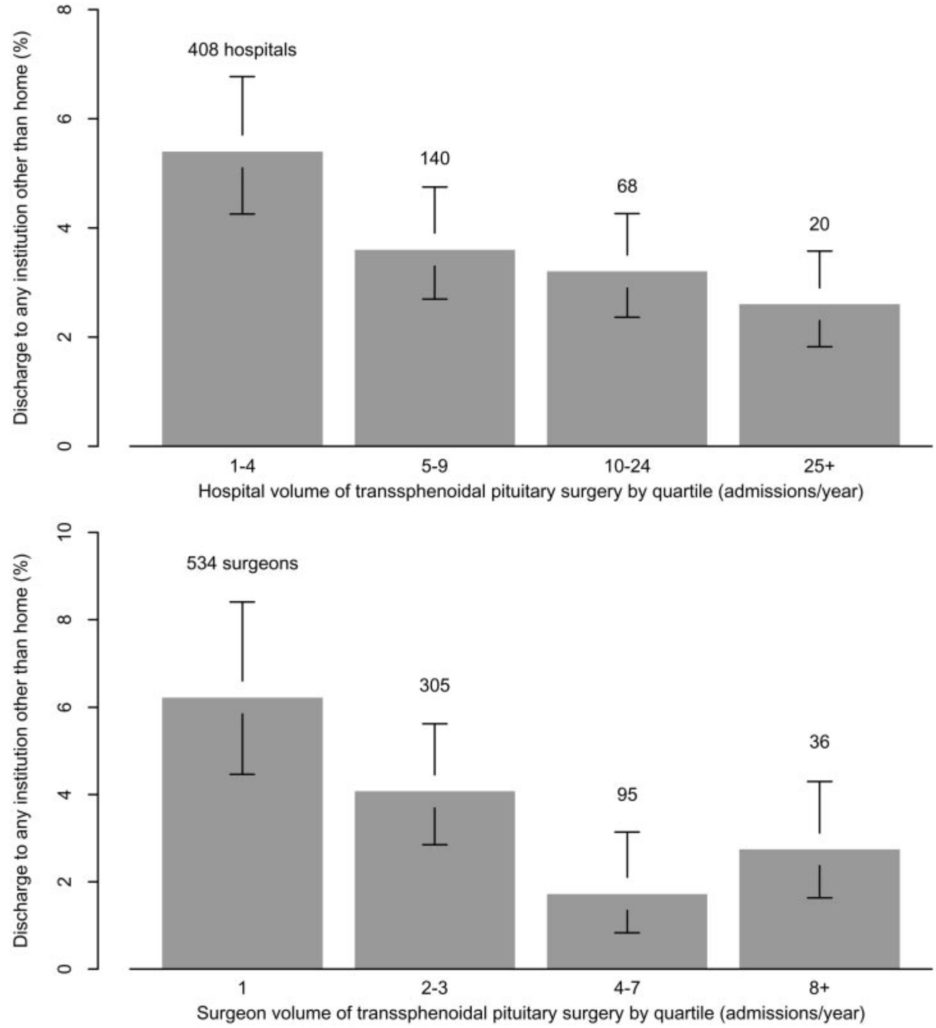

FIG. 2. Bar graph showing probability of discharge other than to home as a function of hospital and surgeon volume of transsphenoidal pituitary tumor surgery, by quartile. The relationship between larger caseload and better outcome was significant in multivariate analysis both for hospitals ($P = 0.007$) and for surgeons ($P = 0.02$).

at highest-caseload-quartile hospitals. A total of 1.1% of patients whose surgeons were in the lowest caseload quartile died, compared with 0.2% for patients of highest-caseload-quartile surgeons.

After adjustment for annual hospital caseload, neither hospital teaching status nor hospital bed size were significant additional predictors of outcome at hospital discharge, although there were trends toward better outcomes at teaching hospitals (OR 0.71, 95% CI 0.50–1.04, $P = 0.08$) and at smaller hospitals (OR 0.80, 95% CI 0.62–1.02, $P = 0.07$). After adjustment for surgeon caseload, whether one surgeon or more than one performed operations at a given hospital was not a significant predictor of outcome.

We tested patient characteristics as potential predictors of care at high-volume hospitals (Table 2) or by high-volume surgeons. Older patients were less likely to have a high-volume hospital ($P < 0.001$ or surgeon ($P = 0.003$). Race was a significant predictor of hospital volume ($P < 0.001$) and surgeon volume ($P = 0.03$). Hospital and surgeon caseloads were higher for white patients than for black patients. Primary payer for care was a significant predictor of both hospital ($P < 0.001$) and surgeon volume ($P = 0.04$), with highest provider volumes for those who had private insurance. Patients from higher-income areas of residence had higher-volume hospitals ($P < 0.001$), but not surgeons ($P = 0.3$). Emergency or urgent admissions were more common to lower-caseload surgeons ($P = 0.02$) but not significantly related to hospital caseload ($P = 0.3$). Patients with more medical comorbidity tended to have lower-volume hospitals ($P = 0.002$) and surgeons ($P = 0.06$). Patients with Cushing's disease were more commonly treated at high-volume hospitals and by high-caseload surgeons ($P < 0.001$ for both), as were patients with acromegaly ($P = 0.08$ for hospitals and $P = 0.03$ for surgeons). (Some of these admissions may have represented second operations at high-volume centers after unsuccessful surgery elsewhere, but this could not be determined from the database.) Patients with noniatrogenic panhypopituitarism were more commonly treated at low-volume hospitals ($P < 0.001$) and by low-volume surgeons ($P = 0.008$), as were patients with visual loss ($P < 0.001$ for hospitals and $P = 0.001$ for surgeons).

Complications and provider volume

We studied several complications of surgery or perioperative care: postoperative neurological complications, including those due to infarction or hemorrhage (reported in 254/5497 patients, 4.6%), hematoma complicating a procedure (86

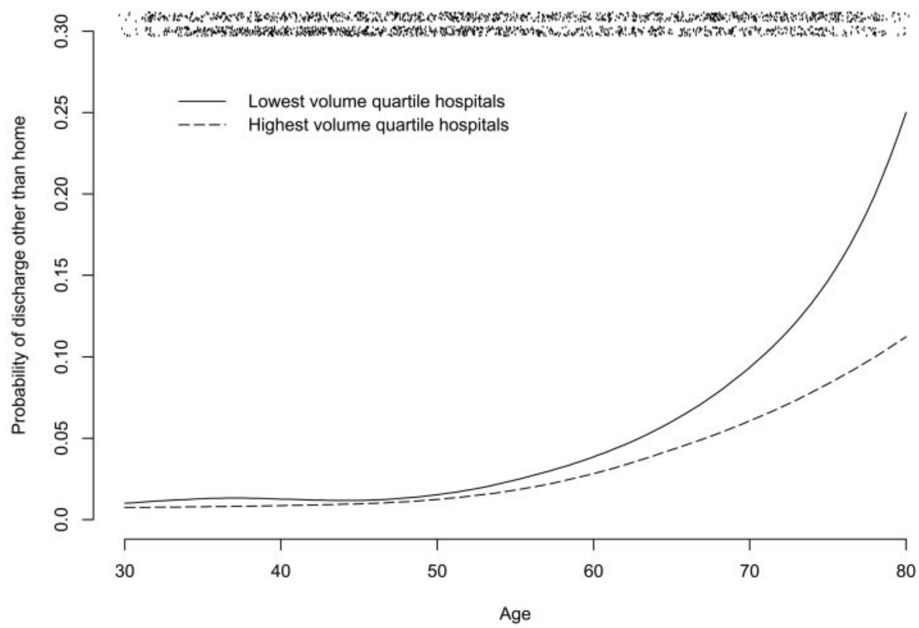

FIG. 3. Probability of discharge other than to home as a function of age for highest- and lowest-volume quartiles of hospitals and surgeons, plotted using local-likelihood fitting.

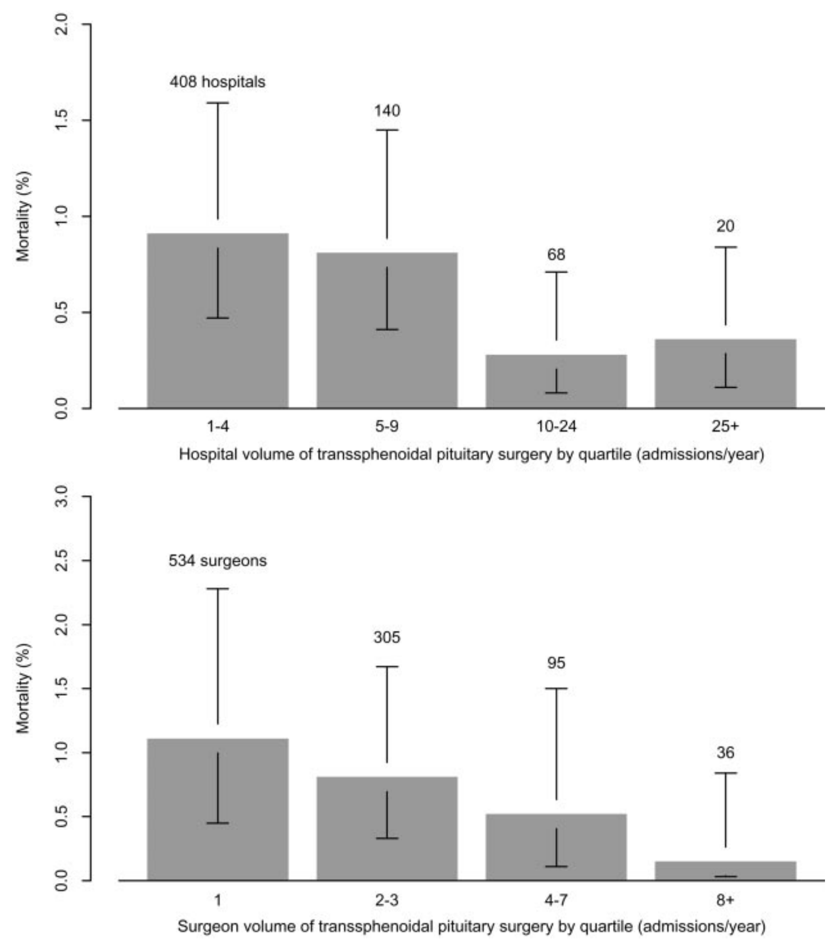

FIG. 4. Bar graph showing probability of in-hospital mortality as a function of hospital and surgeon volume of transsphenoidal pituitary tumor surgery, by quartile. Mortality was lower with higher-volume hospitals ($P = 0.02$) and surgeons ($P = 0.09$).

patients, 1.6%), any intracranial hemorrhage (126 patients, 2.3%), mechanical ventilation (63 patients, 1.1%), fluid and electrolyte abnormalities (486 patients, 8.8%), DI (578 patients, 10.5%), iatrogenic panhypopituitarism (46 patients, 0.8%), performance of a cerebral arteriogram (70 patients, 1.3%), cerebrospinal fluid rhinorrhea (77 patients, 1.4%), cranial nerve 3, 4, or 6 palsies (176 patients, 3.2%) postoperative thrombotic disorders (deep venous thrombosis, pulmonary embolism, or placement of an inferior vena cava filter; 31 patients, 0.6%), and transfusion of packed RBCs (63 patients, 1.1%). We omitted noniatrogenic hypopituitarism, coded in 46 patients (0.8%), from these analyses because this condition is almost always identified after hospital discharge; this code was not significantly associated with mortality or discharge disposition (Table 3) or with hospital or surgeon caseload (data not shown), and repeat analyses including this code in the aggregate definition of complications gave essentially identical results.

One or more of these complications was coded in 1457 patients (26.5%). The presence of one or more of these diagnoses was significantly correlated with mortality (in multivariate analysis adjusted for variables described above, OR 26, 95% CI 7–99, $P < 0.001$) and with worse outcome at hospital discharge (multivariate OR 3.8, 95% CI 2.8- 5.1, $P < 0.001$). Most of the individual complications were also strong predictors of mortality and worse disposition at discharge (Table 3).

In multivariate analysis, a complication was more likely in patients with more medical comorbidity ($P < 0.001$) or Cushing's disease ($P = 0.06$). Larger provider caseloads were associated with less frequent complications. Odds ratios for occurrence of one or more complications were 0.77 for a 5-fold larger hospital caseload (95% CI 0.61- 0.97, $P = 0.03$) and 0.76 for a 5-fold larger surgeon caseload (95% CI 0.65–0.89, $P = 0.005$). Complications occurred during 31.1% of admissions to lowest-quartile-volume hospitals, compared with 23.0% of admissions to highest-quartile-volume hospitals; corresponding rates for surgeon volume were 33.2% (lowest volume) and 23.7% (highest volume; Fig. 5). After adjustment for hospital caseload, hospital teaching status and bed size were not significantly related to complication probability.

Most individual complications showed no significant relationship with hospital or surgeon caseload, although most were less frequent with higher-volume providers (Tables 4 and 5). Higher hospital and surgeon caseload were both significantly associated with lower rates of fluid and electrolyte abnormalities ($P < 0.004$ for both) and DI ($P < 0.03$ for both), and there was a trend toward less frequent mechanical ventilation at higher-volume hospitals ($P = 0.06$).

LOS and hospital charges

LOS decreased significantly during the study period (by 4.6% per year, $P < 0.001$), although the median was 4 d both in 1996 and in 2000. After multivariate adjustment for the variables described above and stratification by treatment year, LOS was significantly shorter at larger-volume hospitals ($P = 0.02$). Adjusted for hospital caseload, neither hospital teaching status nor hospital bed size was correlated with LOS. In a similar multivariate model, larger surgeon caseload was also associated with shorter LOS ($P < 0.001$).

Total hospital charges increased significantly during the study period, from a median of $17,100 in 1996 to $20,200 in 2000 (by 4.3% per year, $P = 0.02$). After multivariate adjustment for the variables described above and stratification by treatment year, there was a trend toward lower charges at higher-volume hospitals (7.6% lower charges for a 5-fold larger caseload, 95% CI 5% higher to 18% lower, $P = 0.2$). Adjusted for hospital caseload, neither hospital teaching status nor hospital bed size was correlated with charges. The relationship between surgeon caseload and hospital charges was not significant ($P = 0.7$).

Discussion

We studied 5497 transsphenoidal pituitary tumor surgery admissions to U.S. nonfederal hospitals during 1996–2000, approximately 20% of all U.S. cases during this period. In-hospital mortality was 0.6% and another 3.2% of patients were not discharged directly home. Complications were coded in 26.8% of patients. Patients of higher-volume hospitals and surgeons had lower mortality rates, better hospital discharge disposition, and fewer complications. Patients of high-volume providers were younger, healthier, and white, more often had private insurance, and resided in wealthier areas. Our data source did not allow us to consider the effect of caseload on the efficacy of surgery—relief of preoperative endocrine and visual complaints.

Surgical excision is the primary treatment for most pituitary tumors. Our data indicate that adverse outcomes are less common after pituitary surgery by higher-volume providers. Most of the differences in outcome we found were statistically significant after casemix adjustment using patient-related risk factors such as age, comorbidity, and Cushing's disease, previously reported to be associated with

TABLE 3. Relationship between complications, mortality, and outcome at hospital discharge

Complication	Mortality			Outcome at hospital discharge		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Neurological complications	21	(9–49)	<0.001	5.1	(3–9)	<0.001
Hematoma	8.7	(2.4–31)	0.001	6.0	(3.2–11)	<0.001
Any intracranial hemorrhage	23	(9–58)	<0.001	11	(6–19)	<0.001
Mechanical ventilation	110	(43–281)	<0.001	23	(10–53)	<0.001
Fluid and electrolyte abnormalities	4.7	(2–11)	<0.001	2.3	(1.6–3.4)	<0.001
Diabetes insipidus	3.9	(1.4–11)	0.007	2.5	(1.7–3.9)	<0.001
Performance of an arteriogram	11	(3.6–31)	<0.001	7	(3.4–14)	<0.001
CSF rhinorrhea	5.3	(1.2–24)	0.03	1.7	(0.6–5)	0.3
Cranial nerve 3, 4, 6	1.0	(0.1–8)	1.0	1.5	(0.8–2.9)	0.2
Thrombotic complications	47	(15–146)	<0.001	32	(12–86)	<0.001
Transfusion of RBCs	2.1	(0.4–12)	0.4	5.0	(2.1–12)	<0.001
Any complication	26	(7–99)	<0.001	3.8	(2.8–5.1)	<0.001

CSF, Cerebrospinal fluid.

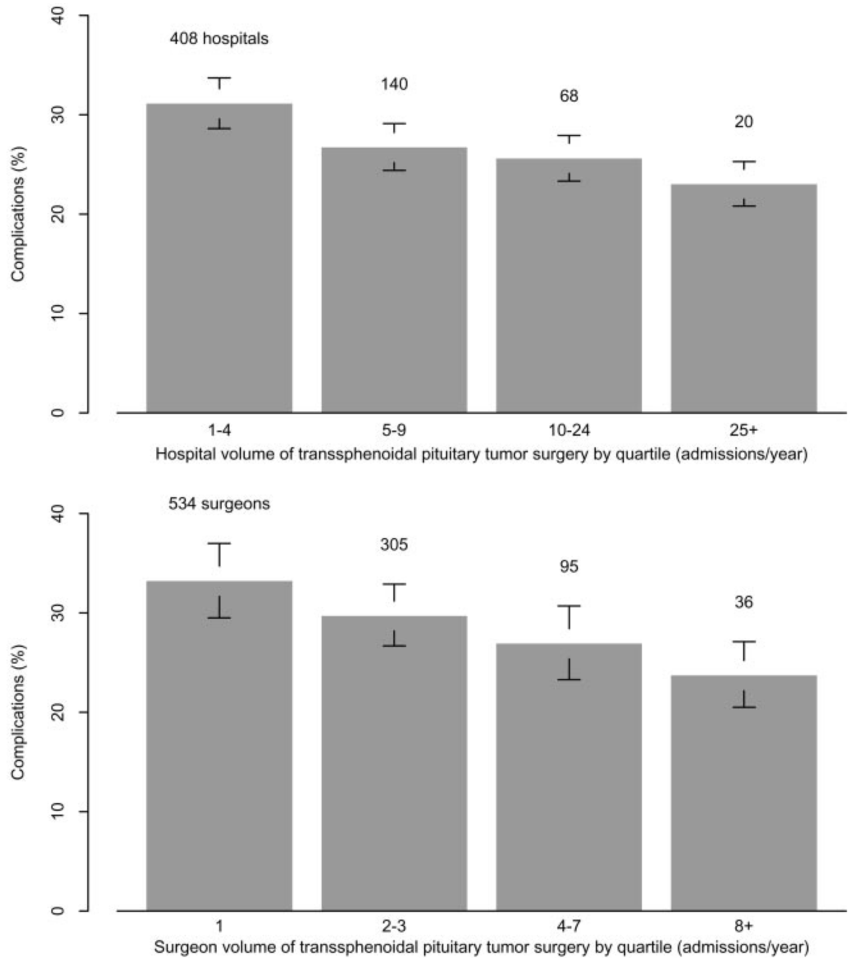

FIG. 5. Bar graph showing probability of one or more postoperative complications as a function of hospital and surgeon volume of transsphenoidal tumor surgery, by quartile. (See text for definition of complications.) The relationship between larger caseload and lower complication rates was significant both for hospital volume ($P = 0.03$) and for surgeon volume ($P = 0.005$).

TABLE 4. Complications of transphenoidal pituitary tumor surgery in relation to annual hospital caseload

	1–4 Admissions/yr	5–9 Admissions/yr	10–24 Admissions/yr	25+ Admissions/yr	*P* value[a]
Neurological complications	50/1313 (3.8%)	56/1356 (4.1%)	68/1436 (4.7%)	80/1392 (5.7%)	0.8
Hematoma	22/1313 (1.7%)	26/1356 (1.9%)	22/1436 (1.5%)	16/1392 (1.1%)	0.5
Any intracranial hemorrhage	33/3313 (2.5%)	33/1356 (2.4%)	31/1436 (2.2%)	29/1392 (2.1%)	0.9
Mechanical ventilation	21/1313 (1.6%)	21/1356 (1.5%)	12/1436 (0.8%)	9/1392 (0.6%)	0.06
Fluid and electrolyte abnormalities	164/1313 (12.5%)	128/1356 (9.4%)	112/1436 (7.8%)	82/1392 (5.9%)	0.003
Diabetes insipidus	169/1313 (12.8%)	145/1356 (10.7%)	131/1436 (9.1%)	133/1392 (9.6%)	0.02
Performance of an arteriogram	23/1313 (1.8%)	17/1356 (1.3%)	22/1436 (1.5%)	8/1392 (0.6%)	0.15
CSF rhinorrhea	20/1313 (1.5%)	15/1356 (1.1%)	23/1436 (1.6%)	19/1392 (1.4%)	0.6
Cranial nerve 3, 4, 6	53/1313 (4.0%)	34/1356 (2.5%)	48/1436 (3.3%)	41/1392 (2.9%)	0.2
Thrombotic complications	8/1313 (0.6%)	7/1356 (0.5%)	9/1436 (0.6%)	7/1392 (0.5%)	0.9
Transfusion of RBCs	20/1313 (1.5%)	14/1356 (1.0%)	12/1436 (0.8%)	17/1392 (1.2%)	0.4
Any complication	408/1313 (31.1%)	362/1356 (26.7%)	367/1436 (25.6%)	320/1392 (23.0%)	0.03

CSF, Cerebrospinal fluid.

[a] *P* value calculated for each complication type separately in multivariate models including demographic, acuity, and comorbidity variables.

adverse outcomes (19, 20). High-volume provider care was also associated with significantly shorter hospital stays and a trend toward lower total hospital charges.

Better patient outcome after transsphenoidal pituitary tumor surgery by a more experienced surgeon was first reported by Cushing, who noted a progressive decrease in mortality rates from 40% (multiple earlier surgeons), to 13.7% in his own early series (21), to 3.9% by the end of his career (22). In modern series reported by specialist surgeons, transsphenoidal pituitary surgery mortality rates are about 1% or less (19, 23–32). These series may not reflect results in less specialized practice settings, and the extent to which pituitary surgery is concentrated in specialized centers and the results achieved outside these settings both remain largely unknown. We found that most transsphenoidal pituitary surgery in the United States during 1996–2000 was performed in low-volume hospitals, by low-volume surgeons. The median annual hospital caseload was 10 admissions, and the median annual surgeon caseload was three admissions. Almost one quarter of patients represented the

TABLE 5. Complications of transphenoidal pituitary tumor surgery in relation to annual surgeon caseload

	1 Admission/yr	2–3 Admissions/yr	4–7 Admissions/yr	8+ Admissions/yr	*P* value[a]
Neurological complications	24/627 (3.8%)	43/861 (5.0%)	23/581 (4.0%)	36/658 (5.5%)	0.3
Hematoma	9/627 (1.4%)	15/861 (1.7%)	13/581 (2.2%)	8/658 (1.2%)	0.9
Any intracranial hemorrhage	16/627 (2.6%)	22/861 (2.6%)	16/581 (2.8%)	11/658 (1.7%)	0.5
Mechanical ventilation	8/627 (1.3%)	16/861 (1.9%)	10/581 (1.7%)	5/658 (0.8%)	0.6
Fluid and electrolyte abnormalities	90/627 (14.3%)	96/861 (11.1%)	49/581 (8.4%)	37/658 (5.6%)	0.0002
Diabetes insipidus	79/627 (12.6%)	106/861 (12.3%)	50/581 (8.6%)	57/658 (8.7%)	0.005
Iatrogenic panhypopituitarisum	5/627 (0.8%)	6/861 (0.7%)	3/581 (0.5%)	5/658 (0.8%)	0.9
Performance of an arteriogram	18/627 (2.9%)	13/861 (1.5%)	5/581 (0.9%)	9/658 (1.4%)	0.1
CSF rhinorrhea	10/627 (1.6%)	14/361 (1.6%)	8/581 (1.4%)	9/658 (1.4%)	0.9
Cranial nerve 3, 4, 6	25/627 (4.0%)	33/861 (3.8%)	22/581 (3.8%)	21/658 (3.2%)	0.5
Thrombotic complications	4/627 (0.6%)	7/861 (0.8%)	3/581 (0.5%)	2/658 (0.3%)	0.6
Transfusion of RBCs	15/627 (2.4%)	8/851 (0.9%)	13/581 (2.2%)	6/658 (0.9%)	0.4
Any complication	208/627 (33.2%)	256/861 (29.7%)	156/581 (26.9%)	156/658 (23.7%)	0.005

CSF, Cerebrospinal fluid.

[a] *P* value calculated for each complication type separately in multivariate models including demographic, acuity, and comorbidity variables.

only transsphenoidal pituitary operation in the database that year for their surgeon.

Recent series have suggested that surgeons who are pituitary tumor specialists have higher endocrine cure rates for Cushing's disease and acromegaly (25, 27, 33). When one surgeon or a few operate at a specialized center, larger cumulative personal experiences result, with better outcomes—the surgical learning curve (34). Better acromegaly cure rates with greater experience were reported by one surgeon operating in Oxford, United Kingdom, 1974–1995 (35) and by three surgeons operating in Boston, Massachusetts, 1978–1996 (23). We found no evidence that having only one pituitary surgeon per institution improved outcome, other than through larger personal caseload.

Provider caseload effects on mortality or operative morbidity after transsphenoidal surgery are more difficult to detect in single-institution studies because these endpoints are infrequent. Rees *et al.* (25) reported lower hypopituitarism rates when Cushing's disease surgery shifted from three surgeons to one, but there was no clear decrease in other complications. Ciric *et al.* (36) reported a survey study on transsphenoidal surgery complications, based on 958 responding U.S. surgeons (37% response rate). Surgeons with larger cumulative experience reported significantly lower rates of 13 of 14 complications assessed. We found a weaker correlation between complication rates and surgical caseload than did Ciric *et al.* (36). Possible explanations include undercoding or miscoding of complications in NIS data, reducing statistical power, or underreporting of complications by experienced surgeons, overreporting by inexperienced surgeons, or both in the survey study.

Our enforced use of outcomes measured during hospitalization means that our rates of some complications differ from those previously reported. The 26.5% combined incidence of complications we report, and even the 23.0% rate at high-volume centers, is higher than usually recorded in single-center series (19, 30–32). Many coded events we classified as complications were either DI or other fluid and electrolyte abnormalities, which likely resolved soon after surgery. Although permanent DI—1–2% of patients treated in specialized centers (19, 31)—is a more meaningful endpoint, both DI and fluid and electrolyte abnormalities coded before discharge were associated with higher rates of death and adverse discharge disposition (Table 3). Conversely, because iatrogenic hypopituitarism is assessed after discharge, our reported rate (0.8%) is probably an underestimate, and could reflect the results of prior surgery in some cases. We found no correlation between coded iatrogenic hypopituitarism and provider caseload, mortality rates, or discharge disposition.

Another difficulty that affects studies using administrative databases to measure postoperative outcomes is that some adverse events also represent surgical indications, and the NIS database does not distinguish between the two. We were unable to study postoperative increase in visual loss for this reason, although these patients should have been coded as neurological complications of surgery.

Demonstrations of better outcomes after complex surgical procedures performed at higher-volume centers often lead to a call for concentration of care in a limited number of hands, as by regionalizing care or by requiring special certification for surgeons (37–39). Our study's limitations should be carefully weighed before our conclusions are accepted as supporting regionalization of transsphenoidal pituitary surgery.

Administrative databases are accurate sources for "hard" endpoints such as mortality rates and discharge disposition, but coding of comorbidities and complications is known to be incomplete (40–45). The low rates we report for acromegaly and Cushing's disease in comparison to other registry-based studies (46–51) probably indicate undercoding in the NIS, reducing sensitivity to the effects such factors have on outcome (42). (Some subpopulations are probably also overrepresented at tertiary centers, typically the source of large case series.) Although incomplete coding of complications, overcoding of risk factors, or misclassification of other, low-risk operations as transsphenoidal pituitary resections at high-volume centers could account for our results, such large-scale biases appear unlikely. Less aggressive resections at high-volume centers could cause the effect we observed. Specialist surgeons, however, uniformly advocate the most aggressive adenoma resection consistent with patient safety, and the higher endocrine cure rates they achieve (23, 25, 27, 33, 35) indicate that this goal is typically realized.

Our study assessed only short-term endpoints because of the limitations of our data source. Because many patients discharged to short-term rehabilitation centers return home when recovery is complete, using short-term outcomes exaggerates the magnitude of the difference in long-term functional outcomes (and other potentially transient adverse outcomes such as DI) between high- and low-volume hospitals. Some important long-term outcomes, such as cure of Cushing's disease or acromegaly and relief of preoperative visual loss, could not be assessed for the same reason. Our surgeon-caseload analyses do not account for the participation of two cosurgeons (a neurosurgeon and an otolaryngologist) in some transsphenoidal operations. The NIS identifies one primary surgeon per admission, whose specialty is not indicated. Whether the experience level of one or both surgeons, or of their combination as a team, affects outcome most has not yet been studied for any operation involving cosurgeons, including transsphenoidal surgery.

The most likely bias that could cause the volume-outcome effect we observed is the concentration of low-risk patients at high-volume centers. We found substantial evidence of this bias in our study: high-volume providers' patients were younger, had admissions that were more often routine rather than urgent or emergent, and had less medical comorbidity, as well as higher socioeconomic status and better insurance—both likely to prompt more liberal use of screening studies for minor symptoms (and presentation with smaller tumors). Noniatrogenic panhypopituitarism and visual loss, both hallmarks of macroadenomas, were more common at low-volume centers. Cushing's disease was the only unfavorable patient characteristic more common at high-volume centers.

Although we adjusted for these factors, adjustment for a risk index incorporating both clinical data (*e.g.* tumor size, history of prior transsphenoidal surgery, and preoperative endocrine and visual status) and the administrative data we used would likely reduce the magnitude of the volume-outcome effect we observed. A population-based study that incorporated clinical data would be valuable in confirming our findings.

Figures 1, 2, and 5 suggest that adverse outcomes become progressively less likely as provider caseload increases. Without clinical data on baseline risk or surgical efficacy, such as endocrine and visual cure, choosing a single, minimal acceptable caseload for providers (above which care is "optimal" and below which care is "unacceptable") might be misleading. Our results and studies linking more-experienced surgeons and higher endocrine cure rates (23, 25, 27, 33, 35) suggest that care will be optimized by choosing the most experienced surgeon and hospital available.

Ideally, a study on pituitary tumor surgery outcomes would describe surgical efficacy (probability and durability of endocrine and visual cure) as well as safety, but our data source lacked this information. Measures of surgical appropriateness at high- and low-volume centers would also be of interest. Sosa *et al.* (6) found that high-caseload surgeons had lower thresholds to perform parathyroidectomy than low-caseload surgeons; neither group followed consensus guidelines for the operation. A similar study on transsphenoidal pituitary surgery should be a priority for future research. A national or regional registry of pituitary tumor treatment outcomes, with input from both endocrinologists and surgeons, would facilitate such studies, as well as identification of factors leading to better outcomes at high-volume centers.

Conclusions

We studied a large representative sample of patients who underwent transsphenoidal surgery for pituitary tumors in the United States between 1996 and 2000. After adjustment for risk factors such as age, medical comorbidity, and Cushing's disease status, adverse outcomes (mortality, morbidity at hospital discharge, and operative complications) were less frequent after surgery at high-volume centers or by high-volume surgeons. The difference in outcome at hospital discharge was most important for older patients. LOS was shorter at high-volume centers and there was a trend toward lower treatment charges. A bias toward preferential treatment of low-risk patients at high-volume centers probably affected our study, and we were unable to study the efficacy of surgery in relieving preoperative endocrine and visual symptoms because of the nature of our data source. However, our findings have significance for patients with pituitary tumors, and for their physicians and ensurers, when seeking high-quality surgical care for transsphenoidal surgery.

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