

ORIGINAL ARTICLE

Complications and death among elderly patients undergoing pituitary tumour surgery

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Summary

Background Preoperative determinants of surgical risk in elderly patients with pituitary tumour are not fully defined. The aim of this study was to quantify operative risk for these patients.

Design and methods We performed a retrospective analysis of the Nationwide Inpatient Sample (1998–2005), a database containing discharge information from a stratified, random sample of 20% of all non-federal hospitals in 37 states. Patients >65 years old who underwent pituitary tumour resection were identified by ICD-9 coding. Primary outcome was inpatient death. Other outcomes included post-operative complications, length of stay (LOS) and total charges.

Results A total of 8400 patients (53.7% male) were identified. Mean age was 72.2. Mean co-morbidity score was 5.3. A majority were white (82.0%) admitted to academic hospitals (69.5%) for elective procedures (55.7%). Inpatient mortality was 3.8%. The most common complication was fluid and electrolyte abnormalities (14.3%). Mean LOS was 8.5 days. In multivariate analysis, patients >80 years old had 30% greater odds of death, relative to 65–69 year old counterparts. Each complication increased LOS by an average of at least 4 days. These associations were statistically significant (*P*-values <0.05).

Conclusions New clinically relevant risk stratification information is now available to assist clinicians in operative decision-making for elderly patients with pituitary tumour considering operative intervention.

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Introduction

Populations in the United States, Europe and other developed countries are progressively ageing.¹ During the 20th century, life expectancy in most developed countries increased by approximately 30 years.¹ Recent estimates show that life expectancy in such countries continues to rise almost linearly.¹ With more individuals now living beyond 65 years of age, an increasingly large proportion of this population is being evaluated for surgical treatment.²

Traditionally, 65 years of age has been widely used as a cut-off for defining elderly, with patients over 80 years of age falling within the very elderly category.³ Increasingly, many individuals categorized as elderly or very elderly continue to be physiologically similar to their younger counterparts.⁴ Yet, the impact of surgery upon inpatient complications and outcomes in this older subset of patients has yet to be fully explored.

Given the poorly understood contribution of surgical procedures to morbidity and mortality within this ageing population, the decision to recommend operative care to elderly patients often remains a difficult one.⁵ While there are large series detailing morbidity and mortality among the elderly and very elderly in the general surgery literature, including cardiothoracic,⁶ vascular,⁷ pancreatic⁸ and colorectal procedures,⁹ there have thus far been only few studies analysing outcomes within this patient population following surgery for pituitary tumours.^{10–13} This study was undertaken to help define age criteria for worsening odds of post-operative complications and death in older patients with pituitary tumour undergoing surgical resection using a national inpatient database. Through this unique analysis of over 8000 patients using a national, multi-institutional database, for the first time we are able to quantify the operative risk of inpatient death for pituitary patients over 65 years old, providing new risk stratification data to inform operative decision-making.

Materials and methods

Patient population

We obtained the National Inpatient Sample (NIS) in-hospital discharge database for the years 1998–2005, compiled by the Agency

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for Healthcare Research and Quality (Rockville, MD, USA).¹⁴ The NIS database contains discharge information from a stratified random sample of 20% of all non-federal hospitals in 37 participating US states. The database compiles discharge information on 100% of discharges from sampled hospitals. Over 1000 hospitals are sampled by the NIS, with more than seven million patient discharge records per year available in this database. This publicly available, de-identified data set was exempt for review by the Johns Hopkins Institutional Review Board.

Inclusion and exclusion criteria

Inclusion criteria included patients ≥ 65 years old with a primary diagnosis of a pituitary tumour (malignant or benign) who underwent a primary neurosurgical resection (hypophysectomy), as identified by ICD-9 diagnosis codes (194.3, 227.2, and 237.0) and ICD-9 procedural codes (07.61–07.69), respectively.

Characteristics of interest

Independent patient level variables included patient age, sex, race, Charlson co-morbidity score, type of insurance or primary payer, hospital academic status, and elective status of the procedure. Age was analysed as a continuous variable and stratified into four intervals: 65–69 (baseline), 70–74, 75–79, 80 years old and above. Sex was a binary covariate, either male or female. Race was categorized as white, African-American, Hispanic, Asian, Native American or Other. The Charlson score is a well-validated, weighted patient co-morbidity index.¹⁵ The Charlson index provides a score accounting for various co-morbidities, including history of cancer, as well as cardiac, vascular, pulmonary, neurologic, endocrine, renal, hepatic, gastrointestinal and immune disorders (Table 1). Type of insurance or primary payer was divided into several categories: Medicare, Medicaid, private insurance or self-paid. Other covariates included elective status of the neurosurgical procedure and hospital teaching status, data elements inherent to the NIS.

Outcome variables

Post-operative complications were identified using the following ICD-9 diagnosis codes: post-operative fluid and electrolyte abnormalities (276.0–276.9), cerebrospinal fluid (CSF) rhinorrhea (349.81), pulmonary complications including acute respiratory

distress syndrome (518.81–518.85 and 997.3), iatrogenic pan-hypopituitarism (253.7), stroke (253.5, 998.11, 997.02) and central diabetes insipidus (DI) (253.5). The primary outcome was inpatient death. Secondary outcomes included total hospital charges and total hospital length of stay (LOS).

Statistical analysis

Multivariate logistic and linear regression models were constructed to analyse binary and continuous outcomes, respectively. Multivariate analyses were adjusted for age, sex, race, Charlson co-morbidity score, hospital academic status, type of insurance or primary payer and elective procedure status. *P*-values < 0.05 were considered to be statistically significant. All data were analysed using the software package STATA/MP 10 (College Station, TX, USA).

Results

Univariate analysis

A total of 8400 patients were identified with slightly male predominance (53.7%). Mean (median) age was 72.2 (72). The majority of patients were white (82.0%), with most patients being admitted to academic hospitals (69.5%) for elective procedures (55.7%). Most of the patients underwent transsphenoidal resection, with only 2.6% of patients undergoing a trans-cranial approach, such as a transfrontal approach. Additionally, virtually all patients had benign lesions, with only 1.6% of patients having malignant pituitary neoplasms. Patients had a mean (median) Charlson score of 5.3 (6). The most common post-operative complications were fluid and electrolyte abnormalities (14.3%), followed by CSF rhinorrhea (5.4%), pulmonary complications (3.5%), iatrogenic pan-hypopituitarism (3.5%), stroke (2.5%) and central DI (2.2%). Mean (median) LOS was 8.5 (6) days with a range of 1–41 days. Patients had mean (median) total hospital charges of \$53 486.36 (\$38 770.75). Overall inpatient mortality was 3.8% (Table 2).

Multivariate analyses

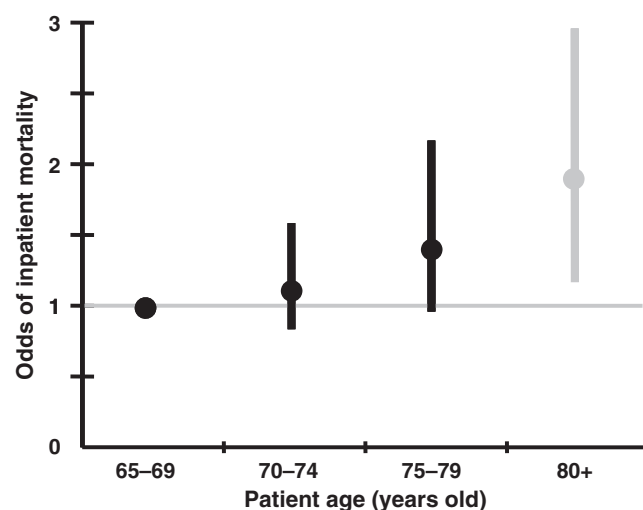
Factors associated with inpatient death. In multiple logistic regression models adjusted for age, sex, race, Charlson score, hospital academic status, elective procedure status and complications, odds of death increased among patients above 80 years old (Odds Ratio, OR: 1.85, *P* = 0.009) relative to 65–69 year olds (Fig. 1). Each 1 year increase in age was associated with a 5% higher odds of death (OR: 1.05, *P* = 0.001). Each one point increase in Charlson score was associated with an 11% increased odds of death (OR: 1.11, *P* < 0.001). Among complications, those patients who developed pulmonary complications like acute respiratory distress syndrome (OR: 8.64, *P* < 0.001) or stroke (OR: 5.23, *P* < 0.001) had 8.64 times and 5.23 times increased odds of inpatient mortality, respectively. The few patients who underwent non-transsphenoidal procedures, including transfrontal procedures, have significantly higher inpatient mortality (OR: 2.24, *P* = 0.01) than transsphenoidal counterparts. Elective procedure status (OR: 0.55, *P* < 0.001) was associated with 45% less odds of death (Tables 3 and 4).

Table 1. Co-morbidities included in the Charlson co-morbidity score

Weights	Clinical conditions
1	Myocardial infarct, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, peptic ulcer disease, or chronic liver disease
2	Hemiplegia, moderate or severe kidney disease, uncomplicated diabetes, diabetes with complications, tumour, leukaemia, lymphoma
3	Moderate or severe liver disease
6	Malignant tumour, metastasis, AIDS

Table 2. Demographics of 8400 elderly patients with pituitary tumour undergoing resection, 1998–2005

Patient demographics	<i>n</i>	%
Males	4502	53.7
Age, in years		
Mean (median)	72.2 (72)	
Race		
White	5249	82.0
African-American	578	9.0
Hispanic	319	5.0
Asian	118	1.8
Native American	11	0.2
Other	126	2.0
Charlson index score		
Mean (median)	5.3 (6)	
Academic hospital admission	5837	69.5
Elective procedures	4095	55.7
Primary payer		
Medicare	7256	86.4
Medicaid	106	1.3
Private Insurance	924	11.0
Self-Pay	48	0.6
Complications		
Fluid or electrolyte abnormality	1203	14.3
Cerebrospinal fluid rhinorrhea	452	5.4
Pulmonary complications	294	3.5
Pan-hypopituitarism	292	3.5
Stroke	212	2.5
Central diabetes insipidus	182	2.2
Outcomes		
Mortality	314	3.8
Length of stay, in days		
Mean (median)	8.5 (6)	
Total hospital charges		
Mean (median)	\$53 486.36 (\$38 770.75)	

**Fig. 1** Adjusted odds of inpatient death among elderly patients with pituitary tumours undergoing neurosurgical resection. Adjusted odds of post-operative inpatient death significantly rose in patients ≥ 80 years old, relative to their 65–69 year old counterparts.

Factors associated with inpatient complications. In multiple logistic regression models adjusted age, sex, race, Charlson score, hospital academic status, and elective procedure status, increasing patient age was associated with significantly higher odds of fluid and electrolyte abnormalities (patients aged over 70 had an OR = 1.24, 95% Confidence Interval, CI: 1.05, 1.56) or stroke (patients aged over 80 had an OR: 1.87, 95% CI: 1.04, 3.33). Each one point increase in Charlson co-morbidity score was associated with a 1% higher odds of developing CSF rhinorrhea (OR = 1.05, $P = 0.04$). Elective procedure status was associated with lower odds of developing post-operative pulmonary complications (OR: 0.70, 95% CI: 0.47, 0.96) or fluid and electrolyte abnormalities (OR: 0.48, 95% CI: 0.40, 0.57) relative to patients undergoing emergency cases, for instance for pituitary apoplexy. Minority patient race was not consistently associated with any major inpatient complications.

Factors associated with hospital LOS. In multiple linear regression models adjusted age, sex, race, Charlson score, hospital academic status, and elective procedure status, the following independent variables were associated with significantly longer mean inpatient LOS days: patients ≥ 75 years of age (up to 1.3 days increased LOS, $P < 0.001$) compared to patients < 75 years of age (whose LOS increased by a non-statistically significant 0.31 days, $P = 0.19$), African-American or Hispanic race (2.38 and 2.03 increased days, respectively, with $P < 0.001$ for both races), higher Charlson score (0.24 increased days, $P < 0.001$), pulmonary complications (increased 10.83 days, $P < 0.001$), post-operative stroke (increased 8.15 days, $P < 0.001$), central DI (increased 5.41 days, $P < 0.001$), fluid and electrolyte abnormalities (increased 4.09 days, $P < 0.001$) and non-elective procedure status (increased 4.46 days, $P < 0.001$) (Table 5). Patients who underwent non-transsphenoidal procedures has significantly longer LOS (4.95 days, $P < 0.001$) than transsphenoidal counterparts.

Factors associated with total hospital charges. In multiple linear regression models adjusted for age, sex, race, Charlson score, hospital academic status, and elective procedure status, significantly higher mean total hospital charges were present among African-Americans (\$8328.45 higher charges, 95% CI: \$2298.36–\$16 011.33) and Hispanics (\$19 275.24, 95% CI: \$9980.91–\$29 350.94), as well as those with higher Charlson scores (\$1284.69 higher charges, 95% CI: \$877.93–\$1834.48). Among complications, those with central DI (\$23 727.35 higher charges, 95% CI: \$15 438.83–\$58 231.26), stroke (\$49 487.78 higher, 95% CI: \$42 830.39–\$78 274.87), pulmonary complications (\$74 465.58 higher, $P < 0.001$) or fluid and electrolyte disorders (\$13 755.21 higher, $P < 0.001$) had higher charges. Patients who underwent non-transsphenoidal procedures have significantly greater total charges (\$27 697.90; $P < 0.001$) than transsphenoidal counterparts. Non-elective procedure status was associated with \$17 425.88 higher charges (95% CI: \$16 283.52–\$22 928.73).

Insurance type, hospital academic status and tumour histology (malignant vs benign lesion) were not significantly associated with death, post-operative complications, hospital LOS or total hospital charges.

Table 3. Complications and outcome divided by age groups of 8400 elderly patients with pituitary tumour undergoing resection, 1998–2005

Outcome	65–69 years	70–74 years	75–79 years	80 + years	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Death	93 (2.94)	92 (3.59)	79 (4.59)	50 (5.40)	314 (3.75)
Fluid or electrolyte abnormality	383 (12.06)	368 (14.32)	289 (16.75)	163 (17.53)	1203 (14.32)
Cerebrospinal fluid rhinorrhea	188 (5.92)	138 (5.37)	82 (4.75)	44 (4.73)	452 (5.38)
Pulmonary complications	119 (3.75)	84 (3.27)	61 (3.54)	30 (3.23)	294 (3.50)
Pan-hypopituitarism	19 (0.60)	14 (0.54)	5 (0.29)	4 (0.43)	42 (0.50)
Stroke	61 (1.92)	76 (2.96)	44 (2.55)	31 (3.33)	212 (2.52)
Central diabetes insipidus	33 (1.04)	30 (1.17)	25 (1.45)	9 (0.97)	97 (1.15)

Discussion

The presence of pituitary lesions in patients over 65 years old is a relatively common occurrence, with autopsy studies in the elderly and very elderly demonstrating a prevalence of approximately 11–14%.¹⁶ Such findings are supported by the clinical observation that the frequency of pituitary adenomas increases with age.¹⁷ Furthermore, elderly patients with pituitary adenomas often present with more advanced disease, including visual field loss, than their younger counterparts.¹⁸ Data from the literature suggest that elderly

patients with pituitary tumours have highly variable range of outcome compare to their younger counterparts. While Sheehan *et al.*¹³ and Ferrante *et al.*¹⁹ showed minimal post-operative complications without mortality, Pietila *et al.*²⁰ reported 11% perioperative mortality, and 11% post-operative deterioration following surgery among patients aged from 80 to 86 underwent brain tumour surgery.

The safety and efficacy of neurosurgical intervention for elderly patients with pituitary disorders, however, has thus far not been fully characterized, potentially complicating the surgical decision-making process for such patients and their providers.⁵ We report outcomes on 8400 elderly and very elderly patients with pituitary tumours undergoing resection between 1998 and 2005 from a nationally representative sample of US hospitals.

Table 4. Odds of inpatient death in multivariate logistic regression among elderly patients with pituitary tumour undergoing resection, 1998–2005*

Patient factors	OR (95% CI)	P-value
Age (years)		
65–69	1.00	–
70–74	1.14 (0.82–1.61)	0.42
75–79	1.45 (0.97–2.16)	0.07
>80	1.85 (1.16–2.97)	0.009
Females	0.75 (0.54–1.03)	0.08
Race		
White	1.00	–
African-American	1.25 (0.79–1.98)	0.33
Hispanic	0.55 (0.22–1.39)	0.21
Asian	1.62 (0.49–5.28)	0.42
Other	0.45 (0.095–2.17)	0.32
Charlson score	1.11 (1.05–1.17)	<0.001
Academic hospital admission	0.91 (0.69–1.18)	0.48
Elective procedures	0.55 (0.39–0.76)	<0.001
Primary payer		
Medicare	1.00	–
Medicaid	1.06 (0.23–4.97)	0.94
Private insurance	1.03 (0.62–1.71)	0.91
Self-pay	1.32 (0.45–3.85)	0.62
Complications		
Fluid or electrolyte abnormality	1.48 (0.98–2.24)	0.06
Cerebrospinal fluid rhinorrhea	1.15 (0.64–2.08)	0.63
Pulmonary complications	8.64 (5.88–12.71)	<0.001
Pan-hypopituitarism	0.59 (0.17–2.03)	0.41
Stroke	5.23 (2.98–9.2)	<0.001
Central diabetes insipidus	2.24 (1.73–6.86)	0.16

*Bold phase indicates statistically significant relationship.

Descriptive data

Our distribution of patient age and sex is similar to trends seen in previous studies focusing on elderly patients with pituitary tumour.^{13,16,20–24} However, less Hispanics were included within our study (5%) than one would expect based upon general demographics within the United States, in which Hispanics make up 15% of the population.¹ This discrepancy has been reported in many NIS-based studies, and it is likely caused by an underrepresentation of hospitals from the Southwest of the country, where the Hispanic population is most prevalent.²⁵ The relatively high mean (median) Charlson score of 5.3 (6) indicates that, as expected, the elderly pituitary patient population has a higher number of co-morbidities than middle-aged adult patients with pituitary tumours.^{10,11,15} The distribution of varying insurance or payer type is as we would expect for an elderly population, with most coverage coming from Medicare, followed by private insurance.

Inpatient mortality

In our analysis, in-hospital mortality was 3.8%, and adjusted odds of inpatient death increased by 85% in patients above 80 years old (compared to 65–69 years old counterparts). This finding is in line with several single-institution studies that retrospectively reviewed their outcomes among elderly patients undergoing neurosurgical intervention for pituitary lesions.^{12,13,20,24,26} Such studies reported inpatient mortality rates ranging from 0 to 11.4% in series

Table 5. Increased length of stay in multivariate linear regression among 8400 elderly patients with pituitary tumour undergoing resection, 1998–2005*

Patient factors	Increased days (95% CI)	P-value
Age (years)		
65–69	–	–
70–74	0.31 (–0.16, 0.78)	0.19
75–79	0.58 (0.07, 1.10)	0.03
>80	1.3 (0.59, 1.95)	<0.001
Females	0.41 (–0.002, 0.82)	0.05
Race		
White	–	–
African-American	2.38 (1.32, 3.44)	<0.001
Hispanic	2.03 (0.93, 3.13)	<0.001
Asian	–0.27 (–2.58, 2.05)	0.82
Other	0.28 (–0.77, 1.32)	0.61
Charlson score	0.24 (0.18, 0.31)	<0.001
Academic hospital admission	0.19 (–0.25, 0.64)	0.40
Elective procedures	–4.46 (–5.03, –3.89)	<0.001
Primary payer		
Medicare	–	–
Medicaid	2.44 (–1.32, 6.21)	0.20
Private insurance	0.45 (–0.26, 1.17)	0.21
Self-pay	–0.22 (–2.51, 2.08)	0.85
Complications		
Fluid or electrolyte abnormality	4.09 (3.37, 4.81)	<0.001
Cerebrospinal fluid rhinorrhea	0.68 (–0.45, 1.80)	0.24
Pulmonary Complications	10.83 (8.57, 13.09)	<0.001
Pan-hypopituitarism	1.10 (–0.00, 2.19)	0.05
Stroke	8.15 (5.22, 11.07)	<0.001
Central diabetes insipidus	5.41 (2.45, 8.37)	<0.001

*Bold phase indicates statistically significant relationship.

including 3–59 patients.^{20,26} Other reports which tracked patients post-operatively for 2–5.2 years had slightly higher long-term mortality rates, up to 18%.^{12,13,24,27} Our reported inpatient mortality among the elderly of 3.8% is much higher than the 0.6% and 0.7% mortality rates reported by Barker *et al.*¹⁰ and Patil *et al.*,¹¹ respectively, in their NIS-based analysis of adult-aged patients, a majority of which were undergoing neurosurgical resection of pituitary lesions in their fifth or sixth decade of life.^{10,11} This disparity in inpatient mortality between adults and elderly patients seems to further highlight the importance of age as a predictor of inpatient mortality. Our findings mirror findings in previous studies evaluating the impact of age upon inpatient mortality for other types of brain tumours. For instance, Bateman *et al.* reported in a NIS-based study that patients older than 70 years old were three times more likely to die in-hospital after meningioma resection, and these patients were five times more likely to have an adverse inpatient outcome, relative to their younger counterparts.²⁸

Predicting which elderly patients will do well following surgery has been the subject of much investigation.⁵ We have found that in addition to age, other risk factors that influence post-operative mortality rate include higher overall Charlson co-morbidity score, non-elective procedure status, and patients who developed post-operative pulmonary complications, stroke or fluid and electrolyte abnormalities, findings that mirrored similar results in the general

surgery literature.^{15,29} Thus, individual patients 65 years of age and older may further be stratified into high-risk categories for post-operative inpatient death based upon not only age, but also based in part upon co-morbidities and type of procedures. Potential treatment protocols for patients deemed to be an overly high risk for surgical intervention have not been fully defined. Furthermore, it is not clear from any rigorous prospective trials whether a greater number of these high-risk patients would develop serious sequela, such as blindness or new neurological deficits, from their primary disease more readily without aggressive neurosurgical intervention. Future strategies for high-risk patients may include more aggressive medical management or radiotherapy, but such approaches would best be tested in rigorously designed and implemented prospective studies which also take into account patient quality of life metrics.

Sex, race, insurance/provider type and academic hospital status were not significantly associated with inpatient mortality. Previous studies in the neurosurgical literature have similarly not shown any significant association between sex or race and inpatient outcomes.³⁰ An analysis by Gerszten *et al.* demonstrated that patients with private health insurance tended to be ready for discharge 1.1 days sooner than their public health insurance and non-insured counterparts, but this trend within the data did not reach statistical significance, and the Gerszten group did not find any association between type of insurance and inpatient, post-operative mortality.³¹ Our lack of association between academic centre status and mortality is in contrast to the work done by Long *et al.*, who, using a different data set, demonstrated that high-volume, tertiary care neurosurgical centres had better outcomes than their low-volume, community hospital counterparts.³² Our lack of association between academic centres and inpatient mortality may be, in part, because of our inability to definitely identify academic centres as being either tertiary care or community hospitals.

Inpatient complications

Our analysis demonstrated a total post-operative complication rate of 32.6%. This rate is similar to the overall 33.2% and 42.1% complication rates published in the Barker *et al.*¹⁰ and Patil *et al.*¹¹ NIS-based studies.^{10,11} This complication rate appears to be in line with previous reports, although studies with longer follow-up time periods often have higher complication rates.^{18,20,22}

Specifically, our post-operative rate of 14.3% fluid and electrolyte abnormalities, including hyponatremia, is similar to previous reports, including retrospective studies by Tao *et al.* and Wei *et al.* demonstrating a greater incidence of post-operative hyponatremia in elderly patients undergoing resection of pituitary adenomas.^{21,23} Our rate of post-operative hyponatremia is also similar to the rate of 9.1% demonstrated in Fraioli *et al.*'s small case series of 11 elderly patients.²⁴ Our rate is slightly higher than the 12.5% rate reported by Patil *et al.* in this NIS-based analysis focusing on adult-aged Cushing patients undergoing transsphenoidal resection.¹¹ This difference in complication rate may reflect some differences in propensity to develop this complication in the elderly subset, although further study of the impact of age upon fluid and electrolyte abnormalities may be required in future prospective studies.

CSF rhinorrhea, mostly occurring beyond the eighth decade of life within our patient population, was 5.4%, again higher than the rate reported of 1.4% by Patil *et al.* who studied patients mostly in their second to fifth decades of life.¹¹ Other studies focused on outcomes following transsphenoidal resection in patients specifically in the elderly population have demonstrated CSF rhinorrhea rates of up to 15%.¹⁶ One likely reason for this difference in reported complication rates may be that other studies followed subjects for up to 4 years, thus likely capturing a greater number of cases than our study, which focused on inpatient complications.¹⁶

Other complications, including post-operative pulmonary complications and iatrogenic pan-hypopituitarism, are reported with varying degree throughout the elderly pituitary tumour literature. Our reported rates of post-operative pulmonary complications (3.5%), iatrogenic pan-hypopituitarism (3.5%) and post-operative stroke (2.5%) are significantly lower than in other, smaller, single-institution studies. The Pietila *et al.*²⁰ series reported post-operative pulmonary complication rates of 14% and pan-hypopituitarism rates of 5%. However, the Pietila study reported aggregate data from elderly patients with numerous types of tumours, including meningiomas and gliomas, in addition to the elderly patients with pituitary tumour we have focused on in our study.²⁰ In fact, the Pietila study had only three patients with pituitary tumour in their total population of 44 patients, and the authors did not separately report complication rates for patients with pituitary tumour from the overall population studied.²⁰ Regarding our relatively low rate of pan-hypopituitarism, because the diagnosis of hypopituitarism is often made several weeks or months after surgery, it likely to be underestimated in our data set. A separate study by Hong *et al.* reported a post-operative stroke rate of 5% in a study of 103 elderly patient with pituitary adenomas following transsphenoidal resection at a single institution.²² The authors of this study followed patient complications for a mean follow-up period of 6.1 years. The difference in our reported post-operative stroke rate of 2.5% and the Hong *et al.* rate of 5% may thus also be in large part because of the longer follow-up period of the latter study.²²

Our reported rate of post-operative central DI (2.2%) was markedly lower than reported rates in other series^{22,24} with rates in ranging from 10.2 to 55%, likely reflecting permanent DI studying over a long follow-up period. The relatively low incidence of DI in our current study may only represent transient DI. Determining the rate of permanent DI would require an assessment of endocrine function several months after surgery. Given that the NIS contains information on inpatient admissions only and does not track patients after discharge, determining the true incidence of permanent DI was not possible in this analysis.

In several multivariate analysis assessing the impact of various patient and procedure-related factors on inpatient complications, we found that older age was associated with increased risk of post-operative stroke (above 80 years old) and fluid and electrolyte abnormalities (above 70 years old); greater Charlson score was associated with greater risk of post-operative CSF leak; finally, non-elective procedure status was associated with greater risk of post-operative pulmonary complication or fluid and electrolyte disorder. These findings are consistent with studies in the general surgery literature demonstrating that greater age and non-elective

procedure status are associated with greater risk of post-operative complications.^{6,9}

LOS and total hospital charges

Similar factors, including age, race, Charlson score, elective procedure status and complications, were associated with both increased LOS and total hospital charges. Median LOS in our study, focused on elderly patients, was 2 days longer than LOS reported by other pituitary surgery outcome studies using the NIS database, which had a median LOS of 4 days and focused on adult-aged patients.^{10,11} Our reported LOS is significantly less than other reports, including the series by Fraioli *et al.* and Kurosaki *et al.*, in which mean LOS was greater than 16 days.^{16,24} It is difficult to verify for certain the cause of the prolonged LOS in these two studies, but it is possible that additional factors unaccounted for in these studies, including patient co-morbidities or a full reporting of complications, may have prolonged patient stay. The Patil *et al.* study reported that LOS was prolonged for older patients, those with multiple co-morbidities and those with post-operative complications.¹¹ Our findings expand upon these observations by specifically quantifying the degree to which patient age, individual Charlson score and specific conditions, such as fluid and electrolyte abnormalities, pulmonary complications, stroke and central DI, contribute to increased LOS (and secondary cost), while other conditions do not significantly contribute to the stated outcomes. Additionally, our study demonstrated that LOS was prolonged among African-Americans and Hispanics, possibly reflecting difficulty in having these patients referred to outpatient therapy or rehabilitation facilities in a timely manner.³⁹ Finally, our results demonstrating reduced LOS for patients undergoing elective procedures has also been well documented in the general surgical literature and is now defined for elderly pituitary patients undergoing surgical resection.³³ Additionally, all associations with increased LOS were reflected in increased total hospital charges.

Study limitations

There are several limitations to the NIS database. Its retrospective nature carries a potential bias. Although this study is powered by a large number of patients over several years, the NIS database does not include all specific characteristics we would desire, including tumour size, tumour secretory status (non-secreting tumour vs acromegaly, Cushing, or prolactinoma) or Karnofsky performance score. Furthermore, as reported Woodworth *et al.*, the overall sensitivity and specificity of administrative databases such as the NIS may often be sub-optimal, and such vast databases may contain some inaccuracies.³⁴ Given that data collection on patients ended with their discharge from the hospital, it was not possible to track important long-term outcomes, such as tumour recurrence or long-term complications or mortality. As a result, the true longitudinal morbidity and mortality is likely to be underestimated. Additionally, given limitations of the database, we were not able to identify surgery vs anaesthesia-related complicated nor were we able to adjust for tumour size or the use of endoscopy.

Despite such limitations, we believe that this study provides important new information regarding clinically relevant risk factors, with high fidelity, in elderly patients with pituitary tumours. While previous studies have noted some associations between patient age and post-operative outcomes, our study is the first to define a specific age threshold among patients with pituitary adenoma beyond which patients are at higher risk of post-operative inpatient mortality, greater LOS, higher total charges and a higher number of post-operative complications. Furthermore, increased Charlson co-morbidity was found to be a risk factor for inpatient mortality, greater LOS, higher total charges and a higher number of post-operative complications. Based on our study results, in the near future, it will be possible to characterize the surgical risk of every individual patient, based not only on his age, but also on his co-morbidities.

Conclusions

The current study suggests that surgical treatment is a safe treatment modality among patients with pituitary tumours up to their ninth decade of life. Higher Charlson co-morbidity score is an important prognostic factor for inpatients death, greater length of stay, higher total hospital charge and higher risk of post-operative cerebrospinal fluid leak.

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Competing interests/financial disclosure

The authors have no conflicting interests or financial disclosures.

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