Comparative preoperative characteristics and postoperative outcomes at a private versus a safety-net hospital following endoscopic endonasal transsphenoidal resection of pituitary adenomas

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OBJECTIVE Sociodemographic disparities in health outcomes are well documented, but the effects of such disparities on preoperative presentation of pituitary adenomas (PA) and surgical outcomes following resection are not completely understood. In this study the authors sought to compare the preoperative clinical characteristics and postoperative outcomes in patients undergoing PA resection at a private hospital (PH) versus a safety-net hospital (SNH).

METHODS The authors conducted a retrospective review over a 36-month period of patients with PAs who underwent endoscopic endonasal transsphenoidal surgery performed by the same attending neurosurgeon at either a PH or an SNH at a single academic medical institution.

RESULTS A total of 92 PH patients and 69 SNH patients were included. SNH patients were more likely to be uninsured or have Medicaid (88.4% vs 10.9%, $p < 0.0001$). A larger percentage of SNH patients were Hispanic (98.7% vs 32.6%, $p < 0.0001$), while PH patients were more likely to be non-Hispanic white (39.1% vs 4.3%, $p < 0.0001$). SNH patients had a larger mean PA diameter (26.2 vs 22.4 mm, $p = 0.0347$) and a higher rate of bilateral cavernous sinus invasion (13% vs 4.3%, $p = 0.0451$). SNH patients were more likely to present with headache (68.1% vs 45.7%, $p = 0.0048$), vision loss (63.8% vs 35.9%, $p < 0.0005$), panhypopituitarism (18.8% vs 4.3%, $p = 0.0031$), and pituitary apoplexy (18.8% vs 7.6%, $p = 0.0334$). Compared to PH patients, SNH patients were as likely to undergo gross-total resection (73.9% vs 76.1%, $p = 0.7499$) and had similar rates of postoperative improvement in headache (80% vs 89%, $p = 0.14$) and vision (82% vs 84%, $p = 0.74$), but had higher rates of postoperative panhypopituitarism (23% vs 10%, $p = 0.04$) driven by preoperative endocrinopathies. Although there were no differences in tumor recurrence or progression, loss to follow-up was seen in 7.6% of PH versus 18.6% ($p = 0.04$) of SNH patients.

CONCLUSIONS Patients presenting to the SNH were more often uninsured or on Medicaid and presented with larger, more advanced pituitary tumors. SNH patients were more likely to present with headaches, vision loss, and apoplexy, likely translating to greater improvements in headache and vision observed after surgery. These findings highlight the association between medically underserved populations and more advanced disease states at presentation, and underscore the likely role of academic tertiary multidisciplinary care teams and endoscopic PA resection in somewhat mitigating sociodemographic factors known to portend poorer outcomes, though longer-term follow-up is needed to confirm these findings.

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KEYWORDS adenoma; transsphenoidal resection; health disparities; safety-net hospital; oncology; pituitary surgery

ABBREVIATIONS ACTH = adrenocorticotrophic hormone; DI = diabetes insipidus; DVT = deep vein thrombosis; GH = growth hormone; GTR = gross-total resection; IGF-1 = insulin-like growth factor-1; PA = pituitary adenoma; PH = private hospital; SNH = safety-net hospital; TSH = thyroid-stimulating hormone.

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SOCIODEMOGRAPHIC disparities in healthcare outcomes are well documented in the medical literature.^{8,23,29,35} Over the past 2 decades, factors such as race, ethnicity, and socioeconomic status have been identified as major barriers to neurosurgical care in the US.^{11,12,26,27,31,33} Large retrospective studies using nationwide databases have found that compared to white patients, African American and Hispanic patients have disproportionately less access to high-volume neurosurgical treatment centers,^{6,11,12,27} which is a known predictor of poor neurosurgical outcomes.^{4,9,10,20,22} Disadvantaged groups often present with more advanced disease states and experience delays in obtaining neuro-oncological treatment, particularly postoperative therapies such as chemotherapy and radiation following tumor resection.^{7,12,32} Studies have shown that uninsured patients have worse neurosurgical outcomes compared to their insured counterparts,^{15,25} and African Americans have higher rates of postoperative complications resulting in longer hospital stays and greater healthcare utilization.^{26,31,33}

Recent studies have compared neurosurgical outcomes at safety-net hospitals (SNHs) and private hospitals (PHs). One study found that patients with glioblastoma treated at an SNH or those who did not have insurance had higher mortality rates than patients treated at a PH.^{5,7} According to a recent study at our center, SNH patients with brain metastases treated with stereotactic radiosurgery alone had less follow-up care and a higher rate of poor neurological outcomes than PH patients,¹⁴ highlighting the importance of considering patient access to follow-up care when deciding on optimal treatment strategies.

Although several studies have investigated sociodemographic barriers to neuro-oncological care in the US, few have looked at disparities in the treatment of pituitary disease. Pituitary adenomas (PAs) are relatively common, with an estimated overall prevalence of 16.7%.¹⁶ Although typically benign, PAs can cause profound disability and have significant adverse impacts on quality of life.¹ One study examined predictors of access to PA resection and found that racial minorities and patients from high-poverty areas were less likely to be admitted to high-volume pituitary centers than were patients from higher income brackets.²⁸ However, the effect of sociodemographic disparities on outcomes following resection of PAs is unknown. In this study of patients undergoing PA resection at an SNH and patients receiving the same treatment at a PH, we compared the clinical presentation, hospital course, and surgical outcome in the 2 patient groups by using a single-surgeon design, with all resections performed by the same attending neurosurgeon and all patients under the care of the same tertiary multidisciplinary team at a single institution.

Methods

Study Design

This retrospective cohort study was approved by the institutional review board of the University of Southern California (USC) Keck School of Medicine. Patients were identified from our electronic pituitary tumor database (RedCap¹⁸), which includes information about

patient demographics, preoperative symptoms and endocrine status, surgical characteristics, pathology, postoperative course, and follow-up details. We included patients who underwent endoscopic transsphenoidal resection of PAs between January 2015 and December 2017 at a single academic medical institution consisting of one PH (Keck Hospital of USC) and one SNH (Los Angeles County + University of Southern California [LAC+USC] Medical Center) located in Los Angeles, CA. All procedures at both hospitals were performed by the same neurosurgeon (G.Z.).

Imaging Evaluation

MR imaging was obtained preoperatively and prior to each follow-up visit. The imaging procedure followed standard pituitary protocol, with T1- and T2-weighted images and T1 postcontrast imaging of thin-cut regions of the sella. Dynamic imaging was used in cases of equivocal diagnosis, using a 1-Tesla MRI at the SNH and 1- or 3-Tesla MRI at the PH. Knosp scores were determined in cases of bilateral cavernous sinus invasion, with grade 0 representing no invasion and grade 4 representing total encasement of the carotid artery. Knosp scores are described in detail elsewhere.^{21,24}

Surgical Intervention

All patients underwent endoscopic endonasal approaches via a 2-surgeon binostril technique that has been described in detail elsewhere.³⁴ Direct approaches are typically performed by the neurosurgery team at our institutions, with otolaryngology involvement for extended approaches requiring flap reconstruction. Intraoperative CSF leak repair is typically performed with autologous fat and/or fascial repair, with lumbar drainage and pedicled nasoseptal flap reconstruction reserved for extended approaches or high-grade CSF leaks. Patients at both hospitals were approached with the same adherence to standard-of-care principles (e.g., medical therapies for prolactinomas were used as first-line treatment regardless of resource constraints).

Endocrine Evaluation

Preoperative symptoms were recorded, and endocrine status was determined using serum pituitary laboratory analyses, including serum thyroid-stimulating hormone (TSH), free T4, prolactin, and insulin-like growth factor-1 (IGF-1). Diagnosis of Cushing's disease was made according to the most recent Endocrine Society guidelines, using salivary cortisol and dexamethasone testing.³⁰ Acromegaly was defined as serum IGF-1 level above the age-adjusted normal range and growth hormone with lack of suppression below 1 ng/ml, accompanied by signs and symptoms of growth hormone (GH) excess.² Oral glucose tolerance testing was performed in selected equivocal cases. Prolactin values greater than 200 ng/ml were considered diagnostic of prolactinoma. Serum prolactin levels below 100 ng/ml were deemed consistent with stalk effect, and values between 100 and 200 ng/ml were considered consistent with stalk effect in macroadenomas. Panhypopituitarism was defined as ≥ 3 pituitary axis deficiencies.

TABLE 1. Comparison of demographic data between patients undergoing PA resection at the PH versus the SNH

	PH (n = 92)	SNH (n = 69)	p Value
Age in yrs, median (range)	55.6 (21–84)	48.2 (16–77)	0.31
Female sex, %	57.6	49.3	0.30
Race/ethnicity, n (%)			
Non-Hispanic—white	36 (39.1)	3 (4.3)	<0.0001
Hispanic—any race	30 (32.6)	55 (79.7)	<0.0001
Asian/Pacific Islander	17 (18.5)	5 (7.2)	0.044
Black	2 (2.2)	2 (2.3)	0.97
Other	7 (7.6)	4 (5.8)	
Insurance, n (%)			<0.0001
Private/Medicare	82 (89.1)	8 (11.6)	
Medicaid/uninsured	10 (10.9)	61 (88.4)	
Household income in US\$, mean ± SD	63,936 ± 23,401	49,987 ± 16,783	<0.0001

Boldface type indicates statistical significance.

Patient education and consult, and obtaining of consent, were performed in the same manner at both hospitals, with discussion of risks, benefits, need for continual endocrine supplementation, etc. Translators were used at both institutions when indicated.

According to institutional guidelines used at both hospitals, determination of postoperative persistence of disease for Cushing's and acromegaly was based on clinical judgment and supportive laboratory values obtained within 3 months of surgery. Remission of acromegaly in equivocal cases was considered to have occurred after normalization of IGF-1 determined by oral glucose tolerance testing with suppression of GH below 1 ng/ml. Cushing's remission was confirmed by low levels of postoperative cortisol (2–5 ng/dl) after withdrawal of glucocorticoids started during the perioperative timeframe. Surgical remission of prolactinomas was defined as postoperative normalization of prolactin without the need for ongoing medical therapy. Remission for nonfunctional tumors was based on radiographic imaging.

Follow-up was conducted with the surgeon at 1 week postoperatively, at 6 weeks with hormonal analysis as indicated, and at 3 months with MRI, visual fields, and hormonal testing as indicated. Further discussion of follow-up methodology is discussed in the *Limitations* section.

Laboratory tests performed at both PH and SNH were sent to Quest Diagnostics.

Statistical Analysis

Patient demographics, presenting symptomatology, preoperative endocrine status, surgical characteristics, postoperative course, and follow-up details were reviewed. Comparisons were made using Pearson's chi-square test for categorical variables and a two-tailed t-test or Mann-Whitney U-test for continuous variables, with an alpha

TABLE 2. Comparison of presenting symptoms in PH versus SNH patients

Symptoms	PH	SNH	p Value
Headache	42 (45.7)	47 (68.1)	0.0055
Vision loss	33 (35.9)	44 (63.8)	0.0011
Decreased libido	15 (16.3)	6 (8.7)	0.16
Amenorrhea*	15 (28.3)	9 (26.4)	0.56
Galactorrhea	9 (9.8)	2 (2.9)	0.087
Fatigue	32 (34.8)	9 (13.0)	0.0022
Cranial nerve palsy	5 (5.4)	4 (5.8)	0.91
Acromegaly	19 (20.7)	14 (20.3)	0.95
Cushing's disease	4 (4.3)	3 (4.3)	1.00
Incidental finding	7 (7.6)	4 (5.8)	0.66
Pituitary apoplexy	7 (7.6)	13 (18.8)	0.033

SNH patients presented with higher rates of headache, visual loss, fatigue, and pituitary apoplexy. Values are presented as number of patients (%) unless otherwise indicated. Boldface type indicates statistical significance.

* Female patients only.

level of 0.05. Household incomes were based on self-reported zip codes and aggregate zip code data from the 2016 American Community Survey.

Results

Baseline Patient Demographics

In total, 170 patients, including 95 PH patients (56%) and 75 SNH patients (44%), underwent transsphenoidal PA resection during the period from January 2015 to December 2017. Three PH patients (3%) and 6 SNH patients (8%) were excluded due to lack of preoperative data, resulting in a total of 161 patients (92 PH patients and 69 SNH patients) analyzed.

Demographic comparisons between the 2 hospitals are shown in Table 1. The median age for PH patients was 55.6 years (range 21–84 years) compared to 48.2 years (range 16–77 years) in SNH patients ($p = 0.31$). In the SNH cohort, 4.3% of patients were non-Hispanic white, compared to 39% of patients in the PH cohort ($p < 0.0001$); conversely, 79.7% of SNH patients were Hispanic (any race), compared to 32.6% of PH patients ($p < 0.0001$). A significantly higher percentage of SNH patients compared to PH patients were uninsured or on MediCal (Medicaid), (88.4% vs 11.6%, $p < 0.0001$). SNH patients had a lower median household income than PH patients (\$49,987 ± \$16,783 vs \$63,936 ± \$23,401, $p < 0.0001$).

Symptoms at clinical presentation and preoperative endocrine status of patients at both hospitals are shown in Tables 2 and 3, respectively. Compared to PH patients, SNH patients presented with higher rates of headache (68.1% vs 45.7%, $p = 0.0048$), vision loss (63.8% vs 35.9%, $p < 0.0005$), and pituitary apoplexy (18.8% vs 7.6%, $p < 0.0334$). PH patients presented with a higher rate of self-reported fatigue than SNH patients (34.8% vs 13.0%, $p = 0.0017$). In terms of endocrine status, SNH patients presented with a higher rate of preoperative panhypopituitarism (18.8% vs 4.3%, $p = 0.0031$), and PH patients pre-

TABLE 3. Preoperative endocrine status of PH versus SNH patients

Endocrine Status	PH	SNH	p Value
Hyperprolactinemia	22 (23.9)	9 (13.0)	0.083
Hypocortisolemia	5 (5.4)	6 (8.7)	0.41
Hypogonadism	36 (39.1)	16 (23.2)	0.032
Hypothyroidism	18 (19.6)	14 (20.3)	0.91
Acromegaly	18 (19.6)	12 (17.4)	0.72
Cushing's disease	4 (4.3)	3 (4.3)	1.00
Panhypopituitarism*	4 (4.3)	13 (18.8)	0.0031
Normal	20 (21.7)	15 (21.7)	1.00

SNH patients had a significantly higher rate of panhypopituitarism than PH patients. Values are presented as number of patients (%) unless otherwise indicated. Boldface type indicates statistical significance.

* Panhypopituitarism was considered an independent category (e.g., there were 4 PH patients and 13 SNH patients with panhypopituitarism in addition to the PH and SNH patients with hypocortisolemia).

sented with a higher rate of documented hypogonadism (39.1% vs 23.2%, $p = 0.0320$).

Baseline Tumor Characteristics

Tumor characteristics are reported in Table 4. SNH patients had a significantly larger mean tumor diameter than PH patients (26.2 ± 11.2 vs 22.4 ± 11.2 mm, $p = 0.0347$). There was no significant difference in the percentage of patients who presented with any cavernous sinus invasion (33.7% of PH vs 40.6% of SNH patients, $p = 0.4388$); however, SNH patients presented with a significantly higher rate of bilateral cavernous sinus invasion ($n = 9$, 13%) compared to PH patients ($n = 4$, 4.3%, $p = 0.0451$). Of the patients who had cavernous sinus invasion, the mean Knosp score for SNH patients was 2.5, versus 2.7 for PH patients ($p = 0.345$). Further analysis by chi-square test of differences in Knosp score among patients with cavernous sinus invasion with scores of 3 and 4 grouped together showed no significant difference in Knosp score between the cohorts ($p = 0.1815$).

Surgical Resection

Resection of tumor was performed by the same neurosurgeon at both the SNH and PH. Surgical characteristics and outcomes are reported in Table 4. Rates of gross-total resection (GTR), assessed by postoperative MRI at 3 months, were similar between the groups (PH 76.1% GTR, SNH 73.9% GTR, $p = 0.7499$). There was a significantly higher rate of intraoperative CSF leak in the PH cohort compared to the SNH group (37% vs 22%, $p = 0.037$). Eleven SNH patients (15.7%) underwent follow-up stereotactic radiosurgery or other radiation, compared to 4 (4.34%) PH patients ($p = 0.014$).

Tumor Pathology

Tumor pathology is reported in Table 5. Nonfunctional PAs represented the majority of cases in both PH patients (62 [67.4%] vs 46 [66.7%], $p = 0.92$). The second most common tumors were GH-secreting somatotrophic ade-

TABLE 4. Surgical and tumor characteristics of PH versus SNH patients

	PH	SNH	p Value
Reoperation*	16 (17.4)	10 (14.5)	0.62
Macroadenoma at presentation	83 (90.2)	66 (95.7)	0.19
Giant adenoma†	9 (9.8)	7 (10.1)	0.95
Max tumor diameter in mm, mean $\pm$ SD	22.4 ± 11.2	26.2 ± 11.2	0.035
Tumor invasion	70 (76.1)	56 (81.2)	0.44
Cavernous sinus	30 (33.7)	28 (40.6)	0.37
Right	16 (17.4)	12 (17.4)	1.00
Left	10 (10.9)	7 (10.1)	0.87
Bilateral	4 (4.3)	9 (13.0)	0.045
Suprasellar	52 (56.5)	39 (56.5)	1.00
Infrasellar	16 (17.4)	8 (11.6)	0.31
Sinus	14 (15.2)	5 (7.2)	0.12
Clivus	7 (7.6)	8 (11.6)	0.39
Ventricle	1 (1.1)	1 (1.4)	0.87
Cavernous sinus invasion, Knosp score			0.18‡
Mean	2.7	2.5	
1	5	1	
2	6	7	
3/4	20	15	
Postop GTR	70 (76.1)	51 (73.9)	0.75
Intraop CSF leak	34 (37.0)	15 (21.7)	0.037

SNH patients had significantly larger tumors and significantly lower rates of intraoperative GTR and intraoperative CSF leak. Values are presented as number of patients (%) unless otherwise indicated. Boldface type indicates statistical significance.

* Percentage of patients from each cohort who were undergoing a second operation.

† Tumor diameter ≥ 4 cm.

‡ Pearson's chi-square test comparing proportions of patients with Knosp scores of 1, 2, and 3 and 4 combined.

nomas, comprising 19.6% ($n = 18$) of the PH group tumors versus 18.8% ($n = 13$) of the SNH group tumors ($p = 0.89$). Prolactinomas represented 5.4% ($n = 5$) of tumors resected at the PH, versus 2.9% ($n = 2$) of tumors resected at the SNH ($p = 0.44$). There were 4 adrenocorticotrophic hormone (ACTH)-secreting tumors in the PH patients (4.3%) versus 3 (4.3%) in the SNH patients ($p = 1$). There were 2 TSH-secreting adenomas in the PH patients (2.2%) and zero in the SNH patients.

Surgical Complications and Immediate Outcomes

There were no significant differences in complication rates between the 2 groups, as shown in Table 6. There were 5 cases of CSF leak requiring reoperation or lumbar drain in each group (5.4% vs 7.2% in the PH vs SNH group, respectively, $p = 0.64$). There were 6 cases of hyponatremia at the PH group versus 1 in the SNH group (6.5% vs 1.4%, $p = 0.11$). There were 8 cases of transient diabetes insipidus (DI) in the PH group versus 6 in the

TABLE 5. Pathologically confirmed tumor subtypes in PH and SNH patients

PA Subtype	PH	SNH	p Value
ACTH	4 (4.3)	3 (4.3)	>0.99
GH	18 (19.6)	13 (18.8)	0.89
GH and PRL	1 (1.1)	1 (1.4)	0.86
TSH	2 (2.2)	0 (0)	
Prolactinoma	5 (5.4)	2 (2.9)	0.44
NFPA	62 (67.4)	46 (66.7)	0.92

NFPA = nonfunctional pituitary adenoma; PRL = prolactin.

Values are presented as number of patients (%) unless otherwise indicated.

SNH group (8.7% vs 8.6%, $p = 0.98$). There was 1 case of each the following: deep vein thrombosis (DVT; SNH group), permanent DI (SNH group), and abdominal hematoma (PH group). There was 1 case of hydrocephalus in each group. There were 2 cases of hematoma, 1 case of stroke, and 2 cases of sinusitis in the PH group, but none of these complications occurred in the SNH group. There were no deaths in either group.

There was no significant difference between the 2 groups in rates of early readmission (15.2% in the PH vs 12.9% in the SNH group, $p = 0.71$) or in rates of reoperation (7.6% in the PH vs 4.3% in the SNH group, $p = 0.38$). PH patients had a median postoperative length of stay of 2 days compared to 3 days for the SNH patients ($p = 0.5099$).

Postoperative Outcomes

Follow-up data are presented in Table 7. Mean follow-up times were 13.9 months for PH patients and 13.4 months for SNH patients. Seven (7.6%) PH patients were lost to follow-up versus 13 (18.6%) SNH patients ($p = 0.04$). Of those patients with adequate follow-up, 89% of PH patients achieved postoperative improvement in headache, versus 80% of SNH patients ($p = 0.14$). SNH patients and PH patients achieved similar rates of postoperative improvement in vision (82% SNH vs 84% PH, $p = 0.74$), based on patient self-assessment and formal visual field testing.

PH patients demonstrated improved endocrine outcomes in 47% of cases, versus 17% of cases in SNH patients ($p < 0.0001$). For hyperfunctioning adenomas, improved endocrine status was defined as hormonal remission without the need for medications postoperatively. Of patients with prolactinomas, 3 out of 5 PH patients required cabergoline postoperatively compared to 2 out of 2 SNH patients. For ACTH-secreting adenomas, 1 patient at each hospital required postoperative medication. For GH-secreting adenomas, 3 out of 15 cases (20%) in PH patients required postoperative somatostatin analog medications compared to 4 out of 9 (44%) cases in SNH patients.

Postoperative hypopituitarism was identified by either follow-up endocrine laboratory tests or persistence of symptoms requiring hormone supplementation. Of patients with preoperative hypogonadism, 12 out of 16 cases (75%) in SNH patients persisted compared to 10 out of 36 cases (28%) in PH patients. There were no new cases of hypogonadism reported postoperatively. Of patients

TABLE 6. Postoperative complications in SNH versus PH patients

Complication	PH	SNH	p Value	Risk Difference (95% CI)
CSF leak	5 (5.4)	5 (7.2)	0.64	-1.8% (-0.09 to 0.06)
Hyponatremia	6 (6.5)	1 (1.4)	0.11	5.1% (-0.01 to 0.11)
DI, transient	8 (8.7)	6 (8.6)	0.98	0.1% (-0.09 to 0.09)
DI, permanent	0 (0.0)	1 (1.4)		-1.4% (-0.04 to 0.01)
Meningitis	1 (1.1)	1 (1.4)	0.24	-0.3% (-0.04 to 0.03)
Sinusitis	2 (2.2)	0		2.2% (-0.01 to 0.05)
Bacteremia/sepsis	1 (1.1)	0		1.1% (-0.01 to 0.03)
Pneumonia	0	1 (1.4)		-1.4% (-0.04 to 0.01)
DVT	0	1 (1.4)		-1.4% (-0.04 to 0.01)
Abdominal hematoma	1 (1.1)	0		1.1% (-0.01 to 0.03)
Visual loss	0	0		
Epistaxis	2 (2.2)	2 (2.9)	0.77	-0.7% (-0.06 to 0.04)
Cranial nerve palsy	0	0		
Hematoma	2 (2.2)	0		2.2% (-0.01 to 0.05)
Stroke	1	0		1% (-0.01 to 0.03)
Carotid artery injury	0	0		
Hydrocephalus	1 (1.1)	1 (1.4)		-0.3% (-0.04 to 0.03)
Death	0	0		
Other	4 (4.3)	3 (4.3)	1	
None	65 (70.7)	55 (78.6)	0.27	-7.9% (-0.21 to 0.06)

There were no significant differences in rates of complications between the 2 groups.

TABLE 7. Long-term headache and visual and endocrine outcomes during follow-up after PA resection

	PH	SNH	p Value
Headache			
Improved	89%	80%	0.14
Stable	11%	18%	0.25
Worse	0.0%	2.0%	
No. of patients	84	52	
Visual outcomes			
Improved	84%	82%	0.74
Stable	16%	18%	0.75
Worse	0%	2.0%	
No. of patients	85	58	
Endocrine outcomes			
Improved	47%	17%	<0.0001
Stable	48%	65%	0.04
Panhypopituitarism			
All	10%	23%	0.04
New	5.5%	5.6%	0.98
No. of patients*	72	53	

Improved outcomes represent patients with preoperative deficits that were self-reportedly improved postoperatively. SNH patients had lower rates of improved endocrine outcomes. See the *Postoperative Outcomes* section for more endocrinopathy results. Boldface type indicates statistical significance.

* Patients with perioperative endocrinopathies.

with preoperative hypocortisolemia, 3 out of 6 cases persisted in SNH patients compared to 2 out of 5 cases in PH patients. There were 13 new cases of hypocortisolemia in SNH patients compared to 6 new cases in PH patients. SNH patients as a cohort had a higher rate of postoperative panhypopituitarism than PH patients (23% vs 10%, $p = 0.046$), although this outcome was driven by a higher degree of preoperative panhypopituitarism. In patients with preoperative panhypopituitarism, it persisted in 9 out of 13 (69%) SNH patients compared to 3 out of 4 (75%) PH patients. There were 3 new cases of panhypopituitarism in SNH patients compared to 4 new cases in PH patients ($p = 0.98$). Patients with postoperative isolated hypocortisolemia or panhypopituitarism required long-term steroids. There was no statistical difference in rates of tumor recurrence or progression over the follow-up period (3.5% [PH] vs 6.7% [SNH], $p = 0.38$).

Discussion

Patients with PAs who receive surgical treatment at an SNH are of lower socioeconomic status; present with larger, more advanced and invasive PAs; and have a higher propensity for headaches, vision loss, endocrinopathy, and pituitary apoplexy. Postoperatively, both cohorts had similar overall postoperative courses and complication profiles, with a comparable rate of resection despite the higher rates of more advanced disease in SNH patients. Despite barriers to diagnosis and care of patients with advanced PA disease, safe and durable outcomes were

achieved in both cohorts by providing similar multidisciplinary neurosurgical and endocrinological care teams for both the SNH and PH patients. All patients at both sites were managed by the same teams of neurosurgeons and endocrinologists, and all cases were reviewed in a weekly multidisciplinary pituitary tumor board conference. Our conclusion is that a tertiary multidisciplinary care approach can partially mitigate the obvious disparities in presentation and clinical and imaging findings of advanced disease encountered in the public SNH compared with the PH setting.

Literature involving the impact of sociodemographic status on outcomes following pituitary neurosurgery remains sparse. SNHs serve poorer, underinsured patients. As a result of limited access to care, patients present with more advanced pathology, which our data demonstrate, as SNH patients had higher rates of headache and visual loss, which are symptoms of mass effect, more advanced endocrinopathies, and larger mean tumor diameter. Jahangiri et al. suggested a relationship between lower socioeconomic status and pituitary apoplexy.¹⁹ A similar association was seen in our study, in that SNH patients had a significantly lower median household income (socioeconomic status) and corresponding higher rate of pituitary apoplexy upon presentation.

In terms of the relationship between sociodemographic identifiers and outcomes, data from the National Inpatient Sample showed that in patients undergoing uncomplicated transphenoidal surgery for PA resection, lower median income and Hispanic ethnicity were factors that drove longer hospital lengths of stay.¹⁷ Our data did not demonstrate these trends; SNH patients had a significantly lower median income, and a significantly higher percentage of patients were Hispanic, but they experienced lengths of stay similar to those of PH patients. Perhaps one explanation for this trend, or lack thereof, is due to both the SNH and PH in our study being high-volume hospitals. Barker et al. have asserted that higher-volume hospitals and surgeons correlate with superior short-term outcomes for pituitary neurosurgery, and this trend has been demonstrated for other neurosurgical pathologies as well.^{3,4,9}

Rates of GTR and subsequent long-term outcomes were also similar in both of our study groups. In terms of headache and visual loss, there were similar rates of symptom improvement (between those in both groups who presented with headache and vision loss) postoperatively ($p = 0.14$ and 0.74 , respectively). This finding implies that surgical intervention can lead to dramatic improvements in quality of life that are distributed relatively equally throughout sociodemographic strata. However, SNH patients had worse endocrine outcomes, suggesting that the perceived similar rates of symptomatic improvement may be due to differences in reporting between the 2 groups.

Recurrence rates demonstrated no significant differences between SH and PH patients ($p = 0.67$) over the relatively short follow-up period. This finding can be partially attributed to the generally slow-growing nature of pituitary tumors.¹³ However, this analysis has information from just over 1 year of follow-up. A larger, longer-term study is needed to determine what environmental factors put patients at risk for recurrence.

Future Directions

Our data suggest that while lack of insurance, low socioeconomic status, and Hispanic ethnicity are all correlated with more advanced disease progression, these factors are potentially mitigated by surgery being performed by an experienced surgeon at a high-volume center. The differences between high-volume centers and lower-volume centers and PA resection outcomes should be further explored to determine specific features associated with optimal quality of care.

As the field of neurosurgery continues to explore the effects of sociodemographic factors on outcomes, the role of primary care must be equally explored. Chandra and colleagues have discussed the impact of primary care providers in early diagnosis and continued care of glioblastoma⁷; the role of primary care providers is equally important in the management of PAs. Our SNH patients had a higher rate of endocrinopathy on presentation, and as a result many of them were on long-term endocrine therapy at the time of this report. Similarly, with regard to perioperative endocrine status, rates of hypogonadism were higher in the PH patients. We consider this finding to be due to ascertainment bias; patients at the PH are more likely to receive an endocrine workup that results in documentation/treatment of hypogonadism and are more likely to have had extensive endocrine workups prior to seeing a specialist at a tertiary center. These biases are likely not well captured within our model and represent a future direction of research. The role of primary care providers in diagnosing these tumors early could potentially save some pituitary function and ultimately improve quality of life. In addition, it is important for the field of neurosurgery to identify the causes of potential systematic disparities between groups of patients. In our cohort specifically, many of the differences seen in presentation are largely due to lack of engagement with the healthcare system. This disengagement is multifactorial; it results from a lack of insurance, language barriers between patients and providers, general mistrust of Western healthcare, and—particularly important in a cohort with low socioeconomic status—the fact that the hours required to see a doctor largely take away from work hours in patients who may not receive paid sick leave.

Limitations

Our study has several limitations. In addition to the inherent limitations of a retrospective study, the majority of PH patients undergoing PA resection were undergoing elective procedures, whereas many of the SNH patients were admitted from the emergency room—accordingly, the circumstances by which preoperative symptoms were recorded were not entirely equal. Lastly, a larger portion of SNH patients were lost to follow-up, and thus the long-term outcome data may not be truly representative of the entire cohort. It is important to note that follow-up at the 2 institutions varies widely. At the PH, there is an established pituitary center with protocols that provide consistency in follow-up care. Conversely, SNH patients are followed separately by individual neurosurgery and endocrinology clinics that are staffed by various attending physicians with no set protocol followed. Both hospitals have

equal operative resources (imaging, staff, technology, etc.) for PA resection as part of a concerted effort to build the SNH into a tertiary pituitary center. As a result, the external validity and generalizability of this study may be limited as other SNHs may not have the equivalent resources necessary to care for similarly complex pathologies.

Conclusions

Our study is to our knowledge the first to compare clinical characteristics and outcomes of PA resection in a PH setting versus an SNH setting when the patients in both groups are cared for by similar multidisciplinary teams, with a single-surgeon model, at academic hospitals. The single-surgeon design of our study allowed us to uniquely examine the effects of sociodemographic variables on presentation and outcome. We show that SNH patients present with significantly more advanced disease states and lower socioeconomic status but ultimately have similar short-term and midterm outcomes, demonstrating that an experienced surgical and endocrine team working together at a high-volume academic center may partially mitigate against factors that historically portend negative outcomes in PA patients.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Cyprich, Pangal, Zada. Acquisition of data: Cyprich, Pangal, Shiroishi, Liu. Analysis and interpretation of data: all authors. Drafting the article: Cyprich, Pangal. Critically revising the article: Cyprich, Pangal, Rutkowski, Donoho, Carmichael, Zada. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Cyprich. Statistical analysis: Cyprich, Pangal.

Supplemental Information

Previous Presentations

The abstract was included as a poster presentation at the American Association of Neurological Surgeons Annual Meeting on April 13–17, 2019, in San Diego, CA.

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