

Introduction

Somatostatin analogue administration is a first line treatment used to reduce tumor volume prior to or after transsphenoidal surgery. However, despite their widespread usage there is a subset of tumors that do not respond significantly to medical therapy and require intervention through transsphenoidal surgery (TSS). There has been a paucity of data on the preoperative and postoperative endocrinological characteristics of this subset of lesions as well as overall clinical outcomes to TSS with regards to lesion size in acromegaly patients.

We aimed in this study to characterize the clinical characteristics and postoperative outcomes in acromegaly patients receiving transsphenoidal surgery for macroadenomas versus microadenomas. In addition, we assessed relationships to preoperative therapy such as preoperative somatostatin analogue administration.

Methods and Materials

In this single institution retrospective study a large cohort of 158 acromegaly patients who underwent TSS for acromegaly were examined. Lesions 1 centimeter or greater in maximum diameter were considered macroadenomas. Radiological, surgical, clinical, and endocrinological characteristics preoperatively and postoperatively were documented for analysis. Hormone values were determined at preoperatively and up to 3 years postoperatively for most patients. Pituitary adenoma size, location, and dimensions were determined using preoperative magnetic-resonance-imaging (MRI) and computerized-tomography (CT) imaging. T tests and chi-square tests were not performed due to a high type-1 error rate, as such a multivariate logistic regression model was created to determine which characteristics were predictive of postoperative outcome.

Results

Among the 158 patients with data available, 112 (70.9%) had macroadenomas and 46 (29.1%) had microadenomas. The rates of common preoperative symptoms were largely similar in large versus small tumors, such as headache (41.1% vs 39.1%) and acromegalic-bone changes (75.1% vs 73.9). Unsurprisingly, tumor induced visual field or visual acuity deficits were more common in macroadenomas (23.2% vs 13%). The rates of preoperative comorbidities and medication prescription were overall similar between groups.

Preoperatively, macroadenomas experienced higher rates of hyperprolactinemia (26.5% vs 12.8%), hypocortisolism (17.5% vs 4.7%), and hypothyroidism (23.6%). However, rates of preoperative hypercortisolism were higher in patients with microadenomas (16.3% vs 4.9%). Postoperatively, hypercortisolism and hypoprolactinemia remained the most common types of endocrine dysfunction. The majority of lesions included were intrasellar, with suprasellar-extension occurring in 48.1% of macroadenomas. Average diameter for macroadenomas was 1.8 ± 0.7 cm while average lesion volume was 2.8 ± 3.6 cm. Tumor histology, including hormone co-staining and the MIB index were overall similar between groups. Nearly all patients received endoscopic TSS (98.7% overall) with the most common sellar reconstruction method being nasal packing.

Despite a lower rate of gross total resection in macroadenomas (79.5% vs 93.5%) the rates of biochemical remission (76.7% vs 73.3%) and recurrence (10.7% vs 8.7%) rates were largely similar between groups. Multivariate logistic regression demonstrated that large lesion size was not associated with a greater odds of developing complications such as a CSF leak, dysnatremia, recurrence, or failure of biochemical remission.

Conclusions

Overall, despite differences in preoperative hormone dysfunction and gross total resection rates lesion size was not associated with a greater risk of developing postoperative complications or failure to achieve biochemical remission in patients undergoing surgery for growth hormone secreting adenomas.

Preoperative Characteristics

	Size >1cm (n=112)	Size <1cm (n=46)
Age	46.43 ± 15	50.4 ± 13
Male Gender	47 (42%)	23 (50%)
BMI	28.9 ± 5.1	30.4 ± 5.4
Height (in)	67.7 ± 4.5	67.6 ± 4.5
Weight (lbs)	192.2 ± 46	198.3 ± 39
Hypopituitarism	4 (3.6%)	0 (0%)
Weight Gain	25 (22.3%)	6 (13%)
Skin Changes	36 (32.1%)	20 (43.5%)
Infection	1 (0.9%)	1 (2.2%)
Skin Hyperpigmentation	6 (5.4%)	1 (2.2%)
Depression	2 (1.8%)	4 (8.7%)
Hypertrichosis	3 (2.7%)	1 (2.2%)
Anxiety	2 (1.8%)	0 (0%)
Cognitive Dysfunction	2 (1.8%)	2 (4.3%)
Headache	46 (41.1%)	18 (39.1%)
Tumor Induced Visual Loss	26 (23.2%)	6 (13%)
Acromegalic Bone Changes	83 (74.1%)	34 (73.9%)
Diabetes Mellitus	20 (17.9%)	7 (15.2%)
Hypertension	42 (37.5%)	22 (47.8%)
Coronary Artery Disease	1 (0.9%)	1 (2.2%)
Stroke	0 (0%)	1 (2.2%)
Hyperlipidemia	19 (17%)	9 (19.6%)
Tobacco	5 (4.5%)	2 (4.3%)
Obesity	16 (14.3%)	6 (13%)
Synrhoid	20 (17.9%)	2 (4.3%)
Diabetes Mellitus Oral	15 (13.4%)	5 (10.9%)
Insulin	5 (4.5%)	1 (2.2%)
GH	0 (0%)	0 (0%)
Testosterone	4 (3.6%)	1 (2.2%)
Desmopressin	1 (0.9%)	0 (0%)
HTN	25 (22.3%)	16 (34.8%)
Beta Blocker	14 (12.5%)	9 (19.6%)
Statins	19 (17%)	11 (23.9%)
Cabergoline	7 (6.2%)	3 (6.5%)
Somatostatin Analogues	0 (0%)	0 (0%)

Endocrinological Labs

	Size >1cm (n=112)	Size <1cm (n=46)
Preoperative	Hyponatremia	5 (4.5%)
	Hypnatremia	2 (1.1%)
	Hyperprolactinemia	27 (26.5%)
	Hypoprolactinemia	8 (7.8%)
	Hypocortisolism	18 (17.5%)
	Hypercortisolism	5 (4.9%)
	Hypothyroidism	25 (23.6%)
	Hyperthyroidism	0 (0%)
	Hypoadrenalism	8 (7.5%)
	Hyperadrenalism	4 (3.7%)
	Hypogonadism	20 (19.6%)
	Low GH	0 (0%)
Postoperative	High GH	93 (86.1%)
	Low ADH	2 (5.7%)
	High ADH	0 (0%)
	Hyponatremia	32 (29.1%)
	Hypnatremia	5 (4.5%)
	Hyperprolactinemia	8 (7.3%)
	Hypoprolactinemia	37 (33.9%)
	Hypocortisolism	2 (1.9%)
	Hypercortisolism	66 (61.7%)
	Hypothyroidism	18 (17.1%)
	Hyperthyroidism	0 (0%)
	Hypoadrenalism	12 (11.2%)

Macro vs. Micro Adenoma Characteristics

		Size >1cm (n=112)	Size <1cm (n=46)
Lesion Characteristics	Adherent	14 (12.5%)	2 (4.3%)
	Invasive	16 (16.3%)	2 (4.9%)
	Suprasellar	50 (48.1%)	0 (0%)
	Maximum Diameter (cm)	1.8 ± 0.7	0.7 ± 0.2
	ABC/2 (cm^3)	2.8 ± 3.6	0.2 ± 0.1
	MIB Index	2.44 ± 2.2	2.2 ± 1.9
	Cystic	16 (15.8%)	6 (15.4%)
	Atypical	8 (7.6%)	1 (2.3%)
Surgical Approach	Microscopic Approach	9 (8%)	6 (13%)
	Endoscopic Approach	110 (98.2%)	46 (100%)
	Combined Approach	7 (6.3%)	6 (13%)
	Fat Graft	46 (41.1%)	14 (30.4%)
	Fascia	0 (0%)	0 (0%)
	Nasal Packing	55 (49.1%)	15 (32.6%)
	Lumbar Drain	1 (0.9%)	0 (0%)
	Nasoseptal Flap	6 (5.4%)	0 (0%)
IHC Staining	Intraoperative CSF Leak	33 (29.5%)	10 (21.7%)
	FSH	9 (8.3%)	2 (4.5%)
	LH	11 (9.9%)	2 (4.4%)
	GH	112 (100%)	45 (97.8%)
	ACTH	31 (27.9%)	7 (15.6%)
	TSH	16 (14.4%)	2 (4.4%)
	Prolactin	70 (63.1%)	25 (55.6%)
	P53	41 (51.9%)	21 (63.6%)

Postoperative Outcomes

		Size >1cm (n=112)	Size <1cm (n=46)
Complications	SIADH	10 (8.9%)	1 (2.2%)
	Transient Diabetes Insipidus	8 (7.1%)	7 (15.2%)
	Permanent Diabetes Insipidus	1 (0.9%)	1 (2.2%)
	Postoperative CSF Leak	2 (1.8%)	0 (0%)
	Epistaxis	4 (3.6%)	3 (6.5%)
	ICA Injury	0 (0%)	0 (0%)
	Abscess	0 (0%)	0 (0%)
	Meningitis	2 (1.8%)	0 (0%)
	Site Infection	1 (0.9%)	0 (0%)
	Visual Deficit	1 (0.9%)	0 (0%)
	Hemorrhage	2 (1.8%)	0 (0%)
	Sinusitis	0 (0%)	0 (0%)
	Readmission Within 30 Days	9 (8.1%)	2 (4.3%)
	Reoperation Within 30 Days	3 (2.7%)	0 (0%)
Postoperative Course	Recurrence	12 (10.7%)	4 (8.7%)
	Gross Total Resection	89 (79.5%)	43 (93.5%)
	ICU Admission	8 (7.3%)	4 (8.7%)
	Biochemical Remission	69 (76.7%)	22 (73.3%)
Hormone Replacement	Dopamine Agonist	1 (2.2%)	7 (6.4%)
	Thyroid Hormone Replacement	22 (19.8%)	2 (4.3%)
	Testosterone Replacement	8 (7.2%)	3 (6.7%)
	Estrogen Replacement	0 (0%)	1 (2.2%)
	Cortisol Replacement	22 (20%)	7 (15.2%)
	Sandostatin	2 (1.8%)	1 (2.2%)
	Desmopressin	2 (1.8%)	2 (4.4%)

Macroadenoma Predictive Power

	Odds Ratio	Lower Bound	Upper Bound
Any CSF Leak (n=45)*	0.43	0.2	44
Dysnatremia (n=17)**	0.99	0.39	3.74
Recurrence (n=16)***	1.33	0.4	4.4
Biochemical Remission (n=91)****	1.28	0.48	3.41

* Other covariates included suprasellar location and gross total resection

** Other covariates included gross total resection

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**** Other covariates included gross total resection, preoperative visual loss, and preoperative GH hypersecretion