

Determinants of Remission Following Transsphenoidal Surgery for Cushing's Disease



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Introduction

- •Cushing's disease (CD) is caused by ACTH-producing pituitary adenomas leading to elevated levels of cortisol secreted from the adrenal glands.
- •The adenomas causing CD are most commonly microadenomas (<1cm). In about half of cases, the adenoma is not visible on radiological examination (MRI negative).¹
- First-line treatment for CD is transsphenoidal surgery.
- •Early postoperative remission rates range from 67-95% with subsequent recurrence in up to 36% of patients.²
- It is controversial whether surgical outcomes in patients with MRI negative tumors are less favorable compared to patients with MRI visible tumors.³⁻⁵
 More generally, there is lack of consensus on the determinants of biochemical remission following surgery for CD.⁶⁻⁸

Table 3. Outcomes stratified by MRI-visibility

	MRI-negative	MRI-visible	p-value
Preoperative morning cortisol (ug/dL)	21.5 ± 5.2	$\textbf{26.4} \pm \textbf{16.4}$	0.243
Preoperative salivary cortisol (ng/dL)	$\textbf{393.6} \pm \textbf{401.4}$	450.6 ± 595.9	0.743
Preoperative urine free cortisol (ug/day)	154.0 ± 107.2	140.3 ± 239.6	0.831
Preoperative serum ACTH (pg/mL)	$\textbf{49.0} \pm \textbf{26.2}$	132.7 ± 158.1	0.031
Intraoperative identification of adenoma	14 (77.8%)	33 (94.3%)	0.093
Histopathological confirmation of ACTH-secreting			
adenoma	9 (50%)	32 (91.4%)	0.002
Ki-67 index, ≥3%	3 (21.4%)	19 (61.3%)	0.019
Postoperative day 5 morning cortisol (ug/dL)	$\textbf{15.2} \pm \textbf{10.3}$	11.0 ± 12.0	0.239
Postoperative month 3 morning cortisol (ug/dL)	$\textbf{22.2} \pm \textbf{24.2}$	$\textbf{10.2}\pm\textbf{6.8}$	0.009
Postoperative serum ACTH (pg/mL)	$\textbf{30.9} \pm \textbf{20.9}$	$\textbf{43.5} \pm \textbf{32.3}$	0.144
Short term remission	14 (77.8%)	30 (85.7%)	0.469
Long term disease control	13 (72.2%)	25 (71.4%)	0.952

Pre- and Post-operative Morning Cortisol

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35

Pre- and Post-operative ACTH

Methods

<u>Study design</u>

- Retrospective chart review analysis
- Univariate and multivariate regression

Inclusion criteria

- Clinically and biochemically-confirmed CD
- Treated with transsphenoidal surgery at University of Rochester Medical Center from 2010–2020

Exclusion criteria

- Clinically silent ACTH-secreting tumors
- Ectopic ACTH-secreting tumors
- Prior pituitary surgery

Results

Table 1. Preoperative evaluation		Table 2. Intraoperative and postoperative evaluation		
	N(%). Mean \pm SD		N(%), Mean \pm SD	
Number of patients	53	Operating room time (min)	134 ± 23	
Demographics		Intraoperative identification of an adenoma	47 (88.7%)	
Female	36 (67.9%)	Histopathological confirmation of an ACTH-secreting adenoma	41 (77.4%)	
Age	45.8±13.1	Type of surgery		
BMI	34.2 ± 9.2	Selective adenomectomy	38 (71.7%)	
CD evaluation		Enlarged adenomectomy	9 (17.0%)	
Morning cortisol (ug/dL)	24.7±13.7	Partial hypophysectomy	6 (11.3%)	
Late night salivary cortisol		Ki-67 index, ≥3%	22 (49%)	
(ng/dL)	430.2 ± 530.1	Length of stay (days)	1.2 ± 0.5	
Urine free cortisol (ug/day)	145.6 ± 197.0	Outcomes		
Serum ACTH (pg/mL)	103.7±134.2	Gross total resection ^c	22/35 (62.9%)	
Abnormal DST ^a	30/34 (88.2%)	Short term remission ^d	44 (83.0%)	
IDSS porformod ^b	26 (40, 106)	Long term disease control ^e	38 (71.7%)	
IPSS performed	20 (49.1%)	Remission from surgery alone	26 (49.1%)	
ACTH source	25/26 (96.2%)	Remission from surgery plus complementary interventions	12 (22.6%)	
Visual symptoms	9 (17.0%)	Uncontrolled disease	15 (28.3%)	
Radiologic evaluation		Time to recurrence (years)	2.2 ± 1.5	
Mean tumor axis length (cm)	0.9±1.0	Complementary interventions		
MRI negative	18 (34.0%)	Medication	23 (53.0%)	
Microadenoma (<1cm)	18 (3/ 0%)	Radiotherapy	8 (15.1%)	
		Repeat transphenoidal surgery	17 (32.1%)	
Macroadenoma (≥1cm)	17 (32.1%)	Adrenalectomy	0	
Giant adenoma (≥4cm)	2 (3.8%)	Complications	- /	
Suprasellar extension	14 (26.4%)	Transient AVP-D	5 (9.4%)	
Knosp grade		Permanent AVP-D	0	
0	23 (43,4%)	SIADH Devoietent edvened in sufficience	5 (9.4%)	
1		Other new hyperituiteriers	2 (3.8%)	
T	14 (26.4%)	Eniotoxio		
2	4 (7.5%)	CSElook	2 (3.8%)	
3	3 (5.7%)	Moningitie	0	
4	2 (3.8%)	Vascular injury	0	
Unknown	7(13,2%)	Duration of follow up (years)	67+25	
			0.7 - 0.0	



180



Conclusions

- Rates of remission did not significantly differ between MRI-negative adenomas and MRI-visible adenomas
- In a univariate model, gross total resection, low postoperative 3-month morning cortisol, and low preoperative morning cortisol were predictive of achieving remission from surgery alone

• In a multivariate model, only gross total resection remained an independent predictor of achieving remission from surgery alone

a. Dexamethasone suppression test

b. Inferior petrosal sinus sampling

c. Lack of residual tumor on postoperative MRI. Determined for MRI-visible tumors only.
d. Either (1) symptom improvement plus cortisol <10ug/dL during postoperative week one, or (2) symptom improvement plus normal 3-month salivary/UFC/morning cortisol
e. At time of last follow-up (at least 1 year)

Contact

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