

# Surgical outcome and factors associated with Cushing's disease recurrence in 101 consecutive patients operated on by a single pituitary neurosurgeon: the Cleveland Clinic experience

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## INTRODUCTION

- Cushing's disease is rare and results from excess cortisol from hypersecretion of ACTH by a pituitary gland tumour, it has an incidence of 0.7 and 2.4 cases per million persons/year and is associated with a poor prognosis if undiagnosed or untreated.
- Transsphenoidal tumour resection (TSS) is the first-line treatment for Cushing's disease (CD). With an experienced neurosurgeon, immediate remission rates > 80% are expected for patients with microadenomas ( $\leq 10$  mm).

## AIMS & METHODS

- To report initial and long-term remission rates in a specialist center, and to ascertain factors associated with disease recurrence after TSS.
- Clinical data was obtained from a CD database in addition to online patient medical records [EPIC].
- Patients with CD (N=101, 28M, 73F) having TSS by one neurosurgeon (RJW) at Cleveland Clinic between 2004 and 2013, with a minimum one-year follow-up.
- Glucocorticoids were withheld during and immediately after surgery; ACTH and cortisol were closely monitored post-operatively with a standard protocol to determine initial remission.
- After discontinuing hydrocortisone for surgically-induced adrenal insufficiency, long-term remission ( $\geq 12$  months) was defined by 24h UFC < ULN, and/or late night salivary cortisol < ULN, and/or 8 AM serum cortisol < 1.8 mcg/dl after 1mg overnight dexamethasone.
- Statistical analyses were performed using SAS software (Version 9.2; Cary, NC).

## CONCLUSION

In patients with CD undergoing TSS, post-operative nadir cortisol and ACTH levels are predictive of immediate and long term remission status. Presence of macroadenoma and tumour extension beyond the pituitary are highly predictive of initial non-remission and risk of late recurrence.

## RESULTS

- 101 patients (F:73,M:28) underwent their 1st TSS for CD, median age 46 years (range 15-87), median follow up 52 months (12-118), pituitary microadenoma 74 (73%), macroadenoma 27 (27%).
- Initial remission rates were: microadenoma 89% (66/74), macroadenoma 63% (17/27).
- Initial non-remission occurred in 18 patients, 10 macro- and 8 microadenoma. Six of the 83 patients with initial remission have had recurrence of hypercortisolism requiring either repeat TSS or adjunctive therapy. At last follow-up, continuing remission rates are: microadenoma 90%, macroadenoma 74%; 14 (7 macro, 7 micro) have persistent hypercortisolism.
- Macroadenoma ( $p=0.003$ ) and tumour invasion beyond the pituitary ( $p<0.001$ ) were associated with failure of initial remission and greater likelihood of late recurrence. Absence of tumour on pre-operative imaging was not associated with failure of initial remission.
- Those with initial remission had significantly lower nadir cortisol < 3  $\mu\text{g}/\text{dl}$  [remission  $n=67$  v non-remission  $n=1$ ,  $p<0.001$ ] and ACTH <20 pg/ml [remission  $n=70$  v non-remission  $n=2$ ,  $p<0.001$ ] this was also true for current remission status.

## DISCUSSION

- Surgery by a dedicated neurosurgeon in a specialized pituitary center gives excellent initial and long-term results for CD.
- Remission rates for TSS in patients with CD have varied in published studies due to variability in the definition, the number of patients involved in each study and the inclusion or not of macroadenomas.

