

POST-OPERATIVE SERUM CORTISOL LEVELS AS PREDICTORS OF RECURRENCE IN CUSHING'S DISEASE



D. Martins¹, D. Guelho¹, I. Paiva¹, C. Baptista¹, N. Vicente¹, L. Cardoso¹, D. Oliveira¹, M. Balsa², F. Carrilho¹

¹Endocrinology, Diabetes and Metabolism Department of Coimbra Hospital and University Centre, Portugal

²Endocrinology, Diabetes and Nutrition Department of Baixo Vouga Hospital Centre, Portugal

Introduction

Cushing's disease (CD) is characterized by increased secretion of ACTH generally as a result of a pituitary adenoma. The surgical success rates after transsphenoidal pituitary surgery (TSS) range from 53-96% in different centres. Postoperative cortisol levels have been proposed as the standard criteria for prediction of surgical remission.

Objectives

Evaluate the potential of post-transsphenoidal pituitary surgery cortisol levels to predict surgical remission or recurrence of CD.

Material and methods

Retrospective cohort study of patients with clinical and biochemical diagnosis of CD, submitted to TSS and followed in our centre, from 1977 to 2013 (n=84). Patients who lost follow-up or with insufficient data (n=52), were excluded.

Remission criteria:

- absence of clinical and laboratory signs of hypercortisolism;
- normal urinary free cortisol (UFC);
- cortisol levels < 1,8 µg/dL at 8.00 am after 1mg overnight dexamethasone suppression test.

Recurrence criteria:

- absence of clinical and/or analytical signs of hypercortisolism at least 1 year after TSS

Statistical analysis: IBM SPSS 21.0 software.

Statistical significance: $p < 0,05$

Results (II)

Serum cortisol and UFC – Pre-operative and post-operative assessment

Analyte	Pre-operative assessment			Post-operative assessment				
	Remission	p	Recurrence	Persistence	Remission	p	Recurrence	Persistence
UFC (µg/24h)	186,50	0,955	240,00	396,00	19,50	0,723	25,30	305,00
Cortisol 0 am (µg/dL)	14,00	0,478	18,00	14,00	1,70	0,004	10,00	5,60

Table 1. UFC and midnight cortisol before and 2 months after TSS

Serum cortisol evolution

Cortisol measurement (µg/dL)	Remission	P Remission/ Recurrence	Recurrence	Persistence	P Remission/ Recurrence and Persistence
Cortisol 9 am (A)	9,47	0,047	10,92	16,05	0,076
Cortisol 0 am (A)	4,46	0,008	9,24	14,50	0,027
Cortisol 9 am (B)	5,30	0,039	8,10	16,10	0,032
Cortisol 0 am (B)	2,58	0,031	7,76	8,57	0,021

Table 2. Cortisol levels : one week (A) and 2 months after TSS (B).

Analyte	One week evaluation (A)	2 months after TSS (B)	P
Midnight Cortisol measurement (µg/dL)	3,90±7,45	4,05±6,74	0,224

Table 3. Midnight cortisol levels : one week (A) and 2 months after TSS (B). Patients with persistent disease were excluded.

Disease free survival (DFS): 6,97±4,27 years
Inverse correlation with morning cortisol levels $r = -0,81; p < 0,01$

Number of recurrences: 0,41±0,665
Significant correlation with higher midnight cortisol levels $p < 0,01$

Results (I)

Baseline data

Patients included: 33

87,9% Women
12,1% Men

Median age: 33 years (range 14-70)

Types of lesion

(Imagiology):

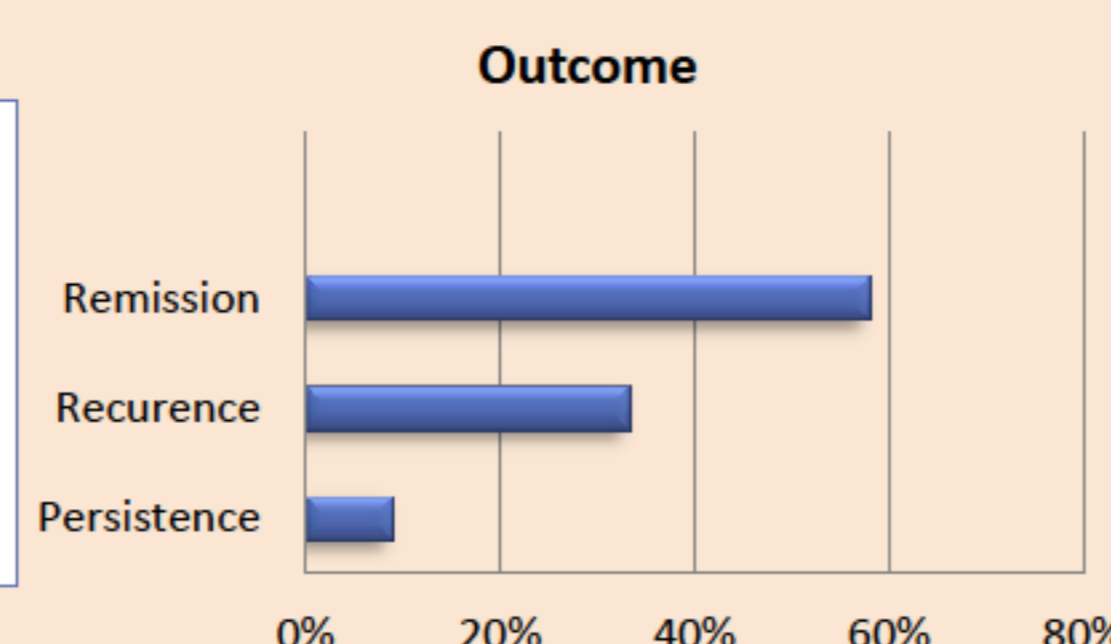
18 patients (54,6%) - Microadenoma
6 patients (18,2%) - Macroadenoma
3 patients (9,0%) - Invasive macroadenoma
6 patient (18,2%) - No adenoma visible on MRI/CT-SCAN

Surgical approach

31 patients (93,9%) – Transsphenoidal approach
2 patients (6,1%) – Transfrontal approach

Outcome aftersurgery

19 patients (57,6%) – Remission
11 patients (33,3%) – Recurrence
3 patients (9,1%) – Persistence



All patients were followed postoperatively during a median period of 8 years (1-28)

Conclusions

- This study states that treatment of Cushing's disease is difficult.
- 57,6% of the patients of this cohort achieved remission after TSS.
- Serum cortisol levels at 0:00am in the post-operative period were significantly different in patients with remission compared with the other groups.
↳ Good predictor of remission
- The usefulness of midnight cortisol levels after TSS was demonstrated.
↳ These values predicted CD remission, with the optimal predictor at two months of TSS
- Lower accuracy in predicting remission with morning serum cortisol values at one week evaluation after TSS.
- The disease free period had a strong inverse correlation with morning serum cortisol levels.

Bibliography

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