Rapid Cortisol Decay Predicts Persistent Remission After Removal Of Functional Corticotroph Adenomas

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Disclosures

None
Introduction

• Despite an 86% initial post-operative biochemical remission rate, up to 25% of patients with Cushing’s disease (CD) recur within 5-years.

• Immediate post-operative cortisol decay, or clearance, results in adrenal insufficiency.

• The objective of this pilot study was to identify the cortisol decay rate that predicts definitive surgical remission at last follow-up.
Methods

- Inpatient cortisol levels were modeled using the decay function $y = Ae^{(-Bx)}$
  - $y$ is the cortisol level
  - $x$ is the post-operative time (hours)
  - $A$ is a scaling parameter to account for different starting cortisol levels
  - $B$ is the decay rate
- Single patient fitting algorithms were created.
- For visualization, we normalized data by the first post-operative cortisol level (within 6 hours of surgery) in order to account for variable initial cortisol levels.
- Crude data were plotted using scatter and individual decay rate violin plots to identify potential bimodal conditions for the decay rate.
Results

Individual patient data

Group trends

Normalized Cortisol Values
Results

- N=44
- Confirmed follow-up time was 64.4 person-years (i.e. time at risk for recurrence calculated by # patients x years at risk)
- 20% Male; 80% Female
- Cortisol decay correlated with need for steroid replacement at last follow up
- Violin plots showing crude data on decay rate by remission status at last follow up
- Asterisks indicate \( p<0.05 \)
- Decay rate appears bimodal

Decay rate of 0.15 means cortisol will decrease to 36.8% \( (1/e) \) of the original value over 6.7 hours
Results

Rapid-decay is $\geq 0.15$

Rapid-decay is $\geq 0.1$
Discussion

• Cortisol levels in patients with definitive biochemical remission at last follow-up appear to follow the exponential decay model.
• In pharmacokinetics, this is known as clearance.
• Cortisol clearance appears bimodal even in patients with initial remission based on current diagnostic criteria.
• In this pilot study, a decay rate of ≥0.15 predicts definitive remission and does not differ greatly from a cutoff of ≥0.1.
• A decay rate of 0.15 falls within 1 standard deviation of mean population half-life of hydrocortisone administered in a single dose.
• Due to limited power (sample size) and relatively short follow-up, further investigation is needed in order to confirm the utility of this biomarker for definitive disease remission.
Summary Points

• The biochemical diagnosis of remission is critical in patients with Cushing’s disease.

• In the immediate post-operative period, a bimodal distribution of initial cortisol clearance exists in patients with initial remission.

• Here we show that when cortisol drops to approximately 30% of its original value every 6 hours until the patient enters adrenal crisis definitive remission is more likely.
References

1. Lonser, Nieman, Oldfield. J Neurosurg 126; 404-417, 2017
4. Ironside et al. Eur J Endocrinol 83; 255-263, 2018