

Utility of Simple and Non-Invasive Strategies Alternative to Inferior Petrosal Sinus Sampling and Peripheral CRH Stimulation in Differential Diagnosis of ACTH-Dependent Cushing Syndrome

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ABSTRACT

We aimed to evaluate the utility of simple, cost-effective, and non-invasive strategies alternative to BIPSS and peripheral CRH stimulation in differential diagnosis of ACTH-dependent CS. First, we performed ROC analysis to evaluate the performance of various tests for differential diagnosis of ACTH-dependent CS in our cohort (CD, n = 76 and EAS, n = 23) and derived their optimal cut-offs. Subsequently, combining various demographic (gender), clinical (hypokalemia), biochemical (plasma ACTH, HDDST, peripheral CRH stimulation) and imaging (MRI pituitary) parameters, we derived non-invasive models with 100% PPV for CD. Patients with pituitary macroadenoma (n = 14) were excluded from the analysis involving non-invasive models. Relative percent ACTH (AUC: 0.933) and cortisol (AUC: 0.975) increase on peripheral CRH stimulation demonstrated excellent accuracy in discriminating CD from EAS. Best cut-offs for CD were plasma ACTH < 97.3 pg/ml, HDDST ≥ 57% cortisol suppression, CRH stimulation ≥ 77% ACTH increase and ≥ 11% cortisol increase. We derived six models that provided 100% PPV for CD and precluded the need for BIPSS in 35/85 (41.2%) patients with ACTH-dependent CS and no macroadenoma (in whom BIPSS would have otherwise been recommended). The first three models included basic parameters and avoided both peripheral CRH stimulation and BIPSS in 19 (22.4%) patients, while the next three models included peripheral CRH stimulation and avoided BIPSS in another 16 (18.8%) patients. Using simple and non-invasive alternative strategies, BIPSS can be avoided in 41% and peripheral CRH stimulation in 22% of patients with ACTH-dependent CS and no macroadenoma; such patients can be directly referred for a pituitary surgery.

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