Diagnostic performance of first line biochemical tests to differentiate ACTH-ectopic syndrome among ACTH dependent Cushing’s syndrome.

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This study evaluates the diagnostic accuracy of clinical features and first line routine screening tests to differentiate ACTH-ectopic syndrome from Cushing’s disease.

Materials and methods:
Patients: The retrospective clinical and biochemical presentations of 180 patients with histologically proven ACTH-dependent Cushing’s syndrome (CS) were compared according to the cause of hypercortisolism.
Assay: Serum cortisol and plasma ACTH were assayed by electrochemiluminescence Cobas e601 Roche. 24hUFC was measured by an immunochromiluminescence assay (extraction with diethyl ether) on a Vitros Eci
Statistics: ROC-analysis was performed to estimate the diagnostic accuracy of the first line tests (23:00 serum cortisol, 24 hours urinary free cortisol (24hUFC) and ACTH rhythm in plasma) proving ACTH-ectopic syndrome. A threshold for the test with the highest area under the curves (AUC) was chosen based on the maximum sum of sensitivity and specificity.

Results:
ACTH-ectopic syndrome; 21
Cushing’s disease; 159

N=180 (Me of age 34 (16-77))

15 cases of bronchial carcinoid, 4 – carcinoid of thymus, 1 – small cell carcinoma of the lung 1 – carcinoid of the appendix

Late-night plasma ACTH showed the highest AUC (0.845 (95% CI 0.764-0.926)) to differentiate ACTH-ectopic syndrome from CD versus morning plasma ACTH – 0.790 (95% CI 0.673-0.908); late-night serum cortisol – 0.754 (95% CI 0.622-0.886) or 24hUFC 0.619 (95% CI 0.481-0.758).

A cut off value of 108.9 pg/ml for late-night ACTH yielded a sensitivity of 70.6% and a specificity of 81.7%.

Conclusions: Of all the clinical features and first line tests, the disturbance of the ACTH rhythm and high late-night plasma ACTH values in patients with proven CS is the most suggestive of ACTH-ectopic syndrome.