The National Research Center for Endocrinology
Moscow, Russia

Department of
Neuroendocrinology
and Bone Diseases

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

Belaya Z.E. (jannabelaya@gmail.com), Rozhinskaya L.Y., Dragunova N.V., Dzeranova L.K., Arapova S.D., Marova E.I., Melnichenko G.A.

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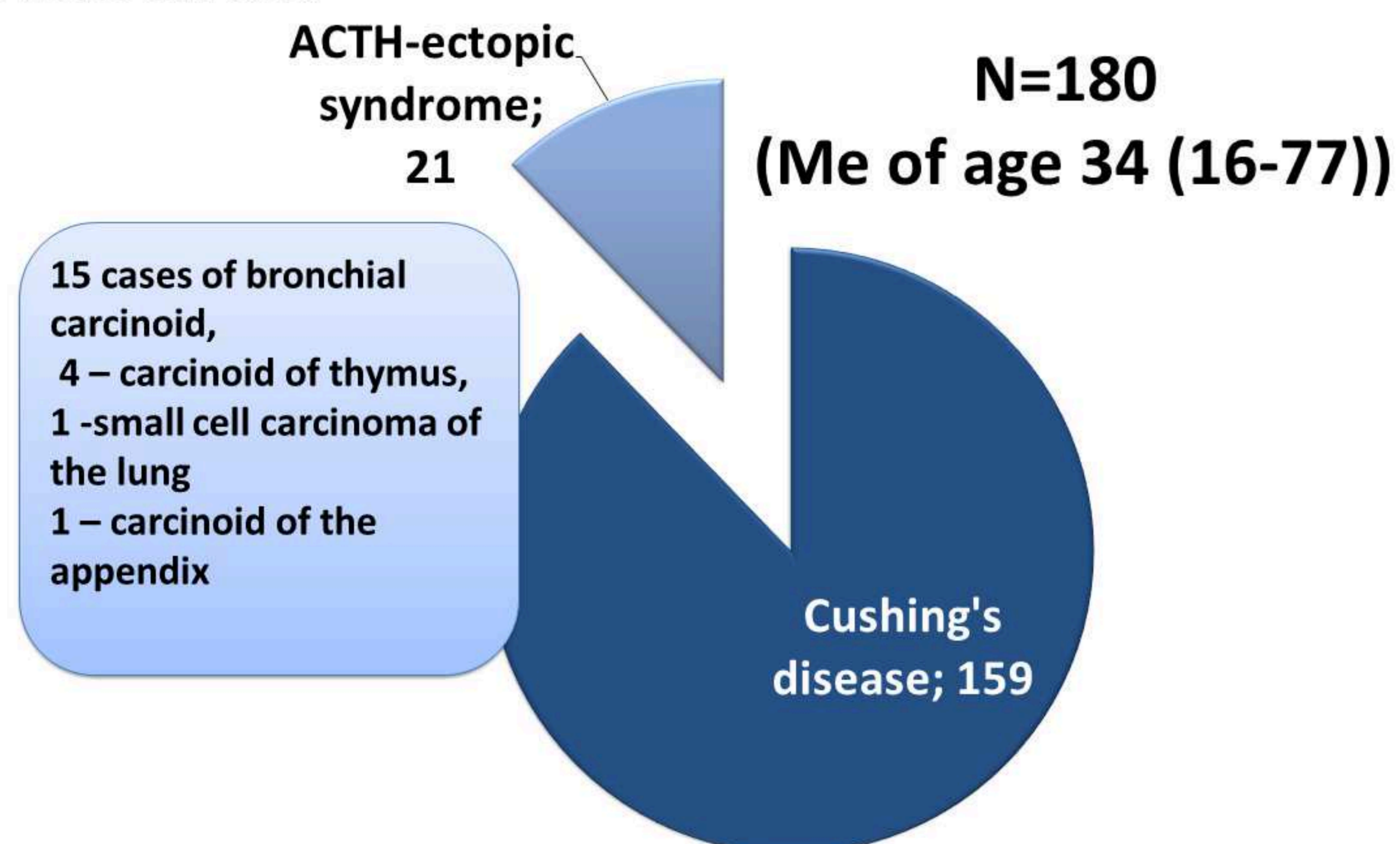
General characteristics of participants

	Cushing's disease (n=159)	ACTH-ectopic CS (n=21)	P
	Me (Q25-Q75) Min -Max		
23:00 serum cortisol (nmol/l)	615 (420-801) 23-1450	1019 (608-1490) 65-2430	0,003
24 h urinary free cortisol (nmol/24h)	1535 (900-2776) 138-8938	2643 (1437-4459) 733-11040	0,018
8:00 ACTH (pg/ml)	89,4 (63,3 -118,6) 20,8-499,9	137,0 (85,0-201,3) 10,2 – 420,8	<0,01
23:00 ACTH (pg/ml)	73,4 (48,8-101,5) 9,7-508,0	128,8 (85,9 – 188,6) (7,4-385,5)	<0,01

The patients with ACTH-ectopic syndrome (had higher rates of low traumatic fractures (p=0.04), but did not differ in other clinical presentations including age or body mass index

ROC curves of the different early tests to evaluate ACTH-ectopic CS

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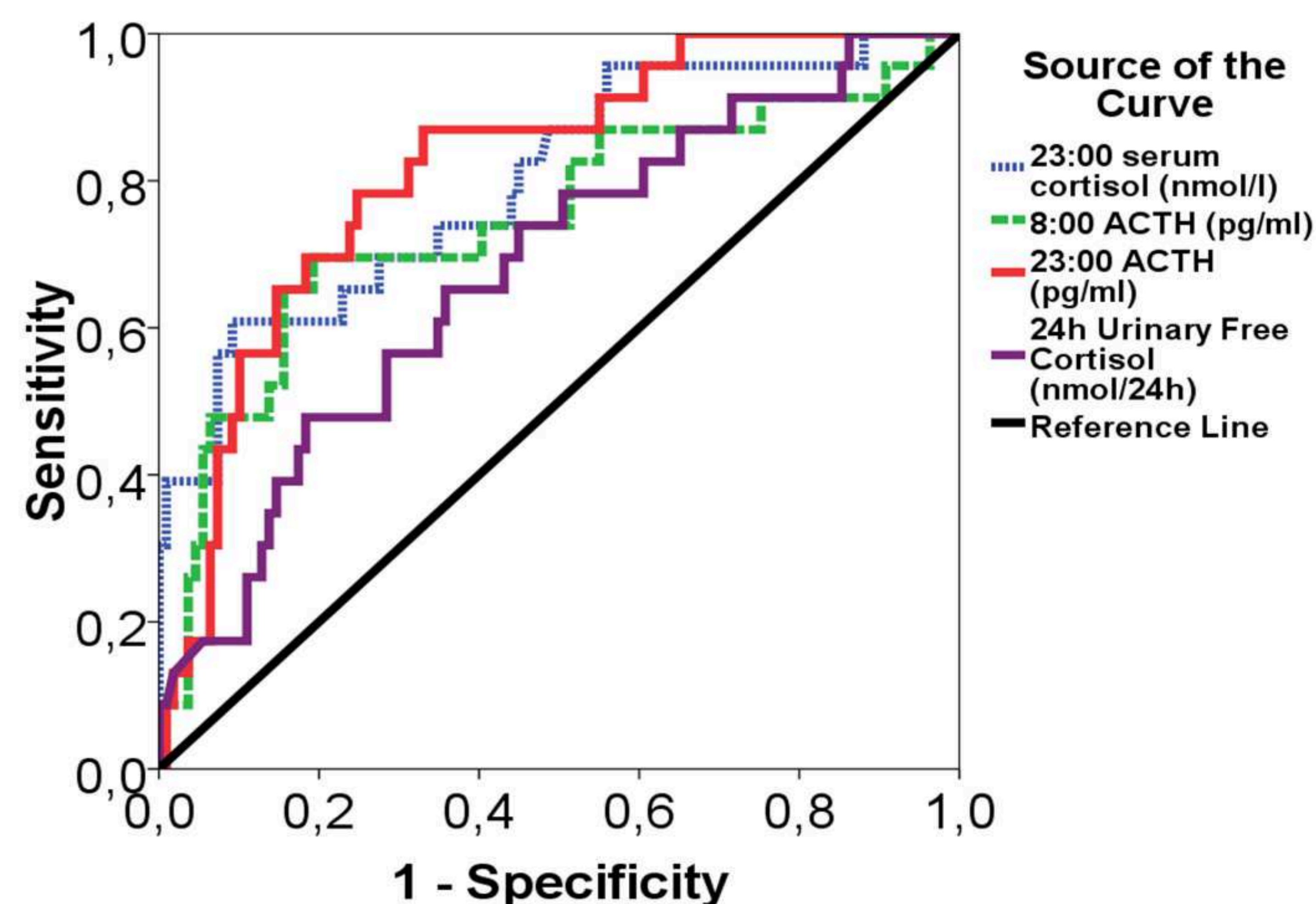
Late-night plasma ACTH showed the highest AUC (0.845 (95% CI 0.764-0.926)) to differentiate ACTH-ectopic syndrome from CD versus morning plasma ACTH – 0.790 (95% CI 0.673-0.908); late-night serum cortisol - 0.754 (95% CI 0.622-0.886) or 24hUFC 0.619 (95% CI 0.481-0.758).

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%.

Results:

ACTH-ectopic syndrome; 21

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

Cushing's disease; 159

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.