Does measurement of serum dexamethasone increase diagnostic accuracy of the overnight dexamethasone-suppression test?

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Background

The 1-mg overnight dexamethasone-suppression test (DST) is commonly used to screen for hypercortisolism. Sensitivity is high (95%), but specificity is lower (80%), leading to false positive results. Identifying individuals with abnormal dexamethasone absorption or metabolism could enhance diagnostic accuracy

Aims

- Define the concentration of s-Dexamethasoen (s-DXT) after DST, sufficient to suppress cortisol <50 nmol/L
- Estimate the proportion of positive DSTs explained by insufficient levels of s-DXT
- Evaluate the reproducibility of s-Cortisol with repeated DSTs

Materials and methods

Table 1: Patient characteristics

	Incidentalomas	Suspected CS	Healthy controls	Total
Patients, N	152	50	101	303
Women N (%)	94 (62%)	38 (76%)	64 (63%)	196 (65%)
Age, yrs Median (range)	62 (29-86)	43 (17-77)	49 (23-81)	56 (17-81)
BMI Median (range)	28 (16-43)	31 (19-56)	25 (18-62)	27 (16-62)
Hypertension N (%)	74 (49%)	12 (24%)	19 (19%)	105 (35%)
Diabetes N (%)	19 (13%)	13 (26%)	9 (9%)	41 (14%)
Smokers N (%)	57 (38%)	6 (12%)	7 (7%)	70 (23%)

- **Subjects: patients with clinical suspicion of Cushing's syndrome (CS), incidentaloma, and healthy controls**
- **Steroid assay: S-cortisol and s-DXT were assayed by liquid chromatography tandem mass spectrometry (LCMSMS)**
- **Evaluation: DST results were correlated to the final diagnosis based on current clinical guidelines**

Results

- **A s-DXT cut-off level at 3.3 nmol/L was chosen based on the 2.5% quantile of DXT in those suppressing s-cortisol < 50 nmol/L (fig.1)**
- **Applying this cut-off, 10/302 (3.3%) DSTs were false positive with both inadequate s-DXT-levels and elevated s-cortisol, i.e., 12% of the positive DSTs could be explained by low levels of s- DXT (fig.2)**
- **Of these, three were misdiagnosed as subclinical-CS**

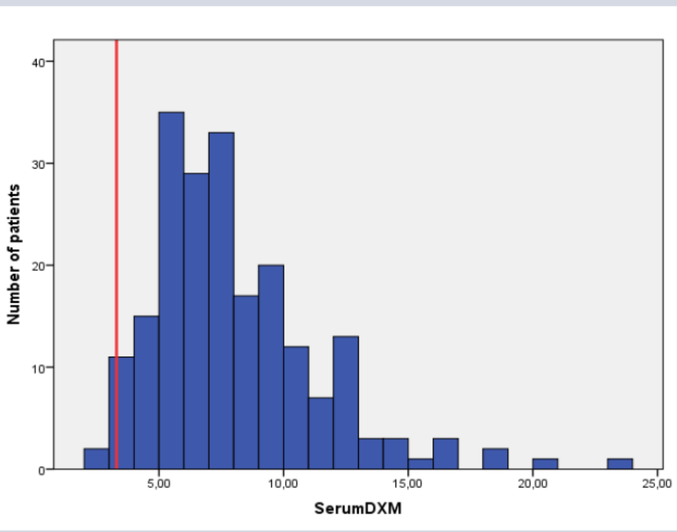
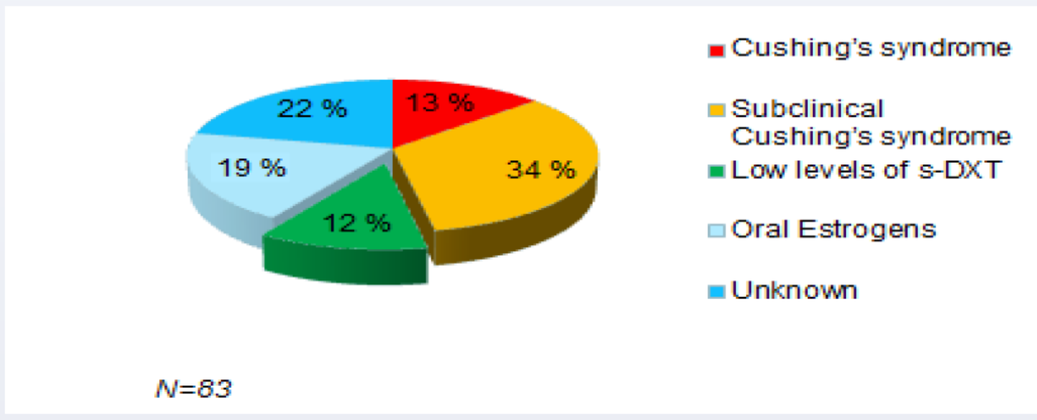


Fig. 1- The distribution of s-DXT in all persons suppressing cortisol <50nmol/L

N=208
s-DXT 7.8 (2.3-24) nmol/L, Median (range)

- **83/302 did not suppress s-cortisol (<50 nmol/L). Of these 11 had overt CS, and 27 subclinical CS (fig.2)**

Fig. 2- Classification of positive DST results



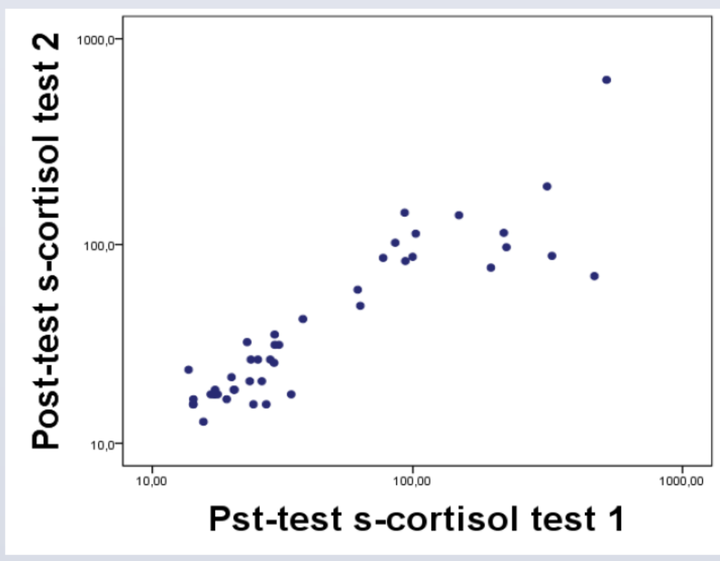
- **Among non-CS samples, s-cortisol values were significantly (p<0.01) higher in the incidentaloma-group compared with the two other groups**

Table 2. Post-DST s-cortisol and s-DXT in different subgroups of patients

	Incidentalomas	Suspected CS	Healthy controls
S-Cortisol (nmol/L) Median (range)	42.6 (13-577)	22.7 (9.9-289)	22.2 (8.4-103)
S-DXT (nmol/L) Median (range)	7.8 (0.0-23.9)	7.3 (0-20.8)	7.0 (3.0-18.5)

- **Inter-individul reproducibility of DST for s-cortisol is excellent (fig. 3)**

Figure 3- Reproducibility of the DST



ρ=0.87, P<0.01

N=44 (28 healthy controls, 16 patients)

Intra-class coefficient ICC=0.94

Conclusions

- **A minimum s-DXT level of 3.3 nmol/L is needed to suppress s-cortisol < 50 nmol/L**
- **Simultaneous measurement of s-DXT and S-cortisol after DST increases the accuracy of the test, and reduces the risk of falsely diagnosing subclinical CS**
- **Abnormal absorption or metabolism of DXT is a common reason for false positive DSTs**
- **Post-test cortisol is significantly higher in incidentaloma patients compared with healthy controls and patients with suspected CS**
- **The reproducibility of DST is excellent**

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