

Low positive predictive value of midnight salivary cortisol measurement to detect hypercortisolism in type 2 diabetes

Charlotte Steffensen¹, Henrik H. Thomsen^{1,2}, Olaf M. Dekkers^{3,4,5}, Jens S. Christiansen¹, Jørgen Rungby⁶, Jens Otto L. Jørgensen¹

¹Department of Endocrinology and Internal Medicine, Aarhus University Hospital, ²Department of Medicine, Viborg Regional Hospital, ³Department of Medicine, Section Endocrinology, Leiden University Medical Center, Leiden, The Netherlands, ⁴Department of Clinical Epidemiology, Aarhus University Hospital

⁵Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands, ⁶ Centre for Diabetes Research, Gentofte University Hospital, DK - 2900 Hellerup, Denmark

OBJECTIVES

- Hypercortisolism is prevalent in type 2 diabetes (T2D), but analytical and functional uncertainties prevail
- The usefulness of salivary cortisol in the context of T2D is uncertain
- **The objective** of this study was to determine sensitivity, specificity and accuracy of a single LNSC with the 1 mg DST as reference standard in T2D patients.

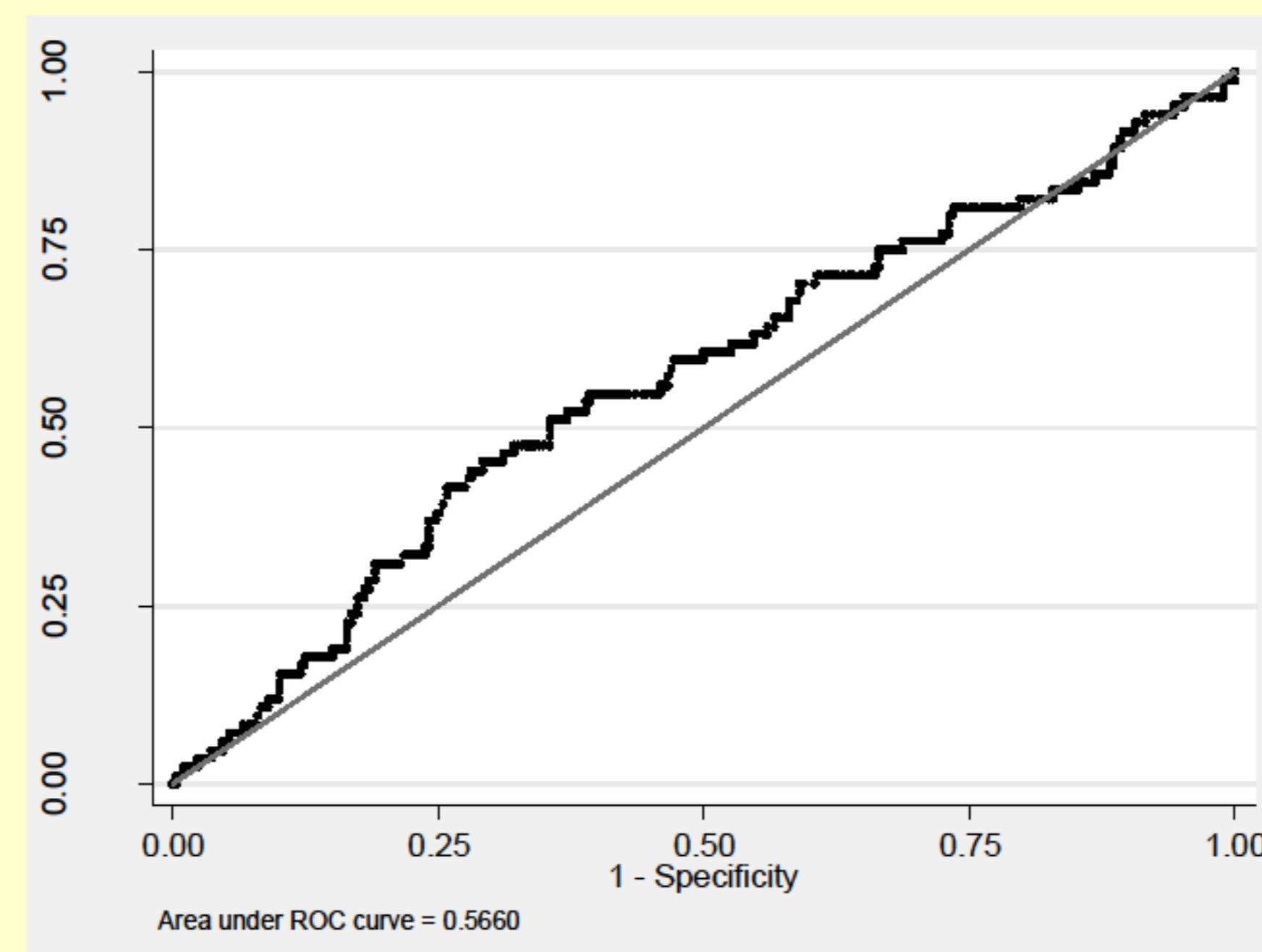
METHODS

- 382 patients (150 women and 232 men, median age 62 (range 23 - 85) years) recruited from the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Project (12), and diagnosed with T2D after January 2009, participated in the study.
- Exclusion criteria were: use of any kind of exogenous glucocorticoids or estrogen containing medications, psychiatric disease, alcohol intake > 14 units/week for men and 7 units/week for women, and evidence of any acute medical condition
- Cut - off values for hypercortisolism: LNSC \leq 3.6 nmol/l and DST \leq 50 nmol/l.

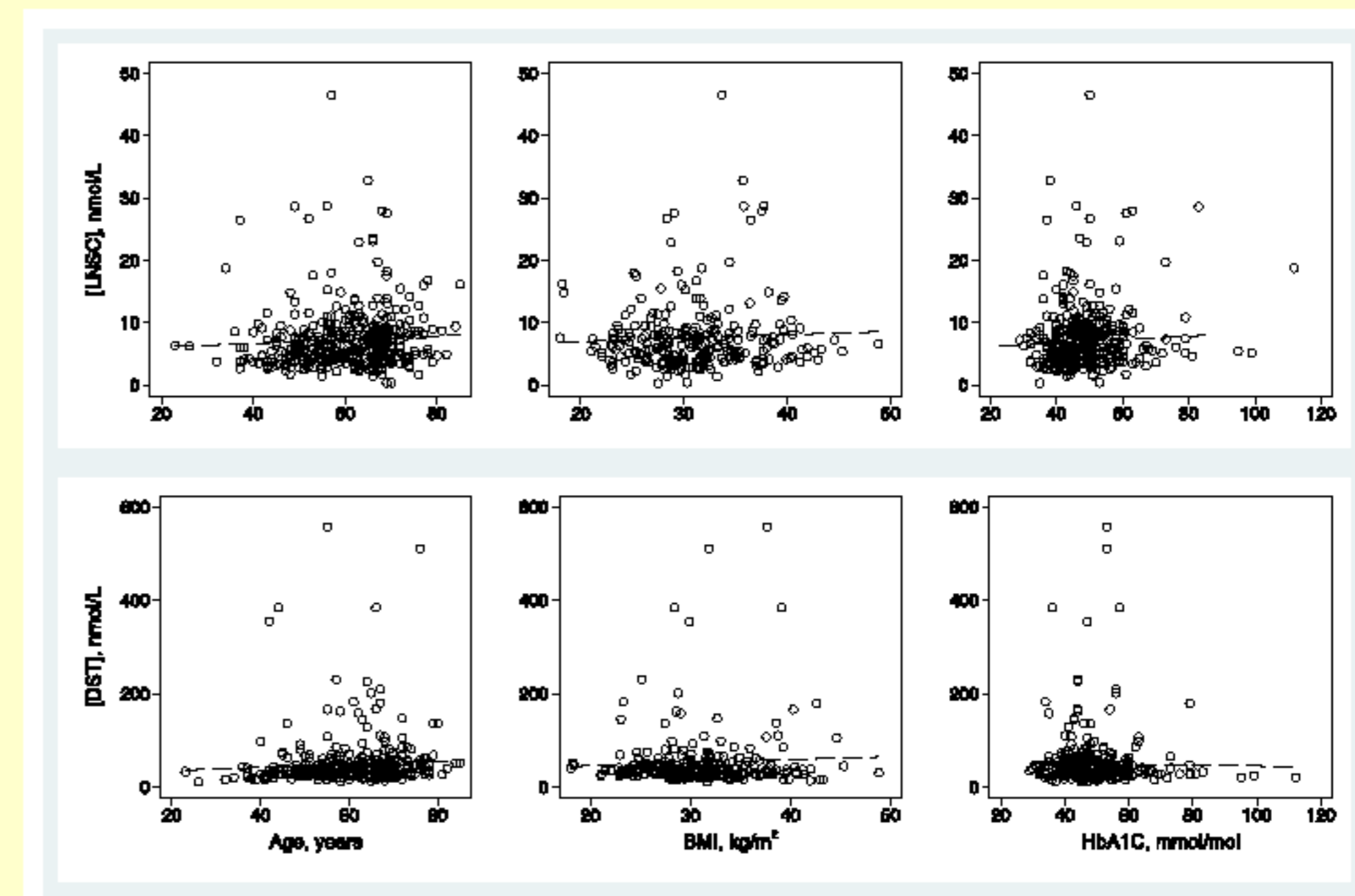
| | Hypercortisolism: DST > 50 nmol/L | No hypercortisolism: DST \leq 50 nmol/L | |
|-----------------------|--------------------------------------|--|----------------------|
| LNSC \geq 10 nmol/L | 15 | 44 | PPV: 25.4% (15/59) |
| LNSC < 10 nmol/L | 69 | 254 | NPV: 78.6% (254/323) |
| | Sensitivity: 17.9% (15/84) | Specificity: 85.2% (254/298) | |

| | Hypercortisolism: DST > 50 nmol/L | No hypercortisolism: DST \leq 50 nmol/L | |
|------------------------|--------------------------------------|--|---------------------|
| LNSC \geq 3.6 nmol/L | 71 | 256 | PPV: 21.7% (71/327) |
| LNSC < 3.6 nmol/L | 13 | 42 | NPV: 76.4% (42/55) |
| | Sensitivity: 84.5% (71/84) | Specificity: 14.1% (42/298) | |

Number of patients with hypercortisolism (DST > 50 nmol/L) and measurements of LNSC with cut - off value \geq 3.6 nmol/L and \geq 10 nmol/L. PPV, Positive Predictive Value; NPV, Negative Predictive Value



The area under the ROC curve (AUC) describes accuracy of LNSC compared to DST. An AUC value of 0.57 indicates very low discriminative value



Association between age, BMI, and HbA1c and cortisol concentration in T2D patients. LNSC, late - night salivary cortisol; DST, Dexamethasone suppression test; BMI, body mass index. LNSC and DST are in units of nmol/L, age in years, BMI in kg/m².

RESULTS

- 84 T2D patients (22%) did not suppress serum cortisol < 50 nmol/L after 1 mg DST
- 329 T2D patients (86%) had elevated LNSC
- The **sensitivity** of LNSC was 85% and the **specificity** was 14%
- **Positive predictive value** of LNSC was 22% and the **negative predictive value** was 76%
- ROC curve: the area under the curve revealed **an accuracy of LNSC of 0.57** (95% CI: 0.49 - 0.64)
- Linear regression established that **neither age, BMI, nor HbA1c could predict LNSC or DST**

CONCLUSIONS

- **LNSC is characterized by very low specificity and poor positive predictive value to detect hypercortisolism in T2D**
- **LNSC is not suitable as a stand-alone test to screen for hypercortisolism in T2D**
- **Further methodological and clinical studies are needed to substantiate the relevance of cortisol status in T2D**

References

Chiodini I, Torlontano M, Scillitani A, Arosio M, Bacci S, Di Lembo S, et al. Association of subclinical hypercortisolism with type 2 diabetes mellitus: a case-control study in hospitalized patients. Eur J Endocrinol [Internet]. 2005 Dec [cited 2014 Sep 23];153(6):837-44.

Raff H, Raff JL, Findling JW. Late-Night Salivary Cortisol as a Screening Test for Cushing 's Syndrome*. J Clin Endocrinol Metab. 1998;83(8):2681-6.

