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## **Adrenal (Excluding Mineralocorticoids)**

**OR30-01**

### ***Waking Salivary 11-hydroxyandrostenedione And Cortisone As A Novel Non-invasive Test For Adrenal Insufficiency***

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**Background:** The ACTH (Cosyntropin) stimulation test (AST) is the reference standard for diagnosis of adrenal insufficiency. We have demonstrated recently that home waking salivary cortisone accurately predicts the ACTH stimulation test outcome and confirms or excludes adrenal insufficiency in 70% of high-risk patients (*in press*: Home Waking Salivary Cortisone to Screen for Adrenal Insufficiency *NEJM Evidence*). 11-hydroxyandrostenedione (11-OHA4) is a weak adrenal androgen whose synthesis is dependent on *CYP11B1*. Since ACTH drives steroidogenesis, and adrenal androgens are low in patients with adrenal insufficiency, we hypothesised that waking 11-OHA4 could also predict adrenal status. **Methods:** A prospective, diagnostic accuracy study of waking salivary cortisone was performed in 173 patients at high risk of AI. All patients collected a salivary sample on waking, and then attended the endocrine clinic for an AST with the 30-minute cortisol used to diagnose AI. Salivary cortisone and 11-OHA4 was measured in the waking salivary sample. Biomarker discrimination was assessed by calculation of area under the curve (AUC) of the receiver operator characteristics (ROC) plot. Equivocal results were defined to maintain a sensitivity of 95% and specificity of 95%, and percentage of AST saved by calculating the number of AST needed if used only in equivocal cases. **Results:** The median (IQR) for 11-OHA4 for patients with AI and no AI was 55 (45 to 110) pmol/l vs 508 (255 to 765) pmol/l;  $p < 0.0001$ . Salivary 11-OHA4 on waking was highly predictive of adrenal insufficiency ( $R^2=0.63$ , ROC AUC 0.94), similar to waking salivary cortisone alone ( $R^2=0.65$ , AUC 0.94). Waking 11-OHA4 performed better than either serum cortisol ( $R^2=0.65$ , AUC 0.88) or salivary cortisone ( $R^2=0.74$ , AUC 0.93) collected at the baseline of the AST. Combining both waking salivary 11-OHA4 with waking salivary cortisone further improved discrimination ( $R^2=0.70$ , AUC 0.96), and using this combination would mean that 78% of ACTH-stimulation tests could be avoided. **Conclusion:** Waking salivary 11-OHA4 can accurately predict AI with similar discriminatory value as waking salivary cortisone. Combining waking 11-OHA4 with waking salivary cortisone improves discrimination for adrenal insufficiency, is a simple non-invasive test that can be used widely in clinical practice in the ambulatory setting, and obviates the need for AST in 78% of cases with greater patient convenience and lower costs.

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