# Biochemical Evaluation of Adrenal Incidentalomas Referred to Endocrine Surgery in a Large Teaching Hospital

AS Davison,[1,3*] C Fairclough,[1] NJ Russell,[2] AJ Waghorn,[2] SL Shore[2]

Departments of Clinical Biochemistry and Metabolic Medicine, Liverpool Clinical Laboratories,[1] and Endocrine and Breast Surgery,[2] Royal Liverpool and Broadgreen University Hospitals Trust, Liverpool, UK; Manchester Academic Health Science Centre, University of Manchester, UK[3]

## Background and Aims

An adrenal 'incidentaloma' (AI) is an adrenal mass that is discovered serendipitously during a radiologic examination performed for reasons other than an evaluation for adrenal disease (1). AI frequently pose a diagnostic dilemma owing to the increasing use of diagnostic imaging. The incidence of AI is estimated to be 6% based on reports summarizing the result of 25 autopsy studies (1-2). The majority of AI are non-functional, benign adrenocortical adenomas (2).

There is much debate around the investigation of AI due to the absence of current UK guidelines (3). More recent guidelines published by the American Association of Clinical Endocrinologists and American Society of Endocrine Surgeons (AACE/AAES) (4) propose patients should undergo clinical, biochemical and radiological evaluation. This retrospective observational study evaluated biochemical investigations performed in patients referred to Endocrine Surgery with AI and assessed adherence to Guidelines.

## Methods

Biochemical, histological and radiological data from referrals made to Endocrine Surgery between January 2012 and April 2014 were collected from Hospital clinical case notes and the Laboratory IT system Telepath (iSoft, Leeds).

## Results

125 patients were referred to Endocrine Surgery for evaluation of an adrenal pathology. 21 were excluded as they were not considered to have AI. 70/104 were female and the median age of all patients was 63 years (range 17-87).

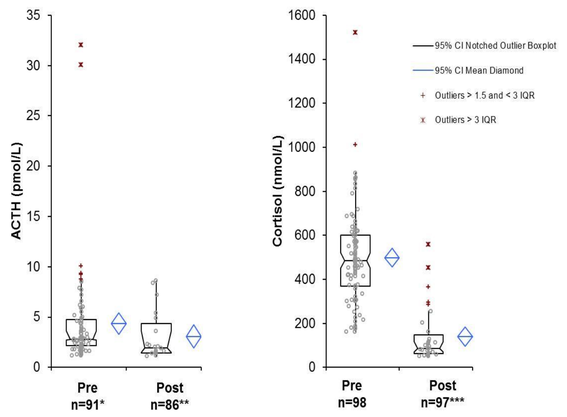
88 patients had adrenal CT and or MRI reports available. 87 had tumour dimensions, 22/87 were ≥4cm. 13/22 were resected (including 6 phaeochromocytoma (PCC), 2 cortisol secreting adrenocortical adenoma). 9 patients had bilateral; 45 left and 34 right AI.

20/104 referrals were surgically removed. 6 PCC (metadrenalines in urine and or plasma were >3 times the upper reference range in all cases, Table 2 shows histological features); 11 adrenal cortical adenomas (5 secreted excess cortisol); 1 adrenal myelolipoma; 1 adrenal ganglioneuroma and 1 adrenal angiomyolipoma.

90 and 96% of patients had ACTH and cortisol measured following an overnight dexamethasone (2mg) suppression test (ON-DXMST) (Figure 1). 75% of patients (n=24) that failed the ON-DXMST also had a low dose DXMST (0.5mg dexamethasone/6h/48h). Renin and aldosterone were measured in 80 and 88% of patients (Figure 2), and urine and or plasma metadrenalines were measured in 89% of patients (Figure 3).

Supine (n=13) and upright (n=84) renin activities were increased in 1 and 8 patients, respectively (Table 1). Aldosterone concentrations were not increased in any of these patients. Aldosterone (upright measurement, n=91) was increased in one patient that did not have a suppressed renin activity.

32/97 patients failed to suppression cortisol <50nmol/L following an ON-DXMST (Table 1). 3/32 had normal urinary free cortisol results (<165nmol/24h). 24/32 also had a low dose DXMST. 23/24 failed to supress cortisol <50nmol/L. 1/24 also had a high dose DXMST (2mg DXMST every 6h/48h), which also failed to supress cortisol <50nmol/L. Using a cortisol concentration of ≥138nmol/L (3) as a cut off to diagnose subclinical Cushing's syndrome (SCS), 7.7% (n=8) of patients referred had SCS.




*10/91 <1.1, **66/86 <1.1; 13 patients that had ACTH >1.1 had cortisol <50, *** 65/97<50

**Figure 1.** ACTH and cortisol results pre- and post 2mg overnight dexamethasone

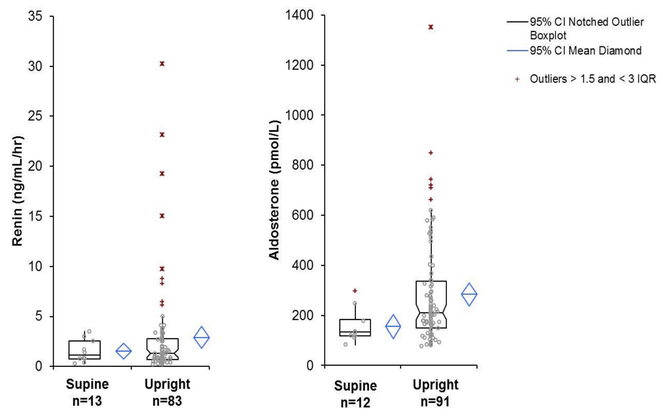



**Figure 2. Supine and upright** renin and aldosterone results

| Analyte | n | Range | Reference range/Normal response |
|---|---|---|---|
| **Urinary free normetadrenaline** | 5 | 1509-28512 | <650nmol/24h |
| **Urinary free metadrenaline** | 5 | 93-2526 | <350nmol/24h |
| **Plasma metadrenaline** | 2 | 373-1275 | <510pmol/L |
| **Plasma normetadrenaline** | 2 | 17759->25000 | <1180pmol/L |
| **Aldosterone (upright)** | 1 | 1351 | 140-850pmol/L |
| **Renin (supine)** | 1 | 3.5 | 0.2-2.8ng/ml/hr |
| **Renin (upright)** | 8 | 6.1-30.2 | 1.5-5.7ng/ml/hr |
| **Cortisol (post-overnight DXMST)** | 32 | 51-801 | <50nmol/L |
| **ACTH (post-overnight DXMST)** | 4 | 1.3-1.6 | <1.1pmol/L |
| **Cortisol (post low dose DXMST)** | 23 | 53-555 | <50nmol/L |
| **ACTH (post low dose DXMST)** | 7 | 1.2-7.2 | <1.1pmol/L |

**Table 1.** Summary of all abnormal biochemical results

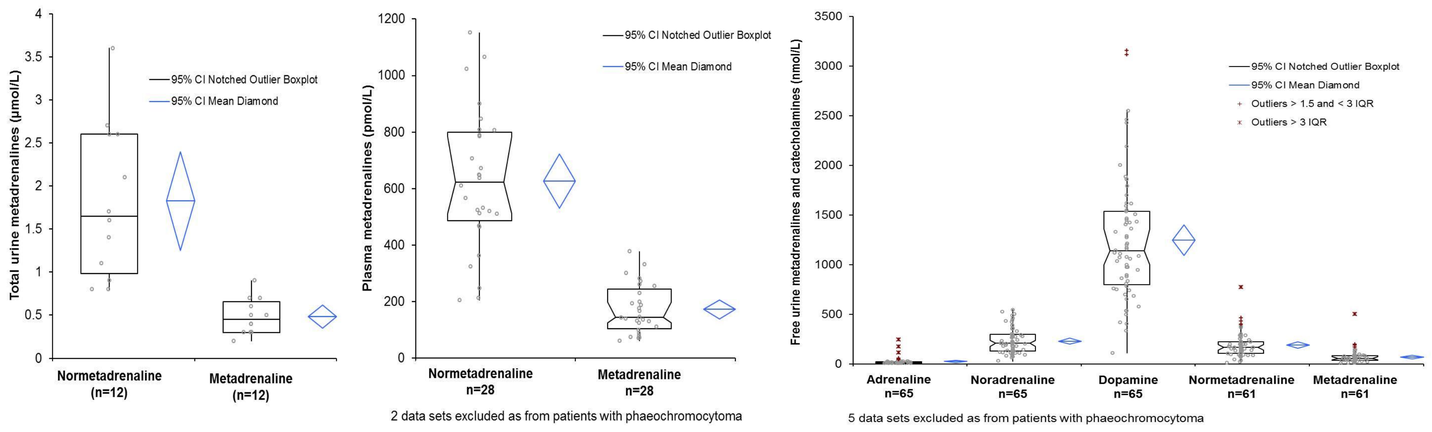



**Figure 3.** (a) Total fractionated urine metadrenalines (b) plasma free metadrenalines and (c) urine free catecholamines and metadrenalines

| Age | Size | Necrosis present | Hypervascularity present | Haemorrhage present | Mitotic index | Positive immunohistochemical staining | Benign/ Malignant |
|---|---|---|---|---|---|---|---|
| 67 | ≥4cm | N | N | N | 1/10 | Chromogranin Synaptophysin S-100. Ki-67 1-2% | Benign |
| 30 | ≥4cm | Y | N | Y | <1/20 | N | Benign |
| 73 | ≥4cm | N | Y | N | <1/10 | N | Benign |
| 70 | ≥4cm | N | N | Y | <1/10 | N | Benign |
| 63 | ≥4cm | N | Y | Y | 2/10 | N | Malignant |
| 51 | ≥4cm | N | N | N | <1/10 | Chromogranin Synaptophysin S-100 | Benign |

**Table 2.** Summary of histological features in 6 cases of phaeochromocytoma. Y – yes; N- no

## Conclusions

This retrospective observational study confirms that in our Unit the majority of patients referred for evaluation of AI are investigated appropriately. It also shows that Clinical Biochemists and Endocrine Specialists should work closely to ensure the appropriate investigation of patients referred with AI in absence of current UK guidelines.

The incidence of PCC discovered in this study (6/104) is in keeping with published reports of ~5% (5). SCS was observed in 7.7% (8/104) of patients in this study (literature estimates >5% (5)). No cases of Conns syndrome were discovered in this study, this is not surprising as 1% of AI are aldosteronomas and the cohort was fairly small.

**References**

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