Endocrine (2011) 40:80–83
DOI 10.1007/s12020-011-9445-6

ORIGINAL ARTICLE

The prevalence of adrenal incidentaloma in routine clinical practice

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Received: 1 February 2011 / Accepted: 12 February 2011 / Published online: 10 March 2011

Abstract The prevalence of adrenal incidentaloma (AI) on computed tomography (CT) in the general population has been reported to be as high as 4.2%. However, many of the previous studies in this field utilised a prospective approach with analysis of CT scans performed by one or more radiologists with a specialist interest in adrenal tumours and a specific focus on identifying the presence of an adrenal mass. A typical radiology department, with a focus on the patient's presenting complaint as opposed to the adrenal gland, may not be expected to diagnose as many adrenal incidentalomas as would be identified in a dedicated research protocol. We hypothesised that the number of AI reported in routine clinical practice is significantly lower than the published figures would suggest. We retrospectively reviewed the reports of all CT thorax and abdomen scans performed in our hospital over a 2 year period. 3,099 patients underwent imaging, with 3,705 scans performed. The median age was 63 years (range 18–98). Thirty-seven true AI were diagnosed during the time period studied. Twenty-two were diagnosed by CT abdomen (22/2,227) and 12 by CT thorax (12/1,478), a prevalence of 0.98 and 0.81% with CT abdomen and thorax, respectively, for AI in routine clinical practice.

Keywords Adrenal incidentaloma · Adrenal tumours · Adrenal adenomas · Prevalence · Cushing's

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Introduction

Adrenal incidentaloma (AI) is defined as an adrenal mass discovered serendipitously during a radiological examination performed for reasons other than adrenal disease. The classic definition excludes patients with clinically overt adrenal hormone hypersecretion, and those with concurrent malignancy known to metastasise to the adrenals [1, 2]. These tumours, once discovered, necessitate radiological and biochemical assessment to determine their risk of malignancy, and whether they are hypersecreting hormones.

At autopsy, the prevalence of adrenal tumours in the general population has been reported to be as high as 6% [1]. Not all of these tumours can be identified on radiological imaging, and the prevalence of adrenal tumours when established by computed tomography (CT) varies from 2.5 to 4% for CT abdomen, and 4.2% for CT thorax, in adult populations [1, 3–5]. In the seminal article on AI by Young et al. [1], a prevalence of 4% for CT abdomen was reported.

Based on these figures, a typical radiology department could expect to report on AI and refer to endocrinology for appropriate endocrine testing, one out of every 25 patients who attend for a CT scan of the thorax or abdomen. However, in the majority of the previously mentioned radiological studies, the authors took an approach in which scans were prospectively reviewed by radiologists with a specialist interest in the adrenal gland, with the specific aim of

identifying any adrenal masses that are present. Screening of this nature, as is the case with pulmonary nodules, tends to diagnose smaller masses than are normally detected in routine clinical practice. In a busy radiology department, with a primary focus on the pathology for which the scan was initially requested, one might expect a significantly lower pick-up rate for AI. Therefore, we hypothesised that while previous articles have accurately reported the absolute numbers of adrenal masses that can be detected by a dedicated, prospective research protocol, this figure does not reflect the number of AI that are diagnosed in normal routine clinical practice.

The primary aim of this study was to determine how many AI had been diagnosed on CT scans of the thorax and abdomen performed during both the acute and out-patient care of both medical and surgical adult patients attending our hospital over a 2-year period. As much of the clinical relevance of this tumour stems from its propensity for hormonal hypersecretion, the secondary aim of our study was to determine whether the identification of an AI in the radiology department led to appropriate endocrine referral and investigation for excess adrenal hormone hypersecretion [1, 2].

Methods

This study was conducted in Beaumont Hospital, a large teaching hospital in the Dublin area. This hospital is the national referral centre for neurosurgery, renal transplantation and cochlear implants, but otherwise provides emergency and acute medical and surgical care to the local population of 290,000 people.

We conducted a retrospective chart and database review of a 2-year period (January 2006–December 2007). A database search was conducted to identify all the patients who had undergone CT abdomen and/or thorax with a view of the adrenals during this time. All CT imaging were performed on two CT scanners; a Siemens Somatom Emotion 6+ and a 16 Slice Sensation non-adaptive array with various standard protocols. For the purposes of this study, we included CT abdomen and CT thorax (with or without contrast). We did not attempt to assess the prevalence of AI on MRI, as we hypothesised that we would have insufficient numbers of AI diagnosed with this imaging modality.

The official radiology report of each individual CT scan was reviewed. Patients with any abnormality of the adrenal glands in their report were noted and entered in the second stage of the study, whereas patients with normal glands on their report were excluded from the study. The scans themselves were not reviewed as part of this study; hence, all adrenal findings were genuine incidental pick-ups as part of routine clinical practice.

In the second stage a chart and laboratory database review was performed. Radiological and biochemical data, choice of treatment/follow-up and demographic details were recorded in all the patients with true AI as per the classic definition. Definite nodule visibility was required for the diagnosis of AI. If a biochemical assessment had not been performed, then the chart was reviewed to identify any possible reason.

As per guidelines, an adequate endocrine assessment was qualified as a 1 mg overnight dexamethasone suppression test or 24-h urinary-free cortisol to assess for hypercortisolism in *all* the patients, a 24-hour collection for urinary catecholamines and metanephrines (or measurement of plasma metanephrines) in *all* the patients, and measurement of plasma renin activity and aldosterone concentration *if* hypertension or hypokalaemia were present [1, 2].

Results

Between January 2006 and December 2007, 3,099 patients attended our radiology department for 3,705 CT scans which included the adrenal glands. 1,648 were male, and 1,451 were female. The vast majority were Caucasian. The median age was 63 years (range 18–98). This represented our overall study population.

Thirty seven true AI were identified. Twenty were male (54%). Median age for the AI patients was 68 years (range 45–92). Twenty were right-sided, (54%), and one case involved bilateral adenomas. Twenty two were diagnosed by CT abdomen (22/2,227) and 12 by CT thorax (12/1,478). Therefore, for AI we calculate a prevalence of 0.98% with CT abdomen, and a prevalence of 0.81% with CT thorax. Two AI were initially diagnosed by renal ultrasound (US), and one AI by CT pulmonary angiography (CTPA) before going on to receive definitive CT adrenal imaging.

Risk of malignancy (size, Houndsfield units and appearance) was commented upon in the official radiology report for every AI. Mean size ($\pm$ standard deviation) was 2.6 ± 1.2 cm. One patient underwent laparoscopic adrenalectomy for a tumour measuring 7.5 cm in diameter. The histology in this case was benign. No cases of malignancy of the adrenal glands (primary or secondary) were diagnosed in this group of 37 AI.

With regard to endocrine function, complete biochemical assessment took place in 19/37 patients (51%). Four out of 19 patients failed their screening investigations and underwent further testing (21%). Three were diagnosed with subclinical cortisol hypersecretion and one with subclinical

Table 1 Rates of endocrine assessment and results of assessments performed

Status	*N*	Comment	Outcome
Adequate endocrine assessment	19	3 patients with cortisol hypersecretion	1 cortisol adenoma and 1 phaeochromocytoma cured by laparoscopic surgery
		1 patient with phaeochromocytoma	1 cortisol adenoma treated with metyrapone
		15 patients with non-functioning adenomas	1 cortisol adenoma under observation
Incomplete or no endocrine assessment	18	8 patients had no endocrine testing	N/A
		5 patients had incomplete endocrine testing	
		5 patients had severe illness precluding testing	

phaeochromocytoma. 1 patient with hypercortisolaemia and one patient with phaeochromocytoma underwent curative laparoscopic surgery. One patient with hypercortisolaemia was placed on metyrapone and is currently controlled on this medication. The remaining patient with hypercortisolaemia remained under observation due to the mild nature of his disease. Five patients had incomplete endocrine testing (1 mg dexamethasone test only), with no hypersecretion identified. Five patients had severe illness at the time of diagnosis of AI that precluded testing during the study period (3 subsequently died from unrelated causes, two patients had prolonged stays in ICU and were subsequently followed up in another centre). Eight patients received no endocrine testing without any reason apparent (Table 1).

With regard to metabolic disease amongst the incidentaloma cohort, type 2 diabetes was present at diagnosis of incidentaloma in six out of thirty seven patients (16%). None of the four patients with a hypersecreting adenoma had diabetes. A total of twenty five out of thirty seven patients (68%) were receiving treatment for hypertension at diagnosis of incidentaloma. All of the four patients with a hypersecreting adenoma had hypertension, although none met the criteria for treatment-resistance hypertension.

Discussion

This is the first study to clearly differentiate between the identification of adrenal tumours diagnosed during routine clinical practice versus those diagnosed as part of a dedicated radiological review. Using our approach we report significantly lower rates of AI than quoted in a number of recent articles. Based on the data reported here, one out of every 101 patients who undergo CT abdomen and 1 out of every 123 patients who undergo CT thorax will be diagnosed with AI and require further radiological and endocrine assessment. The strengths of our study include the relatively large sample size and the comprehensive nature of the database review. With regard to MRI imaging, only 224 MRI abdomens had been performed in the time-period studied, and none had diagnosed AI, and therefore we cannot report AI rates with this imaging modality. Three AI were diagnosed by imaging modalities other than CT abdomen or CT thorax, two by US and one by CTPA.

With regard to other studies in this field, both Herrera et al. and Eldiery et al. [6, 7] adopted a similar approach to our own with large patient cohorts, reporting prevalence rates of 0.4 and 2.5%, respectively, for AI with CT scanning. The novel aspect of our study is its illustration of the difference between rates of AI derived from dedicated research protocols and those derived from clinical practice, moving the focus to the latter, which has greater clinical relevance. This difference also helps one to explain some of the wide variation seen in AI prevalence rates reported in the literature, and should be taken into account in future research in this field. Furthermore, it should be noted that Herrera et al. reviewed CT scans from 1985 to 1989, and imaging technology has advanced significantly in the intervening time, with an increased pick-up rate for AI expected in a modern series. Finally, Song et al. [8] also adopted a similar approach to our own, reporting a prevalence of 5% for AI in a retrospective review of CT scan results, but this study included a radiological review of the CT images in a significant percentage of cases, and again, may have diagnosed more AI than would be encountered in normal clinical practice.

A key issue in the relevance of AI to clinical practice is the importance of subclinical hormone hypersecretion. In this study four patients had hypersecreting tumours. These patients were termed subclinical as none exhibited the specific physical stigmata of Cushing's or persistent/severe hypertension as may be found with an active phaeochromocytoma. All AI should undergo formal endocrine testing, but in our study one third of patients with AI did not receive these tests as indicated. Although we cannot extrapolate this aspect of our data to other centres, it nonetheless raises the concern that hormonally active tumours may escape diagnosis in hospitals that do not have a formal protocol in place for the assessment of AI. Interestingly, Eldeiry et al. [7] also reported a significant

percentage of patients who did not undergo endocrine investigations, and recommended increased education of clinicians regarding AI. Our data, gathered 3 years later, suggests that there may have been little improvement in adherence to international recommendations over this time. In our own centre, we now plan to initiate a policy whereby the endocrinology service is automatically notified by the radiology department when the diagnosis of AI is made, ensuring appropriate follow-up.

In recent years, a number of groups have suggested that adrenal incidentalomas may exert detrimental metabolic effects even when they do not meet diagnostic criteria for hormonal hypersecretion. In 2009, Erbil et al. [9] compared a group of patients with confirmed non-functioning adenomas against age and body-mass index matched controls. They reported decreased flow mediated dilatation, along with an increased prevalence of the metabolic syndrome, in the adenoma group. In a similar fashion, Terzolo et al. [10] reported decreased insulin sensitivity in patients with non-functioning adenomas compared to controls. Finally, Midorikawa et al. [11] reported that surgical resection of non-functioning adenomas increased insulin sensitivity in eight patients. It has been suggested that a spectrum exists between non-functioning adenomas, subclinical Cushing's and overt Cushing's, and current diagnostic tests for Cushing's may fail to identify adrenal adenomas with a low level of autonomous cortisol production. With regards to our study, we report a high prevalence of diabetes (16%) and of hypertension (68%) in our incidentaloma cohort, equally distributed between patients confirmed as non-functioning and patients who did not receive adequate testing. The retrospective nature of our study does not allow suitable comparison with a matched cohort to allow further conclusions to be drawn, but the high prevalence of metabolic disease reported is in agreement with the aforementioned studies. Further research is necessary to clarify the metabolic effects of the supposedly benign non-functioning adrenal adenoma.

There were no malignant adrenal tumours diagnosed in this study. The risk of malignancy in AI has been estimated as high as 4.7% previously [1]. However, in recent times, such a high percentage has been challenged, and it is possible that the risk is lower than previously estimated [8]. Our results, although limited with regards to follow-up, would support this hypothesis. Nonetheless, radiological assessment for malignant phenotype remains the first priority in all newly diagnosed AI.

Our study shows the rate of reported AI to be 0.98% on CT abdomen, and 0.81% on CT thorax in the Irish adult population. These figures are significantly lower than the previously published reports, and highlights, for the first time, the difference between the surreptitious finding of an adrenal adenoma in routine clinic practice, and the finding of an adrenal adenoma specifically searched for and identified in a research study.

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