A Practical Approach to the Incidental Adrenal Mass

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About the Author

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Introduction

With modern use of abdominal imaging, incidental detection of adrenal masses is increasingly common. These lesions are estimated to be present in 4% of all patients and in up to 10% of the elderly population.[1,2] Fortunately, most adrenal masses are benign non-functioning adenomas.[3] However, some of these lesions are hyperfunctioning or harbour malignancy. A familiarity with the evaluation and management of incidental adrenal masses is of interest to endocrinologists as well as surgeons and primary care providers who order abdominal imaging tests.

In 2023 a multidisciplinary working group of Canadian radiologists, endocrinologists, and radiologists published an updated guideline on the diagnosis, management, and follow-up of the incidentally discovered adrenal mass.[4] This publication has helped clarify the necessary imaging and biochemical testing required prior to creating a management plan for a patient with an incidental adrenal lesion.

When faced with an adrenal mass, the clinician must answer 3 essential questions: **1)** Is the mass benign or malignant? **2)** Is the mass hormonally functional or non-functional? **3)** How should the mass be managed?

Imaging Evaluation: Is the mass benign or malignant?

The first step in the evaluation of an adrenal mass is to establish if it is benign or malignant. Non-contrast CT of the abdomen is the most validated test for this purpose due to the well-established characteristics of benign lesions. A low-density lesion (<10 Hounsfield units [HU]) that is homogenous and well circumscribed can be confidently diagnosed as a benign adenoma. A retrospective cohort study that included 2219 adrenal incidentalomas determined the risk of finding adrenocortical carcinoma was 0% if the HU value was <10, 0.5% if the HU value was 10–20, and 6.3% if the HU value was >20.1 Similarly, masses with large areas of macroscopic adipose tissue can be diagnosed as a benign myelolipoma on CT.

Not all masses will have benign features on non-contrast CT and indeed many adrenal masses will be classified as indeterminate. Up to 30% of adrenal adenomas will have densities of >10 HU and exhibit characteristics that overlap with those of pheochromocytoma and malignant lesions.[5-7] If an adrenal mass is classified as indeterminate then further evaluation with contrast enhanced washout CT or chemical shift MRI is needed. Few studies have directly compared the two modalities, thus it is difficult

to recommend one modality over the other. However, there are limitations to both CT and MRI which are outlined in **Table 1**.

Endocrine Evaluation: Is the mass hormonally functional or non-functional?

Screening for adrenal hyperfunction is an important step in the evaluation of an incidental adrenal mass. Both benign and malignant entities can lead to elevated and autonomous production of adrenal hormones (cortical and medullary). Specific elements of the history and physical examination in addition to the radiological findings will dictate which adrenal hormones should be evaluated. Many patients will not require all of the various screening tests.

Many incidental adrenal masses can be confidently described as benign adenomas on initial imaging. In the absence of hypertension or hypokalemia, screening for primary aldosteronism can be omitted for such cases.[8-10] Similarly, observational studies support not screening for pheochromocytoma if the HU is <10 on a non-contrast CT scan.[11-13] A summary the patients who should be screened, and the recommended screening tests is included in **Table 2**.

Management of Incidental Adrenal Masses: Surgery, monitor or ignore?

A management plan for an adrenal mass is predicated on both the functional status and the malignancy risk. There is an opportunity to intervene surgically when needed while also avoiding unnecessary testing and follow-up in low-risk patients.

Surgery

Surgery is the treatment of choice for many functional and malignant lesions, although there are some patients who will not benefit from surgical excision. While patients with unilateral cortisol hypersecretion and signs and symptoms of Cushing's syndrome should undergo extirpative surgery, it is less clear whether patients should undergo surgery if their condition is subclinical.[14] Mild autonomous cortisol secretion can be associated with conditions such as diabetes, hypertension, and dyslipidemia, however, very few of these patients progress to Cushing's syndrome.[15] Surgery may impact some of these comorbidities but the impact is not as profound as when patients have the full constellation of Cushing's symptoms. To this end, the role of surgery in mild autonomous cortisol secretion (MACS) is on a case-by-case basis.

Patients with primary aldosteronism and unilateral hypersecretion often benefit from adrenalectomy. Several studies have confirmed that this surgery can lead to a substantial improvement or resolution of hypertension and hypokalemia. Adrenal vein sampling should be performed in all patients considering surgery since CT or MRI imaging can be discordant with the actual site of hypersecretion in 37.8% of cases.[10] Many cases of primary aldosteronism will display bilateral hypersecretion even in the presence of a unilateral adenoma.

Surgery is the treatment of choice for adrenal pheochromocytoma. Pre-operative patient preparation with pharmacologic alpha blockade is critical to limit the impact of catecholamine surges at the time of excision.

Adrenocortical carcinoma (ACC) is an aggressive malignant tumour of the adrenal gland. When localized, surgical excision is the only opportunity for cure.[16] All patients with suspected ACC limited to the adrenal gland should be considered for surgical resection. While minimally invasive surgery is likely safe for small lesions, large or locally advanced tumours often require open surgical approaches and concurrent lymphadenectomy.

Monitor

Historically, the size of an incidental adrenal mass was one of the main indications for surgical excision.[3] Retrospective studies show that most surgically treated malignant tumours (ACC and pheochromocytoma) were larger than 4 cm at the time of treatment.[17] Nonetheless, when an adrenal mass has benign features on CT, the final pathology is concordant regardless of the size of the lesion.[11] With this in mind, the Canadian Urological Association now recommends that radiologically benign masses >4 cm should undergo repeat imaging in 6–12 months rather than surgical excision.[4] If a mass grows more than 5 mm per year the patient should be offered adrenalectomy. If a radiologically benign mass has minimal growth (<3 mm per year) then no further follow-up is required.

A greater challenge is to manage a non-functional but radiologically indeterminate mass. While many of such lesions will ultimately have benign pathology, this cannot be confirmed with conventional imaging tests. Such circumstances require shared decision making between patients and providers. Management options include repeat imaging in 3–6 months or proceeding with surgical resection.

	CT	MRI
Advantages	Adenoma has a rapid contrast washout Adrenocortical carcinoma has less contrast washout	Can detect adenomas with high sensitivity and specificity No radiation or iodinated contrast agents
Limitations	False positives: 1/3 of lipid-poor adenomas do not exhibit the typical contrast washout in the adenoma range False negatives: 1/3 of pheochromoctyomas and some malignant lesions will exhibit the typical contrast washout in the adenoma range	Decreased performance on lesions with an unenhanced HU of >30 Cost/availability

Table 1. Advantages and limitations of CT and MRI; *courtesy of Neal Rowe, MD*.

Hormone Excess	Population	Tests	Interpretation	Ancillary Testing
Cortisol	All incidentalomas	1 mg Dexamethasone suppression test	≤50 nmol/L excludes cortisol hypersecretion 51–138 nmol/L possible autonomous cortisol secretion >138 nmol/L evidence of cortisol hypersecretion	ACTH testing (independency) 24-hour urinary-free cortisol, midnight salivary cortisol DHEAS
Aldosterone	Hypertension or hypokalemia	Aldosterone-to-renin ratio	20 ng/dL per ng/mL/hr, with a sensitivity and specificity of >90%	Saline suppression test Adrenal vein sampling for lateralization
Catecholamines	HU >10	24-hour urinary fractionated metanephrines Or Plasma free metanephrines	>2 times the upper limit of normal	N/A
Androgens	Virilization Suspected adrenocortical carcinoma	DHEAS, testosterone	Higher levels suggest a greater burden of disease	17β-estradiol, 17-OH progesterone, androstenedione, 17-OH pregnenolone, 11-deoxycorticosterone, progesterone, and estradiol

Table 2. Recommended screening tests for incidental adrenal masses; *courtesy of Neal Rowe, MD*.

Abbreviations: ACTH: adrenocorticotropic hormone, **DHEAS:** dehydroepiandrosterone sulfate, **HU:** Hounsfield unit

Ignore

Radiologic and hormonal evaluation of an incidental adrenal mass often confirms a small (<4 cm), benign (<10 HU) adenoma that is non-functioning. One study of over 2300 patients did not find any progression to malignancy if the initial workup identified an adrenal adenoma.[18] Similarly, in a large study of over 2000 such lesions, the risk of developing functionality was less than 2%.[19] Considering the very low rate of hormonal hypersecretion, it is reasonable to not subject such patients to routine hormonal screening. Overall, patients with small, benign, non-functional lesions do not require close follow-up and special testing. The main trigger for repeat evaluation would be symptoms or signs of hormone excess identified during routine medical history and physical examination.

Conclusions

Detection of an adrenal mass incidentally when imaging is performed for an unrelated indication is a common clinical circumstance. Fortunately, most incidental adrenal masses are non-functional and benign. However, a systematic evaluation of such lesions is paramount to rule out hormonal excess and to assess for malignant features. Patients with unilateral hormonal hypersecretion or suspected malignancy may benefit from timely surgical treatment.

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Financial Disclosures

Board of Directors: Canadian Urological Association and the Urologic Society for Transplantation and Renal Surgery
Consultant: Olympus, Laborie
Honoraria for speaking engagements: Canadian Urological Association and Société Internationale d'Urologie

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