Medical and Surgical Evaluation and Treatment of Adrenal Incidentalomas

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Introduction: Adrenal incidentalomas are detected in approximately 4% of patients undergoing high-resolution abdominal imaging studies. The majority of adrenal incidentalomas are benign, but careful evaluation of all patients is warranted to be certain that primary adrenocortical carcinoma and functional adenomas are not missed.

Methods: The diagnostic approach in patients with adrenal incidentalomas should focus on two main questions: whether the lesion is malignant, and whether it is hormonally active. Radiological evaluation including noncontrast and contrast computed tomography attenuation values expressed in Hounsfield units is the best tool to differentiate between benign and malignant adrenal masses. All adrenal tumors with suspicious radiological findings, most functional tumors, and all tumors more than 4 cm in size that lack characteristic benign imaging features should be surgically excised. All patients should undergo hormonal evaluation for subclinical Cushing’s syndrome and pheochromocytoma, and those with hypertension should also be evaluated for hyperaldosteronism. Combined 1-mg dexamethasone suppression test, plasma metanephrines, and aldosterone/plasma renin activity measurements (if hypertensive) are reasonable initial hormonal evaluations.

Results: Annual biochemical follow-up of most patients with adrenal incidentalomas, especially if the tumor is more than 3 cm in size, for up to 5 yr may be reasonable. Patients with adrenal masses less than 4 cm in size and a noncontrast attenuation value of more than 10 Hounsfield units should have a repeat computed tomography study in 3–6 months and then yearly for 2 yr. Adrenal tumors with indeterminate radiological features that grow to at least 0.8 cm over 3–12 months may be considered for surgical resection.

An adrenal incidentaloma is defined as an adrenal lesion that is discovered when a radiological study is performed for indications other than suspected adrenal disease. This definition should exclude patients undergoing imaging studies as part of staging and workup of an underlying malignancy unless the radiological features are consistent with a benign lesion, and patients who had medical history or physical exam that was inadequate but that would have led to a suspicion of an underlying adrenal disorder if taken or performed (1, 2).

The prevalence of adrenal incidentalomas based on reports summarizing the result of 25 autopsy studies is about 6% (1, 3, 4). The mean prevalence of adrenal incidentalomas using high-resolution computed tomography (CT) scans is about 4%, close to the percentage reported in autopsy series (5, 6). The prevalence of adrenal incidentalomas increases with age; it is less than 1% in patients younger than 30 yr of age and up to 7% in patients over age 70 (3, 4, 7). In a comprehensive review by Cawood et al. (2), the authors argue that many series in the literature represent an overestimation of malignant lesions and functional adrenal tumors for a variety of reasons, such as: inclusion of surgical series with patients who had significant clinical findings; inclusion of patients with suspi...
cious radiological features; exclusion of those with benign imaging studies; small sample size; inclusion of a patient population who were referred to tertiary centers; exclusion of patients with small tumors; inclusion of patients with a history of cancer or suspicion of malignancy; usage of ultrasonography for tumor detection; and finally, methodological error in reporting tumor prevalence (2).

The distributions of the pathological origins of adrenal incidentalomas vary with regard to several clinically important factors, including cancer history and tumor size. Among patients with cancer (most commonly carcinomas of the lung, breast, kidney, and melanoma), up to three-fourths of incidentalomas are metastases (4, 8). In contrast, the lack of a primary cancer site in a patient with a true adrenal incidentaloma would make the diagnosis of a metastatic lesion very unlikely. In such cases, primary adrenocortical carcinoma would be a more common etiology for a malignant adrenal tumor (9, 10).

When clinicians face an adrenal incidentaloma, there are mainly two questions that need to be answered: 1) is the lesion malignant, and if so, is it a primary or a metastatic tumor; and 2) is it functional. Patients with an adrenal incidentaloma should undergo a thorough clinical evaluation. The history and physical exam should be aimed at excluding a functional tumor or an underlying malignant disease.

**Hormonal Evaluation**

All patients with an adrenal incidentaloma should be evaluated for autonomous cortisol secretion referred to as subclinical Cushing’s syndrome (SCS), pheochromocytoma, and (if hypertensive) hyperaldosteronism. In most patients, a combination of 1-mg dexamethasone suppression test (DST), plasma metanephrines, along with aldosterone and plasma renin activity (PRA) measurements (if hypertensive) is a reasonable initial hormonal workup. Further hormonal evaluation is based on clinical and radiological findings.

**Adrenal Imaging**

With modern CT scanners, both adrenal glands are now easily recognized. On rare occasions, it is even possible to distinguish between cortex and medulla on CT scans (Fig. 1, A and B). The three most important imaging criteria to distinguish between benign and malignant adrenal lesions are: 1) size of the lesion; 2) the CT attenuation value on an unenhanced CT scan; and 3) the pattern of enhancement and deenhancement (so-called “washout”).

**Adrenal tumor size**

Adrenal tumor size is an important determinant to help differentiate adrenal adenomas from nonadenomas; the majority of tumors less than 3 cm are benign, and the malignant adrenal lesions are generally more than 6 cm in size (11–20). Different cutoff values ranging from 4–6 cm have been proposed for surgical resection of adrenal masses (12, 17, 18, 20–24). The risk of malignancy increases significantly with tumor size greater than 4 cm, and therefore, in the authors’ opinion, all adrenal incidentalomas more than 4 cm in size that lack characteristic benign radiological features should be surgically removed, regardless of whether or not they are functional (19, 21, 25). At the same time, the risk of malignancy in a 5-cm homogenous adrenal mass with noncontrast attenuation value of less than 10 Hounsfield units (HU) is close to 0% (12, 15, 26–33). The noncontrast CT attenuation coefficient expressed in HU is superior to adrenal size in differentiating between benign and malignant adrenal tumors (12, 15, 26, 28, 30, 33, 34).

Lack of change in the size of an adrenal mass has also been proposed as an indicator of the benign nature of an adrenal tumor (20, 35). However, follow-up of patients with nonfunctioning adrenal masses suggests that 5 to 25% of adrenal masses increase in size by at least 1 cm (20, 36–38). Furthermore, there are reports of cases of adrenal metastases with no change in CT appearance over a period of 36 months (10, 27). In a recent study by Pantalone et al. (10) reporting on 75 surgically resected adrenal masses with at least two imaging studies 3 to 12 months apart, a change in tumor size of 0.8 cm provided the highest com-
bined sensitivity (60%) and specificity (84.6%) for the differentiation of a benign vs. a malignant adrenal mass. The authors could not find any adrenal size cutoff value that would provide 100% sensitivity or specificity to confirm or exclude malignancy. Therefore, change in tumor size should be used in conjunction with other imaging and clinical characteristics when considering surgical resection (10).

Adrenal protocol CT scan

An adrenal protocol is used to further assess a newly discovered adrenal lesion. It consists of unenhanced images, images obtained 1 min after iv injection of contrast media, and imaging after a 10- to 15-min delay (Figs. 2 and 3). In a study by Hamrahian et al. (12) looking at 299 adrenal masses, a noncontrast CT of less than 10 HU or a combination of no more than 4 cm adrenal mass size and a noncontrast CT scan with no more than 20 HU had a 100% specificity in the identification of benign adrenal tumors (Fig. 4).

A relative or absolute percentage deenhancement of 40 and 60% in 10 or 15 min, respectively, is an excellent means of distinguishing between adenomas and metastases. Pheochromocytomas, however, may mimic adenomas (Figs. 2 and 3) (39). Caoli et al. (40) characterized 127 adrenal masses and reported the criteria for benign lesions of less than 10 HU on unenhanced CT scan and absolute percentage enhancement washout of at least 60% was 98% sensitive and 92% specific. Some adrenal lesions such as myelolipomas have characteristic CT scan findings with HU often below −40 (Fig. 5).

Subclinical Cushing’s Syndrome

The first reports on SCS were published by Beierwaltes et al. (41) in 1973 and subsequently by Charbonnel et al. (42) in 1981. The authors suggested that the adrenal tumors produced autonomously small amounts of cortisol, insufficient to result in the typical clinical manifestations of Cushing’s syndrome, but enough to suppress ACTH. This would result in decreased stimulation of the contralateral adrenal gland and lack of iodocholesterol uptake, which would increase after ACTH administration.

Most studies report a prevalence of 5–24% for SCS in patients with adrenal incidentalomas. This broad range is likely the result of differences in the diagnostic criteria that have been used (4, 7, 22, 43–46). Young (1) reported a
prevalence of about 5% after summarizing the data on over 2000 patients from 13 different studies. This percentage is closer to our clinical experience and a recent critical review of the literature (2, 7).

**Diagnosis of SCS**

In the largest study of patients with adrenal incidentaloma, a combination of a positive 1-mg DST and low ACTH was the most common biochemical abnormality in patients with SCS (19). Comparing patients with unilateral and bilateral adrenal iodomethyl-norcholesterol uptake, the 1-mg DST and morning serum ACTH levels were superior to 24-h urinary free cortisol in differentiating between the two groups (47). Despite the lack of a single “gold standard” test to diagnose SCS, the authors consider a combination of the 1-mg DST and plasma ACTH level as the best diagnostic tool for evaluation of patients suspected to have SCS (20, 21). Others have advocated different test combinations, including 1-mg DST, 24-h urinary free cortisol, and plasma ACTH level (49, 50).

There has been disagreement among authors about the best cortisol cutoff value for the diagnosis of SCS, and cortisol levels ranging from 27.6 to 138 nmol/liter (1 to 5 μg/dl) have been proposed (20, 22, 46, 51–53). In a study by Barzon et al. (54), all patients with plasma cortisol greater than 138 nmol/liter after 1-mg DST had only uptake on the side of the adenoma during adrenal scintigraphy. Based on these results, and because the 1-mg DST has the highest impact in both diagnosing SCS and subsequent surgical decisions, the authors recommend using 138 nmol/liter as the cortisol cutoff value during 1-mg DST (1, 20, 21). Using lower cutoff values for cortisol after 1-mg DST would result in an increased test sensitivity but lower specificity (49). With the availability of further prospective studies to better define the value of a surgical approach in patients with SCS, using lower cortisol cutoff values after 1-mg DST may be indicated. Based on limited data, the late-night salivary cortisol should not be used as an initial screening test in patients suspected to have SCS (55). Despite potential usefulness of adrenal scintigraphy for diagnosis of SCS in patients with adrenal incidentalomas, the lack of widespread availability and the time required to complete the test limit its usage (56, 57).

**Treatment of SCS**

Studies on the natural history of SCS are limited, and long-term morbidity and mortality data are still lacking (45, 52, 58). In a study by Vassilatou et al. (59) among 77 patients with an adrenal incidentaloma who were followed for a mean duration of 62 months, only two patients developed Cushing’s syndrome, and neither of these had SCS. With regard to developing SCS in a nonfunctioning adenoma, Barzon et al. (60) followed 130 patients with an adrenal incidentaloma, and the estimated cumulative risk of developing SCS at 1 and 5 yr was 3.8 and 6.6%, respectively. Most studies have reported a higher prevalence of hypertension, obesity, insulin resistance, dyslipidemia, and osteoporosis in patients with SCS (22, 52, 53, 61–66). There is growing evidence for the deleterious effects of excess cortisol on bone in patients of both sexes with SCS. A high prevalence of vertebral fractures (43 to 72%) has been reported in patients with subclinical hypercortisolism (67–69). A possible role of glucocorticoid receptor polymorphism in determining metabolic and bone complications in patients with adrenal incidentaloma has recently been suggested (70).

The decision to operate should take into account the presence of the metabolic consequences of cortisol excess, as well as the severity of the hypothalamic-pituitary-adrenal (HPA) axis abnormality. In general, the more severe the abnormality of the HPA axis, the more likely the patient would benefit from surgery. In a recent retrospective study of 41 patients with adrenal incidentaloma and SCS, there was a significant improvement in blood pressure and fasting blood glucose in patients who underwent surgery, but a worsening of blood pressure and fasting blood glucose in those who chose to be managed conservatively during a follow-up period of 18–48 months (71). Until the results of prospective studies are available, a reasonable strategy may be to consider adrenalectomy for younger patients and those with new onset or a worsening of un-
underlying comorbidities such as diabetes mellitus, hypertension, obesity, or osteoporosis (1, 21, 72).

Perioperative management of patients with SCS

Patients with Cushing’s syndrome or SCS have adequate circulating glucocorticoids and therefore do not require glucocorticoid therapy during surgery. Such patients can safely undergo surgical resection of their tumor, have cortisol levels measured in the morning of postoperative d 1, and then be started on hydrocortisone 30 mg in the morning and 10 mg in the early afternoon until the result of the cortisol level becomes available (73). This would provide an early and accurate evaluation of surgical success in patients with underlying Cushing’s syndrome or SCS. Another approach would be to cover all patients with glucocorticoids perioperatively and evaluate their HPA axis at a later date (71, 74).

Pheochromocytoma

A prevalence of 1.1–11% for pheochromocytomas in patients with adrenal incidentalomas has been reported, but it is probably closer to 3% (2, 7, 75, 76). In approximately 4–14% of patients with a pheochromocytoma, the tumor is discovered incidentally and up to 50% of patients with incidentally discovered pheochromocytoma may be normotensive (3, 20, 77).

Pheochromocytomas are usually well circumscribed on CT scan and mostly inhomogeneous due to areas of cystic changes and hemorrhage. They exhibit increased vascularity with marked enhancement during contrast studies (Fig. 3). A noncontrast CT of less than 10 HU makes the diagnosis of pheochromocytoma extremely unlikely (12, 34, 78–83). One cannot distinguish benign from malignant pheochromocytomas on CT scan unless there is obvious local tumor invasion or evidence of metastasis. A high signal intensity on T2-weighted magnetic resonance imaging is highly characteristic for pheochromocytomas, but its absence does not rule out such diagnosis (84).

Biochemical evaluation

There is a lack of consensus on the best initial diagnostic test for the evaluation of pheochromocytomas in patients with adrenal incidentalomas (1, 85–91). Both plasma and 24-h urinary metanephrines are reasonable initial screening methods for such patients. From a practical standpoint, normal plasma metanephrine rules out a diagnosis of pheochromocytoma in almost all patients except the very rare dopamine-secreting tumor and avoids the deadly consequences of a missed diagnosis (88). Accordingly, the authors favor plasma metanephrines as the first-line diagnostic test due to its excellent diagnostic sensitivity and convenience (21, 88, 92). Patients with elevated plasma metanephrines within three to four times the upper limit of normal need to proceed further with measurement of 24-h urine metanephrines (91, 93).

Perioperative management

All patients with pheochromocytoma should be treated with an α-adrenoceptor antagonist for at least 1–2 wk before surgery (94–96). Phenoxybenzamine (POB) is a long-acting, nonspecific α-adrenergic antagonist that is usually started at 10 to 20 mg/d, with further adjustment until hypertension is controlled or the patient develops side effects, which may include stomach upset, nausea,
stuffy nose, drowsiness, sexual problems in males (e.g. trouble ejaculating), and weakness (95). POB may be associated with significant orthostatic hypotension, reflex tachycardia, and prolonged postoperative hypotension, and it is expensive (97). A selective postsynaptic α1-adrenergic antagonist such as doxazosin is less costly and usually does not result in reflex tachycardia (87). It should be administered at bedtime at 1 to 2 mg/d to avoid significant orthostatic hypotension, with a gradual increase in dosage to 8–12 mg/d at bedtime as tolerated. In the authors’ experience, POB provides better α-blockade and control of paroxysmal hypertension but with increased side effects, which may be prohibitive in some patients (98). The choice of α-blocker often ultimately depends on the level of comfort of the medical team (including the endocrinologist, surgeon, and anesthesiologist) with a particular medication.

Calcium channel blockers may be used to control hypertension or tachycardia or may be used in those patients who cannot tolerate α-blockade (87, 99). Only after adequate α-blockade may patients be started on a β-blocker such as metoprolol or atenolol to control persistent tachycardia or arrhythmias (21, 95). α-Methyltyrosine (metyrosine), a tyrosine hydroxylase inhibitor responsible for the rate-limiting step in catecholamine synthesis, may be used in association with an α-adrenergic antagonist in patients with hemodynamic instability before surgery and may be associated with less intraoperative hemodynamic instability compared with use of an α-blocker alone (100, 101).

With advances in surgical techniques and minimally invasive surgery, most tumors can now safely and successfully be resected laparoscopically (102). All patients should have their biochemical evaluation reassessed a few weeks after surgery, with further assessment intervals based on the overall clinical picture. Because there are no definitive diagnostic criteria for malignancy, patients with an apparently benign pheochromocytoma should be followed annually for at least 5 yr and then intermittently afterward (103, 104).

Primary Aldosteronism

All patients with an adrenal incidentaloma who have hypertension should be screened for primary aldosteronism (44). It is important to note that patients with an aldosterone-producing adenoma (APA) may be normokalemic, and therefore a normal serum K should not preclude further evaluation (105, 106). The estimated prevalence of an APA among patients with adrenal incidentaloma is less than 1%, but a prevalence as high as 2% has been suggested by some (3, 5, 7, 19, 75, 107–109). APA are often small (usually <2 cm in diameter) on CT scan (Fig. 4) (110).

Diagnosis of primary aldosteronism

Since its introduction in 1983 by Hiramatsu et al. (111) and, despite its shortcomings, measurement of plasma aldosterone to renin ratio (ARR) is the best initial test for the evaluation of primary aldosteronism (44, 106, 111). A range of ARR cutoff values from 20 to 100, where plasma aldosterone and renin activity are measured in nanograms per deciliter and nanograms per milliliter per hour, respectively, is used in different institutions before proceeding with confirmatory tests (7, 19, 44). The sensitivity of the assay (level of detection) for PRA can have a significant impact on ARR (112). A PRA of 0.1 ng/ml/h, even in the presence of a serum aldosterone of only 5 ng/dl, will result in an ARR of 50. Therefore, the plasma aldosterone level needs to be considered when evaluating the ARR. A serum aldosterone level below 0.25 nmol/liter (9 ng/dl) makes a diagnosis of primary aldosteronism highly unlikely (113, 114). On the contrary, requiring an aldosterone level of 0.42 nmol/liter (15 ng/dl) as an additional criterion prior to proceeding with confirmatory tests will miss some patients with primary aldosteronism (114). From a practical standpoint, ARR may be measured at the time of an initial patient visit. However, borderline values should be repeated: 1) after correcting hypokalemia; 2) while the patient is on salt restriction; 3) in the morning in a sitting position; and 4) after resting for at least 15 min before proceeding with confirmatory tests (44, 91).

Patients with an elevated ARR should proceed with a confirmatory test such as the salt loading test or saline suppression test (44, 115). Patients may be treated with a non-dihydropyridine calcium channel blocker (verapamil slow release) as a single agent or in combination with α-adrenergic blockers (e.g. doxazosin, to be given at bedtime) and hydralazine for blood pressure control while undergoing confirmatory biochemical evaluation (44). Proceeding with salt loading in some patients with severe uncontrolled hypertension and significant hypokalemia may be unsafe and unnecessary.

Preoperative and surgical management

The majority of patients with primary aldosteronism need to proceed with bilateral adrenal venous sampling to confirm the presence of a unilateral source for hyperaldosteronism. The approach in patients with a well-defined adrenal adenoma more than 1 cm in size and a normal contralateral adrenal gland is somewhat controversial (91). Although in some institutions almost all patients with primary aldosteronism undergo adrenal vein sam-
pling, others may proceed with surgery in patients with an isolated well-defined adrenal nodule more than 1 cm in size (106, 116, 117). Some experts recommend adrenal vein sampling in all patients with primary aldosteronism older than 40 yr due to the increased prevalence of adrenal incidentaloma in such a population (118).

Adrenalectomy in patients with a documented unilateral source of primary aldosteronism is more cost effective compared with lifelong medical therapy. Medical therapy with mineralocorticoid receptor antagonists should be reserved for those who are unable or unwilling to undergo surgery (44). Laparoscopic adrenalectomy compared to an open procedure is associated with a shorter hospital stay, fewer complications, and faster recovery. Resection of the adrenal tumor in a patient with APA will result in resolution of hypokalemia and improvement in hypertension in almost all patients.

Postoperative management

Potassium supplementation and mineralocorticoid receptor antagonists should be stopped on postoperative d 1, and there should be close monitoring of serum potassium. A temporary state of hypoaldosteronism may also develop in some patients with primary aldosteronism postoperatively. In the majority of cases, this condition can be managed by increasing salt intake. Rarely, treatment with fludrocortisone 0.1 mg/d for several weeks may be required (119, 120).

Fine-Needle Aspiration (FNA)

Image-guided FNA of an adrenal tumor occasionally may be helpful in the diagnostic evaluation of patients with a

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Prevalence</th>
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<tr>
<td>Adrenal cortical tumors</td>
<td></td>
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<tr>
<td>Nonfunctional adenoma</td>
<td>85 (71–93)</td>
</tr>
<tr>
<td>Subclinical Cushing’s syndrome</td>
<td>6.4 (4.4–8.3)</td>
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<tr>
<td>Conn’s syndrome</td>
<td>0.6 (0–1.2)</td>
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<tr>
<td>Adrenocortical carcinoma</td>
<td>1.9 (0.8–3)</td>
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<tr>
<td>Adrenal medullary tumors</td>
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<tr>
<td>Pheochromocytoma</td>
<td>3.1 (1.8–4.3)</td>
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<tr>
<td>Metastasis</td>
<td>0.7 (0–1.4)</td>
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<tr>
<td>Others</td>
<td>&lt;5</td>
</tr>
</tbody>
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In patients with a history of cancer or clinical features suggestive of an underlying adrenal etiology have been excluded. Data are expressed as percentage (range).

All patients should be evaluated for subclinical Cushing’s syndrome, pheochromocytoma, and if hypertensive, primary aldosteronism. MRI, Magnetic resonance imaging; DHEAS, dehydroepiandrosterone sulfate; DM, diabetes mellitus; HTN, hypertension; POD, postoperative day 1.
history of cancer (particularly lung, breast, kidney, and melanoma), no other signs of metastasis, and an adrenal mass with noncontrast CT attenuation value more than 10 HU and a CT examination showing less than 60% absolute deenhancement. To avoid the potential for a hypertensive crisis, pheochromocytoma should always be excluded before FNA of an adrenal mass is attempted (121). FNA should not be considered in the diagnostic approach of a tumor suspected to be an adrenocortical carcinoma because it may not be informative and may be hazardous due to the potential for tumor seeding (18, 23).

Bilateral Adrenal Lesions

Adrenal incidentalomas are bilateral in less than 15% of cases (60, 122). The most common underlying etiologies include metastatic disease, congenital adrenal hyperplasia, bilateral cortical adenomas/hyperplasia, bilateral pheochromocytomas, or infiltrative diseases (1) (Tables 1 and 2). Measurement of cortisol precursors such as 17-hydroxyprogesterone during a cortrosyn stimulation test should be considered to rule out congenital adrenal hyperplasia.

Long-Term Follow-Up of Patients with Adrenal Incidentalomas

The optimal duration of biochemical follow-up for patients with adrenal incidentalomas is unknown. Excess hormone secretion may develop in up to 20% of patients with previously nonfunctional adrenal tumors during follow-up (37, 38, 123). The transformation rate of nonfunctional adrenal masses to functional tumors seems to be higher in adrenal masses greater than 3 cm in size (38). The National Institutes of Health consensus statement included recommendations for limited follow-up only for nonfunctional adenomas of less than 3 cm with no specific recommendations (20). Until data from large prospective studies are available, annual biochemical follow-up for up to 5 yr may be reasonable for patients with adrenal incidentalomas, especially if the tumor is more than 3 cm in size (20, 21, 37, 45).

The most appropriate radiological follow-up of a nonfunctional adrenal mass is unknown. Although some authors recommend no routine follow-up of adrenal incidentalomas with a noncontrast attenuation value no greater than 10 HU, a one-time follow-up scan in 6–12 months may be reassuring to the physician and the patient (2, 12, 40, 124). Frequent adrenal imaging is associated with additional cost, anxiety, and exposure to radiation, which may theoretically induce cancer at an estimated rate similar to the chance of developing adrenal malignancy (2). Patients with adrenal masses less than 4 cm in size and a noncontrast attenuation value more than 10 HU should have a repeat CT study in 3–6 months and then yearly for 2 yr. There is no good evidence supporting continued radiological surveillance if the follow-up imaging studies show no change in the adrenal tumor size (20). Surgical excision may be considered for tumors with indeterminate radiological features that grow at least 0.8 cm over 3- to 12-month follow-up (10).

Summary

The diagnostic approach in patients with adrenal incidentalomas should focus on two main questions: 1) whether the lesion is malignant; and 2) whether it is hormonally...
active (Fig. 6). Radiological evaluation including noncontrast CT attenuation value expressed in HU is the best tool to differentiate between benign and malignant adrenal masses. All adrenal tumors with suspicious radiological features, most functional tumors, and all tumors more than 4 cm in size that lack characteristic benign imaging features should be removed. All patients should undergo hormonal evaluation for SCS and pheochromocytoma, and those with hypertension should also be evaluated for primary hyperaldosteronism. Annual biochemical follow-up of most patients with an adrenal incidentaloma (especially if the tumor is more than 3 cm in size) for up to 5 yr may be reasonable. Patients with adrenal masses less than 4 cm in size and a noncontrast attenuation value greater than 10 HU should have a repeat CT study in 3–6 months and then yearly for 2 yr. Adrenal tumors with indeterminate radiological features that grow at least 0.8 cm over 3–12 months should be considered for surgical resection once other imaging and clinical characteristics have been taken into consideration.

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