The Incidental Adrenal Mass on CT: Prevalence of Adrenal Disease in 1,049 Consecutive Adrenal Masses in Patients with No Known Malignancy

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OBJECTIVE. The purpose of our study was to determine the nature and prevalence of adrenal lesions identified on CT in patients with no known malignancy.

MATERIALS AND METHODS. A computer search of abdominal CT reports using the term "adrenal" was performed in 65,231 consecutive patients with examinations performed from January 2000 to December 2003. An adrenal mass was identified in 3,307 (5%) patients. Patients with no known malignancy and no suspicion for a hyperfunctioning adrenal mass were further isolated. Nine hundred seventy-three patients with 1,049 adrenal masses fulfilled the study criteria. The nature of each lesion was determined by histopathology; imaging characterization with CT, MRI, or washout; a minimum of 1 year of stability on follow-up imaging; or clinical follow-up of at least 2 years.

RESULTS. One thousand forty-nine adrenal masses were characterized with the following methods: histopathology (n = 12), imaging characterization (n = 909), imaging follow-up (n = 87), and clinical follow-up (n = 41). There were 788 adenomas constituting 75% of all lesions. There were 68 myelolipomas (6%), 47 hematomas (4%), and 13 cysts (1%). Three pheochromocytomas (0.3%) and one cortisol-producing adenoma (0.1%) were found incidentally. One hundred twenty-eight lesions (12%) were presumed to be benign by imaging or clinical stability. No malignant adrenal masses were found, even among the 14 patients who later developed malignancy elsewhere.

CONCLUSION. In 973 consecutive patients with an incidental adrenal mass and no history of cancer, no malignant lesions were identified. Adenomas (75%) and myelolipomas (6%) were the most common lesions.

Keywords: adrenal gland, CT; adrenal gland, diseases; adrenal gland, neoplasms; adrenal mass

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The adrenal gland is a common site of disease, with a prevalence of abnormality reported to be as much as 9% in autopsy series [1]. With the increasing use of CT, adrenal lesions are frequently found in the daily practice of radiology, diagnosed on up to 5% of CT examinations performed for various reasons [2]. Imaging features on CT can establish a specific diagnosis of many of these lesions, including myelolipoma, hematoma, and cysts. Once a diagnostic dilemma, now adenomas can be accurately diagnosed using unenhanced CT [3–5], chemical shift MRI [6–8], and CT contrast washout analysis [9–11]. Because the adrenal gland is also a frequent site of metastasis, recent literature has focused on imaging characterization of adrenal masses to differentiate adenomas from metastases. In patients without known malignancy, most adrenal lesions are benign, and a specific diagnosis can now be made on the basis of imaging features.

However, there are scant data in the imaging literature about the prevalence of different adrenal masses. Much of the prevalence information quoted is derived from autopsy series from the 1950s and 1960s [1, 12]. In studies with imaging and surgical correlation, selection bias is frequently present because these surgical lesions are typically large or have malignant imaging features requiring histologic evaluation. In addition, many of these studies have a mixed population of low-risk and cancer patients. Prevalence of adrenal abnormalities is important to understand because the adrenal gland is a common site of disorders, and the increased use of cross-sectional imaging has increased the frequency of detection of adrenal lesions.

The purpose of our study was to determine the prevalence and cause of adrenal masses

incidentally identified on CT in low-risk patients. The prevalence of disease is important in predicting the risk of malignancy when an adrenal mass is discovered in a patient without known cancer. Our hypothesis is that most of these incidentally found adrenal lesions are benign, and some of these benign lesions may be more prevalent than has been previously reported in the pathology literature.

Materials and Methods

Subjects

This retrospective study was approved by our institutional review board, and informed consent was waived. This study was also HIPAA-compliant.

The CT reports of 128,401 consecutive chest or abdominal CT examinations from our academic institution performed on 65,231 patients from January 2000 to December 2003 were searched for the word "adrenal" in the impression. The search identified 3,307 (5%) patients with adrenal lesions. Two authors retrospectively reviewed these CT reports independently and further identified patients at low-risk for metastasis. For 150 patient reports (5%) with ambiguous findings (e.g., possible adrenal nodule, probable adrenal adenoma), the CT images were reviewed to confirm the presence or absence of a mass. We considered any available clinical history or current imaging evidence of malignancy to be high-risk for adrenal metastasis, and we excluded 2,227 patients with known cancer. Patients with indeterminate adrenal lesions on initial CT who were diagnosed with malignancy after the initial CT were included in the study cohort. We excluded six patients with an adrenal mass who had a clinical suspicion of a functioning adrenal lesion. One hundred one patients were further excluded because of less than 1-year imaging or 2-year clinical follow-up ($n = 63$) or lost follow-up ($n = 38$).

The remaining 973 low-risk patients with 1,049 adrenal masses constituted the study group. We recorded the number and size of the adrenal mass of each patient. The results of histopathology, specific imaging diagnosis, and a minimum of 1-year stability on imaging or 2-year stability on clinical follow-up were used to establish the diagnosis. The histologic diagnosis was considered to be the reference standard when available ($n = 12$). The diagnostic imaging studies for adrenal mass characterization included enhanced CT, unenhanced CT, adrenal CT with washout, and chemical shift MRI ($n = 909$). For the lesions with no specific histologic or imaging diagnosis, at least 1-year stability on follow-up imaging was used as imaging evidence of benignity ($n = 87$) [13, 14]. For the remaining lesions, clinical stability of at least 2 years ($n = 41$) was considered to indicate a benign process, as discussed in the following text [15, 16].

Imaging Methods and Analysis

The initial CT examinations were performed at two hospitals and outpatient imaging centers, and included both chest and abdominal CT. All studies were performed on helical CT (HiSpeed CT/i and 4-MDCT Lightspeed, GE Healthcare; 4-MDCT Asteion, Toshiba Medical Systems; and 16-MDCT Sensation, Siemens Medical Solutions). Incidental adrenal lesions were identified on unenhanced abdominal CT and on contrast-enhanced abdominal CT, typically performed during the portal venous phase (60–70 seconds) after the IV administration of 100 mL of low-osmolar contrast material at collimations ranging from 3 to 7 mm, depending on body part imaged, scanner used, and the year of the examination. Most chest CT examinations were performed as unenhanced studies. Contrast-enhanced chest CT was performed with the IV administration of 100 mL of low-osmolar contrast material using a routine protocol or as chest CT angiography (pulmonary embolism and aortic dissection protocols) with 120 mL of low-osmolar contrast material.

Adrenal mass characterization was performed using unenhanced CT, dedicated adrenal CT with contrast washout, or adrenal MRI with chemical shift imaging as we will describe.

Adrenal CT—For the patients who underwent follow-up dedicated adrenal CT to characterize the incidentally discovered adrenal mass, the following protocol was used: Initially unenhanced sections were obtained using 2.5-mm (MDCT) or 3-mm (single-detector CT) collimation through the adrenal glands using an average field of view at 25–28 mm. An elliptic region of interest (ROI) through the adrenal mass was obtained, and if it measured greater than 10 H, then 100 mL of nonionic contrast material was injected IV at 3 mL/s. Using the same parameters, imaging was repeated at 60 seconds after contrast injection and again after a 10- or 15-minute delay.

Adrenal MRI—MRI was performed on a variety of MR equipment including 1.5-T systems (Vision or Symphony, Siemens Medical Solutions) and 1-T systems (Harmony, Siemens Medical Solutions). A phased-array torso coil was used whenever possible. T1-weighted in-phase and opposed-phase axial breath-hold images were obtained with a 2D gradient-refocused echo sequence using the following parameters: TR range, 150–193 milliseconds; in-phase TE range, 4.4–7.5 milliseconds; and opposed-phase TE range, 2.2–3.7 milliseconds. Additional parameters are as follows: flip angle, 70–90°; field of view, 350–360 mm; matrix, 127–192 × 256; slice thickness, 5–6 mm; intersection gap, 0–1 mm; and 1 signal acquisition. All studies also included a T2-weighted sequence of variable technique.

An adenoma was diagnosed when a lesion had an attenuation coefficient of less than or equal to 10 H on unenhanced CT and absolute contrast washout of greater than or equal to 52% at 10 minutes or 60% at 15 minutes on adrenal CT [13, 14]. For the chemical shift MRI criteria, we used signal cancellation based on subjective analysis of signal dropout on opposed-phased imaging to diagnose an adenoma [8]. The diagnostic criterion for a myelolipoma was the presence of macroscopic fat assessed subjectively or attenuation of less than –20 H. An adrenal hematoma was diagnosed when a high-density mass showed diminished size on follow-up imaging, frequently with diminished density, or complete resolution. On MRI, the signal intensity of a hematoma varied depending on the age of the blood products. The criteria used to diagnose an adrenal cyst on CT were a sharply marginated, well-defined mass of fluid attenuation showing no enhancement.

Clinical Follow-Up

For the 40 patients without a specific histologic or imaging diagnosis and less than 1 year of imaging follow-up, clinical follow-up of at least 2 years was used to assure a benign diagnosis. Clinical information was gathered through the electronic medical record ($n = 25$) and telephone

TABLE 1: Methods to Establish Diagnosis of Adrenal Lesions

Methods	No. of Masses
Histologic diagnosis	12
Imaging diagnosis	909
Unenhanced CT	641
Adrenal CT with washout	71
Contrast-enhanced CT	150
Chemical shift MRI	29
Unenhanced CT and adrenal CT with washout	5
Unenhanced CT and chemical shift MRI	8
Adrenal CT with washout and chemical shift MRI	3
Unenhanced CT, adrenal CT with washout, and chemical shift MRI	2
Imaging follow-up ≥ 1 year	87
Clinical follow-up ≥ 2 years	41
Total	1,049

calls (n = 15) to the referring clinician of the patient, specifically to determine whether malignancy was diagnosed after CT or whether any clinical findings were suspicious for a biochemically active adrenal lesion.

Statistical Analysis

We calculated the 95% CI for the detection of malignancy using the Web program for Exact Binomial and Poisson Confidence Intervals from statpages.org.

Results

The results are summarized in Tables 1–4. The study cohort comprised nine hundred seventy-three low-risk patients (567 women, 406 men) with a total of 1,049 adrenal masses, including 76 bilateral masses. The mean age of the patients in our study group was 64 years (range, 19–100 years). One thousand forty-nine lesions were evaluated as follows (Table 1): histologic diagnosis (n = 12), imaging characterization (n = 909), imaging follow-up (n = 87), and clinical follow-up (n = 41). A specific diagnosis was established in 921 adrenal lesions, whereas a presumed benign diagnosis was made of 128 adrenal masses (Table 2). In 654 (62%) adrenal lesions, a specific diagnosis was made at the time of the initial CT, and the remaining 395 (38%) masses required further workup. The mean size of the adrenal mass was 2.0 cm (range, 0.4–8.2 cm) in 990 lesions (Table 3). The size of the mass was not reported and the images were not available for review in the remaining 59 (5.6%) adrenal lesions.

Of the 12 adrenal masses evaluated histologically, eight lesions were surgically resected and four were biopsied with CT guidance. The mean size of the histologically diagnosed adrenal masses was 3.7 cm (range, 1.4–6.0 cm). There were six histologically proven adenomas, including a 1.4-cm surgically resected serendipitous, cortisol-producing adenoma causing subclinical Cushing's syndrome. The remaining five adenomas were diagnosed histologically because they did not meet the criteria of an adenoma on adrenal CT or MRI. There were three (0.3%) incidentally found pheochromocytomas, two of which (a 6.3-cm heterogeneous and a 2.8-cm homogeneous mass) were surgically resected. The third 3.0-cm pheochromocytoma was biopsied with CT guidance after α-blockade and then subsequently treated with radiofrequency ablation because the patient was a poor surgical candidate. Therefore, four (0.4%) incidentally found hyperfunctioning masses were in the study group. The remaining three surgically resected masses were heterogeneous masses with imaging features suspicious for malignancy: a 6-cm spontaneous hematoma, a 3.5-cm macronodular hyperplasia, and a 4.2-cm adrenal cortical neoplasm of uncertain malignant potential.

TABLE 2: Pathology Results for All Adrenal Lesions

Diagnosis	No. (%) of Lesions
Adenoma	788 (75)
Myelolipoma	68 (6)
Hematoma	47 (4)
Cyst	13 (1)
Pheochromocytoma	3 (0.3)
Macronodular hyperplasia	1 (0.1)
Adrenal cortical neoplasm, unknown malignant potential	1 (0.1)
Presumed benign by imaging or clinical stability	128 (12)
Total	1,049 (100)

Nine hundred nine adrenal lesions were diagnostic on imaging. There were 782 adenomas, accounting for 86% of imaging diagnoses. Six hundred eighty-nine (88%) of these adenomas were lipid-rich (H ≤ 10) and diagnosed on unenhanced (n = 607) or enhanced CT (n = 82); the remaining 93 (12%) adenomas required adrenal CT or chemical shift MRI to confirm the diagnosis (Table 4). Therefore, 788 adenomas (six histologic and 782 by imaging) were found in 725 patients, constituting 75% of all adrenal lesions. Sixty-eight (6%) of the adrenal masses were myelolipomas. There were 47 (4%) hematomas in 43 patients, 36 on the right and 11 on the left. Other than the single case of spontaneous hematoma diagnosed on a surgical specimen discussed previously, the remaining 46 hematomas were diagnosed on imaging. Thirty-six of 47 (77%) hematomas occurred in the setting of trauma. The causes for the remaining hematomas were surgery-related stress (n = 7), sepsis (n = 1), anticoagulation (n = 1), and spontaneous (n = 2). There were 13 (1%) cysts in the study group, seven of which contained peripheral calcification.

Eighty-seven adrenal lesions without a specific histologic or imaging diagnosis had imaging proof of stability of at least 1 year (range, 1–6 years). Adrenal lesions were followed up with CT (n = 84), MRI (n = 2), and PET (n = 1). The mean length of imaging follow-up was 2.8 years (range, 1–2 years in 28 lesions, 2–3 years in 27 lesions, and > 3 years in 32 lesions).

Forty-one lesions in forty patients without histologic or imaging diagnosis and less than 1 year imaging follow-up had available clinical information of at least 2 years from the time of the initial study (range, 2–5 years). None of these patients with clinical follow-up developed malignancy, and their adrenal lesions were presumed to be benign. The

TABLE 3: Size of Adrenal Lesions

Diagnosis	< 2 cm	2–4 cm	> 4 cm	Total
Imaging diagnosis				
Adenoma	395	348	9	752
Myelolipoma	24	31	9	64
Hematoma	6	14	5	25
Cyst	0	6	7	13
Histologic diagnosis				
Adenoma	2	3	1	6
Pheochromocytoma	0	2	1	3
Other	0	1[a]	2[b,c]	3
Presumed benign by stability	60	63	1	124
Total	487	468	35	990

Note—Mass size was not reported and images were not available for review in 59 adrenal lesions.
[a]Macronodular hyperplasia.
[b]Hematoma.
[c]Adrenal cortical neoplasm of unknown malignant potential.

TABLE 4: Technique Used for 782 Adenomas Diagnosed by Imaging

Imaging Study	No. of Masses
Unenhanced CT	592
Adrenal CT with washout	63
Contrast-enhanced CT	82
Chemical shift MRI	28
Unenhanced CT, adrenal CT with washout	5
Unenhanced CT, chemical shift MRI	8
Adrenal CT with washout, chemical shift MRI	2
Unenhanced CT, adrenal CT with washout, chemical shift MRI	2
Total	782

mean length of clinical follow-up was 3.3 years (range, 2–3 years in 21 lesions and > 3 years in 20 lesions).

No malignant adrenal lesions were found in the study population (95% CI, 0.0000–0.0035). Fourteen patients with a total of 15 adrenal masses that were indeterminate on initial CT, later developed malignancy elsewhere (five, lung; three, prostate; one each, breast, melanoma, renal, rectal, biliary tract, and head and neck), but none of their adrenal lesions were metastasis. Of these benign adrenal lesions, one was a histologically proven adenoma, seven were adenomas by imaging, and seven lesions were presumed to be benign based on imaging stability.

Discussion

Incidental adrenal masses are frequently seen on CT with the increasing use of cross-sectional imaging. With the current high-resolution CT scanners, the prevalence of adrenal "incidentalomas" has increased, and our result of 5% prevalence corroborates the 4.4% reported from a recent series [17], compared with the 1–2% reported in the older literature [18]. The prevalence of incidental adrenal mass on imaging now approaches that of autopsy series [19], although not as high as the frequently cited 9% [1], which includes microscopic lesions. Although numerous publications describe the imaging appearance of different types of adrenal pathology, we know of no large published series in the imaging literature reporting the prevalence of adrenal lesions detected on CT. Prior studies reporting the pathology of incidentally detected adrenal masses often had selection bias because only surgically resected masses were analyzed [20, 21]. In addition, the definition of incidentaloma is broad among different series, with many studies including oncologic patients [21–23]. In patients without a known history of malignancy, most adrenal lesions are benign and are frequently detected incidentally. Because of their specific imaging appearance, many adrenal lesions, including myelolipomas, hematomas, and cysts, can be accurately diagnosed on CT. Recent studies have shown that adenomas, too, can be accurately diagnosed using unenhanced CT, adrenal CT, or chemical shift MR [13, 14, 24]. The high yield of imaging characterization was confirmed in our study; we found that imaging provided a specific diagnosis in 910 (87%) of all adrenal masses, of which 654 (62%) were diagnostic at the initial CT.

Only 12 (1%) adrenal masses were histologically evaluated in our series, eight of which were surgically resected. The general consensus is that mass size is an important predictor of risk of malignancy. Although the size threshold for resection varies, adrenal masses larger than 4 cm are frequently resected if there is no firm diagnosis of a benign cause. The mean size of the histologically evaluated masses in our series was 3.7 cm (compared with the mean size of 2 cm in masses diagnosed at imaging or follow-up), and four (33%) of these masses were larger than 4 cm. In our subgroup of 35 adrenal masses larger than 4 cm, 11% of the lesions required histologic diagnosis, compared with 0.8% in the smaller masses.

In our study, adenomas were by far the most common entity, constituting 75% of all adrenal masses, followed by myelolipoma (6%) and hematoma (4%) and others as detailed in Table 2. Of the 788 adenomas, only five (0.6%) required histologic evaluation because of their indeterminate or malignant appearance, and 99.4% of the adenomas were diagnosed on imaging. The number of adrenal adenomas requiring biopsy for diagnosis has declined in recent years with the introduction of dedicated adrenal CT and MRI [25]. In our study, most (78%) adenomas were characterized on unenhanced CT, using the threshold of ≤ 10 H, which is similar to the 83% reported by Caoili et al. [14]. Interestingly, in our series 10% of adenomas were diagnosed on routine contrast-enhanced studies using the same threshold.

Adrenal myelolipomas are reported to be uncommon, accounting for 2.6% of all primary adrenal tumors in pathology series [26] and having a prevalence of 0.08–0.2% in autopsy series [27]. These lesions are easily recognized on imaging because they contain macroscopic fat. Although numerous reports describe the imaging features of adrenal myelolipomas, we know of no reports of the prevalence of myelolipomas on imaging. In our study, myelolipomas were the second most common diagnosis, accounting for 6% of all adrenal lesions, which is higher than has been reported in autopsy series.

Adrenal hematomas are usually easily diagnosed on CT because of their typical appearance of a high-density mass, and also because they occur in distinct clinical settings, with trauma being responsible for 80% of cases [28]. Although adrenal injury has been reported in 28% of autopsy series of severe trauma [29], a much smaller 2% prevalence has been reported in CT of trauma patients with severe abdominal injury [30, 31]. In our series of all adrenal lesions, 4% were hematomas, with trauma as the leading cause in 77%. The right adrenal gland was involved three times more frequently than the left, as typically seen in trauma. In general, adrenal hematomas require follow-up examination to exclude an underlying malignant mass.

In our series of 1,049 incidental adrenal lesions, one adrenal mass was an adrenal cortical neoplasm of unknown malignant potential. There was no adrenal cortical carcinoma, a malignancy rare in the general population but having a reported prevalence of 1–5% among patients with an adrenal mass [15, 18]. Adrenal cortical carcinomas are typically large, with imaging features of malignancy including heterogeneous density, central necrosis, and calcification requiring histologic evaluation. Adrenal cortical carcinomas can also be biochemically active, prompting imaging evaluation for mass detection. No metastatic adrenal lesions were found in our low-risk population, including the patients who subsequently developed malignancy elsewhere. It is rare for an incidental adrenal mass to present as the initial and only manifestation of metastatic cancer [15, 32].

Four (0.4%) hyperfunctioning masses were seen in our study. Subclinical hormone secretion by adrenal masses is well recognized, reported to be as high as 12% of cortisol-producing adenomas [33] and 2–11% of pheochromocytomas [19] among incidentalomas. Pheochromocytomas can be clinically silent, although most patients with an incidentally found pheochromocytoma have a history of hypertension. In a recent series by Motta-Ramirez et al. [34], 58% of all pheochromocytomas were reported to be detected incidentally. The National Institutes of Health (NIH) consensus conference recommends biochemical evaluation for hormonal excess in its guideline for management of clinically unapparent adrenal masses [35]. Our less than 1% incidence of hyperfunctioning masses is likely an underrepresentation because biochemical screening was not routinely performed on all patients.

Our study had several limitations. The gold standard of histologic diagnosis was not available for most of the adrenal masses. Lack of histology result reflects the current acceptance of imaging as highly accurate; thus, histologic evaluation of most of these benign lesions would have been unjustified. A second limitation

is that in this retrospective study involving a large data set of 128,401 examinations on 65,231 patients, in most cases—especially the studies that did not report the presence of an adrenal lesion—it was not feasible to review all the images to confirm the reports. However, because these examinations were interpreted by board-certified radiologists, we believe screening out negative cases based on their reports is a reasonable method in a study of this size. A third limitation of this study is that 101 patients had either less than 1 year of imaging follow-up or less than 2 years of clinical follow-up, and thus the nature of their adrenal lesions is unknown. However, we have no reason to believe any selection bias exists in the 101 excluded patients. A fourth limitation of this study is that by using strict imaging and clinical criteria, we likely underestimated the true incidence of adrenal adenomas. The 128 (12%) adrenal lesions we defined as benign on the basis of the accepted criteria of imaging stability or clinical follow-up were not assigned a specific diagnosis. It is likely that many of these "benign lesions" were additional adenomas. A fifth limitation is the theoretic possibility that an early presentation of adrenal cortical carcinoma could have been miscategorized as a probable benign lesion using our methods; however, that would be a rare exception for adrenal cortical carcinoma. Finally, the functional status of adrenal masses was not routinely addressed in this study and may account for the less than 1% prevalence of functioning masses in our study, lower than in previously published data. Functional status of an incidentaloma has been reported in other studies [15, 20, 21, 36] and was not the focus of this study.

In conclusion, our results showed no malignant mass among incidentally found adrenal lesions in low-risk patients without known malignancy. Adenomas were by far the most common lesion, followed by myelolipoma and adrenal hematoma. Our 6% incidence of incidental adrenal myelolipomas is higher than that reported in the older pathology literature.

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