The Incidental Indeterminate Adrenal Mass on CT (> 10 H) in Patients Without Cancer: Is Further Imaging Necessary? Follow-Up of 321 Consecutive Indeterminate Adrenal Masses

OBJECTIVE. The objective of our study was to determine whether follow-up imaging evaluation is necessary for incidentally discovered indeterminate adrenal lesions (> 10 H) on CT in patients with no known malignancy.

MATERIALS AND METHODS. A computer search of CT reports from January 2000 to December 2003 identified patients with incidentally detected, indeterminate, but benign-appearing adrenal lesions who had no known malignancy and no clinical suspicion of hyperfunctioning adrenal mass. Patients with adrenal masses diagnostic on the initial CT or heterogeneous masses were excluded. Two hundred ninety patients with 321 lesions met the study criteria. Each lesion was determined to be benign or malignant based on histopathology, characterization with diagnostic imaging studies, or a minimum of 1 year of stability on imaging follow-up or 2 years of stability on clinical follow-up.

RESULTS. Of the 321 lesions, 318 masses (99.1%) were confirmed to be benign and clinically insignificant. These included three (0.9%) histologically confirmed adenomas, 198 (61.7%) adenomas by imaging characterization, five (1.6%) other benign lesions, 71 (22.1%) masses stable on imaging follow-up, and 41 (12.8%) masses with clinical stability. There were three (0.9%) clinically unsuspected functioning masses: one cortisol-producing adenoma and two pheochromocytomas. There were no metastatic adrenal lesions, even among the 13 patients who subsequently developed malignancy elsewhere.

CONCLUSION. All of the incidentally detected adrenal masses with a CT attenuation of > 10 H were benign in patients with no known malignancy. Follow-up imaging to characterize an incidental adrenal mass appears to have a limited role in this patient cohort.

Keywords: adenoma, adrenal glands, adrenal mass, benign adenoma, CT, incidental adrenal mass, incidentalomas, neoplasms

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1All authors: Department of Diagnostic Imaging, Rhode Island Hospital, Warren Alpert Medical School of Brown University, 593 Eddy St., Providence, RI 02903. Address correspondence to J. H. Song (jsong2@lifespan.org).

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discovered indeterminate adrenal lesions on CT in patients with no known cancer and, further, whether imaging evaluation is necessary to establish benignity in these patients. Our hypothesis was that most of these incidentally found adrenal masses are benign and would not require a confirmatory imaging study.

Materials and Methods

Subjects

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

The CT reports of 128,401 consecutive chest, abdominal, or chest and abdominal CT examinations from our academic institution performed from January 2000 to December 2003 were queried for the word “adrenal” in the impression section. The search identified 3,307 patients with adrenal masses. Two authors retrospectively reviewed these CT reports and further identified patients with incidentally detected indeterminate adrenal lesions in a population at low risk for adrenal metastases as described in the next sections of text.

Exclusion criteria—We considered patients with any available clinical history or current imaging evidence of malignancy to be at high risk for adrenal metastasis and therefore excluded 2,227 patients with known malignancy. Patients diagnosed with malignancy after the initial CT examination, however, were included in the study cohort. We excluded six patients with an adrenal mass who had clinical suspicion of a functioning adrenal lesion, because these lesions are clinically significant and would warrant further management. Sixty-four patients who had known adrenal masses from previous imaging studies were excluded. In 502 (49.7%) of the remaining 1,010 patients, adenoma was diagnosed on the initial CT on the basis of the currently accepted CT threshold of 10 H, and these patients were excluded. One hundred thirteen patients were excluded because another specific imaging diagnosis, such as hematoma and myelolipoma, could be made on the initial CT on the basis of the currently accepted CT threshold of 10 H, and these patients were excluded adenoma diagnostic on unenhanced CT, adrenal CT with contrast washout, and chemical shift

Imaging Method and Analysis

The initial CT examinations were performed at two hospitals and at outpatient offices and included both chest and abdominal CT images. All studies were performed on a helical CT unit (HiSpeed CT6 [GE Healthcare]; 4-MDCT: LightSpeed [GE Healthcare] and Asteion [Toshiba Medical Systems]; 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 IV administration of 100 mL of low-osmolar contrast material at a collimation ranging from 3 to 7 mm, depending on the body part being imaged, scanner, and the year of the examination. Most of the chest CT examinations were performed as unenhanced studies. Contrast-enhanced chest CT was performed with IV administration of 100 mL of low-osmolar contrast material using routine protocol or as chest CT angiography (pulmonary embolism and aortic dissection protocol) with 120 mL of low-osmolar contrast material. For confirmatory imaging diagnosis, unenhanced CT, dedicated adrenal CT with contrast washout, or adrenal MRI with chemical shift imaging was performed.

Adrenal CT—For the 57 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 at 2.5 mm (multidetector) or 3 mm (single-detector) through the adrenal glands using an average field of view of 25–28 mm. An elliptic region of interest through the adrenal mass was obtained, and if it measured greater than 10 H, then 100 mL of nonionic contrast material was IV injected at 3 mL/s. Sections of the same thickness were then acquired through the adrenal glands at 60 seconds after contrast injection and then after a 10–15 minute delay using the same parameters [10].

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. Axial T1-weighted in-phase and opposed-phase 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 were a flip angle of 70–90°, a field of view of 350–360 mm, matrix of 127–192 × 256, slice thickness of 5–6 mm, intersection gap of 0–1 mm, and 1 signal acquisition. All studies included some type of T2-weighted sequence of variable technique.

Using the current imaging criteria, an adenoma was diagnosed when a lesion had an attenuation coefficient of ≤10 H on unenhanced CT, and absolute contrast washout of ≥52% at 10 minutes or 60% at 15 minutes on adrenal CT [13, 15]. For the chemical shift MR criteria, we used signal cancellation based on subjective analysis of signal dropout on opposed-phase imaging.

Clinical Follow-Up

Electronic medical charts were searched and reviewed for all subjects included in the study group. For the lesions without a specific histologic or imaging diagnosis, less than 1 year of imaging follow-up, or no imaging follow-up, clinical stability was evaluated [16, 17]. Clinical information was gathered from review of electronic medical records (n = 75) and telephone calls (n = 20) to the referring clinician of the patient specifically to determine whether malignancy was diagnosed after CT or whether there were any clinical findings suspicious for biochemically active adrenal lesions.
TABLE 1: Clinical Indications for CT in 290 Patients

<table>
<thead>
<tr>
<th>History</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>143</td>
</tr>
<tr>
<td>Abnormal findings on chest radiography</td>
<td>31</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>21</td>
</tr>
<tr>
<td>Suspected mass</td>
<td>19</td>
</tr>
<tr>
<td>Trauma</td>
<td>13</td>
</tr>
<tr>
<td>Chest pain</td>
<td>10</td>
</tr>
<tr>
<td>Flank pain or possible renal stone</td>
<td>12</td>
</tr>
<tr>
<td>Weight loss</td>
<td>9</td>
</tr>
<tr>
<td>Cough or shortness of breath</td>
<td>8</td>
</tr>
<tr>
<td>Abnormal liver function test or liver disease</td>
<td>6</td>
</tr>
<tr>
<td>Suspected abscess</td>
<td>5</td>
</tr>
<tr>
<td>Suspected bleed (nontrauma)</td>
<td>3</td>
</tr>
<tr>
<td>Hematuria or renal mass</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>290</td>
</tr>
</tbody>
</table>

Statistical Analysis

We calculated the 95% CI for the detection of malignancy using a Web program for calculating exact binomial and Poisson CIs from www.statpages.org [18].

Results

Two hundred ninety patients (196 women, 94 men) with 321 solid adrenal masses, including 31 bilateral lesions, met the final inclusion criteria and constituted the study group. The mean age of the patients was 64 years (range, 20–93 years). The initial CT examination was performed for a wide range of clinical indications (Table 1). Abdominal pain was the most common indication for abdominal CT, followed by abnormal chest radiography findings for chest CT. One hundred ninety-one masses were present on the left, and 130 masses were on the right. The average size of the adrenal masses was 2.1 cm (range, 0.5–6.0 cm). The 321 lesions were evaluated as follows: histologic diagnosis (n = 6), imaging follow-up (n = 274), or clinical follow-up (n = 41).

Of the six lesions with histologic diagnosis, three lesions were biopsied using CT guidance and three lesions were surgically removed. There were four adenomas (1.2%), two diagnosed from biopsy specimens and two surgically resected. One of the surgically resected adenomas was a 3-cm mass that did not meet the criteria of an adenoma on adrenal CT. The second lesion was an incidentally detected 1.4-cm adenoma subsequently found to be a functioning lesion with excess cortisol production, causing subclinical Cushing’s syndrome, on endocrine evaluation.

There were two (0.6%) clinically unsuspected pheochromocytomas, a 2.8-cm mass and a 3-cm mass, that did not fulfill the imaging criteria of adenoma on adrenal CT and chemical shift MRI, respectively. On further clinical investigation, both patients had elevated serum catecholamine levels. The first of these pheochromocytomas was surgically resected. The second was biopsied under CT guidance after α-blockade with phenoxybenzamine and was subsequently treated with radiofrequency ablation because the patient was a poor surgical candidate. Therefore, there were three (0.9%) clinically unsuspected, benign but clinically significant functioning masses discovered incidentally.

Two hundred seventy-four lesions had imaging follow-up. There were 203 lesions for which a specific benign diagnosis could be made and 71 lesions with at least 1 year of stability on imaging studies. Of the 203 diagnostic lesions, 198 (61.7%) were adenomas, three (0.9%) were hematomas occurring in the setting of trauma, and two (0.6%) were cysts. Most of the adenomas were diagnosed on unenhanced CT, with the remaining lesions by adrenal CT, chemical shift MRI, or a combination of these studies (Table 2). Seventy-one lesions had radiologic proof of stability of at least 1 year: 68 were followed with CT, two with MRI, and one with PET. The mean length of imaging follow-up on these lesions was 2.7 years (1–2 years, 24 lesions; > 2–3 years, 22 lesions; and > 3 years, 25 lesions). Five lesions that did not meet the criteria of adenoma on dedicated adrenal imaging were stable for at least 1 year and, therefore, were presumed to be benign on the basis of imaging stability. None of the lesions had increased in size on follow-up study.

Forty-one lesions without histologic diagnosis or adequate imaging follow-up had available clinical information of at least 2 years from the time of the initial study. The mean length of clinical follow-up was 3.3 years (2–3 years, 21 lesions; and > 3 years, 20 lesions). Two lesions that were not diagnostic of adenoma on dedicated adrenal imaging and six lesions with less than 1 year of imaging follow-up had clinical stability for more than 2 years and were presumed to be benign.

When 209 adrenal masses with histologic diagnosis or imaging characterization only were considered for the final diagnoses, there were 202 (96.7%) adenomas, three (1.4%) hematomas, two (1.0%) cysts, and two (1.0%) pheochromocytomas.

There was no malignant adrenal lesion in our study (95% CI: 0.0000–0.0093). Of the study population, 13 patients with a total of 14 adrenal masses subsequently developed malignancy elsewhere (five lung; three prostate; and one each breast, skin [melanoma], kidney, rectum, and head and neck). None of the adrenal lesions was a metastasis. Of these benign adrenal lesions, one was a histologically proven adenoma, seven were adenomas by imaging, and six lesions were presumed to be benign by imaging stability.

Discussion

With the increasing use of cross-sectional imaging, adrenal masses are frequently detected incidentally on CT. Most of these incidentalomas are benign adenomas in patients with no underlying malignancy or biochemical abnormalities. These are typically small, well-defined round or oval masses with homogeneous attenuation. If an incidental adrenal mass has suspicious imaging features including heterogeneity, irregular margins, or change in size, it should be further evaluated with imaging or histology. However, the management of benign-appearing incidental lesions is unclear and is the focus of this study. These “incidentalomas” then pose a dilemma for the radiologist and the referring clinician, frequently leading to patient anxiety and additional imaging studies when there is also increasing concern for economic impact of imaging on health care. This uncertainty is exemplified by a recent review article by

TABLE 2: 198 Indeterminate Adrenal Masses Diagnosed as Adenoma on Imaging

<table>
<thead>
<tr>
<th>Imaging Study</th>
<th>No. of Masses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unenhanced CT</td>
<td>121</td>
</tr>
<tr>
<td>Adrenal CT with washout</td>
<td>39</td>
</tr>
<tr>
<td>Chemical shift MRI</td>
<td>26</td>
</tr>
<tr>
<td>Unenhanced CT and adrenal CT with washout</td>
<td>5</td>
</tr>
<tr>
<td>Unenhanced CT and chemical shift MRI</td>
<td>3</td>
</tr>
<tr>
<td>Adrenal CT with washout and chemical shift MRI</td>
<td>2</td>
</tr>
<tr>
<td>Unenhanced CT, adrenal CT with washout, and chemical shift MRI</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>198</td>
</tr>
</tbody>
</table>

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Young [19] in the New England Journal of Medicine that recommended repeat imaging studies at 6, 12, and 24 months for a benign-appearing incidental adrenal lesion (≤10 HU on unenhanced CT or CT contrast washout of 50%), even though the author acknowledged that there are no data from large, long-term studies to support that recommendation. In a separate review, Copeland [20] advised that masses of more indeterminate nature that are not immediately resected should be followed at 3, 6, and 18 months. These adrenal lesions add to the growing list of serendipitous findings on imaging studies. The American College of Radiology states that extensive and costly workup is usually not justified for small—that is, < 3 cm—adrenal masses [21].

The recommendation for additional imaging to evaluate an adrenal mass is in part due to the recent success of imaging for diagnosing adenoma with high accuracy. Now, most benign adrenal lesions can be distinguished from metastasis based on noninvasive imaging using CT and MRI [13, 15, 22]. As a result, the number of adrenal masses requiring histologic diagnosis has declined recently [23]. In our study, only six (1.8%) lesions required histologic evaluation. There is little debate that imaging evaluation is crucial in oncologic patients presenting with an adrenal mass; however, there is little discussion in the recent literature about whether an adrenal incidentaloma in a patient at low risk for adrenal metastasis should require imaging confirmation of benignity.

In our study, none of the incidentally detected adrenal masses in patients without cancer were malignant. Thirteen patients with a total of 14 adrenal masses subsequently developed malignancy elsewhere, and none of these lesions was a metastasis. Similar findings were reported separately by Lee et al. [24] and Herrera et al. [16], where only 0.2% and 0.3% of incidental adrenal masses were the initial presentation of metastatic cancer. In those studies, the morphology of the masses was not analyzed, but these uncommon metastatic masses were reported to be large (≥ 6 cm and 5.5 cm, respectively). In addition, some of the patients were reported to be asymptomatic and have bilateral masses [24]. The reason for a somewhat higher incidence of metastasis of 4.1% reported by Gajraj and Young [25] is unclear, but it perhaps is related to different imaging practice and technique.

None of the incidental masses in our study was a primary adrenal cortical carcinoma, which is a rare malignancy. In a series of 210 patients with adrenal masses, Terzolo et al. [26] reported the prevalence of adrenal cortical carcinoma to be 13%. However, the average size of the adrenal mass in their study was 9.4 cm and the masses were inhomogeneous with irregular margins. As stated in their work, these findings are imaging features that are suspicious for malignancy and require histologic evaluation. In a multicenter series of 381 patients, Bülow et al. [27] reported a 4% incidence of malignancy including 10 patients with adrenal cortical carcinomas. However, their criteria for incidentaloma were broader than ours: 10% of their subjects had symptoms or signs of malignant disease, including three of the patients with cortical carcinoma. In addition, the mean size of the carcinoma was 10 cm and four of these 10 patients had elevated biochemical activity. Adrenal cortical carcinomas detected on CT are described to be large (4–17 cm) in studies with reported prevalence of 1.2–4.7% in incidentally detected adrenal masses [16, 25, 27]. The average adrenal mass size in our study was 2.1 cm, which is smaller than the studies described, and because none of the masses in our study were malignant, we could not assess for the size threshold for the risk of malignancy. The 6-cm mass, the largest in our study, typically would have been resected; however, instead it was followed up using CT with confirmed stability at 5 years. No lesion in our series had increased in size on follow-up imaging, although previous studies have observed mass enlargement of more than 1 cm over 1 year in approximately 5% of benign adenomas [28, 29].

There were three (0.9%) unsuspected functioning adrenal masses in our study: one cortisol-producing benign adenoma (0.3%) and two pheochromocytomas (0.6%). Subclinical hormone secretion by adrenal mass is well recognized, reported as high as 12% of cortisol-producing adenoma [20] and 9% of pheochromocytoma [26] among incidentalomas. Although most of the patients with incidentally found pheochromocytoma have a history of hypertension, pheochromocytomas can be clinically silent but are potentially lethal. In one autopsy series, 46% of patients with pheochromocytoma did not have a recorded history of hypertension [30]. The 0.9% incidence of unsuspected functioning adrenal mass in our study may be an underrepresentation because biochemical screening was not routinely performed in all patients.

This study has several limitations. Thirty-two patients were lost to follow-up and 66 patients had less than 12 months of imaging follow-up or less than 24 months of clinical follow-up and thus the outcomes of these patients are unknown. The second limitation is the lack of histology results as the gold standard for most of the cases. However, this reflects the shift in management of incidental adrenal masses and the acceptance of imaging diagnosis to be highly accurate. A third limitation is that, although imaging stability is well accepted and clinical stability has been used as evidence of a benign process, it is theoretically possible that a very early presentation of a small adrenal cortical carcinoma can be inaccurately diagnosed as a benign lesion using those two methods. However, that would be a rare exception for adrenal cortical carcinoma, which is a rare malignancy that can also be hormonally active. To minimize such outcome, we used conservative periods of 1 year for imaging follow-up and 2 years for clinical follow-up. A fourth limitation is that we could not address the relevance of the size to the risk of malignancy because there was no malignant mass in our study. Last, the functional status of adrenal masses was not routinely evaluated and may account for the less than 1% prevalence of incidental hyperfunctioning masses. However, the primary goal of our study was to determine the necessity of imaging evaluation, not of biochemical screening which is generally recommended.

In conclusion, the results of our study show that none of the incidentally detected adrenal masses was malignant in patients with no known cancer. If an incidental adrenal mass appears benign on imaging and the patient has no known malignancy, follow-up imaging appears to have a limited role. Further research with prospective studies and cost–benefit analyses would be useful to guide management of the incidentally discovered adrenal mass.

Acknowledgment

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References


Incidental Indeterminate Adrenal Mass on CT

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