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Clinical, Biochemical, and Radiological Characteristics of a Single-Center Retrospective Cohort of 705 Large Adrenal Tumors

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Abstract

Objective: To characterize large adrenal tumors (≥4 cm in diameter) and to identify features associated with malignancy.

Patients and Methods: We investigated the clinical, biochemical, and imaging characteristics in a large retrospective single-center cohort of patients with adrenal tumors of 4 cm or more in diameter during the period of January 1, 2000, through December 31, 2014.

Results: Of 4085 patients with adrenal tumors, 705 (17%) had adrenal masses measuring 4 cm or more in diameter; of these, 373 (53%) were women, with a median age of 59 years (range, 18-91 years) and median tumor size of 5.2 cm (range, 4.0-24.4 cm). Underlying diagnoses were adrenocortical adenomas (n=216 [31%]), pheochromocytomas (n=158 [22%]), other benign adrenal tumors (n=116 [16%]), adrenocortical carcinomas (n=88 [13%]), and other malignant tumors (n=127 [18%]). Compared with benign tumors, malignant tumors were less frequently diagnosed incidentally (45.5% vs 86.7%), were larger (7 cm [range, 4-24.4 cm] vs 5 cm [range, 4-20 cm]), and had higher unenhanced computed tomographic (CT) attenuation (34.5 Hounsfield units [HU] [range, 14.1-75.5 HU] vs 11.5 HU [range, −110 to 71.3 HU]; $P<.001$). On multivariate analysis, older age at diagnosis, male sex, nonincidental mode of discovery, larger tumor size, and higher unenhanced CT attenuation were all found to be statistically significant predictors of malignancy.

Conclusion: The prevalence of malignancy in patients with adrenal tumors of 4 cm or more in diameter was 31%. Older age, male sex, nonincidental mode of discovery, larger tumor size, and higher unenhanced CT attenuation were associated with an increased risk for malignancy. Clinical context should guide management in patients with adrenal tumors of 4 cm or more in diameter.

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Adrenal tumors are encountered in approximately 5% of patients undergoing cross-sectional imaging.[1-3] Prevalence varies with age, ranging from less than 0.5% in children[4,5] to 10% in elderly patients.[6-8] Most adrenal tumors are discovered incidentally on imaging performed for a reason other than suspected adrenal disease; however, at least 15% of patients with adrenal tumors present with signs and symptoms of adrenal hormonal excess.[9] In every patient with a newly discovered adrenal tumor, it is essential to determine whether the adrenal tumor is malignant and/or hormonally active.

Most incidentally discovered adrenal tumors are benign and nonfunctioning adrenocortical adenomas (ACAs).[9] Functional ACAs and pheochromocytomas (PHEOs) are diagnosed in 11% to 15% and 4% to 10% of patients with adrenal incidentalomas, respectively.[9] Malignant adrenal tumors (mainly adrenocortical carcinomas [ACCs]) are diagnosed in up to 11% of patients with adrenal incidentalomas.[7,9] However, in patients with an active extraadrenal malignancy, the likelihood of adrenal metastasis varies widely between 2% and 71% depending on the studied population, clinical presentation, and underlying malignancy.[10-13]

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The imaging characteristics of the adrenal mass are helpful in determining the risk of malignancy. The intracellular lipid content can be approximated by measuring Hounsfield units (HU) on unenhanced computed tomography (CT) and with the use of chemical shift magnetic resonance imaging. Lipid-rich adrenal tumors present with low unenhanced CT attenuation and positive chemical shift on magnetic resonance imaging and are consistent with ACAs. Because most incidentally discovered adrenal tumors are lipid-rich adenomas, guidelines[9,14-16] recommend unenhanced CT as the initial imaging study to exclude malignancy. An attenuation threshold of more than 10 HU has a sensitivity of 93% to 100%, but a specificity of only 71% to 72% for detecting a malignancy.[3] Thus, after imaging, a clinically significant proportion of adrenal tumors remain indeterminate for malignancy and require additional assessment. Additional imaging modalities are often used to further characterize adrenal masses, including CT with contrast administration to assess for absolute and relative contrast washout and [^{18}F]-fluorodeoxyglucose–positron emission tomography integrated with CT to assess for metabolic activity. However, evidence on the diagnostic accuracy of these imaging modalities is limited[3]; a recent publication by our group demonstrated that [^{18}F]-fluorodeoxyglucose–positron emission tomography integrated with CT adrenal liver ratio of more than 1.8 diagnosed malignancy with a sensitivity of 87% and specificity of 84%.[17] When imaging is inconclusive, various strategies may be considered including interval imaging to assess for tumor growth, adrenalectomy, and, in selected cases, adrenal biopsy.[3,9,18,19]

In patients with adrenal masses, the risk of malignancy is directly proportional to the size of the adrenal mass. Although several studies report sensitivities of 80% to 93%, a tumor size threshold of 4 cm is only 34% to 61% specific for the diagnosis of a malignant adrenal mass.[7,20,21] The natural history of patients with large adrenal tumors is not well studied and most evidence originates from surgical series.[7,21,22] Several guidelines recommend consideration of adrenalectomy for adrenal masses greater than 4 to 6 cm.[14-16] However, more recent guidelines on adrenal incidentalomas do not recommend an absolute size cutoff for adrenalectomy, but suggest an individualized approach with consideration of adrenalectomy in large tumors.[9] This equivocal recommendation reflects the paucity of data on the management and natural history of patients with large tumors. An alternative explanation for the lack of a consensus recommendation is that many variables tend to be considered when deciding on surgery, including HU attenuation on unenhanced CT, CT contrast washout behavior (if available), growth or stability on follow-up imaging, patient age, and comorbidities. Our objective was to improve the understanding of the characteristics of large adrenal tumors by retrospectively studying a large cohort of patients with adrenal tumors of 4 cm or more in diameter seen over a 15-year period, in order to identify features associated with malignancy.

PATIENTS AND METHODS

This was a retrospective cohort study performed at Mayo Clinic, Rochester, Minnesota, between January 1, 2000, and December 31, 2014. This study received approval from the Mayo Clinic Institutional Review Board and included only those patients who provided authorization for research. All electronic medical records of patients with adrenal tumors diagnosed during the study period were individually reviewed for inclusion criteria. Adult patients with adrenal tumor size of at least 4 cm in largest diameter were included in the study and detailed clinical, imaging, biochemical, and histopathologic data were collected. The functional status of adrenal tumors was obtained through medical record review. Overt hypercortisolism, primary hyperaldosteronism, and catecholamine excess were diagnosed on the basis of most recent guidelines.[23-25] Mild autonomous cortisol excess was defined as failure to suppress cortisol to less than or equal to 1.8 μg/dL (to convert to nmol/L, multiply by 27.59) after overnight dexamethasone administration (1 mg or 8 mg).[9]

We grouped all adrenal tumors into 5 main diagnostic categories, on the basis of histology for patients who underwent adrenalectomy and on the basis of cytology results if adrenal biopsy was performed. For patients in whom adrenalectomy or adrenal biopsy was not performed, we used information on clinical and radiological characteristics at presentation and follow-up to determine the final diagnosis.