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Prevalence and Characteristics of Adrenal Tumors in an Unselected Screening Population

A Cross-Sectional Study

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Background: With the widespread use of advanced imaging technology, adrenal tumors are increasingly being identified.

Objective: To investigate the prevalence and characteristics of adrenal tumors in an unselected screening population in China.

Design: Cross-sectional study. (ClinicalTrials.gov: NCT04682938)

Setting: A health examination center in China.

Patients: Adults having an annual checkup were invited to be screened for adrenal tumors by adrenal computed tomography.

Measurements: The participants with adrenal tumors had further evaluation for malignancy risk and adrenal function.

Results: A total of 25 356 participants were screened, 351 of whom were found to have adrenal tumors, for a prevalence of 1.4%. The prevalence increased with age, from 0.2% in participants aged 18 to 25 years to 3.2% in those older than 65 years. Among 351 participants with adrenal tumors, 337 were diagnosed with an adrenocortical adenoma, 14 with another benign nodule, and none with a malignant mass. In 212 participants with an adenoma who completed endocrine testing, 69.3% were diagnosed with a nonfunctioning adenoma, 18.9% with cortisol autonomy, 11.8% with primary aldosteronism, and none with pheochromocytoma. Proportions of nonfunctioning adenomas were similarly high in various age groups (72.2%, 67.8%, and 72.2% in those aged <46, 46 to 65, and ≥66 years, respectively).

Limitation: Only 212 of 337 participants with an adrenocortical adenoma had endocrine testing.

Conclusion: The prevalence of adrenal tumors in the general adult screening population is 1.4%, and most of these tumors are nonfunctioning regardless of patient age. Cortisol and aldosterone secretion are the main causes of functional adenomas.

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Adrenal incidentaloma refers to an incidentally found nodule, usually at least 1 cm in diameter, in a patient without apparent clinical signs of adrenal diseases (1). The detection rate of adrenal incidentalomas has increased greatly with the development and widespread use of advanced imaging technology. A recent study showed that the incidence of adrenal tumors has increased 10-fold in the past 20 years (2). A guideline from the European Society of Endocrinology and European Network for the Study of Adrenal Tumors recommends that all patients with an adrenal incidentaloma be assessed for malignancy risk and hormone secretion (1). Among adults, the prevalence of adrenal incidentalomas has been reported to be 0.4% to 7.3% (3–14), with 0% to 30% of these tumors reported to be malignant and 4.1% to 25% reported to cause hormone excess (5, 15–21). The prevalence varies greatly depending on patient selection and diagnostic methods.

Most published literature on the prevalence of adrenal incidentalomas consists of retrospective surveys based on radiographic diagnosis in a medical record system, which might under- or overestimate the prevalence (5, 7, 8, 14). Ebbehoj and colleagues (2) collected data on diagnosis of adrenal tumors from the medical records of a large cohort in Olmsted County, Minnesota. They reported that the sex- and age-standardized prevalence of adrenal tumors was 532 per 100 000 inhabitants (0.5%), whereas in residents who had computed tomography (CT) or magnetic resonance imaging (MRI) scans of the abdomen, 1.54% were diagnosed with an adrenal tumor. Several studies have prospectively investigated the prevalence of adrenal incidentalomas in referral centers. One reported a prevalence of 4.5% in 34 044 patients who had abdominal or chest CT; however, more than half of the patients enrolled had a history of extra-adrenal malignant tumors or were suspected of having malignant disease (6). Another study of 520 patients at high risk for lung cancer reported a prevalence of 4.4% (4). Reimondo and colleagues (12) studied 601 outpatients who had abdominal CT for various reasons (such

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as abdominal pain), and they found that 7.3% had an adrenal tumor found incidentally. The selection bias for patients who had a pathologic reason for having abdominal imaging in these studies might have led to overestimation of the prevalence of adrenal tumors and distorted the data on the causes of incidentalomas (15–17). There is currently a lack of epidemiologic data on the prevalence of adrenal tumors and the frequencies of malignant adrenal tumors and hormone excess in unselected community populations that did not have any indications for abdominal imaging.

We investigated the prevalence and characteristics of adrenal tumors in a large population of persons undergoing routine health checks in China.

METHODS

Study Participants

This study was done in the community health examination center of the First Affiliated Hospital of Chongqing Medical University (ClinicalTrials.gov: NCT04682938). This health examination center is one of the largest in Southwest China; it provides health checks for 26 districts and 12 counties in Chongqing, completing health checks for 150 000 to 180 000 residents per year. These health checks are funded by employment benefits (about 40%), government funding (about 30%), and self-payment (about 30%). People generally attend the center for annual health checks. For residents with acute diseases, including active cancer, the center staff recommend testing in the outpatient department rather than the health examination center. On weekdays from November 2020 to November 2021, the first 100 patients aged 18 to 78 years undergoing health checks in the community health examination center were invited to take part in this study and have adrenal imaging. Exclusion criteria were known adrenal diseases, continuous use of steroids or drug treatment that might influence cortisol secretion or dexamethasone metabolism and could not be stopped, and refusal to participate in the study. This study was approved by the Human Research Ethics Committee of Chongqing Medical University, and each participant provided written informed consent.

CT Scan and Screening of Adrenal Tumors

Unenhanced CT scans of the adrenal glands were done on a 64-slice multidetector CT scanner (SOMATOM Force VA50A, Siemens). Images were reconstructed with a slice thickness of 1 mm. Two radiologists independently screened the CT images for adrenal tumors. The characteristics of all adrenal tumors were recorded, including number, size, attenuation, and other specific features (such as hemorrhage, necrosis, and calcification). When multiple nodules were present, we used only the characteristics of the largest for analysis. Diagnosis of adrenal tumors was based on the detection of adrenal nodules (diameter ≥1 cm) on CT scans. The 2 radiologists further discussed any discordance to reach an agreement on the final diagnosis. We applied diagnostic criteria for malignant and benign adrenal tumors based on guidelines (Supplement Table 1, available at Annals.org). Participants whose tumors had imaging characteristics suggestive of malignancy had an enhanced CT or MRI scan or a positron emission tomography CT scan with fluorodeoxyglucose. To verify the imaging diagnosis, those whose adrenal tumors had an attenuation value on unenhanced CT of more than 10 Hounsfield units (HU) were required to repeat the adrenal CT scan after 6 to 12 months.

Functional Assessment of Adrenal Tumors

Participants with adrenal tumors, except those with typical imaging features of myelolipoma (Supplement Table 1), were required to complete hormonal testing. The methods are described in detail in Supplement Table 2 (available at Annals.org) and in brief in the following paragraphs.

First, we assessed aldosterone secretion (22). Aldosterone–renin ratio was measured to screen for primary aldosteronism. Patients receiving antihypertensive drug treatment, which can interfere with the aldosterone–renin ratio, either stopped or switched to α-blockers or nondihydropyridine calcium antagonists for 2 to 4 weeks before screening. If the screening result was positive, the captopril challenge test was done. For participants with inconclusive captopril challenge test results, a seated saline infusion test was done to further confirm the diagnosis. For those diagnosed with primary aldosteronism, adrenal vein sampling was usually recommended. The subtype diagnosis was based on a comprehensive analysis of the results of adrenal vein sampling (23, 24), consensus criteria from the Primary Aldosteronism Surgery Outcome study (25), and prediction scores for bilateral adrenal hyperplasia (26).

Second, we assessed cortisol secretion (1). Plasma cortisol and adrenocorticotropic hormone (ACTH) were measured at 8 a.m. and a 1-mg dexamethasone suppression test (1mg-DST) was done. We defined cortisol autonomy as failure to suppress morning serum cortisol concentration to less than 50 nmol/L after the 1mg-DST in the absence of clinical features indicative of Cushing syndrome. Patients with cortisol autonomy were further subdivided into those with autonomous cortisol secretion (ACS) (serum cortisol after the 1mg-DST >138 nmol/L) and those with mild ACS (serum cortisol after the 1mg-DST, 50 to 138 nmol/L) (27). For participants with suspected primary adrenal insufficiency, an ACTH stimulation test was done.

Third, we assessed androgen secretion (28). We assayed 6 adrenal androgen hormones (androstenedione, dehydroepiandrosterone sulfate, 17-hydroxypregnenolone, 17-hydroxyprogesterone, progesterone, and testosterone), which were included in a panel of 16 adrenal steroid hormones (Supplement Table 3, available at Annals.org). Participants with androgen abnormalities (such as elevated levels of 17-hydroxyprogesterone) were required to complete further evaluation.

Last, we measured plasma catecholamines (1), including metanephrine and normetanephrine.

Anthropometric, Biochemical, and Hormonal Measurements

Staff recorded anthropometric data for each participant, including height, weight, waist circumference, and

blood pressure. For biochemical measurements, fasting blood samples were obtained. An automated chemiluminescence immunoassay was used to measure plasma concentrations of aldosterone, renin (LIAISON, DiaSorin), cortisol, and ACTH (DxI 800, Beckman Coulter). High-performance liquid chromatography with electrochemical detection was used to measure metanephrine and normetanephrine (Waters). Liquid chromatography–tandem mass spectrometry was used for the simultaneous quantification of 16 steroids (Supplement Table 3).

Statistical Analysis

We present data as means and SDs or, in case of very skewed distributions, as medians and IQRs. Categorical variables are presented as proportions. The generalized linear model was used to calculate marginally adjusted means and 95% CIs for each hormonal measurement. All models were adjusted for age, sex, and body mass index. Variables were log-transformed in the model in case of very skewed distributions.

Missing data were imputed using multiple imputation by chained equations (https://amices.org/mice). Regression models were used to predict the missing values. Supplement Table 4 (available at Annals.org) provides detailed information on the missing covariates.

All analyses were done using R, version 4.0.1 (R Project for Statistical Computing).

Role of the Funding Source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Characteristics of the Study Population

During the study period, 28 046 persons were invited to participate; 2644 declined, 45 were excluded for known adrenal disease, and 1 was excluded for continuous steroid treatment. A total of 25 356 participants were enrolled for adrenal imaging, and 351 were found to have adrenal tumors (Figure 1). Supplement Table 6 (available at Annals.org) shows the regional distribution of participants and the funding sources for their health checks. The average age of the participants was 48 years, and women accounted for 50.2% of the cohort (Table 1). Participants with adrenal tumors were on average older and had higher blood pressure and a higher fasting blood glucose level than participants without adrenal tumors (Table 1). Five participants (1.4%) with adrenal tumors had a history of extra-adrenal cancer, including 3 with lung cancer, 1 with breast cancer, and 1 with thyroid papillary carcinoma. They had been continuously monitored for at least 3 years, and the cancer was in remission.

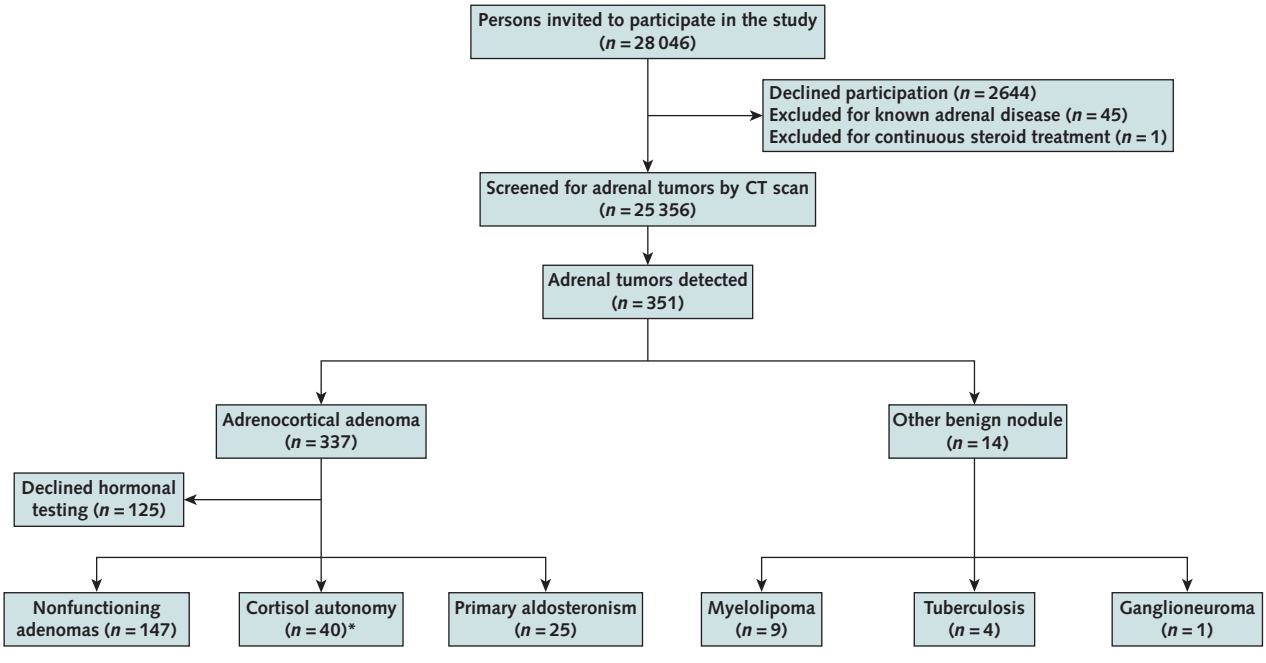
Prevalence of Adrenal Tumors

The prevalence of adrenal tumors was 1.4% (95% CI, 1.2% to 1.5%), and it was higher in men (1.6% [CI, 1.3% to 1.8%]) than women (1.2% [CI, 1.0% to 1.4%]). The prevalence of adrenal tumors increased with age in both men and women (Figure 2).

Characteristics and Causes of Adrenal Tumors

For the detected adrenal tumors, the median diameter of the nodules was 15 mm (range, 10 to 45 mm) (Figure 3). Only 2 tumors had a diameter of 40 mm or

Figure 1. Study flow diagram.



CT = computed tomography.
* Included participants with autonomous cortisol secretion (ACS) (*n* = 7) and participants with mild ACS (*n* = 33).

Table 1. Baseline Characteristics of the Study Population

Characteristic	Total (*n* = 25 356)	With Adrenal Tumors (*n* = 351)	Without Adrenal Tumors (*n* = 25 005)	Standardized Mean Difference
Mean age (SD), *y*	48.0 (12.7)	56.3 (11.1)	47.8 (12.7)	0.71
Women, *n (%)*	12 730 (50.2)	152 (43.3)	12 578 (50.3)	0.14
Mean BMI (SD), kg/m2	23.6 (3.1)	24.6 (3.0)	23.5 (3.1)	0.35
Mean waist circumference (SD), *cm*	81.7 (10.0)	85.4 (9.8)	81.7 (9.9)	0.38
Mean SBP (SD), *mm Hg*	124 (18.2)	130 (18.3)	123 (18.2)	0.34
Mean DBP (SD), *mm Hg*	76.0 (11.3)	80.0 (11.1)	75.9 (11.3)	0.37
Median fasting blood glucose level (IQR)				0.33
mmol/L	5.3 (5.0–5.7)	5.5 (5.2–6.2)	5.3 (5.0–5.7)	
mg/dL	95.5 (90.1–102.7)	99.1 (93.7–111.7)	95.5 (90.1–102.7)	
Median total cholesterol level (IQR)				0.07
mmol/L	4.9 (4.3–5.6)	5.0 (4.4–5.6)	4.9 (4.3–5.6)	
mg/dL	189.2 (166.0–216.2)	193.1 (169.9–216.2)	189.2 (166.0–216.2)	
Median triglyceride level (IQR)				0.17
mmol/L	1.3 (0.9–1.9)	1.5 (1.1–2.2)	1.3 (0.9–1.9)	
mg/dL	115.0 (79.7–168.1)	132.7 (97.4–194.7)	115.0 (79.7–168.1)	
Mean HDL-C level (SD)				0.12
mmol/L	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	
mg/dL	54.1 (15.4)	54.1 (15.4)	54.1 (15.4)	
Mean LDL-C level (SD)				0.08
mmol/L	3.1 (0.9)	3.1 (1.0)	3.1 (0.9)	
mg/dL	119.7 (34.8)	119.7 (38.6)	119.7 (34.8)	
History of hypertension, *n (%)*	9503 (37.5)	133 (37.8)	9370 (37.5)	0.01
History of diabetes, *n (%)*	2999 (11.8)	48 (13.7)	2951 (11.8)	0.06
History of cancer, *n (%)*	405 (1.6)	5 (1.4)	400 (1.6)	0.01

BMI = body mass index; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure.

greater. Among the adrenal tumors, 62.4% (*n* = 219) and 28.5% (*n* = 100) were localized on the left and right, respectively, and 9.1% (*n* = 32) were bilateral.

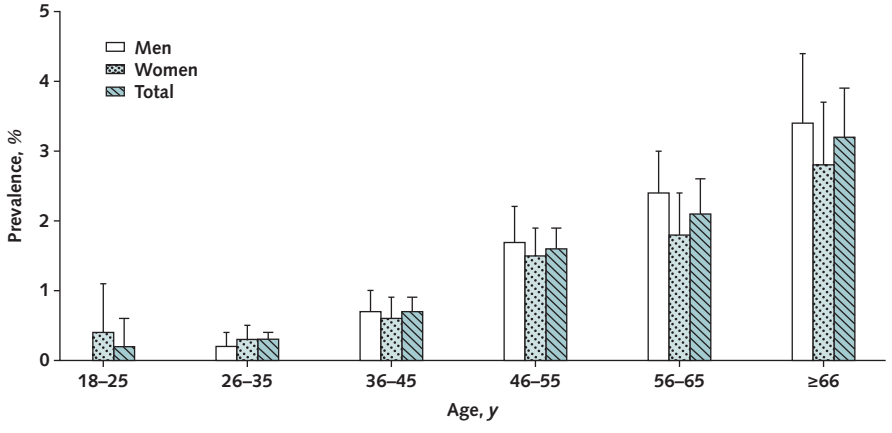
Among 150 adrenal tumors of less than 10 HU on unenhanced CT, 9 were diagnosed as myelolipomas (ranging from −30 to −90 HU, with diameter 13 to 40 mm) and the other 141 were radiologically considered "benign adenomas" (with diameter 10 to 36 mm). In 201 participants with adrenal tumors of more than 10 HU on unenhanced CT (ranging from 11 to 52 HU), 4 were diagnosed with tuberculosis with adrenal insufficiency, 1 (with a tumor diameter of 45 mm and attenuation value of 40 HU on unenhanced CT) had negative results on ^{131}I-metaiodobenzylguanidine scintigraphy and was diagnosed with ganglioneuroma on the basis of histopathology after adrenalectomy, 105 repeated the adrenal CT scan during the 6 to 12 months of follow-up, and none showed tumor growth (<20% of the largest tumor diameter). Of these 201 participants, 47 with tumors of more than 20 HU (ranging from 21 to 42 HU, with diameter 10 to 31 mm) further completed enhanced CT or MRI scans, but the tumors did not show signs of pheochromocytoma or malignancy. The remaining 44 participants had tumors smaller than 4 cm measuring 10 to 20 HU.

In total, 337 participants had a radiologically diagnosed "adrenocortical adenoma," of whom 212 completed functional assessment and 125 declined or did not complete the assessment (**Figure 1**). Participants who did not complete the functional assessment were older and had higher systolic blood pressure than those who completed the functional assessment, whereas other characteristics, including sex, body mass index, diastolic blood pressure, fasting blood glucose level, serum lipid levels, and tumor size, were similar between the groups (**Supplement Table 7**, available at Annals.org). Of the 212 participants who completed functional assessment, nonfunctioning adenomas accounted for 69.3% (*n* = 147) and adrenal tumors with steroid hormone secretion for 30.7% (*n* = 65), including 40 (18.9%) with cortisol autonomy (7 with ACS; 33 with mild ACS) and 25 (11.8%) with primary aldosteronism. No participants had classic pheochromocytoma symptoms or elevated levels of catecholamine metabolites. The proportions of nonfunctioning adenomas among the adrenocortical adenomas were similarly high in various age groups (72.2%, 67.8%, and 72.2% in those aged <46, 46 to 65, and ≥66 years, respectively).

Compared with participants with nonfunctioning adenomas, those with primary aldosteronism had a higher blood pressure, plasma aldosterone level, aldosterone–renin ratio, and 18-oxocortisol level and a lower concentration of plasma renin (**Tables 2** and **3**; **Supplement Table 8**, available at Annals.org). Serum potassium concentration was similar between these 2 groups; only 3 participants with primary aldosteronism had a history of hypokalemia. Of the 25 participants diagnosed with primary aldosteronism, 3 were diagnosed with an aldosterone-producing adenoma, 17 with bilateral adrenal hyperplasia, and 5 with an indeterminate subtype.

Compared with participants with nonfunctioning adenomas, the group with cortisol autonomy had higher levels of cortisol after the 1mg-DST and lower levels of ACTH and adrenal androgens (dehydroepiandrosterone sulfate, 17-hydroxyprogesterone, 17-hydroxypregnenolone, and androstenedione). Metabolic variables—including body mass index, blood pressure, and levels of blood glucose, serum lipids, and other steroid hormones—

Figure 2. The prevalence of adrenal tumors in various age subgroups.



Prevalence, *n*/*N* (%)						
Men	0/212 (0)	4/1859 (0.22)	20/2846 (0.70)	67/3842 (1.74)	60/2475 (2.42)	48/1392 (3.45)
Women	1/272 (0.37)	9/2712 (0.33)	18/2882 (0.62)	51/3496 (1.46)	37/2101 (1.76)	36/1267 (2.84)
Total	1/484 (0.21)	13/4571 (0.28)	38/5728 (0.66)	118/7338 (1.61)	97/4576 (2.12)	84/2659 (3.16)

T bars indicate 95% CIs.

were not obviously different between the groups (Tables 2 and 3; Supplement Table 8).

Four participants with nonfunctioning adenomas (tumor diameter, 30 to 40 mm) and 2 who did not complete functional assessment (tumor diameter, 10 to 20 mm) requested surgery, which confirmed their adrenocortical adenoma on histopathology. Three participants with primary aldosteronism had adrenalectomy, which led to complete biochemical and clinical cure. Two participants with ACS, who had unequivocal glucocorticoid excess (that is, suppressed dehydroepiandrosterone sulfate and ACTH and a cortisol level >138 nmol/L after 1mg-DST) and unilateral adrenal adenomas larger than 30 mm, had adrenalectomy. One was receiving a glucocorticoid replacement 6 months postoperatively, whereas the other had normalization of her 1mg-DST after surgery.

Discussion

In our cross-sectional study, we found that the prevalence of adrenal tumors was 1.4% in an unselected community population in China. Nonfunctioning adenomas accounted for approximately 70% of the adrenal tumors regardless of age. Of the functional adenomas, autonomous cortisol and aldosterone secretion adenomas were the most common. In this study, no malignant tumors or pheochromocytomas were found, again confirming that these are extremely rare causes of adrenal tumors in an unselected adult population.

Previously reported prevalence rates of adrenal tumors have varied from 0.4% to 7.3% depending on the study population and diagnostic methods (3–14). In studies that enrolled older participants with more comorbid conditions (4, 13) and those based on the prospective evaluation of adrenal images by radiologists with a specific interest in adrenal tumors (4, 6, 12), the prevalence was higher (4.4% to 7.3%). In contrast, older studies that used lower-resolution scanners (3) and retrospective studies where the diagnoses were based on CT reports (5, 7, 8, 14) found lower prevalence (0.4% to 1.86%). Epidemiologic data on the prevalence of adrenal tumors in community populations are scarce. Davenport and colleagues (8) reviewed data from a National Health Service foundation trust that encompassed 9 district general or community hospitals; they identified 75 patients with adrenal tumors from 4028 CT scans, giving a prevalence of 1.86%. However, 46.7% of the patients with adrenal tumors had cancer in another organ, which was the indication for their CT scan, reflecting a significant selection bias. In a recent study, Ebbehoj and colleagues (2) retrospectively collected data on patients diagnosed with adrenal masses from the medical records of the entire population of Olmsted County and reported that the sex- and age-standardized prevalence of adrenal

Figure 3. The size distribution of adrenal tumors.

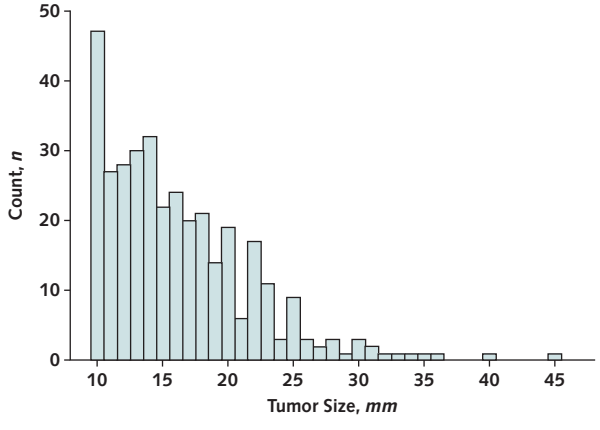


Table 2. Characteristics of Participants With and Without Autonomous Steroid Hormone Secretion

Characteristic	Nonfunctioning Adenoma (*n* = 147)	Cortisol Autonomy (*n* = 40)*	Primary Aldosteronism (*n* = 25)†
General characteristics			
Mean age (SD), *y*	54.6 (10.1)	54.6 (10.2)	55.7 (9.7)
Women, *n (%)*	60 (40.8)	17 (42.5)	13 (52.0)
Mean BMI (SD), kg/m^2	24.8 (3.0)	23.7 (2.5)	25.7 (2.6)
Mean waist circumference (SD), *cm*	85.3 (9.3)	82.6 (10.0)	87.5 (9.0)
Mean SBP (SD), *mm Hg*	127 (16.6)	126 (18.8)	139 (20.0)
Mean DBP (SD), *mm Hg*	80.3 (11.0)	78.1 (9.3)	86.3 (12.5)
Median total cholesterol level (IQR)			
mmol/L	5.0 (4.5–5.6)	5.0 (4.4–5.6)	5.0 (4.2–5.6)
mg/dL	193.1 (173.8–216.2)	193.1 (169.9–216.2)	193.1 (162.2–216.2)
Median triglyceride level (IQR)			
mmol/L	1.5 (1.1–2.3)	1.6 (1.1–1.9)	1.5 (1.3–2.1)
mg/dL	132.7 (97.4–203.5)	141.6 (97.4–168.1)	132.7 (115.0–185.8)
Mean HDL-C level (SD)			
mmol/L	1.4 (0.5)	1.4 (0.4)	1.3 (0.3)
mg/dL	54.1 (19.3)	54.1 (15.4)	50.2 (11.6)
Mean LDL-C level (SD)			
mmol/L	3.2 (0.9)	3.0 (1.1)	3.0 (0.9)
mg/dL	123.6 (34.8)	115.8 (42.5)	115.8 (34.8)
Mean creatinine level (SD)			
μmol/L	68.7 (13.4)	69.4 (15.1)	68.6 (16.0)
mg/dL	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)
Median fasting blood glucose level (IQR)			
mmol/L	5.5 (5.2–6.3)	5.5 (5.2–6.2)	5.7 (5.5–6.5)
mg/dL	99.1 (93.7–113.5)	99.1 (93.7–111.7)	102.7 (99.1–117.1)
Median hemoglobin A_{1c} (IQR), %	5.7 (5.4–6.0)	5.7 (5.5–6.0)	5.8 (5.5–6.4)
Mean serum potassium level (SD), *mmol/L*	4.3 (0.3)	4.2 (0.4)	4.1 (0.6)
Mean serum sodium level (SD), *mmol/L*	142 (1.8)	142 (1.9)	143 (2.1)
Imaging characteristics			
Left, *n (%)*	96 (65.3)	22 (55.0)	13 (52.0)
Right, *n (%)*	39 (26.5)	13 (32.5)	7 (28.0)
Bilateral, *n (%)*	12 (8.2)	5 (12.5)	5 (20.0)
Median tumor size (IQR), *mm*‡	15.0 (11.0–19.0)	16.5 (14.0–21.0)	14.0 (11.5–18.0)
Mean unenhanced CT attenuation (SD), *HU*§	12.2 (15.2)	16.3 (13.1)	11.3 (13.9)
Symptoms of hormone excess			
Hypertension, *n (%)*	47 (32.0)	16 (40.0)	19 (76.0)
Hypokalemia, *n (%)*	1 (0.7)	0 (0)	3 (12.0)
Cushing signs, *n (%)*‖	0 (0)	0 (0)	0 (0)
Diabetes, *n (%)*	15 (10.2)	7 (17.5)	7 (28.0)

BMI = body mass index; CT = computed tomography; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein cholesterol; HU = Hounsfield units; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure.
* Included participants with autonomous cortisol secretion (*n* = 7) and participants with mild autonomous cortisol secretion (*n* = 33).
† Four patients with primary aldosteronism had concomitant cortisol autonomy.
‡ Largest diameter shown (if >1 tumor).
§ Measured in homogeneous tumors only. Highest unenhanced CT attenuation HU value shown (if >1 tumor).
‖ Purple striae, proximal muscle weakness, easy bruising, plethora, round face, and dorsal fat pad.

tumors was 532 per 100 000 inhabitants. However, in residents who had CT or MRI scans of the abdomen, 1.54 patients (CI, 1.46 to 1.63 patients) per 100 residents were diagnosed with an adrenal tumor. This prevalence was similar to that in our study. Some evidence suggests that adrenal lesions may be underreported in clinical practice because of older age and concomitant cancer or other diseases that shifted the radiologist's focus to other pathology. Hammarstedt and colleagues (6) estimated the prevalence of incidentally detected adrenal lesions from the radiology departments of all hospitals in Western Sweden (1.66 million inhabitants). A total of 34 044 CT examinations were done during the study period, and the mean frequency of originally reported adrenal lesions was only 0.9%; however, when 3801 randomly selected cases were reevaluated, the frequency increased to 4.5% (6). Underreporting is not an issue in our study because imaging was intentionally done to screen for adrenal adenomas.

The mean diameter of adrenal tumors in this study was 15 mm, which is smaller than in many previous studies (15–21). This may be due to intentional and careful assessment of adrenal tumors by radiologists leading to more smaller tumors being detected. As for the causes of adrenal tumors, in accordance with previous reports, we found that nonfunctioning adenomas ranked first, whereas cortisol autonomy was the most common adrenal dysfunction (17–19, 21). Of note, mild ACS accounted for most cortisol autonomy. In addition to cortisol autonomy, autonomous aldosterone secretion was also common in our study. The prevalence of primary aldosteronism in various studies depends on whether strict or lax criteria for

diagnosis were chosen. In our study, primary aldosteronism was diagnosed according to a published protocol using rigorous methods, including the withdrawal of interfering medications (29). In contrast to autonomous cortisol and aldosterone secretion, the prevalence of malignant tumors and pheochromocytomas in our study was much lower than in previous studies (16, 18, 19). This might be attributed to our generally healthy community population comprising people who had minimal acute diseases, such as cancer. Previous studies have shown that increased attenuation on unenhanced CT (>20 HU) is one of the typical imaging features of pheochromocytomas and that tumor size less than 4 cm plus attenuation on unenhanced CT less than 20 HU suggests a reassuringly low rate of malignancy (30). In our study, all tumors with attenuation less than 10 HU on unenhanced CT (except 9 myelolipomas, which were all less than −30 HU and therefore easily distinguishable) were diagnosed as benign adenomas. Thus, in adrenal tumors with typical imaging characteristics of an adenoma (attenuation <10 HU on unenhanced CT), the likelihood of a pheochromocytoma is extremely low, and it seems reasonable to not measure metanephrine in such patients.

Among the patients who completed functional assessment, we found that the proportions of nonfunctioning adenomas were similarly high in various age groups. Even in those younger than 46 years, 72.2% of adrenal tumors were nonfunctioning. In previous studies, patients with a functional adrenal tumor were reported to be younger than those with a nonfunctioning adrenal tumor (19, 31) and the risk for functional tumors increased in patients younger than 45 years (32). In clinical practice, the evaluation of adrenal function may be more comprehensive in young patients than in elderly patients, such that functional tumors might have a higher chance of being detected in younger patients. Retrospective studies choosing patients who completed functional tests may lead to an overestimation of the rate of functional tumors in younger patients. Our prospectively collected data indicate that nonfunctioning adenomas are common regardless of age. One caveat in our study is that although the majority (63% [16 of 26]) of participants younger than 40 years had detailed functional testing, as did those older than 40 years (62% [196 of 311]), participants who did not complete functional assessment were older and had higher systolic blood pressure. Although those not tested may exhibit a similar secretory pattern to those tested, this remains unknown.

Some studies have reported a spectrum of changes in steroid hormone production in people with functional adenomas (22, 33, 34). Compared with patients with nonfunctioning adenomas, those with cortisol autonomy showed lower basal levels of dehydroepiandrosterone and androstenedione, whereas 18-oxocortisol measurements in patients with primary aldosteronism were higher (33, 34); these data were similar to ours. Recent studies have suggested that steroid hormone profiling may help classify adrenal tumors in a 1-step diagnostic approach (35). However, given the small number of participants with functional adenomas in our study, we did not analyze the diagnostic accuracy of the steroid hormone panel for either autonomous cortisol or aldosterone secretion. The role of steroid hormone profiling needs to be further investigated in larger studies.

The strength of this study lies in its relatively large sample size, unselected population, and strict diagnostic protocol. It is the first study to our knowledge to systematically evaluate the prevalence, cause, and characteristics of adrenal tumors in an unselected adult population. Our cohort was drawn from the community rather than hospitalized patients or radiologic series, which minimized selection bias. We tested a wide spectrum of adrenal hormones, and the diagnosis was confirmed after

Table 3. Concentration of a Range of Steroid Hormones in Participants With and Without Autonomous Steroid Hormone Secretion*

Hormone	Nonfunctioning Adenoma (*n* = 147)	Cortisol Autonomy (*n* = 40)†	Primary Aldosteronism (*n* = 25)‡
Plasma aldosterone concentration, *pmol/L*	266.3 (246.9–288.5)	296.8 (255.2–335.7)	507.6 (457.7–557.6)
Plasma renin concentration, *μIU/mL*§‖	14.9 (13.0–18.4)	10.6 (7.5–14.9)	5.3 (3.5–8.0)
Aldosterone–renin ratio, *pmol/L/μIU/mL*$^{-1}$§‖	18.4 (14.9–22.6)	29.9 (21.1–42.2)	147.0 (97.0–222.9)
Plasma aldosterone concentration after captopril challenge test, *pmol/L*	163.7 (152.6–177.5)	172.0 (147.0–197.0)	349.5 (316.2–380.0)
Cortisol level, *nmol/L*	362.6 (342.1–383.0)	385.2 (345.67–424.6)	362.6 (313.2–412.0)
ACTH level, *pmol/L*	7.3 (6.7–7.8)	6.1 (5.0–7.2)	6.7 (5.4–8.1)
1mg-DST, *nmol/L*§	29.9 (27.9–32.0)	90.5 (78.8–97.0)	36.8 (32.0–42.2)
Dehydroepiandrosterone sulfate level, *μmol/L*§	0.31 (0.28–0.35)	0.20 (0.16–0.25)	0.29 (0.22–0.38)
17-hydroxyprogesterone, *ng/mL*	1.6 (1.5–1.8)	1.4 (1.0–1.7)	1.6 (1.2–2.0)
17-hydroxypregnenolone, *ng/mL*§	2.2 (2.0–2.5)	1.6 (1.3–1.9)	2.3 (1.8–3.0)
Androstenedione level, *nmol/L*	3.6 (3.4–3.9)	2.8 (2.3–3.3)	3.6 (3.0–4.2)
Progesterone level, *nmol/L*§	2.5 (2.1–3.1)	2.3 (1.6–3.3)	3.3 (2.1–5.2)
Testosterone level, *nmol/L*	0.09 (0.08–0.10)	0.07 (0.05–0.09)	0.09 (0.06–0.11)
Metanephrine level, *ng/L*	106.1 (104.0–108.1)	106.2 (102.3–110.0)	105.1 (100.2–110.0)
Normetanephrine level, *ng/L*	101.7 (98.4–105.0)	101.1 (94.8–107.3)	105.3 (97.3–113.2)

1mg-DST = 1-mg dexamethasone suppression test; ACTH = adrenocorticotropic hormone.
* Values are marginally adjusted means (95% CIs) calculated using a generalized linear model (adjusted for age, sex, and body mass index).
† Included participants with autonomous cortisol secretion (*n* = 7) and participants with mild autonomous cortisol secretion (*n* = 33).
‡ Four patients with primary aldosteronism had concomitant cortisol autonomy.
§ The log-transformed variables were analyzed in the model.
‖ To convert μIU/mL to pmol/L, multiply by 0.037.

surgery or by repeated CT scanning during 6 to 12 months of follow-up.

Our study has several limitations. A significant drawback is that only 212 of 337 participants with an adrenocortical adenoma were assessed for function because of a high rate of refusal of hormonal assessment. Participants enrolled in our study were those who came for regular health checkups, usually with no symptoms of discomfort, whereas hormonal assessment required them to attend the hospital at least twice for blood draws in a short period of time—presumably the main reason for declining further testing. Our data showed that participants who did not complete functional testing were older and had higher systolic blood pressure; therefore, they could have had a higher rate of functional adrenal tumors. The reported prevalence of functional adenomas in our study should therefore be interpreted with caution. In addition, the study was done in a homogenous Chinese population, and characteristics of adrenal tumors might be different in other ethnic groups. Last, because adenomas were mainly diagnosed on the basis of unenhanced CT, a few cysts may have been misdiagnosed as adenomas.

In conclusion, the prevalence of adrenal tumors in the adult population is 1.4%. Nonfunctioning adenomas account for most of the adrenal tumors in both young and old people. Autonomous cortisol and aldosterone secretion are the main forms of adrenal dysfunction in people with incidentally found adrenal tumors.

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