

Predicting Functional Status in Adrenal Adenomas: The Role of Radiological Findings

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Abstract

Aim: The increasing use of imaging modalities has led to a higher detection rate of adrenal incidentalomas. Surgical treatment is recommended for hormonally active (functional) lesions and for non-functional lesions larger than 4 cm due to the risk of malignancy. Determining the functional status of adrenal masses generally requires multiple hormonal tests, which may prolong hospitalization and increase healthcare costs. In this study, we aimed to evaluate whether radiological parameters could help predict the functional adrenal adenomas. **Materials and Methods:** This retrospective study included 60 patients who underwent adrenalectomy between January 2017 and December 2023. Demographic characteristics, clinical findings, hormonal evaluation results, and radiological parameters were analyzed. Computed tomography measurements included the lateral and medial limb lengths and the density of the contralateral adrenal gland. Patients were divided into two groups according to the functional status of their adrenal masses. **Results:** Among the 60 patients, 65% (n=39) were female, and the mean age was 51.5±13.2 years. Functional adrenal tumors were identified in 70% (n=42) of patients. Most surgeries were performed laparoscopically (n=47), with conversion to open surgery in three cases. When the groups were compared according to the functional status of the mass, no significant differences were found in terms of age, sex, tumor localization, contralateral adrenal gland limb lengths, or adrenal density (p>0.05). However, the adrenal gland volume on the tumor side was significantly smaller in patients with functional tumors compared to those with non-functional tumors (p=0.007). **Conclusion:** Radiological parameters alone do not appear to be sufficient for reliably differentiating the functional status of adrenal adenomas. Hormonal evaluation remains essential in determining the functional status of adrenal masses. Larger prospective studies are needed to clarify the potential diagnostic value of radiological findings.

Keywords: Adrenal incidentaloma; Adrenalectomy; Computed tomography

1. Introduction

The adrenal glands are organs located superior to the kidneys and consist of the cortex and medulla. The cortex produces glucocorticoids, mineralocorticoids, and androgens, while the medulla produces catecholamines. The adrenal glands play an important role in metabolic and cardiovascular homeostasis.

Adrenal masses are observed in 3–7% of adults¹. Incidentally detected adrenal masses are referred to as adrenal incidentalomas (AIs). With the advancement of imaging modalities, the prevalence of adrenal incidentalomas has increased. One of the most important considerations in the management of these lesions is the risk of malignancy, while another is determining whether the lesion is hormonally active².

In AIs, adrenalectomy is recommended for functional tumors (those associated with excess cortisol, aldosterone, or catecholamines). Masses suspected of malignancy (≥ 4 cm, heterogeneous appearance, high Hounsfield unit [HU] values, or rapid growth) should also be surgically treated^{1,3}.

Adrenalectomy was first performed in 1894, and the first laparoscopic adrenalectomy was carried out by Gagner et al. in 1992⁴. Previous studies have suggested that chronic ACTH suppression in cortisol-secreting tumors may lead to atrophy of the contralateral adrenal gland. Therefore, radiological measurements of the contralateral adrenal gland may provide clues regarding the functional status of adrenal masses.

In this study, we aimed to evaluate whether radiological parameters could help predict the functional status of adrenal masses.

2. Material and Methods

This study was conducted in accordance with the ethical approval of University of Health Sciences Adana City Training and Research Hospital (decision number 2979, dated 07/12/2023). The study period ranged from January 1, 2017, to December 31, 2023. This retrospective study included 60 patients. Patients were included if they were over 18 years old, had an incidentally detected adrenal mass, underwent surgery, and had accessible data through the hospital information system. Patients whose data were unavailable or who were under 18 years old were excluded from the study.

Patients evaluated in the general surgery outpatient clinic or referred from the endocrinology department were divided into two groups according to the functional status of the adrenal mass. Patients with functional masses were categorized as having pheochromocytoma, primary hyperaldosteronism, or Cushing syndrome/subclinical Cushing syndrome. Appropriate treatments were initiated according to the hormonal status of the mass, and patients were referred for surgery. Non-functional masses larger than 4 cm or masses with suspected malignancy were also planned for surgical intervention. All patients underwent elective surgery.

Demographic, laboratory, and radiological data of the patients were extracted from the hospital information system.

2.1. Hormonal Evaluation

Hormonal activity was assessed in accordance with European and American guidelines^{5,6}. All patients underwent an overnight 1 mg dexamethasone suppression test (DST). Patients received 1 mg of oral dexamethasone at 23:00, and plasma cortisol levels were measured in fasting blood samples the following morning at 08:00. Plasma cortisol levels ≤ 1.8 $\mu\text{g/dL}$ after DST were considered sufficient suppression. Patients with post-DST plasma cortisol levels between 1.8 and 5 $\mu\text{g/dL}$ without clinical signs of Cushing syndrome were defined as having autonomous cortisol secretion (ACS), whereas those with levels ≥ 5 $\mu\text{g/dL}$ were classified as Cushing syndrome^{5,7}.

For pheochromocytoma screening, 24-hour urinary fractionated metanephrine and normetanephrine levels were measured after discontinuation of medications that could affect the results. Patients with levels at least twice the upper reference limit were referred for further diagnostic evaluation.

In the assessment of primary hyperaldosteronism, plasma aldosterone concentration, plasma renin activity, and the aldosterone/renin ratio (ARR) were measured. After withholding medications that could affect the test for at least two weeks, patients with plasma aldosterone levels ≥ 15 ng/dL, suppressed renin activity, and an ARR > 20 were referred for confirmatory testing. Confirmatory tests included the saline infusion test and/or the captopril suppression test.

2.2. Radiological Evaluation

All masses detected on ultrasonography were further evaluated with computed tomography (CT) and, when necessary, magnetic resonance imaging (MRI).

All MRI examinations were performed using a 1.5-T scanner (Ingenia; Philips Healthcare, the Netherlands). The imaging protocol included axial and coronal balanced turbo field echo T2-weighted (T2W) sequences, axial spectral attenuated inversion recovery T2W, diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping, and dual-echo fast field echo (FFE) sequences. In addition, T1-weighted (T1W) fat-suppressed gradient-echo THRIVE sequences were acquired in all patients both before and after intravenous gadolinium administration (0.1 mmol/kg body weight).

Computed tomography imaging was performed using a 128-detector multidetector CT (MDCT) system (Philips Ingenuity 128; Philips Healthcare, Eindhoven, the Netherlands). The acquisition parameters were as follows: tube voltage of 120 kVp, tube current of 200–400 mAs with automatic tube current modulation, rotation time of 0.42 s, pitch of 0.6, and a slice thickness of 3 mm for all phases. All images were transferred to a dedicated workstation (IntelliSpace Portal; Philips Healthcare, Best, the Netherlands) for analysis. Measurements included medial and lateral limb thicknesses of the adrenal glands, adrenal gland volume, gland density and ADC values derived from MRI.

2.3. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, version 27 (IBM Corp., Armonk, NY, USA). The normality of variables was assessed using the Kolmogorov-Smirnov test. Categorical variables were summarized as numbers and percentages, while continuous variables were presented as mean $\pm$ standard deviation, and, when appropriate, as median with minimum–maximum values. For comparison of two groups with continuous variables, the independent samples t-test was used for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. Categorical data were analyzed using the Pearson chi-square test or Fisher's exact chi-square test. A p-value < 0.05 was considered statistically significant for all analyses.

3. Results

A total of 60 patients were included in the study, of whom 65% (n=39) were female. The mean age of the patients was 51.51 ± 13.18 years. Functional adrenal masses were identified in 70% (n=42) of the patients. Laparoscopic surgery was performed in 47 patients, while conversion to open surgery was required in 3 cases. The mass was located in the right adrenal gland in 50% (n=30) of patients, and one patient had bilateral adrenal masses.

Histopathological analysis revealed that 63.3% (n=38) of patients had adrenocortical adenomas. Ten patients were diagnosed with malignancy, and in one of these cases, histopathological examination suggested metastatic carcinoma.

Postoperatively, one patient developed an incisional hernia and one patient experienced a pulmonary complication. No postoperative complications were observed in the remaining 58 patients. The mean length of hospital stay was 4.61 ± 2.31 days.

Sex, mass localization, and malignancy based on histopathological examination according to functional status of the mass are presented in Table 1. As shown in Table 1, no significant association was found between functional status and sex, localization, or malignancy.

Table 1. Demographic characteristics

Parameters		Non-functional n	Non-functional %	Functional n	Functional %	p
Gender	Female	9	52.94%	30	69.77%	0.218*
	Male	8	47.06%	13	30.23%	
Side	Right	7	41.18%	23	53.49%	0.221*
	Left	9	52.94%	20	46.51%	
	Bilateral	1	5.88%	0	0.00%	
Histopathological diagnosis	Benign	14	82.35%	36	83.72%	0.898*
	Malignant	3	17.65%	7	16.28%	

*: Pearson chi-square or Fisher exact test.

Preoperative CT imaging of adrenal masses was performed, and measurements of the adenoma-bearing and contralateral adrenal glands are presented in Table 2. Analysis of radiological measurements revealed that the residual volume of the adenoma-bearing gland was significantly smaller in patients with functional masses compared to those with non-functional masses ($p=0.007$). No significant association was found between functional status and other radiological measurements.

Table 2. CT scan measurements of the gland with the adenoma and the contralateral gland

Location	Parameters	Non-functional Mean $\pm$ SD	Median	Functional Mean $\pm$ SD	Median	p
Contralateral gland	Age (years)	53.35 $\pm$ 13.82	57.00	50.79 $\pm$ 13.02	50.00	0.502 ^s
Contralateral gland	Lateral limb length (mm)	3.76 $\pm$ 0.85	3.66	3.62 $\pm$ 0.92	3.66	0.668 ^o
Contralateral gland	Medial limb length (mm)	4.19 $\pm$ 1.39	3.63	3.72 $\pm$ 1.04	3.63	0.263 ^o
Contralateral gland	Density (HU)	38.99 $\pm$ 15.52	39.66	39.93 $\pm$ 16.92	39.66	0.621 ^o
Contralateral gland	Volume (mm ³)	4.62 $\pm$ 2.86	4.06	5.93 $\pm$ 9.05	4.06	0.854 ^o
Gland with adenoma	Lateral limb length (mm)	3.45 $\pm$ 0.26	3.55	3.71 $\pm$ 1.10	3.55	0.381 ^o
Gland with adenoma	Medial limb length (mm)	3.45 $\pm$ 0.18	3.50	3.65 $\pm$ 0.90	3.50	0.644 ^o
Gland with adenoma	Density (HU)	45.56 $\pm$ 16.21	42.87	41.81 $\pm$ 15.67	42.87	0.314 ^o
Gland with adenoma	Volume (mm ³)	73.63 $\pm$ 77.07	22.34	29.28 $\pm$ 37.01	22.34	0.007 ^o
—	ADC	1.38 $\pm$ 0.22	1.33	1.31 $\pm$ 0.20	1.33	0.522 ^o

^s: independent samples t-test; ^o: Mann-Whitney U.

Functional masses were further categorized individually and compared with non-functional masses in terms of radiological features, as shown in Table 3. In this analysis, although the lateral and medial limb measurements of the contralateral adrenal gland

tended to be shorter in patients with Cushing syndrome and autonomous cortisol secretion (ACS), no statistically significant association was observed.

Table 3. Comparison of non-functional and functional masses separately

Parameters	Non-functional Mean±SD	Median	Cushing/MACS Mean±SD	Median	p
Lateral limb length (mm)	3.89±0.99	3.66	3.54±1.08	3.66	0.366 ^o
Medial limb length (mm)	4.37±1.55	3.63	3.40±0.60	3.54	0.058 ^o
Density (HU)	37.84±15.83	39.66	41.16±19.46	39.66	0.520 ^o
Parameters	Non-functional Mean±SD	Median	Primary hyperaldosteronism Mean±SD	Median	p
Lateral limb length (mm)	3.89±0.99	3.66	3.49±0.87	3.66	0.412 ^o
Medial limb length (mm)	4.37±1.55	3.63	3.60±0.82	3.63	0.087 ^o
Density (HU)	37.84±15.83	39.66	42.59±17.38	39.66	0.296 ^o
Parameters	Non-functional Mean±SD	Median	Pheochromocytoma Mean±SD	Median	p
Lateral limb length (mm)	3.89±0.99	3.66	3.66±0.48	3.66	0.674 ^o
Medial limb length (mm)	4.37±1.55	3.63	3.91±1.11	3.63	0.966 ^o
Density (HU)	37.84±15.83	39.66	37.18±13.44	39.66	0.721 ^o

All parameters refer to the contralateral adrenal gland. ^o: Mann-Whitney U.

4. Discussion

In the literature, the most commonly observed functional adrenal adenoma is autonomous cortisol secretion (ACS)⁸. In our study, functional adrenal masses were observed at comparable rates; however, primary hyperaldosteronism was the most frequent functional subtype (34.88%).

Previous studies have reported a mean hospital stay of 2–4 days^{9,10}. In our study, the mean length of hospital stay was 4 days (range 2–14), which is consistent with the literature.

Adrenal masses located on the right side are in closer proximity to the liver, which increases the difficulty of dissection and the risk of bleeding. Therefore, the likelihood of conversion from laparoscopic to open surgery is higher for right-sided adrenal masses¹¹. In our study, conversion from laparoscopic to open surgery occurred in 3 patients (6%), all of whom had right-sided adrenal masses. In all three cases, dissection was complicated due to bleeding.

As noted in the literature, non-functional adrenal incidentalomas (AIs) smaller than 4 cm have a low risk of malignancy and can be managed with follow-up. However, for lesions larger than 4 cm, the risk of malignancy increases. Surgical treatment is recommended for selected patients with lesions 4–6 cm and for all lesions ≥6 cm¹². In our study, non-functional adrenal incidentalomas larger than 4 cm were surgically treated, which likely explains why the residual volume of the adenoma-bearing gland was higher in non-functional AIs compared to functional AIs.

Kong et al. compared patients with mildly autonomous cortisol secretion (MACS) to those with non-functional adrenal adenomas and reported that the medial limb length of the contralateral adrenal gland was significantly shorter in the MACS group¹³.

Park et al. found that patients with adrenal cortisol hypersecretion exhibited a reduction in the lateral limb length of the contralateral adrenal gland¹⁴. Kim et al. reported that in cases of cortisol hypersecretion and mild cortisol secretion, the contralateral adrenal gland was smaller, whereas no reduction was observed in non-functional masses or primary hyperaldosteronism¹⁵. These findings suggest that chronic ACTH suppression may lead to atrophy of the contralateral adrenal gland.

In our study, radiological evaluation aimed at differentiating functional adrenal adenomas from non-functional adenomas revealed that the lateral and medial limb lengths and density of the contralateral adrenal gland were similar to those of the adenoma-bearing gland.

This study has several limitations, including its retrospective design, small sample size, and single-center nature. We believe that randomized controlled studies with larger patient populations may provide more robust and conclusive results.

5. Conclusion

In our study, no significant differences in radiological parameters were observed between functional and non-functional adrenal adenomas. These findings indicate that hormonal evaluation remains essential for the diagnosis of functional adenomas. It is suggested that larger, prospective studies are needed to more clearly determine the diagnostic value of radiological parameters.

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