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Clinical characteristics of incidental adrenal masses and relationship with hematological indices as indicators of inflammation

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Abstract

Adrenal incidentaloma (AI) is being diagnosed more frequently due to the increase in use of imaging modalities. Inflammatory processes can play a role in the development and prognosis of numerous diseases. We aimed to investigate the clinical and endocrinological characteristics of adrenal adenoma and its relationship with inflammatory markers. The present study retrospectively analysed 111 patients with adrenal incidentaloma who underwent radiological and clinical examinations between January 2018 and January 2022. Patients diagnosed with Cushing's syndrome, pheochromocytoma or primary aldosteronism were classified as functional. Inflammation was assessed using neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), glucose lymphocyte ratio (GLR), systemic immune-inflammation index (SII) and prognostic nutritional index (PNI). Of the 111 patients included, 76.6% (n=85) had nonfunctional adenomas and 23.4% (n=26) had functional adenomas. Of the patients with functional adenomas, 50% (n=13) had Cushing's syndrome, 26.9% (n=7) had pheochromocytoma and 23% (n=6) had primary aldosteronism. The median duration of follow-up was 22.0 (2.0–60.0) months. During the follow-up, two (2.4%) of the 85 patients with non-functional adenomas gained functionality and were diagnosed with Cushing's disease. Functionality was not significantly associated with NLR, PLR, GLR, SII and PNI levels. There was a negative correlation between cortisol level after the overnight 1 mg dexamethasone suppression test and PNI (r:-0.207, p=0.030). Inflammatory hemogram parameters levels were not significantly different between patients with functional and non-functional adenomas. There was a significant negative correlation between the PNI level and cortisol secretion. PNI, which can be easily calculated by serum albumin level and absolute lymphocyte count, can be a useful guide for clinicians in the follow-up for the prognosis of functional adenoma.

Keywords: Adrenal incidentaloma, systemic immune-inflammation index, prognostic nutritional index

Introduction

Adrenal incidentaloma (AI) is as an adrenal mass that is >1 cm in size and is generally incidentally detected during imaging. Recently, it is being diagnosed more frequently due to the increased use of imaging modalities (prevalence, 1.0%–8.7%) [1]. AIs may be malignant or benign. Clinically, the treatment and prognosis of AI depend on whether the mass is functional [2].

A majority of the AI cases are benign and unilateral. Only 0.5%–5% of AIs are malignant and 10%–15% are bilateral. Functional adenomas comprise approximately 10%–15% of all AI cases [3]. While initially diagnosing AI, malignant should be differentiated from benign and hormonal hypersecretion should be considered. Signs of malignancy include a mass >4 cm in size, heterogenous appearance, hypervascular structure and radiodensity of >10 Hounsfield unit. The current guidelines recommend that all patients with AI should be tested for high levels of catecholamine and glucocorticoid [4].

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After excluding malignancy and hormone hypersecretion, patients should be followed up routinely. The diagnosis of functional tumours require comprehensive diagnostic tests. In addition to determining increased hormone levels, all patients should be evaluated for hypertension, hypokalaemia, diabetes mellitus (DM), asymptomatic vertebral fractures, and symptoms consistent with hirsutism, gynaecomastia and virilisation [5]. Hypertension and hypokalaemia are reportedly markers of functional adenoma, causing primary aldosteronism. Patients with functional adenoma have elevated levels of insulin, total cholesterol, LDL, triglyceride and fasting blood sugar. In addition to biochemical parameters, alterations in haematological and inflammatory markers are also expected in patients with AI. Yilmaz et al. established an association between AI and certain endocrine impairments and inflammation [6]. High cortisol levels in patients with AI result in activation of inflammation and high oxidative stress. Recently, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been used as inflammatory markers. Imga et al. reported increases in NLR and arteriosclerosis in patients with AI [7]. In another study, high NLR levels were associated with a higher incidence of malignant adrenal tumours [8].

Newer studies to understand the changes in the biochemical, haematological and inflammatory markers in AI are required. Previous studies have investigated the relationship between AI and the existing diseases using certain biochemical parameters. Herein, we aimed to investigate the relationship between adrenal tumours and the demographic, haematological and inflammatory parameters and prognostic nutritional index to facilitate early diagnosis and reduce unnecessary hormonal testing.

Material and Methods

Study design

This cross-sectional study included patients diagnosed with AI at the Endocrinology Clinic of the Batman Training and Research Hospital between January 2018 and January 2022. The patient files were retrospectively screened and all cases meeting the inclusion criteria were enrolled in the study. Patients aged <18 years, those with acute or chronic inflammatory diseases, acute infections, non-adrenal malignancies and incomplete data and those planning to follow-up and receive treatment at another health institution were excluded from the study. This study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Batman Training and Research Hospital's Non-invasional Research Ethics Committee (No: 347/22.03.2023; |date of approval|:24/03/2023).

Study population

A total of 111 patients diagnosed with AI who met the study criteria were included in the study. The medical and imaging records of the patients were reviewed by the authors to confirm the AI diagnosis. All patients were classified as having functional or non-functional adenoma based on the 'European Society of Endocrinology Clinical Practice Guidelines'. Patients diagnosed with Cushing syndrome, pheochromocytoma or primary aldosteronism were classified as having functional adenoma [4].

Data collection and definitions

The patient's age, sex and existing diseases at diagnosis were retrieved from the hospital information system and patient files. The imaging studies of the patients were reviewed; the size and location of the AI were recorded. Biochemical (glucose and albumin levels) and haematological (neutrophil, lymphocyte and platelet count) parameters were retrospectively recorded. The patient's biochemical and haematological parameters at the time of diagnosis were used to calculate the NLR (neutrophil/lymphocyte), PLR (platelet/lymphocyte), and glucose lymphocyte ratio (GLR) (glucose/lymphocyte). The Systemic immune-inflammation index (SII) and Prognostic Nutritional Index (PNI) were calculated as previously described [9]. The SII was calculated using the following formula: platelet count x neutrophil count/lymphocyte count. The PNI was calculated using the following formula: albumin level (g/L)+total lymphocyte count x 5.

Statistical analysis

The study data were analysed using SPSS (version 22; IBM Corporation, Armonk, New York, USA). The descriptive statistics are described as frequency and percentages for categorical data, mean (standard deviation) for normally distributed continuous data and median (minimum–maximum) for non-normally distributed continuous data. The categorical data were analysed using the Pearson chi-square or Fisher's exact test. The distribution of the continuous variables was analysed using the Shapiro–Wilk test. Normally distributed data were compared between two independent groups using the independent sample t-test. Non-normally distributed data were compared between independent groups using the Mann–Whitey U or Kruskal–Wallis test and the post-hoc Bonferroni correction was used for pairwise comparisons. The relationship between the continuous variables was analysed using Spearman's correlation. A p-value of <0.05 was considered statistically significant.

Results

The study included 111 patients with AI, of which 69.4% (n=77) were females and 30.6% (n=34) were males. The mean age of the patients was 52.38±11.63 years. Of the 111 cases of AI, 76.6% (n=85) were classified as non-functional adenomas and 23.4% (n=26) as functional adenomas. Of the 26 patients with functional adenomas, 50% (n=13) had Cushing's syndrome, 26.9% (n=7) had pheochromocytoma, and 23% (n=6) had primary aldosteronism. Approximately 52.3% (n=58) of the tumours were left-side, 39.6% (n=44) were right-side and 8.1% (n=9) were bilaterally localised to the adrenal glands. The median tumour size was 22.0 (10.0–140.0) mm. The median follow-up duration was 22.0 (2.0–60.0) months. During the follow-up period, two (2.4%) of the 85 non-functional adenomas had gained functionality. Both these patients had Cushing's syndrome. The baseline characteristics of the study population are presented in Table 1.

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Table 1. Baseline characteristics of the study population

Characteristic	All patients (n=111) (%)	Non-functional adenoma (n=85) (76.6%)	Functional adenoma (n=26) (23.4%)
Age	52.38±11.63	51.95±11.45	56.50±12.31
Gender			
Female	77 (69.4)	55 (64.7)	22 (84.6)
Male	34 (30.6)	30 (35.3)	4 (15.4)
Tumour characteristics			
Left	58 (52.3)	46 (54.1)	12 (46.2)
Right	44 (39.6)	31 (36.5)	13 (50.0)
Bilateral	9 (8.1)	8 (9.4)	1 (3.8)
Tumour diameter (mm)	22.0 (10.0–140.0)	20.0 (10.0–65.0)	27.5 (10.0–140.0)
Tumour diameter classification			
10-40 mm	97 (87.4)	78 (91.8)	19 (73.1)
41–60 mm	10 (9.0)	6 (7.1)	4 (15.4)
>60 mm	4 (3.6)	1 (1.1)	3 (11.5)
Functionality classification			
Cushing's syndrome	13 (11.7)		13 (50.0)
Pheochromocytoma	7 (6.3)		7 (26.9)
Primary aldosteronism	6 (5.4)		6 (23.0)
Comorbidities			
Hypertension	62 (55.9)	39 (45.9)	23 (88.5)
Diabetes mellitus	41 (36.9)	26 (30.6)	15 (57.7)
Dyslipidaemia	37 (33.3)	23 (27.1)	14 (53.8)
Coronary artery disease	30 (27.0)	23 (27.1)	7 (26.9)
Biochemical characteristics			
Glucose (mg/dl)	101.0 (64.0–338.0)	100.0 (80.0–325.0)	103.0 (64.0–338.0)
Albumin (g/dl)	4.08 (2.38–8.97)	4.10 (3.27–4.99)	4.00 (3.50–4.50)
Absolute neutrophil count, $10^3/mm^3$	4.38 (2.38–8.97)	4.36 (2.38–8.97)	4.69 (2.70–7.76)
Absolute lymphocyte count, $10^3/mm^3$	2.35 (1.07–4.65)	2.37 (1.07–4.65)	2.28 (1.53–3.73)
Platelet count, $10^3/mm^3$	266.0 (131.0–616.0)	264.0 (131.0–473.0)	274.5 (132.0–616.0)
Inflammatory markers			
NLR	1.90 (0.63–4.55)	1.89 (0.63–4.55)	1.93 (0.99–3.96)
PLR	112.2 (51.1–289.7)	112.0 (51.1–289.7)	112.7 (58.4–236.9)
SII index	480.8 (121.5–1.472.9)	480.8 (121.5–1.472.9)	479.2 (255.9–1.274.7)
GLR	2.41 (1.12–9.86)	2.31 (1.12–9.86)	2.70 (1.22–8.12)
PNI	52.99±4.77	53.25±4.97	52.12±4.03
Tumour histology	**All patients (n=11) (%)**	**Non-functional (n=3) (27.27%)**	**Functional (n=8) (72.72%)**
Benign	8 (72.7)	3 (100)	5 (62.5)
Malignant	3 (27.3)	0 (0.0)	3 (37.5)

NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, SII: systemic immune-inflammation index, GLR: glucose lymphocyte ratio, PNI: prognostic nutritional index

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Functional adenomas had a median size of 27.5 (10.0–140.0) mm and were significantly larger than non-functional adenomas with a median size of 20.0 (10.0–65.0) mm (p=0.007). Median serum cortisol levels were 1.74 µg/dL (0.06–10.20) and 0.98 µg/dL (0.20–4.56) in the functional adenoma and non-functional adenoma group after overnight 1 mg dexamethasone suppression test (DST) respectively. The cortisol levels were significantly higher in the functional group than in the non-functional group (p<0.001). The patients with functional adenoma had higher rates of DM (p=0.012), hypertension (p<0.001) and dyslipidemia (p=0.011) (Table 2). Patients with functional and non-functional adenomas were not different in terms of the levels of inflammatory markers (NLR, PLR, SII, GLR, PNI) (Table 2) and also no correlation was observed between tumor size, inflammation parameters and age (Table 3).

Table 2. Comparison of the baseline characteristics of patients with functional and non-functional adrenal incidentalomas

Characteristic	Non-functional adrenal incidentaloma (n=85) (%)	Functional adrenal incidentaloma (n=26) (%)	p-value
Demographics			
Age (mean±sd)	51.95±11.45	53.77±12.32	0.488
Gender n (%)			
Female	55 (64.7)	22 (84.6)	0.054
Male	30 (35.3)	4 (15.4)	
Adrenal incidentaloma characteristics			
Unilateral	77 (90.6)	25 (96.2)	0.458
Bilateral	8 (9.4)	1 (3.8)	
Adrenal incidentaloma size (mm)	20.0 (10.0–65.0)	27.5 (10.0–140.0)	**0.007**
Serum cortisol after overnight 1 mg DST (µg/dL)	0.98 (0.20–4.56)	1.74 (0.06–10.20)	**<0.001**
Tumour classification			
<40 mm	78 (91.8)	19 (73.1)	**0.012**
≥40 mm	7 (8.2)	7 (26.9)	
Biochemical investigations			
Glucose (mg/dl)	100.0 (80.0–325.0)	103.0 (64.0–338.0)	0.267
Albumin (g/dl)	4.11±0.28	4.03±0.27	
Haematological parameters			
Absolute neutrophil count, $10^3/mm^3$	4.36 (2.38–8.97)	4.69 (2.70–7.76)	0.741
Absolute lymphocyte count, $10^3/mm^3$	2.37 (1.07–4.65)	2.28 (1.53–3.73)	0.666
Platelet count, $10^3/mm^3$	264.0 (131.0–473.0)	274.5 (132.0–616.0)	0.775
Inflammatory parameters			
NLR	1.89 (0.63–4.55)	1.93 (0.99–3.96)	0.862
PLR	112.0 (51.1–289.7)	112.7 (58.4–236.9)	0.807
SII index	480.8 (121.5–1.472.9)	479.2 (255.9–1.274.7)	0.922
GLR	2.31 (1.12–9.86)	2.70 (1.22–8.12)	0.232
PNI	53.25±4.97	52.12±4.03	0.291
Comorbidities			
Diabetes mellitus	26 (30.6)	15 (57.7)	**0.012**
Hypertension	39 (45.9)	23 (88.5)	**<0.001**
Dyslipidaemia	23 (27.1)	14 (53.8)	**0.011**
Coronary artery disease	23 (27.1)	7 (26.9)	0.989

DST: dexamethasone suppression test, NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, SII: systemic immune-inflammation index, GLR: glucose lymphocyte ratio, PNI: prognostic nutritional index

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Age, inflammatory parameters and cortisol levels after the overnight 1 mg DST did not differ according to tumor localization. Tumours located in the right adrenal gland had a median diameter of 24.0 (10.0–140.0) mm and they were significantly larger than the tumours in the left adrenal gland (p=0.027) (Table 4).

Significant positive correlations between the cortisol level after the overnight 1 mg DST and age (r: 0.440, p<0.001), tumour size (r: 0.205, p=0.031) and GLR (r: 0.238, p=0.012). There was a significant negative correlation between the cortisol level and PNI (r: −0.207, p=0.030). The SII had a significant positive correlation with NLR (r: 0.816, p<0.001), PLR (r: 0.698, p<0.001) and GLR (r: 0.293, p=0.002) and a significant negative correlation with PNI (r: -0.380, p<0.001) (Table 5).

Table 3. Correlation between the tumour size and inflammatory parameters and age

	All cases (n=111)		Non-functional		Functional	
Age	r: 0.960	p=0.317	r: 0.981	p=0.374	r: 0.003	p=0.989
NLR	r: −0.167	p=0.079	r: −0.179	p=0.102	r: −0.100	p=0.627
PLR	r: −0.040	p=0.680	r: −0.009	p=0.934	r: −0.045	p=0.826
SII index	r: −0.069	p=0.470	r: −0.063	p=0.568	r: −0.012	p=0.954
GLR	r: −0.035	p=0.713	r: −0.032	p=0.768	r: −0.099	p=0.629
PNI	r: 0.128	p=0.180	r: 0.170	p=0.120	r: 0.050	p=0.808

NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, SII: systemic immune-inflammation index, GLR: glucose lymphocyte ratio, PNI: prognostic nutritional index

Table 4. Comparison of certain characteristics according to the tumour location

	Right (n=44)	Left (n=58)	Bilateral (n=9)	p-value*
Age	52.50 (28.0–79.0)	51.0 (24.0–72.0)	66.0 (18.0–74.0)	0.165
Tumour size	24.0 (10.0–140.0)	20.0 (10.0–50.0)	30.0 (12.0–65.0)	**0.027**[b]
NLR	1.90 (0.88–3.96)	1.94 (0.63–4.55)	1.80 (1.30–3.15)	0.923
PLR	110.6 (58.4–231.1)	110.8 (51.1–289.7)	123.2 (79.5–236.9)	0.533
SII index	473.2 (158.2–1.152.2)	496.7 (121.5–1.472.9)	546.4 (348.2–1.274.7)	0.457
GLR	2.65 (1.22–9.86)	2.31 (1.12–6.88)	2.66 (1.91–8.01)	0.244
PNI	52.83 (44.65–62.75)	50.08 (42.55–68.80)	52.30 (41.70–56.10)	0.426
DST result	1.01 (0.30–10.20)	0.99 (0.06–8.20)	1.40 (0.96–1.60)	0.111

NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, SII: systemic immune-inflammation index, GLR: glucose lymphocyte ratio, PNI: prognostic nutritional index, DST: dexamethasone suppression test

* Multiple comparison, Kruskal–Wallis test; b Pairwise comparison of right and left glands with regard to tumour size (Mann-Whitney U test) was performed, bilateral localisations were not included in the analysis

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Table 5. Correlation between the overnight 1 mg DST cortisol response and the inflammatory parameters

		DST result	Age	Tm diameter	NLR	PLR	SII	GLR	PNI
DST	r	1.000	.440**	.205*	.184	−.015	.066	.238*	−.207*
	p value	.	.000	.031	.053	.879	.490	.012	.030
Age	r	.440**	1.000	.096	.062	.013	.133	.198*	−.030
	p value	**.000**	.	.317	.519	.894	.165	.037	.752
Tm diameter	r	.205*	.096	1.000	−.167	−.040	−.069	−.035	.128
	p value	**.031**	.317	.	.079	.680	.470	.713	.180
NLR	r	.184	.062	−.167	1.000	.530**	.816**	.489**	−.578**
	p value	.053	.519	.079	.	.000	.000	.000	.000
PLR	r	−.015	.013	−.040	.530**	1.000	.698**	.568**	−.592**
	p value	.879	.894	.680	.000	.	.000	.000	.000
SII	r	.066	.133	−.069	.816**	.698**	1.000	.293**	−.380**
	p value	.490	.165	.470	**.000**	**.000**	.	**.002**	**.000**
GLR	r	.238*	.198*	−.035	.489**	.568**	.293**	1.000	−.594**
	p value	**.012**	.037	.713	.000	.000	.002	.	.000
PNI	r	−.207*	−.030	.128	−.578**	−.592**	−.380**	−.594**	1.000
	p value	**.030**	.752	.180	.000	.000	.000	.000	.

NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, SII: systemic immune-inflammation index, GLR: glucose lymphocyte ratio, PNI: prognostic nutritional index

Discussion

The present study included 111 patients with adrenal incidentaloma of which 23.4% had functional adenomas and 2.7% had malignant tumor. All of the malignant tumors were in the functional group. The prevalence of malignant adrenal masses varies between 1% and 5% [10]. In the study by Cho et al. that included 282 patients, only three patients (1.1%) had malignant adrenal tumours [11]. Our study results are consistent with those of previous studies; the majority of the AIs were benign. Furthermore, most of the AIs were non-functional adenomas. A previous case series reported that the rate of non-functional adrenal adenomas were 86.2%, 73.3% and 82% [11-13]. In the present study, 76.6% of the adrenal adenomas were non-functional. Of the patients with functional adenomas, 50% had Cushing's syndrome, 26.9% had pheochromocytoma and 23% had primary aldosteronism. Data from the present study and previous studies indicate that AIs are mostly benign and non-functional masses.

In this study, more than half of the AIs (52.3%) were located on the left side. Our study results are consistent with those of previous studies that adrenal adenomas are predominantly located on the left side [11]. Although there are studies reporting predominantly right-sided adenomas, they are scarce and the difference may be attributed to the use of ultrasound for diagnosis [14]. Comprehensive autopsy studies have revealed that there is no significant difference between the right and left gland in terms of localisation of the adrenal adenomas [15].

In our study the age, sex and tumour localisation were not related to tumour functionality. Furthermore, the incidence of DM, hypertension and dyslipidaemia were higher in patients with functional adenomas. Cho et al. reported that age and tumour localisation were not associated with functionality [11]. Another study conducted in the Republic of Korea reported that age, sex, tumour size and tumour localisation were not risk factors for functionality [16]. However, several studies have reported an increase in the frequency of DM, hypertension and dyslipidaemia in patients with functional adenomas [17]. Our study findings indicate that AI is a disorder with a low prevalence and requires larger case series.

When clinically managing AI, follow-up is recommended to look

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for functionality and potential growth. Usually, the risk for size and functionality change decreases after four years of follow-up [3]. Of our 85 patients with non-functional adenoma, only two (2.4%) exhibited a change in the hormone levels during the mean follow-up duration of 28.5 (2–60) months. Barzon et al. reported that approximately 1.7% of the patients showed a functionality change during follow-up [18]. Cho et al. determined that 4.2% of the patients underwent hormonal alteration during a mean follow-up period of 22.5 months [11]. A few studies have reported the tumour size at diagnosis is associated with functionality. Tumours that were >4 cm at the time of diagnosis were associated with a greater rate of hormonal hypersecretion [19,20]. In the present study, 26.9% of the functional adenomas were >4 cm and were statistically more frequent compared to the non-functional adenomas. However, some studies suggest that tumour size and localisation are not risk factors for functionality [11,16]. New studies with larger populations are needed to elucidate the relationship between tumour size and functionality.

One of the primary objectives of the present study was to investigate the relationship between inflammatory parameters and hormonal secretion. There was no significant difference between the functional and non-functional adenomas with regard to the median NLR, PLR, SII, GLR and PNI levels. Similar to our results, Demirci et al. reported that there was no significant relationship between inflammatory parameters and functionality [13]. The current inflammatory markers have been studied in relation to a multitude of diseases. Elevated NLR is reportedly associated with malignant tumours. Mochizuki et al. reported that an increase in systemic inflammatory parameters was also present in patients with adrenal tumours [8]. The levels of systemic inflammatory markers could increase in chronic diseases such as DM and hypertension [21]. Yilmaz et al. reported that there was no change in the NLR levels in patients with non-functional adenoma [6]. The change in systemic inflammatory parameters may be associated with the activation of endocrine and inflammatory processes. Additionally, the course of these parameters may be affected by the non-functional status or the silent and mild hormonal changes in functional adenomas in AIs.

We determined a significant positive correlation between tumour diameter and cortisol secretion. Barzon et al. reported the tumour size to be a risk factor for functionality [19]. Although there are studies showing that the tumour size and functionality are not related, our study indicate that an increase in cortisol secretion that parallels tumour size requires attention [11,16]. We did not find a significant correlation between cortisol secretion and NLR, PLR, SII. Demirci et al. reported that the NLR and PLR was not significantly correlated with cortisol secretion [13]. Studies on the relationship between AI and inflammatory parameters are limited. Babinska et al. identified an increase in cardiovascular disease risk and hypertension in conditions of elevated cortisol secretion such as Cushing's syndrome [22]. It has been proposed that the inflammatory process could be the underlying mechanism. We did not find a relationship between hormone secretion and inflammatory markers, which contradicts Babinska et al.'s hypothesis. AIs are considered as a non-inflammatory process unless they exhibit malignant qualities. A study by Park et al. attributed the increased cardiovascular risk in patients with adrenal adenoma to the comorbid metabolic dysfunctions such as hypertension, DM and dyslipidemia [23]. We found a significant positive correlation between cortisol secretion and the GLR levels and a significant negative correlation with PNI. Cortisol secretion affects the glucose metabolism and haematological parameters. Cortisol increases the blood sugar level and leads to leucocytosis; however, the increase is seen in polymorphonuclear (PMN) cells, while lymphocytes show a decrease [24]. Thus, the cortisol-induced increase in glucose can explain the positive correlation between cortisol and GLR. Recent studies have focused on the importance of PNI in the evaluation of disease prognosis and severity in malignancies, immune diseases and chronic diseases. PNI is associated with the prognosis and disease severity in certain chronic conditions such as inflammatory diseases, malignant diseases and cardiac failure [25,26]. Although our study determined a negative correlation between cortisol secretion and the PNI level, it may have been attributable to the cortisol levels causing a reduction in the lymphocyte counts. The present study cannot explain the effect of PNI levels on the prognosis of patients with AI. New studies are required to shed light on this relationship. This negative correlation between cortisol secretion and PNI may guide clinicians with regard to the functionality of AIs and hormone secretion levels.

The present study has some limitation. The single-centre and retrospective nature of the study may have resulted in the loss of some data. The mean duration of follow-up was 28 months, which may have been insufficient to detect metabolic or inflammatory changes. Recent years, some studies have been published showing that hemogram parameters and inflammatory response are particularly affected by covid 19 vaccines. Since the vaccination status of the study cases was not known, this may have affected the hemogram parameters. Despite these limitations, a strength of our study was that the diagnosis was confirmed using contrast computed tomography or dynamic adrenal MR imaging in all patients and histopathological examination in patients who underwent surgery.

Conclusion

The present study determined that adenomas with a tumour size of >4 cm showed higher functionality than those with a size <4 cm. Patients with functional adenomas had higher rates of DM, hypertension and dyslipidaemia. Patients with functional and non-functional adenomas were not different in terms of the levels of inflammatory markers (NLR, PLR, SII, GLR, PNI). We found a negative correlation between the cortisol level and PNI. Thus, PNI may be useful in the evaluation of functionality, hormone secretion and prognosis during the follow-up period in patients with AI. Future studies are required in to focus on the relationship between the inflammatory process and hormone secretion.

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Conflict of Interests
The authors declare that there is no conflict of interest in the study.

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Ethical Approval
Batman Training and Research Hospital's Non-invasional Research Ethics Committee (No: 347/22.03.2023;date of approval:24/03/2023).

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