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Original Study

Comparison of CT Scans With And Without Contrast in The Characterization of Adrenal Gland Adenomas

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SUMMARY

Introduction: With the increased use of diagnostic procedures such as computed tomography (CT), the detection of asymptomatic adrenal lesions demonstrates a growing trend. Accurately distinguishing these lesions is essential for guiding future diagnostic and treatment approaches.

Aim: This study aimed to investigate whether it is possible to determine the adenomatous characteristics of adrenal tumors on non-contrast CT scans.

Material and Method: A retrospective observational study was conducted at the University Clinical Center of Vojvodina (UKCV), involving 43 patients who underwent CT imaging following the adrenal protocol. The key parameters examined were: sex, age, antero-posterior (AP) and latero-lateral diameter (LL) of the adenoma, non-contrast density, absolute (APW) and relative (RPW) washout.

Results: Our study has shown a statistically significant negative correlation between non-contrast density and RPW ($p<0.001$), as well as significant positive correlation between APW and RPW ($p=0.007$). The non-contrast density demonstrated a statistically significant positive correlation with the AP diameter of the adenoma ($p=0.035$).

Conclusion: Our research shows that when using unenhanced CT imaging, a non-contrast density significantly below 10 Hounsfield units (HU) and a lesion diameter under 40 mm strongly suggest an adrenal gland adenoma, potentially allowing for diagnosis without multiple scans or contrast.

Keywords: Adenoma, Washout, Non-Contrast Density

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INTRODUCTION

Adenomas are benign tumors derived from epithelial tissue, commonly consisting of epithelial cells from glands or glandular ducts. They generally grow slowly and in a confined manner, meaning they typically do not lead to major complications and often remain asymptomatic [1,2]. Although benign proliferations can develop in any gland, the adrenal gland represents a common site for these lesions. Adrenal adenomas are usually discovered incidentally during cross-sectional imaging of the abdomen, such as a CT or magnetic resonance imaging (MRI) [3,4,5]. In fact, up to 5% of all abdominal CT scans performed for various reasons reveal new adrenal lesions, whether they are adenomas or other types of tumors. For this reason, all incidentally detected adrenal gland tumors are collectively referred to as „incidentalomas" [3,5]. As the most common benign tumors of this region, adrenal adenomas (AAs) must be distinguished from lesions of other origins (non-AAs). The adrenal glands are also frequent sites of malignant tumors, such as adrenocortical carcinoma or metastases and effective treatment relies heavily on a timely and accurate diagnosis [6,7]. This diagnostic challenge becomes even more critical in patients receiving systemic glucocorticoid therapy, which can suppress adrenal cortical function and potentially mask or mimic pathological changes [8].

CT—specifically CT performed according to the adrenal protocol—is the method of choice for accurately characterizing incidentalomas.. This protocol includes precontrast imaging, a post-contrast scan during the portal-venous phase (60–90 seconds after contrast administration), and a delayed scan after 15 minutes [9,10]. One of the key features assessed with this method is the density of the adrenal lesion on the non-contrast CT scan. Adenomas generally show low density values on non-contrast CT, a characteristic that is directly related to the amount of intracellular lipids. Approximately 70% of adenomas are rich in lipids, leading to their classification into two groups: lipid-rich adenomas and lipid-poor adenomas [7,10]. Clinically, an attenuation of ≤10 HU on non-contrast CT is widely used as the diagnostic threshold for a lipid-rich adenoma. Conversely, an attenuation above 10 HU raises the possibility of a lipid-poor adenoma, pheochromocytoma, or even a malignant lesion such as carcinoma, which typically contains fewer lipids [11]. Furthermore, a precontrast attenuation greater than 43 HU in a lesion that lacks calcifications or hemorrhage is almost certainly indicative of malignancy [12].

Contrast-enhanced CT further assistss in characterizing adrenal lesions by revealing their unique perfusion patterns. Adenomas typically enhance rapidly following contrast administration and also exhibit a quick washout of contrast, a phenomenon not typically seen in pheochromocytomas or malignant lesions, which display much slower washout rates [10,11,13]. Washout is calculated based on density values on: Pre-contrast imaging (HUunenhanced), imaging 60 seconds after contrast administration (HUmax) and imaging 15 minutes after contrast administration (HU10/15min). These values allow us to determine both absolute (APW) and relative (RPW) washout percentages using the following formulas:

Relative contrast washout (RPW) =
100 × [(HUmax – HU10/15min) / HUmax]

Absolute contrast washout (APW) =
100 × [(HUmax – HU10/15min) / (HUmax – HUunenhanced)] [14].

An absolute washout of more than 60% and a relative washout of over 40% strongly suggest the lesion is an adrenal adenoma. Additional indicators that may point to a higher likelihood of malignancy include a tumor diameter exceeding 40 mm, irregular contours, and a heterogeneous appearance [10,13]. In summary, low attenuation values on non-contrast CT, together with an absolute washout of over 60% and a relative washout of over 40%, strongly support the diagnosis of an adenoma in the examined lesion.

AIM

This study aimed to assess whether unenhanced CT characteristics (density and diameter) of adrenal gland lesions are associated with the diagnosis of adrenal adenoma, as well as to evaluate the correlation between pre-contrast density and APW and RPW values during contrast-enhanced CT imaging performed according to the adrenal protocol.

	RANGE		AVERAGE		
	From	To	Overall	Female	Male
NON-CONTRAST DENSITY (HU)	-13	10	0,7	-0,4	1,25
AP DIAMETER (mm)	9	39,8	22,2	22,5	21,4
LL DIAMETER (mm)	7	31,3	17	16,6	18,2
APW (%)	61,8	91,4	73,6	74,1	71,8
RPW (%)	51,1	112,5	75,5	76,8	71,8

Table 1. Obtained values for Non-contrast density, AP and LL diameter, APW, RPW

HU - Hounsfield units
AP - Anteroposterior
LL - Laterolateral
APW - Absolute Washout
RPW - Relative Washout

MATERIAL AND METHODS

This retrospective, academic,, academic, observational phase IV study was conducted at the Center for Radiology and the Clinic for Endocrinology, Diabetes, and Metabolic Diseases in the UKCV. A total of 43 participants (33 women and 10 men) were included in the study, all of whom underwent CT imaging according to the adrenal protocol between November 17, 2020, and January 10, 2024. CT examinations were performed with a 128-slice Revolution EVO scanner (GE Healthcare, Chicago, IL, USA) at the Center for Radiology, UKCV. The data used in this study was collected and analyzed from patient histories, the unified electronic information system of UKCV, and the Picture Archiving and Communication System (PACS). Approval from the Ethics Committee of UKCV was obtained on January 26, 2024 (No. 00-25).

The study exclusively included patients with a confirmed diagnosis of adenoma. During the participant selection process, patients with an adenoma density exceeding 10 HU on the non-contrast CT scans were excluded from the study, as well as those with an AP or LL diameter greater than 50 mm. In cases where patients had bilateral adrenal adenomas, only the larger of the two was included in the study.

RESULTS

The total number of participants included in the study was 43 (33 female and 10 male) with the average age of 63 years (SD = 9.8), with a median of 64 years.

Our research showed no statistically significant correlation between the density on the unenhanced CT and APW ($p = 0.53$).

Our study demonstrated a strong negative correlation between adenoma density on unenhanced CT and its RPW on contrast-enhanced CT ($p < 0.001$).

Our study revealed a statistically significant positive correlation between the APW and RPW values of adenomas ($p = 0.007$).

Our study showed a statistically significant positive correlation between non-contrast density and the AP diameter of adenomas ($p = 0.035$), as well as that there is no statisti-

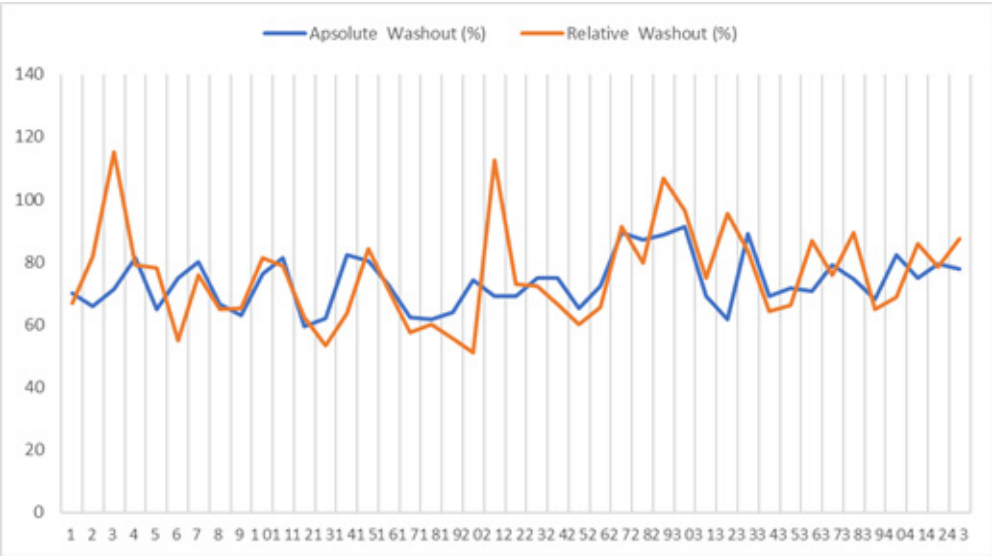

Figure 1. APW and RPW values in adrenal adenomas

cally significant correlation between non-contrast density and the LL diameter of adenomas (p = 0.12).

DISCUSSION

Our study revealed a statistically significant positive correlation between non–contrast density and the AP diameter of adenomas (p = 0.035), whereas no significant association was found between non-contrast density and the LL diameter (p = 0.12). Furthermore, our research demonstrated a statistically significant negative correlation between non-contrast density and RPW, while the correlation between non-contrast density and APW was not significant. Thus, RPW proved to be a better predictor of adenomas than APW. Additionally, we observed a statistically significant positive correlation between APW and RPW.

In our cohort, non-contrast CT densities ranged from -13 to 10 HU. Kirsch et al. reported that using the current cutoff value of <10HU only aids in identifying around half of the adrenal adenomas, and suggested that the threshold be raised to <16HU [15]. Although lipid-rich adenomas can sometimes have a density greater than 10 HU, necessitating additional diagnostic evaluation. However, in most cases, these benign lesions exhibit a non-contrast density of up to 10 HU [16,17]. Recent studies have also shown that the likelihood of a pheochromocytoma displaying a density below 10 HU is nearly zero [18,19]. Taking all this into account, our findings are consistentwith existing literature.

The size of adrenal lesions is considered a potentially strong predictor of malignancy in adrenal incidentalomas. However, relying solely on size as a diagnostic criterion may lead to misclassification, as malignant tumors of atypical dimensions occasionally occur. In numerous studies, a diameter threshold of 40 mm is frequently mentioned as a potential boundary between adenomas and malignant lesions [20,21]. Favia et al. identified 15 adrenocortical carcinomas, seven of which were smaller than 40 mm [22]. In contrast, Ballian et al. found no adrenal carcinomas smaller than 40 mm and proposed this threshold as a criterion for considering adrenalectomy to avoid unnecessary surgical procedures [23].

In our study, adenoma sizes ranged from 9 to 39.8 mm in AP diameter and from 7 to 31.3 mm in LL diameter, aligning with the recommended 40 mm threshold, which is strongly indicative of an adenoma diagnosis [16]. Additionally, our research demonstrated a statistically significant positive correlation between non-contrast density and AP diameter. This suggests that if an adrenal lesion has both a low non-contrast density (typical of adenomas) and small dimensions (also characteristic of adenomas), it further supports the likelihood of an adenoma diagnosis. However, we found no significant correlation between non-contrast density and LL diameter.

APW values in our sample ranged from 61.8% to 91.4%, while RPW ranged from 51.1% to 112.5%.. Although APW >60% and RPW >40% are widely used thresholds for adenoma confirmation, recent studies indicate that these values may be insufficiently accurate [24]. One recent study indicated that applying these reference values could lead up to 22% of malignant tumors being misdiagnosed based on APW and 8% based on RPW, prompting a recommendation to raise the RPW threshold to above 58% [10]. Our research demonstrated no significant correlation between non-contrast density and APW (p = 0.53), but a strong negative correlation between non-contrast density and RPW (p < 0.001). This suggests that as non-contrast density decreases below the 10 HU threshold, RPW values (recognized as a superior predictor of lesion characteristics) increase. Additionally, we observed a statistically significant positive correlation between APW and RPW (p = 0.007).

Our findings align with the 2023 European Society of Endocrinology (ESE) guidelines, which state that if an adrenal lesion is homogeneous in structure, ≤40 mm in size, and has a non-contrast density ≤10 HU, the diagnosis of adenoma is highly reliable, and additional imaging such as adrenal CT protocol is unnecessary [25].

Overall, when considered alongside existing evidence, our findings contribute toa clinically relevant framework that could help streamline the evaluation of adrenal lesions.

Study Limitations

A key limitation of our study is its retrospective nature and the small sample size of 43 patients monitored over the past four years.

Future Research Directions

Based on our findings, several avenues for future research emerge. Future studies should consider incorporating other adrenal lesions, particularly benign ones such as pheochromocytomas, as well as potentially malignant lesions such as adrenocortical carcinomas and metastases. A more extensive comparison of the density of these lesions on non-contrast CT scans with their washout characteristics could provide valuable insights for refining diagnostic criteria.

CONCLUSION

Our study demonstrated that both adrenal lesion diameterand non-contrast CT density with the diagnosis of adrenal adenoma. Additionally, the study demonstrated a significant association between non-contrast density and RPW. If the adrenal lesion measures ≤40 mm, has a non-contrast density below 10 HU, and exhibits a high RPW, this strongly supports a diagnosis of adrenal adenoma. Based on these findings, using only non-contrast CT, if the non-contrast density is significantly below 10 HU and the lesion diameter is well under 40 mm, this provides strong evidence in favor of an adrenal adenoma, potentially allowing for diagnosis without the need for contrast enhancement. This clinically supported and practice-oriented study paves the way for defining new diagnostic algorithms in adrenal imaging.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Komparacija CT pregleda sa i bez kontrasta u karakterizaciji adenoma nadbubrežne žlezde

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KRATAK SADRŽAJ

Uvod: Sa povećanom upotrebom dijagnostičkih procedura visoke rezolucije kao što je kompjuterizovana tomografija (CT), neočekivana detekcija asimptomatskih adrenalnih lezija pokazuje rastući trend. Uspešna diferencijacija ovih lezija je od presudnog značaja za kliničko praćenje i buduću terapiju.
Cilj: Cilj istraživanja bio je da ispita da li je moguće utvrditi adenomske karakteristike tumora nadbubrega CT pregledom bez kontrasta.
Materijal i metode: Istraživanje je rađeno u vidu retrospektivne, opservacione studije u UKCV. U studiju je uključeno 43 pacijenata, kojima je rađen CT po protokolu za nadbubreg. Glavni parametri koji su se koristili su: pol, starost, antero-posteriorni (AP) i latero-lateralni (LL) dijametar adenoma, nativni denzitet, apsolutni (APW) i relativni (RPW) washout.
Rezultati: Naša studija je pokazala da postoji statistički značajna negativna korelacija između nativnog denziteta i RPWa ($p<0,001$) i statistički značajna pozitivna korelacija između APW i RPW ($p=0,007$). Nativni denzitet pokazao je statistički značajnu pozitivnu korelaciju sa AP dijametrom adenoma ($p=0,035$).
Zaključak: Naše istraživanje je pokazalo da upotrebom beskontrastnog CTa, ukoliko nam je nativni denzitet značajno manji od 10 HU a sa njime i dijametar lezije znatno manji od 40 mm, ovo snažno govori u prilog adenoma nadbubrežne žlezde, te se dijagnoza potencijalno može postaviti bez upotrebe kontrastnog sredstva.

Ključne reči: adenom, washout, nativni denzitet

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