ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 2, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

CECT IN THE ADRENOCORTICAL CARCINOMAS: RECOGNIZING THE TYPICAL MORPHOLOGICAL FEATURES

KRITIKAL[1], RAJARAM SHARMA[1], SAMBHAV LODHA[2]*, HEMANGINI THAKKAR[3], PADMA BADHE[3]

[1]Department of Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India. [2]Department of Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India. [3]Department of SGMC Medical College, KEM Hospital, Mumbai, Maharashtra, India. Email: sambhavlodha85@hotmail.com

Received: 09 November 2022, Revised and Accepted: 15 January 2023

ABSTRACT

Objectives: This study was characterization of adrenal masses on computer tomography (CT) using shape, size, and enhancement patterns.

Methods: It is a retrospective study of 86 adrenal masses with morphological differences in the appearance and enhancement patterns (histopathologically proven 36 pheochromocytoma [PCCs], 26 adrenal cortical carcinoma [ACCs], one lymphoma, 22 metastases, and one schwannoma). Two experienced radiologists who were unaware of the histopathological diagnosis reviewed the computed tomography scans, morphological parameters had been noted, along with attenuations measured in Hounsfield units for all the phases of contrast-enhanced computed tomography.

Results: Necrosis had been seen in all the cases of ACCs with a loss of adeniform shape. ACCs were significantly less enhancing in arterial phase and venous phase than PCC; however, no significant difference was seen with lymphomas, metastasis, and schwannoma. 25/33 (75.5%) ACC showed heterogeneous enhancement (due to the presence of necrosis) in the VP.

Conclusion: Heterogenous architecture with a size of more than 5 cm is relatively specific for diagnosing ACC. No specific enhancement pattern could well differentiate ACC from lymphoma, metastases, and schwannoma.

Keywords: Adrenal, Contrast-enhanced computed tomography, Washout, Carcinoma.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i2.47219. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

In recent years, adrenal masses have been receiving increased attention due to the increase in the incidence of adrenal incidentalomas [1]. Classification of the adrenal masses based on etiology has become necessary, because management varies from observation to surgical resection [2]. Moreover, it is essential to avoid missing a significant functional or malignant lesion. Due to the low prevalence of such conditions [2], the investigations need to have a very high sensitivity and specificity to differentiate the adrenal masses. A bucket of investigations is available for diagnosing adrenal masses, including biochemistry and imaging modalities [2]. Still, no single test is fulfilling all the requirements to characterize adrenal masses. Contrast-enhanced computed tomography (CECT) has been used routinely to evaluate adrenal masses. CECT-derived relative and absolute washout percentages (AWP and RWP) are used to differentiate between the adenoma and non-adenoma adrenal masses [3]. All the available literature mainly emphasizes the differentiation of adrenal adenomas from non-adenoma masses depending on the baseline attenuation and washout pattern [3-7]. The literature on further classification of adrenal masses with poor delayed washout on CECT is limited. The masses with poor delayed washout include a broad category of lesions, that is, adrenal cortical carcinoma (ACC), pheochromocytoma (PCC), adrenal metastasis, primary adrenal lymphoma, and adrenal schwannoma (AS). By utilizing multiphase CECT (unenhanced [UE], arterial phase [AP], venous phase [VP], and delayed phase [DP]) for evaluating adrenal masses having poor and delayed washout, we can characterize different masses depending on their dynamic contrast enhancement pattern.

METHODS

Case selection

We reviewed the data on adrenal masses of our institute from January 2016 to August 2021. The Institutional Ethics Committee approval had been obtained for this analysis. A consent waiver was granted, considering the retrospective nature of the study. Patients with adrenal masses who had undergone CECT in all four phases (UE, AP, VP, and DP) showing poor washout on 15 min DP (AWP <60 and/or RPW <40) and having a histopathological diagnosis had been included from the study. Exclusion had been done for patients with inconclusive histopathological diagnosis, motion artifacts, and areas of large necrosis inhibiting us to select an adequate region of interest (ROI) for attenuation measurements. A total of 100 adrenal masses had been identified from the database and on review, out of 100 patients, only 86 were included in the analysis (36 PCCs, 26 ACCs, one lymphoma, 22 metastases, and one schwannoma). The data of biochemical tests had also been noted.

CECT study

Imaging had been performed with a 64-slice multidetector CT system (Brilliance 64, Philips Healthcare) by following standardized protocol: Patients had been placed in a supine position, with arms pulled cranially. The scanning protocol consisted of four identical helical scans obtained in an automated, predetermined, and timed sequence. Scanning parameters were 120 kVp, 140–220 mAs, 0.75 s rotation time, a pitch of 0.797, a 0.625-mm detector configuration, and a beamwidth of 40 mm. The CT sections had been reconstructed at 1-mm centers by "detail" reconstruction kernel. The first phase had been an UE baseline study, followed by injecting 100 mL of iodinated contrast material (Omnipaque 300, GE Healthcare) in the cubital vein (preplaced 18 gauge cannula) at the rate of 3 mL/s and a subsequent saline flush. The second (arterial) phase obtained after 20s of contrast material injection, third (venous) phase and fourth (delayed venous) phase had been obtained at 1 min and 15 min, respectively. Reconstruction of imaging had been done in a standard radiology workstation consisting of axial, sagittal, and coronal projections.

Image interpretation

Two experienced radiologists who unaware of the histopathological diagnosis of the adrenal masses reviewed the CT scans on the workstation. Morphological parameters such as size (maximum size in axial images), shape, necrosis, hemorrhage, and calcification were noted. Attenuation was measured in Hounsfield units (HU) with the elliptic ROI at three separate slices of the particular sequence, and the mean of these three values was calculated. Elliptic ROI being placed over a maximally enhanced area of the AP, which had an area of at least 1 cm [2] and replicated in exact locations during the different stages of the CECT. We covered the enhanced area as much as possible in the ROI after excluding site of calcification, necrosis, and surrounding fat from the ROI placement. For every mass, the HU values calculated in the UE, AP, VP, and DP had been obtained. From these values, the RWP= EVP-DP/EVP and the AWP= EVP-DP/EVP-UE had been calculated. Depending on the enhancement characteristics, the lesions were, further, categorized. If the attenuation value difference was ≥10 HU in the subsequent phase, it was considered significant. Otherwise, it was determined to be a non-enhancing. Percentage arterial enhancement was also calculated as the enhancement in the AP compared to the UE stage. PAE= (HU in AP – HU in UE)/HU in UE × 100.

Statistical calculation

Interobserver variation in the measurement of attenuation values were assessed using an interclass correlation coefficient, with values more than 0.8 being considered a good correlation.

All continuous variables (age, size, HU in different phases, AWP, RWP, and PAE) are expressed in mean±SD. Categorical variables (shape, necrosis, calcification, hemorrhage, and tumor secretion profile) had been expressed in actual numbers and percentage. Categorical variables compared by the Kruskal–Wallis test had been utilized. Age, size, and different CECT-derived variables having being compared between PCC, ACC, lymphoma, metastasis, and schwannoma by performing a one-way analysis of variance test. A *post hoc* test (LSD) had been performed to know the intergroup comparisons.

To evaluate the diagnostic accuracy of varying CECT parameters (AP HU, VP HU, DP HU, APW, RPW, and PAE) in differentiating ACC from other subtypes of adrenal masses, we generated and analyzed receiver operating characteristic curves to determine the cutoff value for differentiating the subtypes with the highest accuracy. $p<0.05$ was considered statistically significant. Statistical analysis had been done on SPSS version 23, IBM, Armonk, NY.

RESULTS

Eighty-six adrenal masses from 100 patients (six patients with bilateral adrenal masses) were included in the study with a mean age of presentation 41.4±16.8 years. The comparison of morphological, contrast enhancement, and washout characteristics are provided in Table 1 and Graph 1. There had been no significant difference in the age-related presentation of different subgroup of adrenal masses (p=0.145).

ACC

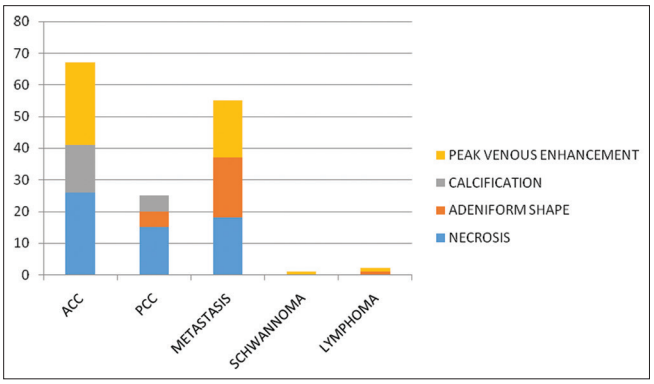
A total of 26 ACCs were included in the study from which ten patients had cortisol secreting tumors, and the other 16 patients comprised biochemically non-secreting tumors. ACC size was more significant compared to the other adrenal masses, all had necrosis, and 31.8% also showed calcification. The enhancement in different phases of CECT was significantly less compared to PCC, but no significant difference could be observed which had been concerning for other subgroups of adrenal masses. All ACCs showed maximum enhancement in the early VP (Figs. 1 and 2). No difference was observed in any of the CECT variables between secretory versus non-secretory lesions. Intraoperatively, the presence of large, lobulated, and yellowish colored masses with internal necrotic areas are shown (Fig. 3), which were subsequently proved by histopathological examination (Fig. 4).

PCC

A total of 36 patients had been included in the study of known PCC. The maximum patients had a small, irregularly shaped mass without significant necrosis or calcification. All the lesions showed a peak enhancement in the AP (Fig. 5).

Metastasis, lymphoma, and schwannoma

In totality, one lymphoma, one schwannoma, and 22 metastatic (3 bilateral) lesions had been included in our study. The adeniform shape (one lymphoma and 4/22 metastasis) being maintained only in this group of patients. Nearly, all the metastases showed necrosis. The enhancement in a different phase of CECT was not significantly further from the ACC (Fig. 6). All metastases cases revealed the primary lesion on the neck to pelvis CECT. Similarly, lymphoma shows homogenous enhancement in the AP and has no necrosis or calcification (Fig. 7), the



Graph 1: Peak enhancement in venous phase. A deformed shape, large, and irregular size mass with internal necrosis and calcification are maximally seen in adrenocortical carcinoma

Table 1: The table describes the comparison between different adrenal lesions i.e., Adrenocortical carcinoma, pheochromocytoma, metastasis, and lymphoma in respect to peak enhancement, size, shape, internal necrosis, and calcification

	Necrosis	Size	Maintain adeniform shape	Irregular shape	Hemorrhage	Calcification	Enhancement pattern
ACC (n=26)	++	++(>5CM) Deformed shaped	–	++	±	++	Peak enhancement in the venous phase
PCC (n=36)	±	–	+	+	+	+	Peak enhancement in the arterial phase
Metastasis (n=22)	±	–	±	±	–	–	Peak enhancement in the arterial phase
Schwannoma (n=1)	–	–	±	–	–	–	Peak enhancement in the delayed phase
Lymphoma (n=1)	–	–	±	+	–	–	Peak homogenous enhancement in the arterial phase

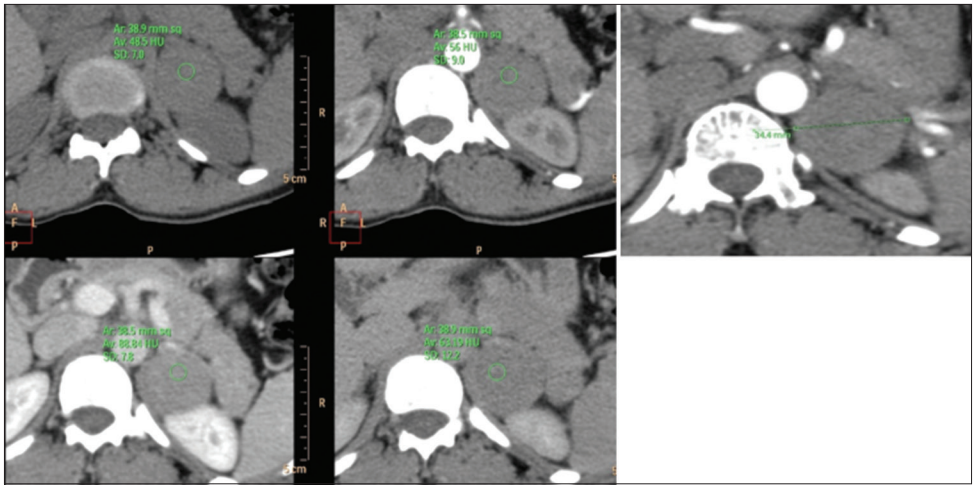


Fig. 1: Post-contrast computed axial tomography scan, illustrating an enlarged left adrenal gland with peak enhancement in the venous phase, suggesting an adrenal cortical carcinoma

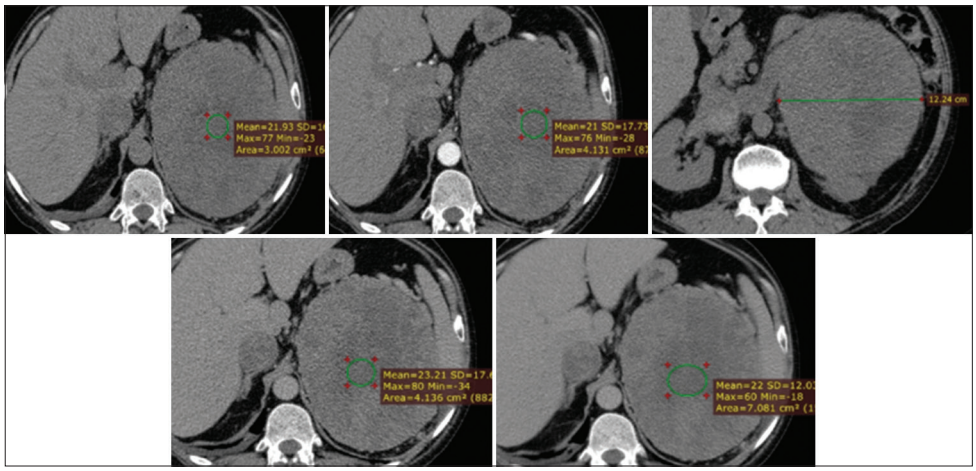


Fig. 2: Post-contrast computed axial tomography scan, demonstrating a large irregular shaped left adrenal gland mass with internal calcification and necrosis, which is showing peak enhancement in the venous phase signifying an adrenocortical carcinoma

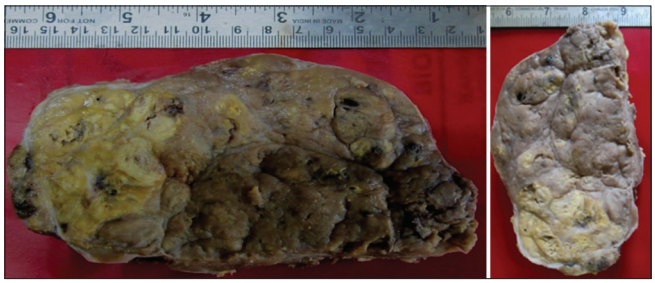


Fig. 3: The gross specimen picture of a large lobulated yellowish-brown adrenal gland mass. The lesion illustrates all features related to adrenocortical carcinoma

schwannoma showed loss of the adeniform shape with a heterogeneous post-contrast enhancement.

DISCUSSION

ACC is a rare but highly malignant lesion with a prevalence rate of approximately one or two in 1 million population with a female-to-male ratio of 1.5:1 and a bimodal age distribution, that is, in the early childhood and second in middle age. Clinical features depend on the hormonally active or inactive status of the tumors; hormonally, dormant tumors present with pain and palpable abdominal mass, while

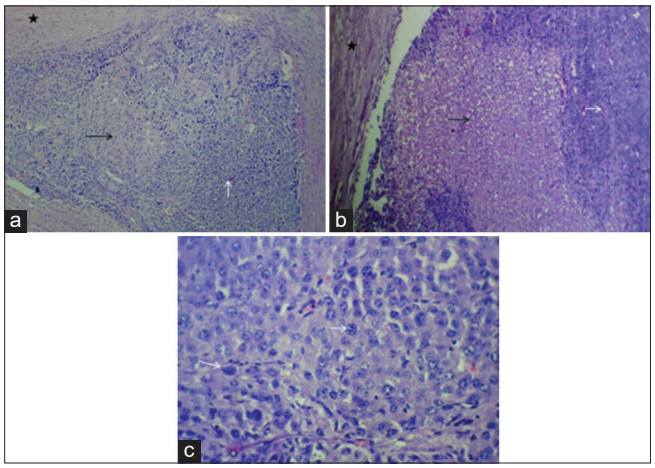


Fig. 4: (a and b) Histopathological slide in low power (H&E ×10) view showing a large sheet of tumor cells (white arrow) surrounded by fibrous stroma (asterisk) and area of necrosis (black arrow) amidst the viable tumor. (c) A high power (H&E ×40) view shows polygonal tumor cells with hyperchromatic, pleomorphic nuclei (white arrows) and prominent chromocenters

hormonally functional tumors present with features of the Cushing syndrome and the Conn syndrome. Grossly, ACCs are bulky and display

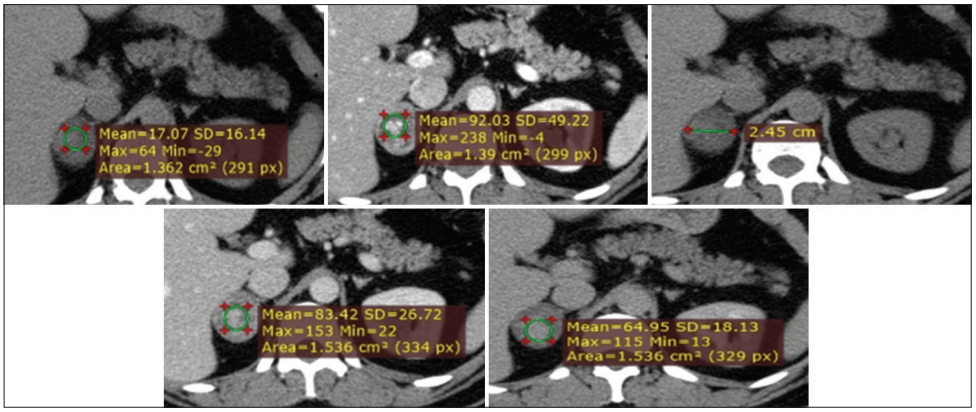


Fig. 5: Post-contrast computed axial tomography scan showing a large right adrenal gland lesion (<5 cm) with irregular shape and internal necrosis but no calcification. The lesion is showing peak enhancement in the arterial phase signifying a pheochromocytoma

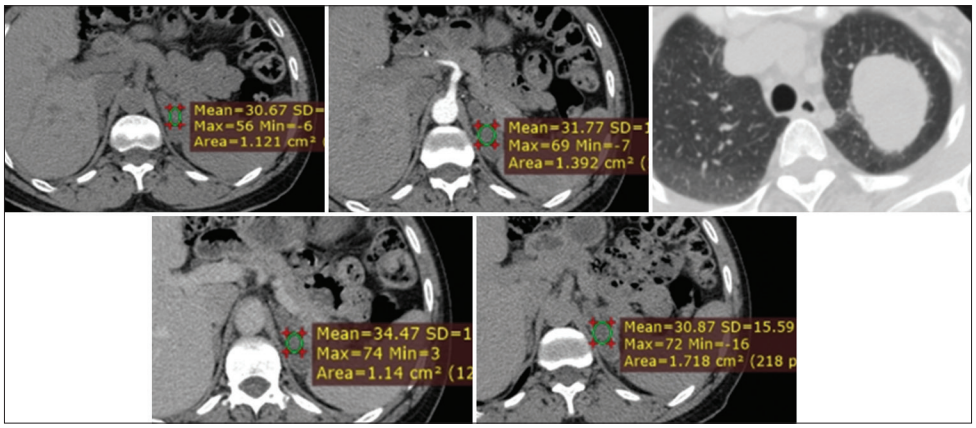


Fig. 6: Post-contrast computed axial tomography scan showing a bulky left adrenal gland maintaining an adeniform shape without any necrosis or calcification, but appears heterogeneously enhancing. In metastatic adrenal lesions, the primary focus of malignancy {; this patient has carcinoma lung (E)} is always present

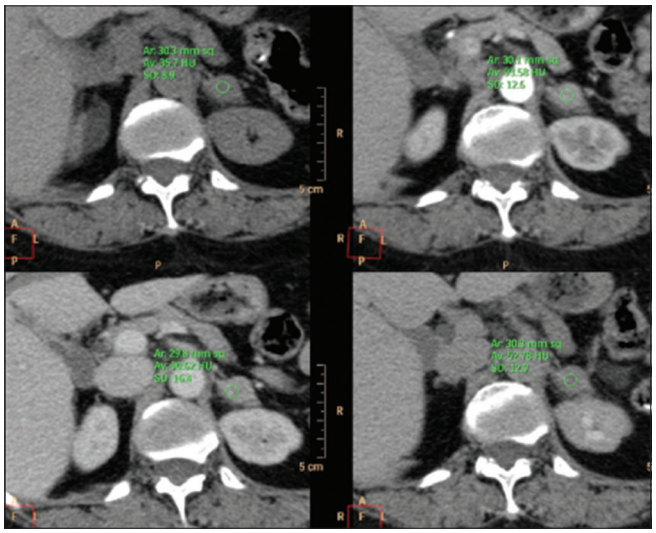


Fig. 7: Post-contrast computed tomography axial scan showing a well-defined left adrenal mass without necrosis or calcification. The lesion illustrates homogenous enhancement in the venous phase signifying a lymphoma

yellow to reddish-brown discoloration with areas of hemorrhages and necrosis.

We assessed the multiphase CECT in the characterization of the adrenal masses with a poor 15 min delayed washout. The ACC showed a heterogeneous enhancement as compared to other subgroups. PAE showed 78.8% sensitivity and 100% specificity at 100 HU cutoff on ROC analysis for the PCCs. The delayed enhancement pattern was 100% specific for the schwannoma.

Characterization of adrenal masses on CT had begun long back; in 1998, Boland *et al*. [8] established an UE attenuation of <10 HU as 98% specific and 75% sensitive for diagnosing adrenal adenoma. Lipid-poor adenoma reduced the sensitivity of the UE attenuation. After that, several authors [3,9,10] studied CT densitometry in the dynamic phase of CECT, but they did not characterize adrenal masses into adenoma versus non-adenoma. Later, the percentage washout values with the corresponding sensitivities and specificities for diagnosing adrenal adenoma were described [9]. On further, subgrouping of the non-adenoma masses by CECT is limited. Extensive investigations such as MIBG scintigraphy and somatostatin receptor (SSTR)-based PET CT are required inpatients to differentiate the non-secretory non-adenoma ACC from the other adrenal masses.

In contrast to the previous studies, the majority (19/26, 75.5%) of our ACCs showed a greater enhancement in the VP. This difference might be due to the younger age (38.8 versus 49.9 years) of our patients, which have a higher incidence of genetic mutation and hypoxia pathway activation [11,12]. The absolute value of attenuation is dependent on multiple factors such as the type of intravenous contrast material, its

total dosage, and injection rate, along with CT technique [11] being used. These parameters had been kept the same in all of our different subgroups of adrenal masses. Other parameters that can affect the enhancement are cardiovascular and intratumoral vascular patterns [11]. In our study, the aortic HU being almost identical between the subgroups; hence, the parameter affecting AP enhancement had been only the intratumoral vascularity. Hypoxia-induced factors are known to modulate the expression of several angiogenic factors and promote the sprouting of blood vessels from the pre-existing vasculature [12].

In our study, no single parameter could differentiate ACCs from other subgroups of adrenal masses. ACC size was statistically significantly different from the metastasis; however, a single value could not determine ACCs from the groups.

The adeniform shape was maintained only in lymphoma and metastasis; no other mass showed this feature. The detections of the primary lesion or other metastatic lesions were also helpful in defining the metastatic adrenal lesion. In our study, all patients had been found to have primary lesions on CECT. The likelihood of an incidental adrenal lesion representing a metastasis without a history of malignancy is exceedingly low, as shown by Song *et al.* [14] in 1049 adrenal masses in low-risk patients.

All AS showed maximum enhancement in the DP of our study.

Study limitations

Limitations of our study are its smaller sample size and retrospective nature. Our study faced selection bias due to inclusion of patients having only surgically/histopathologically proven adrenal masses. This selection bias may overestimate results because patients who did not undergo surgery may be more likely to have a negative or indeterminate effect. We have tried to minimize this selection bias by including all consecutive patients, and the images were reported in a blinded fashion (minimizing observer error).

CONCLUSION

Larger lesion size at presentation, heterogeneous architecture, and delayed peak enhancement are characteristic and specific features of ACC. Specificity and sensitivity of PAE as parameter to differentiate ACC from PCC is pretty accurate. Delayed enhancement is typical for the AS. Adding early AP to routine adrenal protocol CECT (UE, early venous 1 min and delayed venous 15 min) may help differentiate adrenal masses with poor washout on delayed VP.

CONFLICTS OF INTERESTS

None.

AUTHORS FUNDING

None.

REFERENCES

1. Mansmann G, Lau J, Balk E, Rothberg M, Miyachi Y, Bornstein SR. The clinically inapparent adrenal mass: Update in diagnosis and management. Endocr Rev 2004;25:309-40. doi: 10.1210/er.2002-0031, PMID 15082524
2. Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, *et al*. Management of adrenal incidentalomas: European society of endocrinology clinical practice guideline in collaboration with the European network for the study of adrenal tumors. Eur J Endocrinol 2016;175:G1-34. doi: 10.1530/EJE-16-0467, PMID 27390021
3. Szolar DH, Kammerhuber FH. Adrenal adenomas and non-adenomas: Assessment of washout at delayed contrast-enhanced CT. Radiology 1998;207:369-75. doi: 10.1148/radiology.207.2.9577483, PMID 9577483
4. Blake MA, Kalra MK, Sweeney AT, Lucey BC, Maher MM, Sahani DV, *et al*. Distinguishing benign from malignant adrenal masses: Multi-detector-row CT protocol with 10-minute delay. Radiology 2006;238:578-85. doi: 10.1148/radiol.2382041514, PMID 16371582
5. Park BK, Kim CK, Kim B, Lee JH. Comparison of delayed enhanced CT and chemical shift MR for evaluating hyperattenuating incidental adrenal masses. Radiology 2007;243:760-5. doi: 10.1148/radiol.2433051978, PMID 17517932
6. Caoili EM, Korobkin M, Francis IR, Cohan RH, Platt JF, Dunnick NR, *et al*. Adrenal masses: Characterization with combined unenhanced and delayed enhanced CT. Radiology 2002;222:629-33. doi: 10.1148/radiol.2223010766, PMID 11867777
7. Szolar DH, Korobkin M, Reittner P, Berghold A, Bauernhofer T, Trummer H, *et al*. Adrenocortical carcinomas and adrenal pheochromocytomas: Mass and enhancement loss evaluation at delayed contrast-enhanced CT. Radiology 2005;234:479-85. doi: 10.1148/radiol.2342031876, PMID 15671003
8. Boland GW, Hahn PF, Peña C, Mueller PR. Adrenal masses: Characterization with delayed contrast-enhanced CT. Radiology 1997;202:693-6. doi: 10.1148/radiology.202.3.9051018, PMID 9051018
9. Shrimpton P. Assessment of patient dose in CT. In: EUR. European Guidelines for Multislice Computed Tomography Funded by the European Commission 2004: Contract Number FIGMCT2000-20078-CT-TIP. Luxembourg: European Commission; 2004.
10. Korobkin M, Brodeur FJ, Francis IR, Quint LE, Dunnick NR. Londy F. CT time-attenuation washout curves of adrenal adenomas and non-adenomas. AJR Am J Roentgenol 1998;170:747-52.
11. O'Connor JP, Tofts PS, Miles KA, Parkes LM, Thompson G, Jackson A. Dynamic contrast-enhanced imaging techniques: CT and MRI. Br J Radiol 2011;84:S112-20. doi: 10.1259/bjr/55166688, PMID 22433822
12. Favier J, Gimenez-Roqueplo AP. Pheochromocytomas: The (pseudo)-hypoxia hypothesis. Best Pract Res Clin Endocrinol Metab 2010;24:957-68. doi: 10.1016/j.beem.2010.10.004, PMID 21115164
13. Zhang YM, Lei PF, Chen MN, Lv XF, Ling YH, Cai PQ, *et al*. CT findings of adrenal schwannoma. Clin Radiol 2016;71:464-70. doi: 10.1016/j.crad.2016.01.010, PMID 26897337
14. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: Prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. AJR Am J Roentgenol 2008;190:1163-8. doi: 10.2214/AJR.07.2799, PMID 18430826