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ORIGINAL ARTICLE

Value of combined CT parameters in distinguishing benign from malignant adrenal masses in cancer patients

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Abstract The aim of this work was to evaluate the effectiveness of combined CT parameters in distinguishing benign from malignant adrenal masses in cancer patients.
The study included 33 patients with 39 adrenal masses. CT protocol included pre-contrast scan, dynamic and delayed contrast-enhanced scans assessing the mass size, pre-contrast attenuation, histogram & post-contrast absolute percentage washout (APW). Sensitivities, specificities, accuracies & *P*-values were calculated for individual and combined parameters.
Adrenal masses included 13 lipid rich, nine lipid poor adenomas, one carcinoma and 16 metastases. Size was accurate in the differentiation of 26 of the total 39 masses (66.7%). Accuracy (82.05%) & specificity (68.18%) for the 10% negative pixels threshold on histogram were higher as compared to 76.9% & 59% for the 10 HU mean attenuation threshold. Using APW of 55% at 10 min delay, a sensitivity of 88.23%, a specificity of 86.36% & an accuracy of 87.17% were calculated. The

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combination of pre-contrast attenuation & histogram values and the APW were highly significant for the differentiation of benign & malignant adrenal masses (P-value is <0.001).
Combining the CT parameters including the pre-contrast attenuation values, histogram & the post-contrast washout analysis yielded a powerful diagnostic protocol with 74.3% accuracy, excluding the size parameter.

1. Introduction

Adrenal masses—both suspected and incidental—are identified at up to 5% of abdominal CT examinations (1). The adrenal gland is a relatively frequent site for metastatic disease (2). Adrenal adenomas are present in 4–6% of the general population (3). Although most of the adrenal masses turn out to be adenomas, in a patient with a known history of primary extra-adrenal neoplasm especially lung carcinoma, this constitutes a major problem. In this setting to diagnose or exclude an adrenal metastasis is crucial in order to determine a reasonable strategy that requires either follow-up imaging for adenoma or appropriate therapy of the primary tumor (4). The presence of metastases may contraindicate curative surgery or radiotherapy (2). The accurate diagnosis of these masses using CT is important for the staging of malignancies and for the reduction of the need for both percutaneous biopsy and follow-up imaging in patients with adrenal masses (5).

Cross-sectional imaging readily characterizes benign adrenal masses, such as lipid-rich adenomas, myelolipomas, adrenal cysts, granulomas and adrenal hemorrhage as they have characteristic diagnostic imaging findings such as intra-lesional fat, water or blood. A small minority of adrenal masses eludes characterization on cross-sectional imaging and remains indeterminate. These include lipid-poor adenomas, adrenal metastases, adrenal carcinomas, and pheochromocytomas. For this group of adrenal masses, the commonest clinical setting is to differentiate between a benign adrenal adenoma and a malignant lesion, particularly a metastasis (2). Tremendous progress has been made in the radiological evaluation of adrenal masses using unenhanced CT and CT contrast washout analysis (6). The CT histogram analysis is a simple & easily applicable method which provides higher applicable method of unenhanced CT for the diagnosis of an adenoma (4).The two major predictors of malignancy are the tumor's size and its imaging features (7). Kamiyama et al. (5) reported that combining the diagnostic parameters of the CT protocol can yield the best diagnostic results.

The aim of this work was to evaluate the effectiveness of combined CT parameters including the size, pre-contrast attenuation, histogram & the post-contrast washout analysis in distinguishing benign from malignant adrenal masses in cancer patients than the use of individual parameters.

2. Patients & methods

2.1. Patients & masses

This study included 33 patients with known cancer of variable sites of origin, from the oncology department of Ain Shams University hospitals. The primary sites of cancer were lung carcinoma in 8 patients of whom four had bilateral adrenal masses, colon carcinoma in five patients, breast cancer in three patients, larynx carcinoma in three patients, renal cell carcinoma in three patients, gastric carcinoma in two patients, testis carcinoma in two patients, Hodgkin lymphoma in two patients who had bilateral adrenal masses, prostate cancer tumor in two patients, primary adrenal cortical carcinoma in one patient (he was operated upon one year before study & returned with a recurrent adrenal mass), uterine carcinoma in one patient, and bladder carcinoma in one patient. The study was carried over a period of about 24 months. 39 Adrenal masses were detected with a previous imaging study as a part of a cancer workup for staging (six patients had bilateral adrenal masses).

Patients had undergone the dedicated CT protocol for evaluating adrenal masses. All patients were assessed for size stability at previous and/or follow-up imaging examination by CT and/or MRI for one year in view of the patients' history of cancer. Pathologic proof of diagnosis was obtained in six patients according to the results of surgical or percutaneous biopsy specimens.

2.2. Exclusion criteria

- Patients with inadequate follow-up.
- Adrenal cysts (which manifest at CT as water density with lack of enhancement and an imperceptible wall).
- Pheochromocytoma which were diagnosed on the basis of their clinical & hormonal findings).
- Adrenal calcifications or hemorrhage with high CT attenuation values (for not interfering with the pre & post-contrast mean attenuation values calculations of the ROI).

2.3. CT scan technique

The CT examinations were preformed by at least eight multidetector scanners (GE Healthcare, Milwaukee, WI, USA) with 2.5-slice collimation, 3-mm slice thickness, 1.5 reconstruction intervals, a kV of 140, 200–300 mA and 0.8-s gantry rotation time.

Initially, unenhanced images were obtained. IV contrast (Iopamiro 300; Bracco, Milano, Italy) was given as 100–150 mL at a rate of 4 mL/s using an automatic pump injector (Angiomat 6000; Liebel-Flarsheim) via an antecubital vein. Scanning was initiated 60 s after the start of the injection, and delayed images were also obtained 10 min later.

The images were sent to the workstation (Hp xw 8600, AW Volume share 4, GE medical systems SCS, France) where coronal and sometimes sagittal reformats were reconstructed.

CT histogram measurements were performed on the post-processing workstation using the commercially available software. The image showing the maximal cross-sectional area was chosen for each adrenal mass where the long-axis and short-axis diameters were measured. A circular or ovoid region of interest (ROI) was placed on the adrenal mass including as much of the mass as possible but excluding the outer edges to avoid partial volume effects. Approximately half to two-thirds of each mass was included. The mean attenuation over the ROI was recorded. The CT histogram was acquired from the ROI using software application on the workstation where a graph of the number of pixels on the y-axis versus the pixel attenuation on the x-axis was obtained from the ROI. Histogram analysis included recording the total number of pixels, number of negative pixels with attenuation less than 0 HU, and the resulting percentage of negative pixels in each ROI.

2.4. Image analysis

Size was recorded with the CT distance cursor to measure the largest diameter in the axial plane on the unenhanced CT scan. Masses < 4 cm were presumed to be benign while masses > 4 cm were presumed to be malignant.

CT mean attenuation values in Hounsfield units (HU) on the pre-contrast, contrast-enhanced, and delayed contrast-enhanced images were recorded. A threshold value of < 10 HU on the pre-contrast CT scans was chosen for distinguishing benign lesions (e.g. adenomas) from indeterminate lesions (2,8,9). Similarly, non-calcified, non hemorrhagic lesions with attenuation values > 43 HU were considered malignant (10).

CT histogram: The percentage of each type of adrenal mass in terms of containing any negative pixel and at the threshold values of 10% negative pixels on unenhanced CT images was recorded (5). Statistical analysis for correlation between mean attenuation value and percentage of negative pixels was also calculated.

The absolute percentage washout (APW) was calculated as follows:

$APW = 100 \times ([EA-DA]/[EA-PA])$, where EA is attenuation on contrast-enhanced scans, DA is attenuation on delayed contrast-enhanced scans & PA is pre-contrast attenuation. Progressive enhancement of a mass on a delayed scan (i.e., when attenuation on a delayed scan was greater than attenuation on a dynamic scan) was given a washout score of 0. The lowest APW threshold values for best discriminating adenoma were selected (> 52% at 10 min post-contrast) (10).

The final analysis made use of all the imaging information from the protocol & was reviewed by two experienced radiologists; lipid-rich adenomas (which manifest at CT as macroscopic fat) were included in the study.

At follow-up imaging, interval growth or appearance of new lesion was considered to be indicative of malignancy, while one year of stability was considered to be an evidence of benignity to be more conservative in those cancer patients'.

2.5. Statistical analysis

The recorded data were entered into an Excel worksheet (Microsoft, Redmond, Wash). Sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV), and accuracies were calculated for the mass size, the pre-contrast & post-contrast CT analysis and for the combined CT parameters used for the differentiation of benign & malignant adrenal masses. The P-values by Chi-square test were also determined: > 0.05 = non-significant, < 0.05 = significant, & < 0.01 = highly significant.

Table 1 CT features of benign & malignant adrenal masses.

CT parameters		Types of lesions				Chi-square	
		Lipid rich	Lipid poor	Malignant	Total	χ^2	P-value
Size							
< 4 cm	N	9	7	7	23	4.106	0.128
	%	69.23	77.78	41.18	58.97		
> 4 cm	N	4	2	10	16		
	%	30.77	22.22	58.82	41.03		
Pre-contrast attenuation							
< 10 HU	N	13	0	0	13	39.000	< 0.001*
	%	100.00	0.00	0.00	33.33		
> 10 HU	N	0	9	17	26		
	%	0.00	100.00	100.00	66.67		
Pre-contrast histogram							
> 10%	N	13	2	0	15	32.428	< 0.001*
	%	100.00	22.22	0.00	38.46		
< 10%	N	0	7	17	24		
	%	0.00	77.78	100.00	61.54		
APW							
> 60%	N	12	7	2	21	21.926	< 0.001*
	%	92.31	77.78	11.76	53.85		
< 60%	N	1	2	15	18		
	%	7.69	22.22	88.24	46.15		

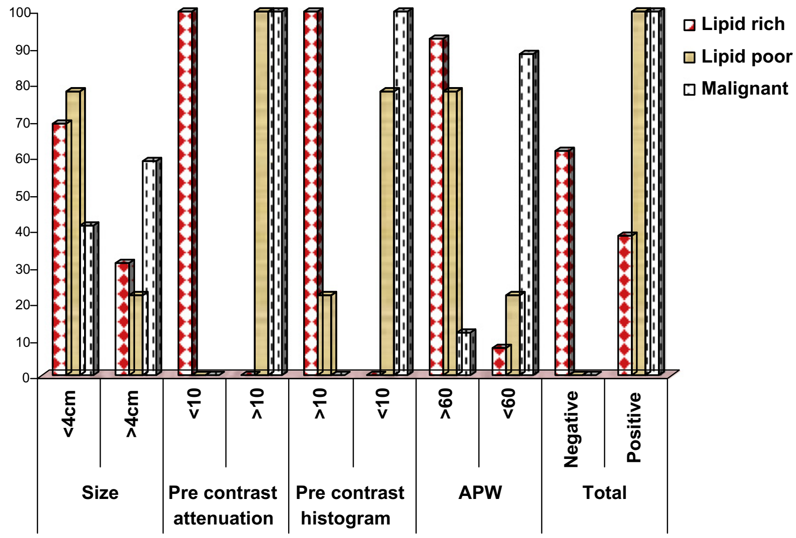

Diagram 1 CT features for lipid rich adenomas, lipid poor adenomas, & malignant adrenal masses.

3. Results

Thirty-nine adrenal masses were detected in 33 patients (21 men & 12 women; their ages ranged from 26 to 65 years). They included 13 lipid rich & 9 lipid poor adenomas (22 benign masses, 56.4%), one adrenal carcinoma and 16 adrenal metastases (17 malignant masses, 43.6%). Characteristic individual CT imaging features of the adrenal masses including the size, the pre-contrast mean attenuation & histogram values and the post-contrast washout analysis (APW)—used for the differentiation of benign & malignant adrenal masses—were summarized in Table 1 & Diagram 1. The sensitivity, specificity, PPV, NPV, & accuracy as well as *P*-values of the individual & combined CT parameters were reported in Table 2 & Diagram 2.

3.1. Individual CT parameters

3.1.1. Size

Sixteen adenomas were <4 cm in maximal diameter (Figs. 1 and 2). Six adenomas were >4 cm in size (6 of 22, 15.38%): four were lipid rich & had low pre-contrast attenuation values ⩽10 HU, negative pixels on histogram >10, and the other two were lipid poor and had intermediate attenuation values of 14 & 31HU (>10 HU), one of them had negative pixels on histogram >10%. They all had AWP > 60% & stable size on follow-up imaging.

Ten malignant masses (nine metastatic & one carcinoma, 58.8%) were >4 cm in size (Figs. 3 and 4).

Seven metastases had small sizes <4 cm (7 out of 17, 17.95%) but their washout was consistent with malignant behavior (Fig. 5) & three of them had attenuation >43 HU favoring malignancy. They were proved to be malignant by histopathology & by increasing size on follow-up imaging.

We concluded that size was accurate in the differentiation of benign & malignant adrenal masses in 26 of total 39 masses (66.7%).

3.1.2. Pre-contrast mean attenuation values

All the lipid rich adenomas (100%) on unenhanced CT had low attenuation values ⩽10 HU & ⩾10% negative pixels on histogram (Fig. 1). The nine lipid poor adenomas (9 of 22 adenomas, 40.9%) had attenuation values >10 HU & <43HU, (range = 13–32 HU, mean = 21 HU). Two of these lipid poor adenomas showed ⩾10% negative pixels on histogram & >60% by AWP favoring benign behavior (Fig. 2). The adrenal carcinoma (Fig. 4) & 12 metastases had attenuation >43 HU (Fig. 3), while the rest of malignant cases (4 of 17 malignant masses, 23.5%) had attenuation values ranging from 27 to 41 HU (mean = 33 HU after exclusion of the cases >43 HU) (Fig. 5).

3.1.3. Pre-contrast histogram

All lipid rich & two lipid poor adenomas had ⩾10% negative pixels on histogram (Fig. 1) ranging from 12% to 52%, mean = 31% (15 of 22 adenomas, 68.18%). Five lipid poor

Table 2 Statistical assessment of the CT parameters used in differentiation of benign & malignant adrenal masses.

CT parameters	Sen.	Spec.	PPV	NPV	Accuracy	Chi-square	
						χ^2	*P*-value
Size	58.824	72.727	62.500	69.565	66.667	4.106	0.128
Pre-contrast attenuation	100.000	59.091	65.385	100.000	76.923	39.000	<0.001*
Pre-contrast histogram	100.000	68.182	70.833	100.000	82.051	32.428	<0.001*
APW	88.235	86.364	83.333	90.476	87.179	21.926	<0.001*
All CT parameters	100.000	36.364	54.839	100.000	64.103	20.129	<0.001*
All excluding the size	100.000	54.545	62.963	100.000	74.359	20.129	<0.001*

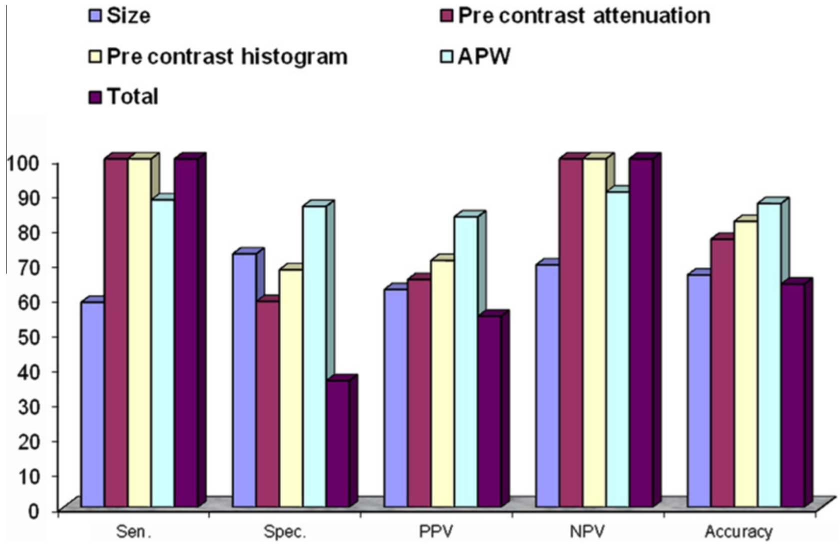

Diagram 2 Statistical assessment of the CT parameters used in differentiation of benign & malignant adrenal masses.

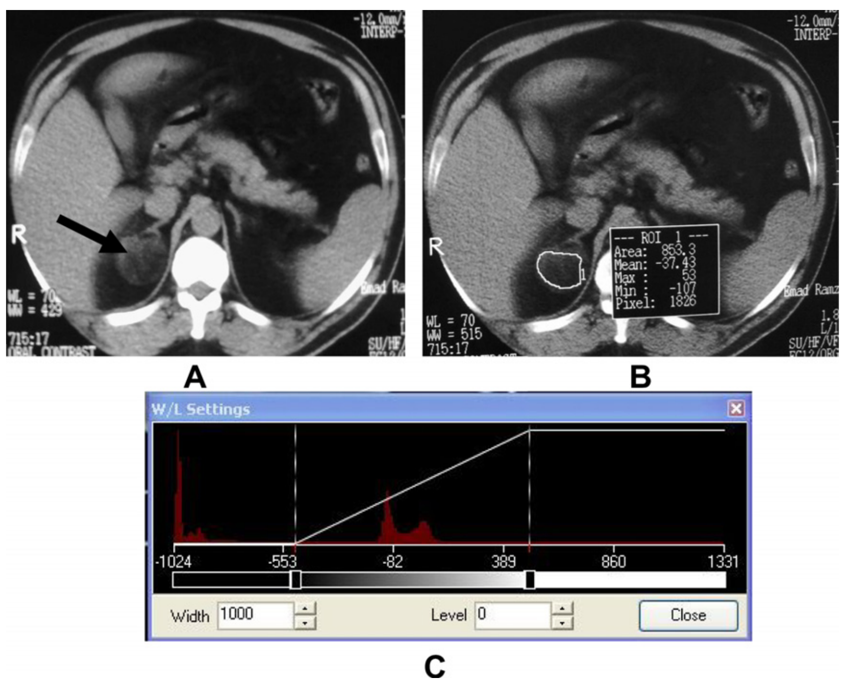

Fig. 1 Lipid rich adenoma: 47 years old man with a history of cancer colon and right adrenal spherical mass 3 cm in diameter (arrow in A). The ROI (B) demonstrates 1026 pixels with a median density of −37 HU. The upper and lower limits of pixel attenuation were 53 & −107, respectively. The histogram analysis (C) shows that more than 50% of the mass contains negative pixels. The APW was 77%.

adenomas had 5–10% negative pixels on the histogram (Fig. 2) & only one had < 5%.

Only five of the malignant masses had < 5% & the rest did not show any negative pixels (Figs. 3 and 4).

We obtained 82.05% accuracy & 68.18% specificity for the 10% negative pixels threshold on histogram as compared to 76.9% accuracy & 59% specificity for the 10HU mean attenuation threshold value for unenhanced CT scan. Both methods resulted in 100% sensitivity for the diagnosis of adrenal masses.

Twenty-six masses had low density < 10 or high density > 43 HU (66.6%) & only 13 (nine lipid poor & four malignant) of 39 lesions had intermediate attenuation (33.3%) which constitute the main group of the diagnostic challenge. Two of the lipid poor adenomas showing ⩾10% negative pixels on histogram were diagnosed to be benign & were excluded from this group reducing it to 11 masses (28.2%). AWP was useful for the diagnosis of 8 of these 11 masses (72.72%): 5 of 7 lipid poor masses (71.4%) & 3 of the 4 malignant masses (75%).

3.1.4. Comparison between the benign & malignant adrenal masses by their washout criteria (APW)

APW threshold of 55% was accurate in diagnosing 19 benign masses (ranging from 63% to 85%, mean = 67%, Figs. 1 and

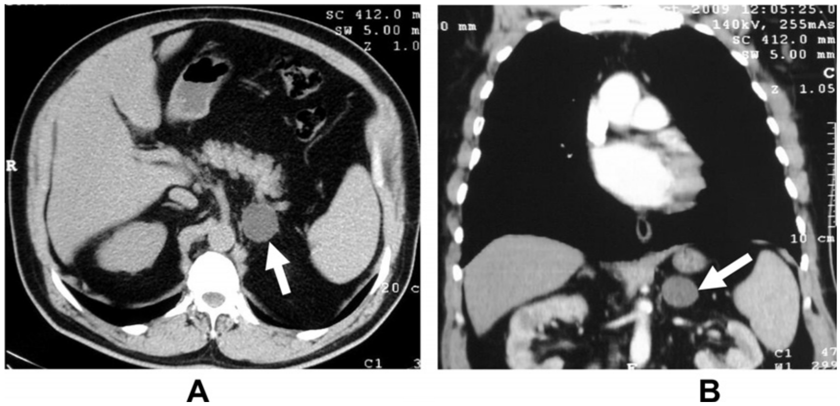

Fig. 2 Lipid poor adenoma: Axial image (A) and coronal reformat (B) of a 26 years old man with a history of orchidectomy for seminoma. The left adrenal mass (white arrows) was 2.2 cm in diameter. Its median density was 27 HU. The upper and lower limits of pixel attenuation were 55 & −4, respectively. The histogram analysis shows that 5.4% of the mass contains negative pixels. The APW was 63%.

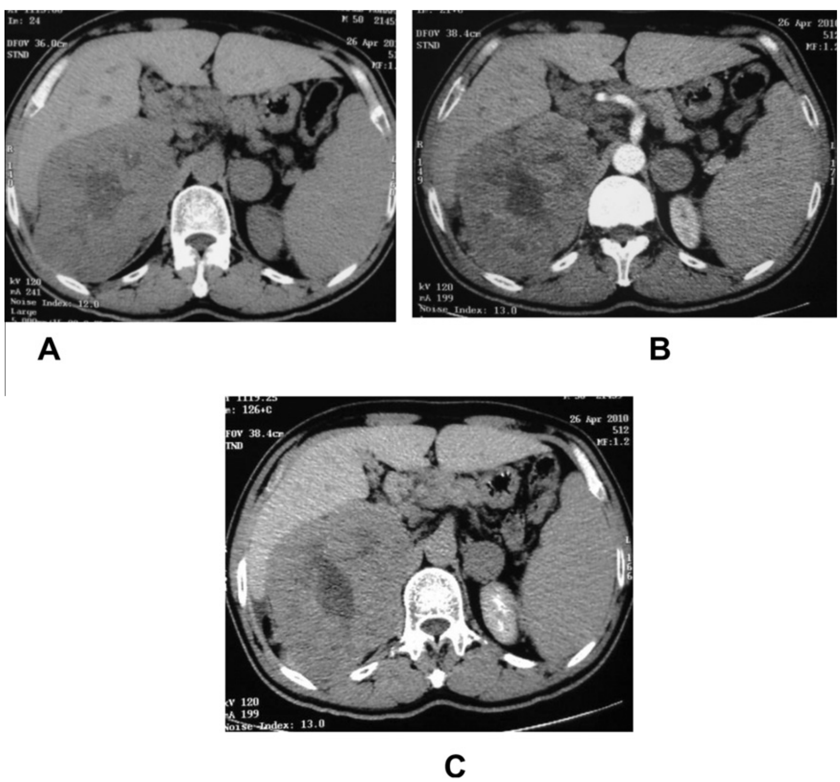

Fig. 3 Bilateral adrenal metastasis: 50 years old man with bronchogenic carcinoma showing newly developed bilateral adrenal masses A, B & C are pre-contrast, dynamic, and 10 min delayed scans. The right adrenal mass had a maximum diameter of 12 cm while the left one measured 2.7 cm in diameter. The right large mass showed a necrotic core which was excluded from the analysis. The two masses had a median density of 47 and 56 HU, respectively. The upper and lower limits of pixel attenuation were 8 & 76 HU for the left mass. The histogram analysis did not show any negative pixels. The APW was 27%.

2) & 16 malignant masses (ranging from 25% to 47%, Figs. 3 and 5) resulting in a total of 35 from 39 masses (89.74%) as compared to the cut-off value of 52% which missed the case of adrenal carcinoma reducing the percentage of diagnosed malignant masses to 15 cases (total 34 of 39 masses, 87.3%). By using an APW of 55% at 10 min delay post-contrast, a sensitivity of 88.23%, a specificity of 86.36% & an accuracy of 87.17% were calculated.

Two of the lipid poor adenomas were misdiagnosed because they did not meet the benign criteria of APW & had intermediate density & 5–10% negative pixels on histogram. One lipid rich adenoma showed progressive enhancement getting a score of 0 but had pre-contrast low attenuation < 10HU (−5 HU), negative pixels > 10% on histogram. They all had small size < 4 cm & were stable on follow-up imaging. The adrenal carcinoma (Fig. 4) showed rapid washout of 55% (> 52% but

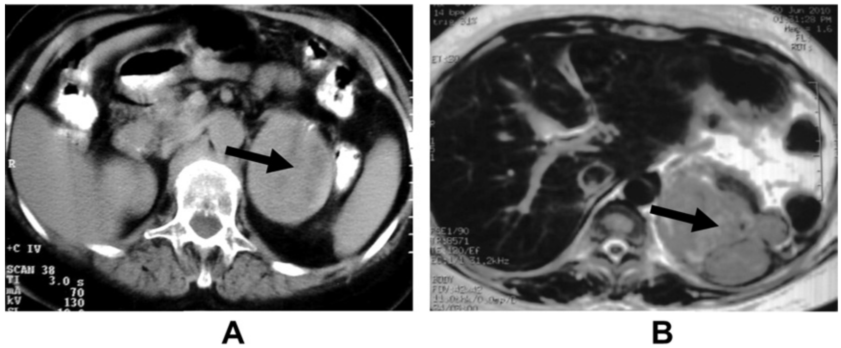

Fig. 4 Left adrenal carcinoma: 55 years old woman with left adrenal mass (arrowed). (A) The mass measured 7 × 5 cm in its axial dimensions with a median density of 52 HU, the upper and lower limits of pixel attenuation were 14 & 73 HU, respectively. The histogram analysis did not show any negative pixels. These figures are consistent with malignant process; however, The APW was 55%. (B) Follow-up was done by MRI revealing a considerable increase of the size mass with 9.5 cm at maximal diameter. Excision and biopsy revealed an adrenal carcinoma.

Fig. 5 Left adrenal metastatic deposit: Coronal reformatted image (A) and axial image with histogram (B) of a 45 years old woman with a history of cancer breast. The study revealed left adrenal mass 2.5 cm in maximum diameter (arrowed). The median density was 37 HU. The upper and lower limits of pixel attenuation were 58 & −2, respectively. The histogram analysis shows that only 0.14% of the mass contains negative pixels. The APW was 33%. Biopsy revealed metastatic disease.

< 60%) & had malignant features by other CT parameters & histopathology. Another adrenal metastasis showed APW > 60%, small size < 4 cm & intermediate density (10–43 HU); it was misdiagnosed as benign but was confirmed by histopathology to be malignant.

3.2. Value of combined CT parameters

The combined CT parameters succeeded in diagnosing 36 (92.3%) of the total 39 cases (100% of the lipid rich, 77.7% of lipid poor & 94.1% of malignant masses). They were able to differentiate benign from malignant masses in 10 of the 13 indeterminate density masses (76.9%). Only 3 of total 39 masses (7.69%) were misdiagnosed: 2 of 9 lipid poor (22.2%) equivalent to 2 of 22 benign masses (9%) & one metastasis case (5.8%) of the 17 malignant masses.

The combination of pre-contrast mean attenuation & histogram values and the post-contrast washout analysis (APW) were highly significant CT parameters for the differentiation of benign & malignant adrenal masses (P-value is < 0.001). Only the size parameter was statistically not significant as an individual CT parameter for this differentiation ($P = 0.128$). The size had the lowest statistical diagnostic values & the AWP had the highest values obtained among the studied CT parameters. The accuracies of combined CT parameters before & after exclusion of the size parameter were 64.1% & 74.3%, respectively.

3.3. Proof of diagnosis

Pathologic proof of diagnosis was able to confirm malignancy in six patients (the patient with recurrent adrenal carcinoma & five patients with adrenal metastasis: two from lung carcinoma, two adrenal lymphomas & one from breast cancer).

The three lesions that did not meet the criteria of adenoma on dedicated adrenal washout study had stable size on follow-up imaging, and therefore, were presumed to be benign on the basis of imaging stability. None of the adenomas had increased in size on follow-up study during the first 6 months.

4. Discussion

Characterizing adrenal masses is important because the nature of the mass may have a profound effect on patient care. Accurate characterization is important for identifying both malignant lesions and benign adenomas because it would obviate both percutaneous biopsy and repeated interval follow-up imaging. Imaging algorithm for assessing adrenal masses in which CT plays the predominant role has been proposed (11).

The probability of a specific type of adrenal mass varies with the clinical picture. For example, in patients with cancer, up to 75% of adrenal incidentalomas are metastatic lesions but in patients with no history of cancer two-thirds are benign (12). The majority of benign lesions are adenomas, of which 80% are benign non functioning adenomas (2). In the current study, 39 adrenal masses were diagnosed, of which 56.4% were benign & 43.6% were malignant.

Considerable overlap in size has been demonstrated between adenomas and nonadenomas, especially metastases in previous studies (13,14). In the current study, the size criterion yielded the lowest sensitivity (58.8%), specificity (72.7%) & accuracy (66.6%) as compared to other studied CT parameters. This was comparable to 98% sensitivity & 53% specificity in Kamiyama et al. (5) study. The incidence of metastatic adrenal lesions increases to 71% if the adrenal mass is larger than 4 cm and demonstrates an increase in size on follow-up imaging within 1 year (15). If the non-contrast CT attenuation value is greater than 10 HU and the mass measures 6 cm or more, Gopan et al. (7) suggested referring the patient for surgery.

In agreement with Hamrahian et al. (9) & Gopan et al. (7), the HU value on non-contrast CT is a better criterion than tumor size for distinguishing adrenal adenomas from non-adenomas. In the current study, it yielded a higher sensitivity (100%), specificity (59%) & accuracy (76.9%) as compared to the size indices. On non-contrast-enhanced CT, up to 30% of benign adenomas have an attenuation value of greater than 10 HU and are considered lipid-poor in Pena et al. (13) study & about 40.9% in the current study. Malignant lesions are also lipid poor (2). Boland et al. (8) in 1998 performed a meta-analysis of 10 studies demonstrating that if a threshold attenuation value of 10 HU was adopted, the specificity was 98% but the sensitivity increased to 71%. In clinical practice, therefore, 10 HU is the most widely used threshold attenuation value for the diagnosis of an adrenal adenoma. In Kamiyama et al. (5) study, this threshold value yielded 100% accuracy for lipid-rich adenomas but 57% (30 of 53) sensitivity for total adenomas because of the 23 lipid-poor adenomas. In the current study, the same threshold was used with comparable results: 100% sensitivity, 59% specificity & 76.9% accuracy for the total adrenal masses & 100% statistical indices for lipid rich adenomas.

In agreement with Blake et al. (10) study, any lesions with pre-contrast attenuation greater than 43 HU should be regarded with suspicion (i.e., considered malignant), regardless of its washout profile. In the current work, thirteen malignant lesions had pre-contrast attenuation values greater than 43 HU (76.4% of malignant masses), whereas none of the benign lesions had pre-contrast attenuation values greater than 43 HU. Also, pre-contrast attenuation of less than 10 HU supersedes APW in importance. One lipid rich adenoma with pre-contrast attenuation of less than 10 HU had progressive enhancement getting an APW value of zero, and one malignancy with pre-contrast attenuation of greater than 43 HU demonstrated a marked contrast material washout with an APW value of 55% at 10 min post-contrast.

The use of CT histogram analysis to evaluate adrenal masses has been proposed by Bae et al. (16). In Halefoglu et al. (4) study, CT histogram analysis using a 10% negative pixel threshold has a higher sensitivity than $\leqslant$10 HU mean attenuation threshold method to discriminate adenomas from non-adenomas on unenhanced CT. In the present study, histogram analysis improved the pre-contrast diagnostic accuracy to 82.05% for the 10% negative pixels threshold as compared to 76.9% for the 10 HU mean attenuation threshold value for unenhanced CT scan. Both methods resulted in 100% sensitivity for the diagnosis of adrenal masses & 100% accuracy for the diagnosis of lipid rich adenomas. Thus, histogram in addition to pre-contrast attenuation could distinguish 71.8% of adrenal masses, being either of low density (lipid rich adenomas) or high density >43 HU (considered malignant until proved otherwise). Unenhanced CT attenuation could not be used to sufficiently differentiate the intermediate density lipid poor adenomas from non-adenomas.

Most lipid-poor adenomas can be separated from the malignant group by recent advances in CT. Lipid-poor adrenal masses should first be evaluated by studying CT contrast medium washout characteristics. Characterization of adrenal masses using contrast-enhanced CT utilizes the different physiological perfusion patterns of adenomas and metastases. Attenuation values of adrenal masses obtained 60 s after contrast medium injection show too much overlap between adenomas and malignant lesions to be of clinical value. Adrenal masses with a CT attenuation value measuring less than 30 HU, on delayed images obtained 10 to 15 min after contrast enhancement, are almost always adenomas (13). However, the percentage of contrast washout between initial enhancement (at 60 s) and delayed enhancement (at 10 min) can be used to differentiate adenomas from malignant lesions. These absolute contrast medium enhancement washout values are only applicable to relatively homogeneous masses without large areas of necrosis or hemorrhage. It has been demonstrated that washout of contrast from adenomas occurs much faster than from metastases. Both lipid-rich and lipid-poor adenomas behave similarly, as this property of adenomas is independent of their lipid content (2). The APW of an adrenal mass may seem to be a more accurate calculation of de-enhancement because the pre-contrast attenuation value is included in the calculation of APW. APW may be the most useful parameter to differentiate lipid-poor adenomas from non-adenomas (5).

In this present study, we followed the 10-min delay protocol which is a more convenient method of adrenal mass characterization because it has the inherent advantage of a shorter examination time as advised by Blake et al. (10) study. The optimal APW threshold values with the 10-min delay used in their study were slightly lower than those with a 15 min delay because there was less time for de-enhancement to occur. The 10-min delay protocol yielded lower threshold values of 52.0%. Caoili et al. (14) recommend the use of 60% APW threshold with a 15-min protocol. On the basis of the results of this current study, in agreement with Blake et al.(10) study, keeping the same high threshold for the 10-min protocol—similar to that adopted for the 15-min protocol—has some merit because it preserves the desired success in the detection of malignancy (e.g. one malignant adrenal mass had AWP of 55% & was proved by biopsy to be metastatic). Delayed enhancement criteria at 5 min may be accurate to differentiate lipid-rich adenomas from nonadenomas, but they yield lower sensitivity for lipid-poor adenomas (5). In the current study, an APW of 55% at 10 min delay post-contrast showed the highest sensitivity of 88.23%, specificity of 86.36% & accuracy of 87.17% as compared to other CT parameters.

In Kamiyama et al. (5) study, they concluded that a combination of the unenhanced and dynamic enhanced CT protocol parameters can yield a high diagnostic accuracy in the differentiation of adrenal adenomas from non-adenomas. Combining the CT parameters studied in the current study yielded a valuable diagnostic protocol with an accuracy of 74.3% for distinguishing the nature of adrenal masses, considering that size criterion should not be used as an individual discriminator.

4.1. Limitations

The majority of the adrenal masses was not pathologically proved and required follow-up imaging for characterization. This has been an accepted method of classifying benign and malignant lesions in previous studies (10,13). Size stability during a 6-month or longer follow-up to confirm adenomas and growth of the mass within 6 months or shrinkage after chemotherapy to confirm metastases was used in most studies as in Blake et al. (10), Kamiyama et al. (5), & Halefoglu et al. (4) studies. Other studies had used one year of stability as a lower limit (13,14). In the current study, 1 year of stability was used to be more conservative for the exclusion of adrenal metastasis as the patients' population was known with cancer of variable origins. Yet, none of the adenomas had increased in size on follow-up study during the first 6 months & they were presumed to be benign on the basis of their imaging stability on follow-up. Therefore, 6 months of follow-up is a sufficient period. No good evidence supports continuing radiological surveillance if the first follow-up study shows no change in tumor size (7).

In conclusion, non hyper-functioning adrenal masses are common even in patients with cancer. Most are lipid-rich adenomas and these can be confirmed on a single unenhanced CT with an attenuation value of less than 10 HU & a histogram threshold of more than 10% negative pixels. Histogram is more accurate than pre-contrast attenuation in detecting intra-lesion fat content & is considered a useful tool in diagnosing lipid rich adenomas. The pre-contrast attenuation value of less than 10 HU supersedes the washout profile in the evaluation of an adrenal mass. Lipid-poor lesions include malignant adrenal lesions and lipid-poor adenomas. All non-calcified, non hemorrhagic adrenal lesions with pre-contrast attenuation of greater than 43 HU should be considered suspicious for malignancy. After these extreme attenuation limits are considered, the APW value is an accurate discriminator of the nature of adrenal masses whether benign or malignant especially for the intermediate density masses. Size is the lowest CT parameter discriminator with considerable overlap between benign & malignant lesions. Combining the studied CT parameters yielded a powerful diagnostic protocol in distinguishing benign from malignant adrenal masses. Six months of size stability is sufficient to confirm benign adenomas without the need for further follow-up.

Disclosure/Conflict of interest

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