DISTINGUISHING BENIGN LESION FROM MALIGNANT ADRENAL MASSES BY CT SCAN WITH 15 MINUTES DELAYED PROTOCOL

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ABSTRACT

BACKGROUND
Adrenal masses are benign, non-hyper functioning adenoma in most of the cases and classified in lipid-rich or lipid-poor adenomas. After injection of contrast with adrenal protocol and delayed washout CT study can differentiate adenomas from other adrenal neoplastic lesions. The aim of this study was to evaluate the effectiveness of MDCT parameters in distinguishing benign from malignant adrenal masses in cancer patients.

MATERIALS AND METHODS
This study included 64 patients with adrenal masses and was carried out in the period from January 2017 to November 2017. MDCT protocol included pre-contrast scan, dynamic and delayed contrast-enhanced scans assessing the mass size, pre-contrast CT density, histogram, delayed post contrast scan apart from 15-min delayed washout rate, relative percentage washout (RPW) and absolute percentage washout (APW) value. Sensitivities, specificities, accuracies & p-values were calculated for individual and combined parameters.

RESULTS
Total 64 adrenal masses were evaluated by using CT attenuation values in pre-contrast, venous and 15 min delayed scans, which showed that 15 min delayed images along with APW/RPW can become useful diagnostic tool in differentiating benign adenomas from malignant adrenal neoplastic adenomas with an accuracy of 98.43%.

CONCLUSION
In adrenal incidentalomas, 15 minutes delayed washout MDCT is mandatory for final diagnosis. Significant accuracy in differentiating adrenal adenomas at APW P60% AND RPW P40%.

KEYWORDS
Relative Percentage Wash Out (RPW), Absolute Percentage Wash Out (APW), Multidetector- CT (MDCT).


BACKGROUND
The detection of adrenal masses both suspected and incidental examined at routine computed tomography (CT) in approximately 5% of cases. The adrenal gland is a common site for metastatic disease. Adrenal masses are common, estimated to occur in approximately 3–7% of the adult population. Although most of the adrenal masses turn out to be adenomas, in a patient with a known history of major extra-adrenal neoplasm especially lung carcinoma that requires either follow-up imaging for adenoma or appropriate therapy of the primary tumor. The presence of metastases may contraindicate curative surgery or radiotherapy. For accurate diagnosis of the masses, CT is important for the staging of primary malignancies and for the reduction of the need for both percutaneous biopsy and follow-up imaging in patients with adrenal masses. Incidental adrenal masses are 3 to 7% common in general population. 80% of all adrenal neoplasms are benign non-hyper functioning adenomas. Benign and malignant adrenal lesions are well differentiated with accurate radiological evaluation. Adenomas appear hypodense on plane CT scan and classified as lipid-rich (70%) or lipid-poor (30%) depending on intracytoplasmatic fat content. Plain CT scan is sensitive in detecting lipid-rich adenomas, while CT washout study can differentiate adenomas from other adrenal neoplasms in indeterminate case. After injection of contrast material at variable period of time, regression in CT HU density in adrenal lesions refers...
as Washout. The Aim of study was role of MDCT with diagnostic value of 15-min delayed washout rate in differentiation of these benign from malignant adrenal lesions

MATERIALS AND METHODS
The ethical clearance of the role of CT scan with 15 min delay in distinguishing benign lesion from malignant adrenal masses was approved by the Gujarat Cancer and Research Institute, Ahmedabad. In addition, the patients with adrenal masses were carried out in the period from January 2017 to November 2017 and Consent was taken prior to conducting the investigations in all patients.

In the study, 64 Out of 100 patients examined for abdominal CT with adrenal incidentaloma, 59 patients (92.2%) with unilateral and 5 patients (7.8%) with bilateral adrenal masses. The exclusion criteria for 36 patients (92.2%) with unilateral and 5 patients (7.8%) with bilateral adrenal masses. Adrenal adenoma is diagnosed in 46 (71.9%) patients while non-adrenaloma were 18 (28.1%) patients. Similarly, non-calcified, non-haemorrhagic lesions with attenuation values >43 HU were considered malignant.

Absolute percentage of washout (APW), as well as the relative percentage of washout (RPW), were calculated by means of the following formulas-

\[ APW = \frac{100 \times (VA - DA)}{VA} \]

\[ RPW = \frac{100 \times (DA - VA)}{VA} \]

Where VA is attenuation on contrast-enhanced scans, DA is attenuation on delayed contrast-enhanced scans & PCA 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.

Statistical Analysis
Data were analyzed to calculate sensitivity, specificity, positive predictive value, and negative predictive value for each individual mass. P values than calculated to declare results to be significant. P< 0.05 considered statistically significant.

RESULTS
64 patients are included in this study having single solid adrenal mass. Adrenal adenoma is diagnosed in 46 (71.9%) patients while non-adrenaloma is diagnosed in 18 (28.1%). Final diagnosis was done with the plain CT scan and/or histopathology after 6 months follow up. Out of 46 adrenal adenoma, 33 patients (71.7%) were lipid rich and 13 patients (28.3%) were lipid-poor adenoma. While out of 18 non-adenomas, 4 patients (22.2%) were adrenocortical carcinoma, 9 patients (50%) were metastasis with largest from bronchogenic carcinoma, 3 patients (16%) were ganglieneuroma and 2 patients (11%) were turned out to be lymphoma.

### Table 1. Demographic and Radiological Data of Patients with Adrenal Masses (n = 64)

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Gender (M/F)</th>
<th>Precontrast Phase (HU)</th>
<th>Venous phase (HU)</th>
<th>Delayed phase washout rate (15 min)</th>
<th>Adenoma Group (Benign) (n=46)</th>
<th>Non-Adenoma Group (Malignant) (n=18)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.7 ± 6.4</td>
<td>18 (28)</td>
<td>13.1 ± 1.2</td>
<td>62.0 ± 12.2</td>
<td>40.0 ± 5.1</td>
<td>46.3 ± 8.3</td>
<td>32.1 ± 6.9</td>
<td>0.592</td>
</tr>
<tr>
<td>48.7 ± 6.4</td>
<td>12 (6)</td>
<td>34.2 ± 6.9</td>
<td>64.5 ± 11.0</td>
<td>78.9 ± 10.2</td>
<td>0.221</td>
<td>0.088</td>
<td></td>
</tr>
<tr>
<td>5.9 ± 3.8</td>
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</table>

Table 1 shows the demographic and radiological data of patients with adrenal masses. Their ages ranged from 25 to 70 years. There was no significant difference between adenoma and non-adenoma groups regarding the age, gender ($P = 0.221$ and $0.088$, respectively). The mean attenuation values of pre-contrast and delayed phase images showed significant differences between the two groups ($P < 0.001$). However, the mean attenuation value of the venous phase enhancement showed no significant difference between the two groups ($P=0.452$).

<table>
<thead>
<tr>
<th>MDCT Sequence</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precontrast phase</td>
<td>95.0%</td>
<td>83%</td>
<td>93.47%</td>
<td>83%</td>
<td>87.87%</td>
</tr>
<tr>
<td>Venous phase</td>
<td>37%</td>
<td>83%</td>
<td>85.00%</td>
<td>27%</td>
<td>50.00%</td>
</tr>
<tr>
<td>Delayed phase</td>
<td>97.8%</td>
<td>94.73%</td>
<td>97.8%</td>
<td>94.73%</td>
<td>98.43%</td>
</tr>
</tbody>
</table>

Table 2. Shows the True Positive (TP), False Negative (FN), True Negative (TN) and False Positive (FP) Values of Different MDCT Phases and the Delayed Washout Rate in the Diagnosis of Adrenal Masses (n=64)

Table 3. Statistical Values of the MDCT Phases and Delayed Washout Rate with the Determination of the Cut-Off Attenuation Values in Adrenal Masses (n=46)

Figure 1 (A–C): A 35-Year-Old Female with Right Adrenal Lesions. Pre-Contrast Axial Image (A) Showed a Well-defined, Hypodense, Homogenous Right Supra-Renal Mass (15x28 mm) with an Attenuation Value of 18.8 HU. It Displayed Attenuation Value of 65.8 HU at Venous Phase. (B) and 41HU at Delayed Phase (C). The APW was 52.8% and RPW was 37.7%. Lesion Diagnosed as Metastasis Later on HPE.

Figure 2 (A–C): A Forty-Seven-Year-Old Female Patient with Left Adrenal Mass. Pre-contrast Axial Image (A) Showed Left Supra-Renal Mass (12x8 mm) with Heterogeneous Density (Attenuation Value of 35HU) and No Associated Areas of Cystic Degeneration or Calcification. It Shows Attenuation Value of 76HU at Venous Phase (B) and 39HU at Delayed Phase (C). The APW was 90.2% and RPW was 48.7%. Lesion Diagnosed as Adenoma Later on HPE. The Final Diagnosis is Based on Histopathological Analysis and 6-Months Followup.
DISCUSSION

Range of neoplasms are invading the adrenal gland including primary and secondary malignant tumors; however incidental benign adenoma is most common tumor with prevalence of up to 9% in the general population. The prevalence of adrenal masses on imaging has increased in high resolution MDCT.

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.6 The majority of benign lesions are adenomas, of which 80% are benign non-functioning adenomas.3 In the current study, 64 adrenal masses were diagnosed, of which 71.9% were benign & 28.1% were malignant.

Sensitivity of Plain CT scan studies to differentiate adenomas from non-adenomas is 70%, as 30% of adenomas are lipid-poor.10 Plain CT scan is important, but its sensitivity is low, and more tests are necessary for the diagnosis of lipid-poor lesions. Plain CT scan and delayed post contrast images mean attenuation value of adenoma is significantly lower than of non-adenoma (P <0.001) in our study. Venous phase is not sensitive as there is no significant difference in mean attenuation value of adrenal adenoma and non-adrenal adenoma.

Measurement of attenuation value of the mass at only venous phase is not sufficient to allow accurate differentiation between adenoma and non-adenoma as it has the sensitivity of 37%, specificity of 83%, PPV of 85%, NPV of 27.0% and an accuracy of 50%. In the study, the use of pre-contrast MDCT for the diagnosis of adrenal adenoma has the sensitivity of 94.7%, specificity of 82.6%, PPV of 93.44%, NPV of 82.7% and accuracy of 87.68%. Delayed images have the sensitivity of 97.6%, specificity of 94.52%, PPV of 97.6%, NPV of 94.54% and an accuracy of 98.36%. This present study results were in agreement with previous studies which stated that the attenuation values of adenomas are significantly lower than non-adenoma at pre-contrast and delayed enhanced MDCT images.6,7 Moreover, they stated that the venous enhanced phase showed too much overlap between the adrenal adenoma and non-adenoma with resultant inaccurate differentiation between the two groups.

Adrenal adenomas of more than 10 HU on pre-contrast CT are of two types, lipid-poor, and lipid rich adenomas. Therefore, it is difficult to differentiate lipid-poor adenoma from non-adenoma by using their increased percentage washout of the contrast material.11

In the current study, we found that all adenomas (lipid-rich and-lipid poor) had APW P60% (sensitivity was 97.8%, specificity was 94.73%, PPV was 97.8 %, NPV was 94.7 % and the accuracy was 98.43 %) and RPW P40% (sensitivity was 100%, specificity was 100%, PPV was 100%, NPV was 100% and the accuracy was 98.9%) while lesions with APW <60% and RPW <40% were non-adenomas. In addition, the sensitivity of 15-min delayed washout rate at RPW threshold of 40% and APW threshold of 60% is 97.8 %, which, in our opinion, is adequate in clinical practice to characterize adenomatous lesions. In the study of Park et al,7 the sensitivity and specificity with a threshold of 55% washout rate at 15-min were 93.9% and 95.8%, respectively. The study showed that there are 18 patients diagnosed with non-adenoma (malignant) with APW <60 and RPW <40. Their diagnosis was confirmed by HPE: 4 patients (22.2%) with adrenocortical carcinoma, 9 patients (50%) with metastasis (5 cases from bronchogenic carcinoma, 2 from cancer breast and 2 from hepatocellular carcinoma), 3 patients (16 %) with ganglioneuroma and 2 patients (11%) with lymphoma. Pheochromocytoma may be associated with other syndromes as neurofibromatosis type II as well as multiple endocrin neoplasm (MEN) syndrome.12

CONCLUSION

15-min delayed washout rate MDCT images are very important for the diagnosis of adrenal adenoma. For accurate diagnosis of adrenal incidentalomas and to differentiate benign and malignant lesions, MDCT with 15-min washout rate with APW P60 and/or RPW P40 is important.

REFERENCES


