CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT – WASHOUT STUDY

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1GDMC Dharmapuri , 2GMKMCH Salem

Abstract – AIM OF THE STUDY: To prospectively characterize adrenal masses as adenomas or non adenomas with Contrast enhanced CT and correlate with histopathological results

MATERIALS & METHODS: Fifty four adrenal masses were evaluated. CT attenuation values were measured using a circular region of interest on images of the lesion, covering at least one half of the mass. Adrenal masses that had attenuation values greater than 10 HU at unenhanced imaging underwent enhanced CT imaging 60 seconds after intravenous administration of contrast material and then underwent delayed enhanced CT imaging at 15 minutes. Enhancement washout percentages were calculated with the following equations: Absolute percentage of enhancement washout : [(Attenuation value at enhanced CT - Attenuation value at delayed enhanced CT) / (Attenuation value at enhanced CT - Attenuation value at unenhanced CT)] * 100. Relative percentage of enhancement washout: [(Attenuation value at enhanced CT - Attenuation value at delayed enhanced CT) / Attenuation value at enhanced CT] * 100. An adenoma was diagnosed if a mass had an absolute percentage enhancement washout value of 60% or higher or relative percentage enhancement washout value of 40% or higher. Results: The pathological diagnosis was 25 adenomas and 29 non adenomas. Absolute percent washout diagnosed 24 of 25 adenomas and 27 of 29 non adenomas. It had a Sensitivity of 96.00%, Specificity of 93.10%, Positive Predictive Value of 92.31% and Negative Predictive Value of 96.43%. Relative percent washout diagnosed 23 of 25 adenomas and 26 of 29 non adenomas. It had a sensitivity of 92%, specificity of 89.66%, Positive Predictive value of 88.46% and Negative Predictive Value of 92.86%. Both were found to be statistically significant.

CONCLUSION. CT contrast washout study is helpful in categorising adenomas and non adenomas in adrenal masses with high degree of accuracy, sensitivity and specificity and helps guide clinical management.

Key words: Adrenal adenoma, Adrenal nonadenoma, CT contrast washout study, Absolute washout percentage, Relative washout percentage

I. INTRODUCTION
Abnormalities of the adrenal gland include primary neoplasm, metastases, hemorrhage, or enlargement of the adrenal gland from external hormonal stimulation. Adrenal masses can be divided into two physiologic categories based on whether they hypersecrete a hormone. Hyperfunctioning adrenal masses produce a hormone that results in a chemical imbalance and include pheochromocytomas, aldosteronomas, and cortisol or androgen-producing tumors. Nonfunctioning adrenal masses cause enlargement of the adrenal gland but no significant increased hormone production. Adrenal adenomas and metastases are the most common nonfunctioning adrenal masses.

The most common lesions, adrenal metastases and adenomas cannot be characterized so easily. This is usually because they are small, without specific diagnostic features, and frequently appear similar to each other when detected. The usual imaging dilemma is therefore to differentiate between these two very different lesions. The diagnosis has profound consequences for the patient.

In a patient with an extrarenal malignancy, the determination that an adrenal mass is metastatic often means the primary disease is incurable and palliative therapy is instituted. On the other hand, characterizing a lesion as benign in these circumstances potentially permits curative therapy for the primary disease.

II. AIM OF THE STUDY
To assess the accuracy of Contrast Enhanced CT - Washout study in characterizing adrenal masses as benign or malignant, i.e as adenomas or non adenomas.

III. REVIEW OF LITERATURE
Melvyn Korobkin and Frederick J Brodeur et al studied contrast enhancement washout curves of 52 adenomas and 24 non adenomas. The optimal threshold value and the
corresponding sensitivity and specificity were calculated for the diagnosis of adenoma. Also the absolute and relative percentage washouts were calculated at time delays from 5 to 45 minutes after contrast enhancement.

The mean percentage enhancement washout for adenosmas was 51% at 5 minutes and 70% at 15 minutes, compared with 8% and 20% respectively for non adenomas. The sensitivity and specificity of diagnosing adenosmas was higher at the 15 minute scan than at the 5 minute delayed scan. Based on the 15 minute delayed scan’s calculation of percentage enhancement washout with 60 HU as threshold, there was a sensitivity of 88% and specificity of 96%. For the relative percentage washout with a 37HU threshold, the sensitivity and specificity both were 96%.

Elaine M. Caolli, MD et al evaluated One hundred sixty-six adrenal masses were evaluated with a protocol consisting of unenhanced CT, and, for those with attenuation values greater than 10 HU, contrast material–enhanced and delayed enhanced CT. Attenuation values and enhancement washout calculations were obtained. An adenoma was diagnosed if a mass had an attenuation value of 10 HU or less at unenhanced CT or a percentage enhancement washout value of 60% or higher.

The final diagnosis was adenoma in 127 masses and nonadenoma in 39. Masses measuring more than 10 HU on unenhanced CT scans were confirmed at biopsy (n = 28) or were examined for stability or change in size at follow-up CT performed at a minimum interval of 6 months (n = 33). Thirty-six (92%) of 39 nonadenomas and 124 (98%) of 127 adenomas were correctly characterized. The sensitivity and specificity of this protocol were 98% and 92%, respectively. This protocol correctly characterized 160 (96%) of 166 masses. The study concluded that With a combination of unenhanced and delayed enhanced CT, nearly all adrenal masses can be correctly categorized as adenomas or nonadenomas.

IV. MATERIALS AND METHODS

STUDY POPULATION
The study group includes a total 50 Patients with 54 adrenal masses who have come to the Department of Radiology at Madras Medical College.

STUDY DESIGN: Prospective Study

INCLUSION CRITERIA: Patients with adrenal masses, measuring more than 1cm, with Hounsfield Unit more than 10.

EXCLUSION CRITERIA: Pregnant women, Severe hypersensitivity or previous allergic reactions, Critically ill patients, Patients in renal failure

DATA ACQUISITION
Adrenal masses were evaluated with an adrenal CT imaging protocol. The dedicated adrenal CT protocol consisted of initial densitometry of the mass on unenhanced CT scans. If the mass had an attenuation of 10 HU or less, it was assumed to be benign and the masses were excluded from the study. Thus, twenty masses with HU below 10 were excluded.

A diagnosis was established in the final study group of 54 masses when histologic proof was obtained at surgery or percutaneous biopsy.

All patients with adrenal masses that had attenuation values greater than 10 HU at unenhanced imaging underwent enhanced CT imaging 60 seconds after intravenous administration of contrast material and then underwent delayed enhanced CT imaging at 15 minutes. The scans were done with 128 slice CT scanner or 4 slice CT scanner. Enhancement washout percentages were calculated for these masses.

To diagnose an adrenal mass as an adenoma, we used the previously reported thresholds of 60% or higher for absolute percentage washout and 40% or higher for relative enhancement washout.

Parameters for the unenhanced and delayed enhanced examinations with the CT scanners were KVP (Peak KY) of 120 kVp, Slice Thickness of 2mm and Slice Interval of 5mm. Enhanced scans were obtained after intravenous injection of 40 mL of iohexol 350

IMAGE ANALYSIS
CT attenuation values were measured by using a circular region of interest on images of the adrenal lesion in question. The region of interest covered at least one-half of the mass, excluding cystic, calcified, or necrotic regions. The edges of the adrenal lesion were avoided to prevent partial volume averaging.

The enhancement washout percentages were calculated with the following equation

![Contrast Washout Formulæ](image)

The maximal diameters and the right or left side locations of the adrenal masses were also recorded.

Statistical analysis of variance was undertaken to examine the significance of the differences between the adenomas and nonadenomas in terms of mean mass size, mean attenuation value at unenhanced CT, mean attenuation value at enhanced
CT, mean attenuation value at delayed enhanced CT, mean percentage of enhancement washout, and mean relative percentage of enhancement washout.

A *p* value less than .05 was considered to indicate a statistically significant difference. The threshold values of 60% or higher for absolute percentage enhancement washout and 40% or higher for relative percentage enhancement washout used in the diagnosis of adenoma were established in prior investigations.

V. RESULTS

Number:
The final clinical diagnosis was adrenal adenoma for 25 masses and nonadenoma for 29 masses, confirmed at pathologic examination.

Size:
The average maximal diameter of the adenomas was 3.5 cm (range, 2.5–5.1 cm, with Standard deviation of 0.6).

Nonadenomas were larger (mean size, 4.2 cm; range, 2.7–6.3 cm, with Standard deviation of 1.0). It was found to be statistically significant with a *p* value of 0.005.

The mean attenuation values of adenomas and nonadenomas on unenhanced, enhanced, and delayed enhanced CT scans are shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Mean attenuation values of Adrenal Masses</th>
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<tbody>
<tr>
<td>Unenhanced</td>
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<tr>
<td>Adenoma</td>
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<tr>
<td>Non adenoma</td>
</tr>
</tbody>
</table>

The nonadenomas included 26 metastases, two pheochromocytomas, one adrenal cortical carcinoma. The primary malignancies in the 26 patients who had adrenal metastases were the following lung cancer (*n* =17), esophageal cancer (*n* = 2), renal cancer (*n* = 2), tongue cancer (*n* = 1), rectal cancer (*n* = 1) and breast cancer (*n* =3).

VI. STATISTICAL ANALYSIS

Absolute percent washout

The use of a threshold of 60% in the differentiation of adenomas from nonadenomas resulted in a sensitivity of 96% (24 of 25 masses) and a specificity of 93% (27 of 29 masses).

<table>
<thead>
<tr>
<th>Table 2: APW Outcome vs Pathological Result</th>
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<tbody>
<tr>
<td>Adenoma</td>
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<tr>
<td>Test + ve</td>
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<tr>
<td>Test - ve</td>
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There was 1 adenoma that did not meet the 60% threshold. The percentage enhancement washout measurements for this mass was 57.4%.

Two nonadenomas had absolute percentage enhancement washout measurements above the 60% threshold. These washout measurements were 99.2% and 65.1%. Both were metastases.

Relative percent washout

The use of a relative percentage enhancement washout threshold value of 40% in the differentiation of the adenomas resulted in a sensitivity of 92% (23 of 25 masses) and a specificity of 89.66% (26 of 29 masses).

<table>
<thead>
<tr>
<th>Table 3: RPW Outcome vs Pathological Result</th>
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<tbody>
<tr>
<td>Adenoma</td>
</tr>
<tr>
<td>Test + ve</td>
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<tr>
<td>Test - ve</td>
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</table>

The relative percentage enhancement washout measurements for the 2 adenomas that did not meet the 40% relative percentage enhancement washout threshold were 37.7%, 34.9%. Each adenoma did not meet either threshold criteria.

3 Non adenomas were wrongly characterised with relative percent washout. The relative percentage enhancement washout measurements for these masses were 41.5%, 42.4% and 47% respectively.

Table 4 APW & RPW

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>APW 96.00%</td>
<td>93.1%</td>
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<tr>
<td>RPW 92.00%</td>
<td>89.66%</td>
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</table>

VII. DISCUSSION

There are two independent properties of adrenal adenomas that can be exploited in characterizing them at CT. First, most adenomas contain large amounts of intracellular lipid, resulting in lower attenuation values at unenhanced CT than nonadenomas. Second, all adenomas, including those without substantial lipid content, tend to have a more rapid loss of attenuation value soon after enhancement with intravenous contrast material.

The purpose of this study was to assess the accuracy, sensitivity and specificity of this method. Absolute percentage enhancement washout threshold of 60% correctly diagnosed 24 of 25 adenomas. This was with a sensitivity of 96%, specificity of 93.1%. The positive and negative predictive values were 92.3% and 96.4% respectively.

Absolute percentage washout failed to correctly characterise two non adenomas. These included a metastasis from lung cancer and an incidentally detected metastasis. The values were 99.2% and 65.1% respectively. It also failed to characterise 1 adenoma. This was in a patient with a lung primary, which it ruled as non adenoma. The value was 57.4%.

Relative percent washout correctly characterised 23 of 25 adenomas and 26 of 29 non adenomas. The sensitivity and specificity were 92% and 89.7% respectively. The positive and negative predictive values were 88.5% and 92.7% respectively.

Relative percentage washout failed to correctly characterise three non adenomas. These included a metastasis from lung cancer and two incidentally detected metastases. The values were 41.5%, 47% and 42.4% respectively.

It also failed to characterise 2 adenomas. These included patients with an incidentally detected adenoma and a case of Cushing’s syndrome which was also pathologically proven to be an adenoma. Both of them were characterised as non adenomas. The value was 34.9% and 37.7% respectively.
The results of this study confirm those of prior studies and demonstrates that the mean attenuation values at unenhanced CT adrenal adenomas and those of nonadenomas are nearly identical. Although the two groups have significantly different mean attenuation values at both enhanced and delayed enhanced CT, the considerable overlap between the two groups is too large to permit sufficiently accurate differentiation between them for any individual case.

The distribution of the enhancement washout calculations for the two groups, however, was significantly different to allow accurate differentiation of individual cases. Absolute percent washout correctly characterised 51 of 54 adrenal masses with an accuracy of 94.44%. Relative percent washout correctly characterised 49 of 54 adrenal masses with an accuracy of 90.74%. Absolute enhancement washout values were more accurate than use of the relative enhancement washout value in the differentiation of adenomas from nonadenomas.

CASE 1-NON ADENOMA –METASTASIS (ABW 34.9%, RPW-29.1%)

CASE 2-NON ADENOMA –METASTASIS (ABW23.8% RPW17%)

VIII. LIMITATIONS OF THE STUDY

Only 50 patients and 54 adrenal masses were included in the study. This patient population may be small. This results are to be considered preliminary and in need of further evaluation. Future studies involving large patient groups may be helpful to determine the usefulness of this technique for specific adrenal lesions.

The study did not include masses with unenhanced attenuation values less than 10HU. Although previous studies have established that masses below 10HU are adenomas, there may be a few cases that could be exceptions.

Third, partial volume averaging errors could have been made in the measurements of smaller masses. This may have falsely lowered or raised the recorded attenuation values.

XI. CONCLUSION

Adenomas can be differentiated from nonadenomas at delayed enhanced CT examinations with absolute and relative percentage enhancement washout calculations. This protocol enables nearly all adrenal masses to be diagnosed with a high sensitivity and specificity. Thus CT contrast washout study for adrenal masses plays a definitive role in guiding clinical management.

BIBLIOGRAPHY