A Crucial Step Adjunct to CT Attenuation Values In Characterizing Adrenal Masses A Prospective Observational Study At Our Institute

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Abstracts: **Aim:** To characterize incidentally detected adrenal masses by CT attenuation values and 15 minutes wash out characteristics at contrast-enhanced CT. **Method :** Prospective observational study from March 2012 -2013 was done, with all the abdominal scan evaluated for adrenal masses. Departmental protocol was followed with15 minutes delayed scan added. CT attenuation values at different phases were used to calculate absolute percentage washout (APW) and relative percentage washout (RPW). The masses with attenuation value ≤10HU on unenhanced scans were diagnosed as lipid rich adenomas and masses with attenuation values >10 on plain scan with APW of >60% and RPW>40% were diagnosed as lipid poor adenomas; rest being non-adenomas, metastasis if there was known malignancy. The masses were evaluated in terms of their sizes, site of involment, stastical significance ($p<0.05$) in attenuation values at different phases and washout studies. **Results:** 96 lesions were detected in 84 patients from March 2012 -2013.M:F ratios of 1.7:1, mean age being 46 years. Lipid poor adenomas (LPA) were the commonest mass followed by metastasis. 64% of patients with malignancy had adrenal metastasis while 36% had adenomas. There was no significant difference in size($p=0.23$) between LPA and non-adenomas (NA) whereas statistical difference was noted in mean attenuation values on unenhanced, delayed, wash-in and wash-out values($p <0.05$).There was no significant difference on enhanced scan ($p=0.95$),but absolute percentage washout (APW) and relative percentage washout (RPW) was statistically significant between LPA and NA ($p<0.05$).**Conclusion:** CT attenuation values, absolute and relative percentage washout values characterize the adrenal masses.[Bhatt Chh NJIRM 2014; 5(5):5-12]

Key Words: Adrenal masses, Attenuation values, Washout studies.

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Introduction: With increased incidence of multi detector CT scan being used for diagnosing the abdominal pathology and for staging of the primary tumors, the incidence of the adrenal masses being detected have increased. Masses like cyst, lipomas, and haemorrhage or functioning masses like pheochromocytomas can be easily differentiated but two commonest other masses i.e. adenomas and non-adenomas needs to be differentiated for better triage of patients. Differentiating adenoma from metastasis is important as detection of later upgrades the tumor.

Aims and Objectives: Characterize adrenal masses by CT attenuation values, and by wash out studies on 15minutes delayed scans.

Material and Method: Prospective observational study of adrenal masses detected on CT scan of abdomen was done from March 2012-2013. Clearance from review board of our institute was obtained prior to the study. No gender bias was followed. Inclusion criteria were, all adrenal masses detected on CT scan of the abdomen for a period from March 2012-2013(n=96). Exclusion criteria: Biochemically active masses like pheochromocytomas, Cushing's disease and functional adrenocortical tumor were excluded (pheochromocytomas in 3 patients and functional adrenocortical tumor in one patient). CT scan was done on 64slice multi detector scanner. Pre procedure preparation was done as per protocol of our department. Three phases of the scans obtained were unenhanced phase, portal -venous phase and 15 minutes delayed phase. Enhanced scan were done by injecting 60-100 ml of non-ionic contrast media (Iopamiror 350mg) though intracubital vein by pressure injector at a rate of 3ml/sec after negative test dose. Scan was obtained 45 sec after starting of the intravenous contrast. Delayed scan was obtained through the adrenal region only, 15 minutes after starting of injection of the IV contrast media. Scan parameter were as follows:-Volumetric data were obtained through the abdomen. Slice thickness-1mm.Collimation= 0.6 mm, Pitch= 1.5, MAS=160, kvp=120. Attenuation values were calculated by using circular region of interest which gives average values. Necrotic, cystic and hemorrhagic

areas were excluded from the region of the interest. Attenuation values measured in Hounsfield Units (HU) of the masses on the unenhanced scan were categorized as follows: masses with attenuation values negative or HU≤10 were categorized as lipid rich adenomas (LRA) or lipomas or myelolipomas, values with fluid density as cysts, HU values >40-60 with history of trauma were considered as hemorrhage. Masses with attenuation values of 10HU and above were indetermined masses. These masses were further studied on 15 minutes delayed phase. Enhancement of masses means difference in attenuation values on unenhanced and enhanced phase while enhancement wash out means attenuation difference between portal-venous and delayed phase. From the values obtained, percentage enhancement also termed as Absolute percentage wash out (APW)and enhancement washout out termed as Relative percentage of enhancement washout (RPW) were calculated as per following equations:-Wash in values: HU at portal venous phase - HU on non-enhanced phase. Wash out values: HU at portal venous phase - HU at delayed scan. Absolute Percentage wash out **=** Wash out/wash in x 100.Relative percentage of Enhancement wash out **=** HU portal venous phase-HU delayed phase/HU portal venous phase x 100. [1] Masses with percentage enhancement of > 60% and enhancement washout out > 40% were diagnosed as lipid poor adenomas(LPA), the other masses being non adenomas(NA) being metastasis if there was known malignancy. Concomitant CT thorax of patients (n =31) and CT neck (n=3) were also available. Patients with known malignancies were lung cancer (n=31), colonic malignancy (n=6), neck malignancy (n=3), breast cancer (n=3) renal malignancy (n=2), hepatic malignancy (n=2), bladder (n=1). Stastical analysis was performed with commercially available software on windows XP. Student t –test analysis was done to evaluate difference in size and attenuation values for lipid rich adenomas, lipid poor adenomas and non-adenomas with wash out studies for lipid poor adenomas and non-adenomas where $p<0.05$ was considered significant. Out of 70 masses with attenuation more than 10HU, biopsy was done in 23patients, 12 with lipid poor adenomas and 11 with metastasis to prove the diagnosis. Follow up studies were available in 7 patients (4patient with LPA &3patients with malignancy). Patients with Koch's and lymphoma were followed up on ultrasonography following anti-tuberculosis and chemotherapy respectively which showed reduction in the size of the lesions. 15 patients with LPA were operated to prove the diagnosis. 5 patients diagnosed as LPA were lost to follow up whereas 17 patients with adrenal metastasis were treated for primary malignancies and no follow up imaging study was carried out. Masses with HU<10 or negative values were diagnostic of benign masses on unenhanced scan and hence no follow up was required.

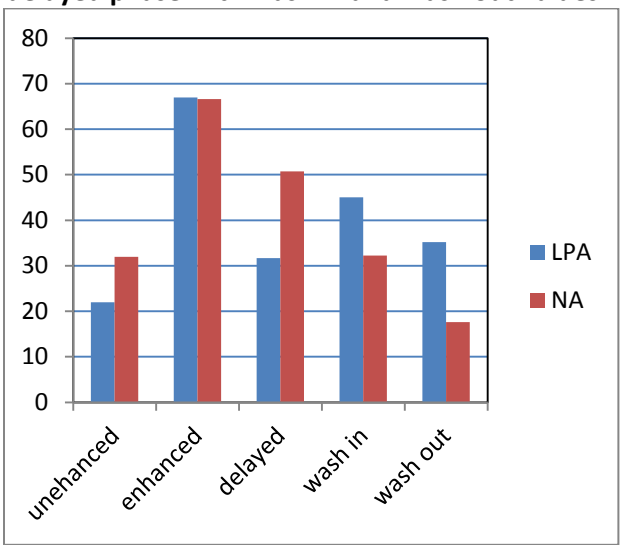
Results: Total of 92 lesions was studied in 84 patients over period of one year from March 2012 - 2013 with incidence being 3.12% in our study. M: F ratios was1.7:1 with mean age being 46years.93% of masses was incidentally detected with bilateral lesions in 8% of patients. Masses were more common on left side seen in 57% which may be incidental. Site of masses included medial limb (29%), entire gland (26%), lateral limb (21%), and stem in (16%). Types of masses as seen in table 1 shows that lipid poor adenomas were the commonest masses followed by non-adenomas.

Table 1: Types Of Masses

Diagnosis	No of masses(n)	Percentage %
Lipid poor adenomas	36	39.13
Non adenomas	31	33.69
Lipid rich adenomas	17	18.40
Haemorrhage	4	4.34
Koch's	2	2.17
Lymphoma	1	1.08
Cyst	1	1.08

Out of 92 masses 70 masses had attenuation values ≥10HU, excluding haemorrhage and cyst. Maximum mean size of LPA was 24.93 mm (SD= 14.93), LRA was 20.76mm (SD=7.9) and NA 28.89 mm (SD=16.84).There was no significant difference in size of LPA and NA (p=0.23) and between LPA and LRA (p=0.33).

Figure 1: shows difference in attenuation values of LPA and NA on unenhanced, portovenous and delayed phase with wash in and wash out values.



There was statistical difference in mean attenuation values on unenhanced, delayed, wash-in and wash-out values between LPA and NA ($p < 0.05$) whereas no significant difference on enhanced scan ($p = 0.95$) suggesting that portovenous phase enhanced scan cannot differentiate between LPA and NA.

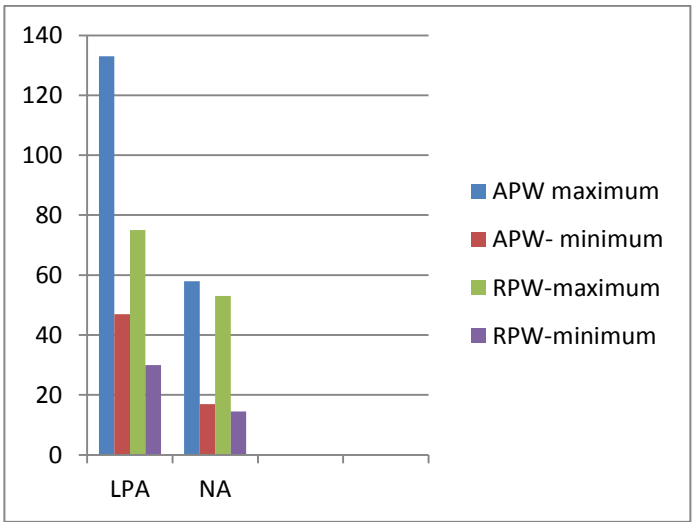
Table 2: Maximum and Minimum Attenuation Values in HU Of LPA and NA

Masses HU>10	LPA(n=36)		NA(n=31)	
	Maximum	Minimum	Maximum	Minimum
Plain	43	10	53	10
Portovenous	123	20	100	40
Delayed	60	11	74	33
Wash in	88	10	66	8
Wash out	83	6	45	4

Table 2 shows that LPA has lower attenuation values as compared to metastasis on unenhanced as well as delayed scan with increased rate of wash in and washout values.

Using the criteria of APW>60% and RPW >40% for lipid poor adenomas, the differences in the maximum and minimum absolute percentage washout (APW) and relative percentage washout (RPW) was stastical significant between LPA and NA ($p < 0.05$) as shown in figure 2.

Figure 2: Maximum and Minimum Absolute and Relative Percentage Washout Values In LPA and NA

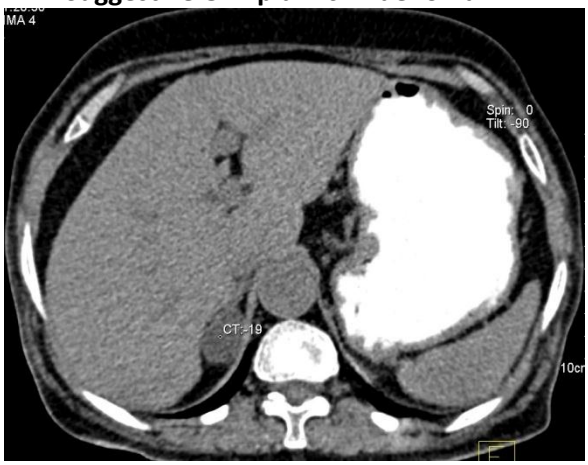


This suggests that enhancement washout is faster and early in adenomas than non-adenomas further differentiating adenoma from non-adenomas.

Out of 48 adrenal masses in patients with known malignancy, 31 adrenal masses (64%) were metastasis while 15 masses (32%) were LPA and 2 masses (4%) were LRA.77% (n=24) of patients with adrenal metastasis had lung malignancy which suggests that lung malignancy was the commonest malignancy to metastasize to adrenal, while 23% (n=7) of patients with lung mass had lipid poor adenomas. 8% of patients with lung malignancy had bilateral adrenal metastasis.

Discussion: Incidence of detecting adrenal masses is increasing as there has been increased use of CT scan to detect abdominal pathologies as well as staging of the malignancies. Incidentally detected adrenal masses needs to be differentiated according to the etiology for prognosis and triage of the patients. Literature states the incidence being around 5%. [2,3,4] Diagnosing adrenal metastasis can alter the prognosis of the patient but at the same time it is important to remember that adrenal adenomas can occur in patients with malignancies as seen in one of our patient (Figure 3).

Figure 3: Axial Post Contrast Image In 70yrs Old Female With Malignancy Of Rectum Showing Right Adrenal Gland Shows Mass With HU Of -19 Suggestive Of Lipid Rich Adenoma In .

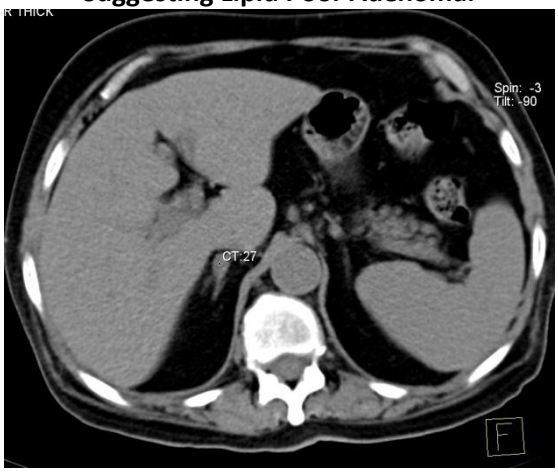


The incidence of an adrenal nodule is approximately 9-13% in patients being scanned for a known malignancy [5] but only 26-36% of these masses turn out to be metastasis. [6]

CT attenuation values play an important role in differentiating the masses like fluid density lesion are cyst and mass with attenuation beyond 40-60 HU represents haemorrhage. Size and shape of the mass may not differentiate benign and malignant masses. [7] In our study we had LPA varying in size from 7mm to80mm with mean being 24mm while metastasis varying in size from 8.6mm to 70mm with mean of 28mm.The mean size of LRA was 20mm. Calculated p values for LPA and NA was 0.23, for LRA and NA was 0.06 and for LPA and LRA was 0.33 all the values were not significant which means size of mass cannot differentiate adenomas and metastasis. However according to the appropriateness criteria of American college of Radiology in patients with no known malignancy, masses <3cms can be considered as benign whereas masses > 5cms should be respected. [8] Benign masses have reduced attenuation on unenhanced scan due to presence of lipid [9] but as many as 10-40% of adenomas may not contain adequate fat and may have values >10 HU and these needs to be differentiated from nonadenomas. [10] Lee et al in his study suggested that mean attenuation of adrenal adenomas (-2.2HU) was significantly lower than that of non-adenomas (28.9HU).With the threshold of 0HU sensitivity and specificity for diagnosing adenomas was 47% and 100% respectively whereas at 10 HU it was 79%:96% .[11] A pooled analysis done by Giles WL et al also showed that at the threshold of 10 HU the sensitivity and specificity was 74% and 98% respectively and thus 10 HU can be used as standard reference to diagnose lipid rich adenoma.[12] The mean relative enhancement of adenomas is 10 times higher than other masses, due to low attenuation of the adenomas on unenhanced scans. In our study portovenous phase showed no difference in the attenuation values between LPA and NA (p=0.95) the fact supported by the study done by Szolar et al [13], but delayed scan showed difference in the attenuation values. Study done by Korobkin et al, showed that mean attenuation for adenomas was 42HU at 5 minutes and 35HU after 45 minutes [14] At 40 HU on delayed phase sensitivity and specificity was 100% for diagnosing adenomas in study done by Szolar et al. [15] In our study the mean attenuation at 15 minutes delay for LPA and NA was 31.7HU and 50.7HU respectively which was significant ($p<0.05$). Attenuation values however may not always be reliable for differentiating LPA and NA and calculating percentage enhancement washout play an important role. Wash out means loss of attenuation values of masses during variable period after contrast injection. Szolar et al in his study showed that on 5,10,and 30 minutes delayed scan absolute percentage loss of enhancement as well as enhancement loss relative to the amount of initial enhancement was statistically significant ($p<0.001$). [13] Absolute percentage wash out threshold of 60% and relative percentage wash out of 40% at 15 minutes delayed scan had a sensitivity of 98% and specificity of 97% in differentiating adenomas versus metastasis ($p<0.001$). [14,16,17,18]. Different method of calculating wash out percentage have been used as in study done at University of Michigan and Massachusetts General hospital wherein the authors calculated RPW as follows 100x(DY A-DA)/DA where DY A= dynamic attenuation and DA = delayed attenuation. [17] In our study the denominator is attenuation values at portovenous phase. The mean APW and RPW was higher for adenomas being 80% and 54% respectively against 41% and 22% respectively for NA was significant ($p<0.05$) helping us to characterize LPA and NA. This shows that

adenomas wash out faster and to a greater extent as compared to metastasis (Figure 4).

Figure 4: Axial Scan In 70 Yrs. Old Female Shows Mass In The Stem Of Right Adrenal Gland With HU Of 27. Absolute Percentage Washout And Relative Percentage Washout Was 71% And 54% Suggesting Lipid Poor Adenoma.



Our continued experience also showed that in cases of incidentally detected adrenal mass being diagnosed as metastasis, primary could be detected in all patients when it was not known. If unenhanced scan are not available which may happen as many a times only dynamic enhanced scan are done, RPW can still be calculated as it does not require attenuation values on unenhanced scan.

The commonest mass to be encountered in adrenal gland is adenoma but adrenal gland is also common site for metastasis most commonly from lung, breast and colon, lymphoma and melanoma. [19] A study done by Lam et al found that metastasis was seen in 3% of patients at autopsy with bilateral disease in 49%.[20] B.J.Vanzquez et al in his study found that out of 24 patient of lung cancer 15% (62%)had adrenal metastasis.[21]In our study 77% of patients with lung malignancy had metastatic disease in adrenal (Figure3)with 8 % being bilateral. Metastasis demonstrates slower washout rate at delayed imaging (APW<60% and RPW<40%) than do adenomas and this is an important factor that helps differentiating the two.[17] CT histogram analysis is another method to differentiate the metastasis as none of these lesion have negative pixels and the sensitivity of this method is 90 %. [22]

The other differential diagnosis for adrenal mass would be adrenocortical carcinoma (ACC) and pheochromocytomas. Attenuation values of ACC and pheochromocytomas on delayed 10 minutes scan is higher 72 HU$\pm$15 and 83$\pm$14 respectively as compared to adenomas and also shows reduced washout pattern as metastasis and can be differentiated from adenomas.[23] However pheochromocytomas may also behave like adenomas in wash out patterns (APW>60%,RPW>40%) [24] and Johnson PT et al , advised considering pheochromocytomas if enhanced CT values are higher than 150HU.[25] The other mass that was seen in our study was non-Hodgkin's lymphoma, showed characteristic of non-adenomas(APW 16% and RPW 7%).This patient had extensive retroperitoneal, pelvic and iliac lymphadenopathy (Figure 5).

Figure5: 50yrs Old Male Patient with Mass In Anterior Segment Of Left Upper Lobe, Showed Left Adrenal Mass With Calculated APW Of 46% And RPW Of 28% Suggestive Of Metastasis.

Lymphoma may involve adrenal gland primarily or secondarily and most frequently bilaterally as seen in our patient. CT findings by Palling and Williamson et al suggested that non-Hodgkin's lymphoma shows discrete mass of variable attenuation. [26] Granulomatous diseases cannot be forgotten in our country. In our study two patients one with Koch's abdomen and other with bilateral sacro-iliac joint Koch's had diffuse enlargement of adrenal gland, bilaterally in later patient, showed washout pattern of adenoma confirming benign masses and these patients were followed on

ultrasonography for response to the treatment which did show reduction in size of the masses. Tuberculosis of adrenal gland has imaging finding like diffuse enlargement with rim enhancement with occasional calcification. Later the gland may show calcification and may lead to Addison's diseases.[27, 28, 29] Adrenal hemorrhage following trauma is commonest cause of enlarged gland and increased attenuation value (50-90HU) of adrenal gland on unenhanced CT as seen in 4 of our patients(Figure 6).

Figure 6: 59 yrs. old male patient presenting with left lower limb edema proved to be Hodgkin's lymphoma, axial scan of abdomen shows diffuse bulky bilateral adrenal gland.

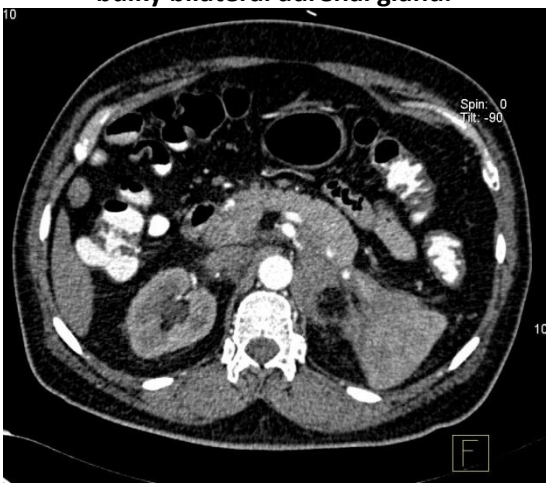
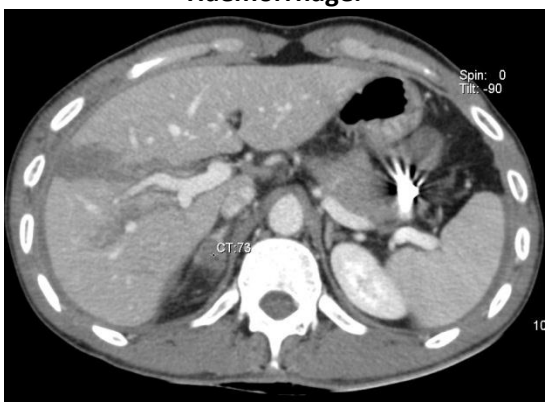


Figure 7: Post Contrast Scan Shows Patient Having Liver Laceration With Adrenal Gland Haemorrhage.



This would gradually decrease in size and attenuation when followed up.[30]

Limitation of our study was that for the masses with HU values in negative or <10 were not studied on delayed washout studies as number of studies have proved beyond doubt benign nature of these masses, reducing the radiation dose to the patient.5 patients diagnosed as LPA on washout studies were lost to follow up.17 metastatic lesion on washout studies were treated for their primary malignancy and status of adrenal lesions were than not followed up.

Thus to summarize one can follow the following protocol for incidentally detected adrenal mass.

Conclusion: CT attenuation values and wash out studies characterizes adrenal masses for better triage of the patients.

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