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Diagnostic Accuracy of Contrast Enhanced Computed Tomography Scan in Characterizing the Adrenal Masses as Adenomas or Non-Adenomas by Taking Histopathology as a Gold Standard

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ABSTRACT

Background: Adrenal masses are a source of diagnostic challenge with distinction of adenomas from non-adenomatous masses serving to guide management. Although readily available and well established as a tool of first choice is contrast-enhanced computed tomography, its sensitivity and specificity compared to histopathological examination require reassessment. **Objective:** To determine the diagnostic accuracy of contrast-enhanced CT in characterizing the adrenal masses as adenomas or non-adenomas by taking histopathology as gold standard. **Study Design:** Cross-sectional validation study. **Duration and Place of Study:** The study was conducted between March 2024 and August 2024 in the Department of Radiology, Liaquat University of Medical and Health Sciences, Jamshoro. **Methodology:** A total of 118 patients aged 20–85 years with adrenal masses >1 cm and attenuation values above 10 Hounsfield units on unenhanced computed tomography were enrolled. Contrast-enhanced computed tomography was performed 60 seconds after intravenous contrast administration and interpreted by a senior radiologist. Imaging findings were compared with histopathology, which served as the reference standard. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. **Results:** The mean patient age was 51.13 ± 11.63 years, with females comprising 65.3% of the cohort. Computed tomography demonstrated a sensitivity of 86.7%, specificity of 93.2%, positive predictive value of 65.0%, negative predictive value of 98.0%, and overall diagnostic accuracy of 92.4%. Stratified analyses confirmed consistent diagnostic performance across gender and body mass index groups. **Conclusion:** Contrast-enhanced computed tomography is a reliable and effective diagnostic modality for evaluating adrenal masses, with high specificity and accuracy when compared with histopathology.

INTRODUCTION

Growing usage of high-quality imaging has meant detection of adrenal masses with increased incidence, resulting in a prevalence of approximately 4% in the general population.[1] Such lesions may be found on imaging performed for some other cause, referred by the term adrenal incidentalomas.[2] Clinical significance of such masses is the potential of them being benign lesions such as adenomas, versus a more sinister group of primary adrenal malignancies, metastatic disease, or even hormonally active tumors such as pheochromocytomas.[3] Differentiation is therefore of utmost significance, because it determines subsequent management, ranging from watchful waiting in benign lesions to surgical resection in malignant/hormonally active tumors.[5]

The differential diagnosis between adrenal adenomas and non-adenomatous lesions is of greatest significance in clinical practice.[5] Adenomas, which are benign and non-functioning by definition, are the leading adrenal masses, but their imaging profiles can be indistinguishable from malignant or metastatic tumors.[6] Non-adenomatous tumors, such as carcinomas, metastases, and pheochromocytomas, tend to necessitate early intervention because of their malignant potential or systemic manifestations.[7] Therefore, radiologic characterization is a cornerstone in minimizing non-therapeutic surgical procedures for benign lesions, ensuring, on the other hand, malignant or hormonally active tumors are appropriately identified by imaging and treated early.[8]

Contrast-enhanced computed tomography scan is a significant tool in diagnosing adrenal lesions, offering high spatial resolution and distinct attenuation values, which facilitate tissue characterization.[9] The differential diagnosis of adenomas versus non-adenomas is aided by contrast enhancement and subsequent studies of contrast

washout, which show rapid contrast washout of lipid-rich adenomas compared with malignant neoplasms.[10] This diagnostic aid is readily available, inexpensive, and has clear definability of diagnosis at the center of clinical decision.[11] When aided by clinical and biochemical workup, contrast-enhanced computed tomographic scans are key in the characterization of adrenal masses, which gives way to proper therapeutic plan and ensuing regimen of follow-up.[12]

We found very limited evidence locally on the diagnostic ability of contrast-enhanced computed tomography in the differentiation between adrenal adenomas and non-adenomas. As adrenal incidentalomas are diagnosed increasingly with the increased usage of imaging, proper and economical characterization is important in order to prevent unnecessary surgical procedures and early detection of malignant or functioning tumors. This study, carried out in the regional clinical setting, would establish the validity of such a modality among the locals, give clinicians evidence-based advice, and aid rationalization of resources utilized in diagnostic and therapeutic decision-making.

METHODOLOGY

This cross-sectional study was carried out in the Department of Radiology at Liaquat University of Medical and Health Sciences, Jamshoro, between March 2024 and August 2024. The research was designed to evaluate the diagnostic accuracy of contrast-enhanced computed tomography in differentiating adrenal adenomas from non-adenomatous lesions, using histopathology as the reference standard. Approval for the study protocol was obtained from the College of Physicians and Surgeons Pakistan as well as the institutional review board of the university prior to the commencement of patient recruitment. The sample size was calculated by considering expected sensitivity of 85%, specificity of 95%, prevalence of adrenal lesions at 13%, with margins of error set at 15% for sensitivity and 5% for specificity, using a 95% confidence interval. Based on these parameters, a minimum of 118 participants was required.

Individuals of either sex, aged between 20 and 85 years, with adrenal masses greater than 1 cm and showing attenuation values above 10 Hounsfield units on unenhanced computed tomography were included. Patients were excluded if they were pregnant, had a history of severe allergic reaction, were critically ill, or had renal failure.

Informed written consent was obtained from all participants before inclusion in the study. Each patient was briefed in detail regarding the objectives and procedures of the study, and confidentiality was ensured by coding data and maintaining secure access to patient records.

Demographic variables including age, gender, height, weight, and body mass index were recorded for all participants. Following demographic documentation, clinical imaging evaluation was conducted. All eligible individuals underwent contrast-enhanced computed tomography scans, performed 60 seconds after intravenous contrast administration. Imaging was interpreted by a senior radiologist with more than five years of experience. Benign adrenal lesions were identified on the basis of well-circumscribed myelolipomas, less than 4 cm in size, with areas of fat density. Malignant masses were considered when large, often bilateral, heterogeneous lesions with internal necrosis or hemorrhage were observed. Tissue samples obtained from these patients were subsequently examined by the histopathology department, which served as the gold standard for diagnosis.

The diagnostic outcome was defined by correlating computed tomography findings with histopathological results. True positive cases were those in which both modalities identified malignancy, while true negatives were defined as cases where both confirmed benign lesions. False positives referred to lesions interpreted as benign on imaging but malignant on histopathology, whereas false negatives denoted those read as benign on imaging but proven malignant on histology. Overall diagnostic accuracy was measured in terms of sensitivity, specificity, positive predictive value, and negative predictive value.

Data were analyzed using SPSS version 21. The Shapiro–Wilk test was applied to assess the distribution of continuous variables including age, height, weight, and body mass index. Normally distributed data were expressed as mean and standard deviation, whereas skewed data were reported as median with range. Categorical variables such as gender were presented as frequencies and percentages. A 2×2 contingency table was constructed to calculate sensitivity, specificity, predictive values, and diagnostic accuracy of contrast-enhanced computed tomography, with histopathology serving as the reference. Stratification was applied for age, gender, and body mass index to address potential confounding, and diagnostic accuracy measures were reassessed post-stratification.

RESULTS

The study included 118 patients with a mean age of 51.13±11.63 years, mean weight of 75.97±11.24 kg, mean height of 1.68±0.05 m, and mean BMI of 26.75±2.85 kg/m^2. The gender distribution showed 41 males (34.7%) and 77 females (65.3%) (as shown in Table-I).

Table I

Patient Demographics

Demographics	Mean ± SD
Age (years)	51.13±11.63
Weight (kg)	75.97±11.24
Height (m)	1.68±0.05
BMI (kg/m^2)	26.75±2.85
Gender	
Male n (%)	41 (34.7%)
Female n (%)	77 (65.3%)

Overall diagnostic outcomes revealed that CT identified 98 cases (83.1%) as benign and 20 cases (16.9%) as malignant adrenal masses, while histopathology classified 103 cases (87.3%) as benign and 15 cases (12.7%) as malignant, with a total of 118 cases (100%) evaluated by both methods (as shown in Table-II).

Table II
Overall results of CT and Histopathology in diagnosis of adrenal masses

Adrenal Masses	CT	Histopathology
Benign	98 (83.1%)	103 (87.3%)
Malignant	20 (16.9%)	15 (12.7%)
Total	118 (100%)	118 (100%)

The comparative analysis between CT and histopathology demonstrated 96 true negatives (TN), 13 true positives (TP), 7 false positives (FP), and 2 false negatives (FN), with totals of 98 benign CT cases, 20 malignant CT cases, 103 benign histopathology cases, 15 malignant histopathology cases, and an overall total of 118 cases. This analysis yielded a highly significant Chi-square value of 59.29 and p-value of 0.000 (as shown in Table-III).

Table III
Comparison of CT versus Histopathology in diagnosis of adrenal masses

CT	Histopathology		Total
	Benign	Malignant	
Benign	96 (TN)	2 (FN)	98
Malignant	7 (FP)	13 (TP)	20
Total	103	15	118

The overall diagnostic performance of CT showed a sensitivity of 86.70%, specificity of 93.20%, diagnostic accuracy of 92.40%, positive predictive value (PPV) of 65.00%, and negative predictive value (NPV) of 98.00% (as shown in Table-IV).

Table IV
Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of CT in diagnosis of adrenal masses

Diagnostic Parameter	Result
Sensitivity	86.70%
Specificity	93.20%
Diagnostic Accuracy	92.40%
PPV	65.00%
NPV	98.00%

Stratified analysis by age groups revealed that for patients ≤50 years (n=57), sensitivity could not be calculated due to absence of malignant cases, while specificity was 94.70%, diagnostic accuracy was 94.70%, PPV could not be calculated, and NPV was 100%. For patients >50 years (n=61), sensitivity was 86.70%, specificity was 91.30%, diagnostic accuracy was 90.20%, PPV was 76.50%, and NPV was 95.50%. Gender-based analysis showed that among males (n=41), sensitivity was 80.00%, specificity was 88.90%, diagnostic accuracy was 87.80%, PPV was 50.00%, and NPV was 97.00%. Among females (n=77), sensitivity was 90.00%, specificity was 95.50%, diagnostic accuracy was 94.80%, PPV was 75.00%, and NPV was 98.50%. BMI stratification indicated that for patients with BMI ≤25 kg/m^2 (n=38), sensitivity and PPV could not be calculated due to absence of malignant cases, while specificity was 100%, diagnostic accuracy was 100%, and NPV was 100%. For patients with BMI >25 kg/m^2 (n=80), sensitivity was 86.70%, specificity was 89.20%, diagnostic accuracy was 88.80%, PPV was 65.00%, and NPV was 96.70% (as shown in Table-V).

Table V
Stratified analysis of Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of CT in diagnosis of adrenal masses with age, gender and BMI

Variables	Groups	Diagnostic Parameter	Result
Age (years)	≤50	Sen	-
		Spec	94.70%
		DA	94.70%
		PPV	-
		NPV	100%
	>50	Sen	86.70%
		Spec	91.30%
		DA	90.20%
		PPV	76.50%
		NPV	95.50%
Gender	Male	Sen	80.00%
		Spec	88.90%
		DA	87.80%
		PPV	50.00%
		NPV	97.00%
	Female	Sen	90.00%
		Spec	95.50%
		DA	94.80%
		PPV	75.00%
		NPV	98.50%
BMI (kg/m^2)	≤25	Sen	-
		Spec	100%
		DA	100%
		PPV	-
		NPV	100%
	>25	Sen	86.70%
		Spec	89.20%
		DA	88.80%
		PPV	65.00%
		NPV	96.70%

DISCUSSION

This study assessed the diagnostic performance of contrast-enhanced computed tomography (CT) to distinguish adrenal masses as benign adenomas or malignant tumors with histopathology as the reference standard. The results show that CT had excellent overall diagnostic performance with sensitivity of 86.70%, specificity of 93.20%, and diagnostic accuracy of 92.40%. High specificity reflects the superior capacity of CT to accurately identify benign adrenal masses and can be related to the enhancement patterns of adenomas that have fast washout of the contrast material due to lipid content and distinctive cellular structure. Relatively low sensitivity implies that there may be malignant tumors with enhancement patterns closely similar to benign adenomas, especially lipid-rich adrenal carcinomas or metastatic tumors with atypical imaging features.

The positive predictive value of 65.00% mirrors relatively low incidence of malignant adrenal masses within this study population (12.7%), which is in accord with known epidemiology wherein benign adenomas prevail among adrenal incidentalomas. The excellent negative predictive value of 98.00% highlights the reliability of CT to exclude malignancy with imaging feature-based suspicion of benign lesion. The highly significant correlation between CT and histopathological diagnosis (Chi-square = 59.29, $p < 0.001$) certifies the diagnostic role of contrast-enhanced CT in characterization of adrenal masses.

Stratification analysis identified significant differences in performance of diagnosis among varying

patient groups. The lack of malignant instances among patients ≤50 years and with BMI ≤25 kg/m^2 is an indication of age-related rise in risk of adrenal malignancy and possible link between metabolic factors and adrenal pathology. The female patients proved to have high diagnostic accuracy (94.80%) as compared to males (87.80%), which could be an indication of differences in adrenal gland structure, influence of hormones and differences in underlying conditions affecting adrenal enhancement patterns between genders.

Our results demonstrate notable concordance with several previous investigations. Shankaranandh et al. [13] reported comparable diagnostic performance with 96% sensitivity and 93.1% specificity for absolute washout criteria, which closely aligns with our specificity of 93.20%. Similarly, Choudhury et al. [14] achieved 89.6% sensitivity and 95.8% specificity at 60% absolute washout threshold, demonstrating results remarkably consistent with our findings. The slight variations in sensitivity may be attributed to differences in study populations, with our cohort showing a lower prevalence of malignant lesions (12.7%) compared to these studies, potentially affecting the positive predictive value calculations. Wang et al. [15] reported 84% sensitivity and 77% specificity for relative washout at 34% threshold, which is lower than our results, possibly due to their use of 7-minute delay imaging versus standard protocols and inclusion of different histological subtypes.

The demographic characteristics of our study population, with a mean age of 51.13±11.63 years and female predominance (65.3%), contrast with Shivapur et al. [16] who reported a higher mean age of 55.7±14.0 years and male predominance (70.7%). This age difference may explain the lower malignancy prevalence in our younger cohort, as malignant adrenal masses typically increase with advancing age. The gender distribution differences could reflect variations in referral patterns or regional epidemiological factors affecting adrenal pathology presentation.

Our diagnostic accuracy of 92.40% compares favorably with established literature benchmarks. Elsayes et al. [17] synthesized multiple studies showing absolute percentage washout ≥60% achieving 88-96% sensitivity and 96-100% specificity, with our results falling within this range. The consistency across multiple studies reinforces the reliability of contrast-enhanced CT washout protocols for adrenal mass characterization. However, Park et al. [18] reported perfect specificity (100%) but lower sensitivity (36-72%) using unenhanced CT attenuation thresholds alone, highlighting the superior diagnostic performance achieved through contrast enhancement protocols as demonstrated in our study. The incorporation of artificial intelligence methodologies as illustrated by Chen et al. [19] with their 99.7% sensitivity and 98.3% accuracy via their 3D V-Net model holds promise for enhanced performance at diagnosis. However, their validation was mainly with pathologically proven cases in a single-center study, whereas our multi-parameter clinical assessment allows broader translation to daily clinical practice. The high negative predictive value (98.00%) seen within our study argues for clinical usefulness of CT to exclude malignancy with confidence and thereby avoid unnecessary invasive procedures and patient anxiety, which is compatible with objectives of precision medicine approaches to adrenal imaging.

A few limitations need to be considered during interpretation of our findings. It was a single-center study and as such may restrict generalizability to other health care settings with varying patient populations, imaging protocols, or specification of equipment. The sample size was relatively small, especially in some of the subgroup analyses such as patients ≤50 years and BMI ≤25 kg/m^2, which might influence the statistical depth for the stratified analysis and render meaningless sensitivity calculations among such groups. The study did not factor variations of contrast injection protocols, timing of imaging, or experience of the reader that might affect performance at diagnosis. Additionally, lack of follow-up data at longer term for those diagnosed as benign restricts evaluating true clinical outcome as well as missed malignancy potential.

CONCLUSION

Our analysis found that contrast-enhanced computed tomography shows high diagnostic accuracy to characterize adrenal masses as adenomas or non-adenomas compared to histopathology as reference standard. The imaging technique had high specificity and negative predictive value, reinforcing its effectiveness to rule out malignancy and detect benign lesions.

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