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ORIGINAL ARTICLE

Diagnostic accuracy of contrast-enhanced CT in diagnosis of adrenal adenoma taking histopathology as gold standard.

Saba Jahangir[1], Amna Rehan[2], Awais Ahmed[3], Zonaira Shabbir[4], Asim Shaukat[5], Muhmmad Zohaib Asgher[6]

ABSTRACT… Objective: To determine the diagnostic accuracy of contrast-enhanced CT in diagnosis of adrenal adenoma taking histopathology as gold standard. **Study Design:** Cross-Sectional Validation Study. **Setting:** Department of Radiology, Allied Hospital, Faisalabad. **Period:** July 2025 to December 2025. **Methods:** A total of 130 patients aged 50–80 years suspected of adrenal carcinoma were enrolled through consecutive sampling. All underwent contrast-enhanced CT (CECT), interpreted by a blinded consultant radiologist. Adenomas were defined as lesions with unenhanced attenuation ≤10 HU and absolute percentage washout >60%. Histopathology after surgical excision or biopsy served as the gold standard. Diagnostic accuracy parameters including sensitivity, specificity, PPV, NPV, and overall accuracy were calculated using a 2×2 table. Data were analyzed with SPSS 25, with stratification for demographic and clinical factors. **Results:** Among 130 patients, CT detected adenoma in 40.8% while histopathology confirmed 75.4%. CT showed high specificity and PPV (93.8% and 96.2%) but low sensitivity and NPV (52.0% and 39.0%), reflecting substantial false-negative rates. **Conclusion:** Although contrast-enhanced CT remains a valuable first-line modality with strong specificity and confirmatory accuracy, its low sensitivity requires cautious interpretation when classic washout features are absent. Emerging quantitative radiomics and functional imaging techniques may enhance diagnostic confidence and support more precise patient management.

Key words: Adrenal Gland Neoplasms, Adenoma, Contrast Media, Diagnostic Accuracy, Tomography, X-Ray Computed.

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INTRODUCTION

Adrenal incidentaloma is defined as an adrenal mass detected incidentally[1-2] with a size of 1 cm or larger and could be detected in approximately 6% of the patients who received imaging studies such as CT or MRI.[3] The incidence and prevalence of adrenal masses have increased between the last 15 and 20 years[4], probably secondary to the development of more advanced imaging techniques and their frequent use, which allow for early visualization.[5]

Their prevalence is age dependent (10–15% in adults >60–70 years), and their detection is increased in recent years, because of the large availability of imaging medical equipment such as CT and MR.[6] Characterization of an adrenal mass as benign or malignant is critical and imaging plays a key role in influencing the clinical management of patients. In this setting, the role of radiologists is crucial in both the choice of imaging modality and protocol technique to be used and interpretation of imaging findings.[7]

CT represents the first-level imaging modality for the evaluation of adrenal lesions, since it permits a quick execution ensuring high spatial resolution, with findings of pre-contrast images and post-contrast behavior being commonly used to achieve a correct diagnosis.[8] In a study, 116 patients were found to have incidental adrenal lesions and 75% were adrenal adenomas and 25% were non ademonas. The sensitivity, specificity, and accuracy for the APW test at a 60% threshold were 52.1%, 93.3%, and 54.0%, respectively.[9]

The most frequent ones, adrenal metastases and adenomas cannot be so described easily. This is mostly because they are small, lack definite diagnostic characteristics and they are often common when they are found seem to be alike.[10-11]

1. MBBS, PGR, Allied Hospital, Faisalabad.
2. MBBS, FCPS, Professor Radiology, Allied Hospital. Faisalabad Medical University, Faisalabad.
3. MBBS, FCPS, EBIR, Assistant Professor Radiology, Fatima Jinnah Medical University, Faisalabad.
4. MBBS, FCPS (Radiology), Senior Registrar Radiology, Sir Ganga Raam Hospital, /FJMU.
5. MBBS, MCPS, FCPS, Professor, Allied Hospital Faisalabad Medical University, Faisalabad.
6. MBBS, FCPS, Consultant Radiologist, IMC Hospital, Lahore.

Correspondence Address:
Dr. Muhmmad Zohaib Asgher
Radiologist, IMC Hospital, Lahore.
mzasgher@gmail.com

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Accuracy of contrast-enhanced CT in the diagnosis of adrenal masses in patients who presented to the Radiology Department of Allied Hospital Faisalabad may be critical in improving clinical decision-making. It will be possible to make more correct diagnoses of adrenal masses by means of introducing a proper idea of sensitivity and specificity of contrast-enhanced CT in this context that will allow providing patients with better management and treatment planning. The results of this study may be used to update the diagnostic procedures and to inform clinicians about the use of the most suitable imaging methods in the assessment of adrenal masses. This may eventually enhance patient outcomes compared to the current situation where delay in diagnosis and failure to deliver accurate diagnosis results leads to invasive procedures, and suboptimal treatment strategies to treat adrenal disorders in future. The diagnosis has far reaching implications on the patient. The importance of the proposed study is to evaluate the accuracy of Contrast Enhanced CT in identifying the adrenal masses to be benign or malignant i.e. adenoma or non-adenoma.

METHODS

This cross-sectional validation study was conducted in the Department of Radiology at Allied Hospital, Faisalabad, to evaluate the diagnostic accuracy of contrast-enhanced computed tomography (CECT) for identifying adrenal adenomas, using histopathology as the reference standard. The study was carried out over a period of six months (July to December, 2025) following approval from the CPSP and Institutional Ethical Review Committee (Ref. No: 48.ERC/FMU/2022-23).

A total sample of 130 patients was calculated using a 95% confidence level, 10% absolute precision, a presumed disease prevalence of 75%, and previously reported sensitivity and specificity values of 52% and 93%, respectively. A non-probability consecutive sampling technique was employed to enroll participants.

The age range of our eligible participants was 50-80 years of either gender group; all participants who were clinically suspected to have adrenal carcinoma were the part of our study whereas all those with renal failure, pregnant females, critically ill or having a history of severe contrast hypersensitivity were excluded from this study. Duly required protocol of written informed consent was also followed. We further recorded relevant history of the patients with demographic data and other co-morbidities like hypertension, diabetes mellitus, smoking status, lesion characteristics.

All participants underwent CECT of the adrenal glands according to departmental protocol. Imaging was performed by a consultant radiologist who was blinded to histopathology results. Attenuation values and absolute percentage washout (APW) were calculated, with lesions demonstrating attenuation ≤10 Hounsfield Units (HU) and APW greater than 60% labeled as adrenal adenomas, while APW less than 60% was categorized as non-adenomas. Subsequent to imaging, all patients underwent surgical excision or percutaneous biopsy of the adrenal mass for histopathological assessment. Histology served as the gold standard, and adenomas were identified based on established microscopic criteria, including the presence of larger cells with variable cytoplasm and nuclear morphology.

We crossed check our imaging findings with the results of histopathology for classification of our results as true negative/true positive/false negative/true negative. A standard 2x2 contingency table was generated to calculate sensitivity/specificity/PPV/NPV and overall diagnostic accuracy. Data were analyzed using SPSS version 25. Quantitative variables such as age and lesion dimensions were expressed as mean ± standard deviation, while qualitative variables including gender, comorbidities, lesion site, and diagnostic categories were presented as frequencies and percentages. Effect modifiers such as age, gender, smoking status, diabetes, hypertension, and mass characteristics were controlled through stratification, followed by post-stratification diagnostic accuracy assessment.

RESULTS

Table-I shows the demographic and clinical details of the 130 patients taking part in the study. Majority participants (75.4%) were in the 50-65 years of age, and 24.6% were aged 66-80 years. Most of them were females (58.5%) against males (41.5%). The overall proportion of patients who were smokers was 28.5%, diabetes mellitus was 33.1% and hypertension was 70.8%. On imaging, 40.8% of patients were diagnosed with adrenal adenoma on contrast-enhanced CT, but histopathology identified adenoma in 75.4% of patients, which is much greater than the prevalence of CT detection. This indicates the possibility of underdiagnosis when using CT.

The table of diagnostic performance of contrast-enhanced CT versus histopathology is summarized in Table-II. This paper has discovered 51 true-positive cases where CT has correctly identified adenoma and 30 true-negative cases where CT has correctly identified non-adenoma lesions. The misclassification was in terms of 47 false negatives, which were missed in CT and 2 false positives where the CT misclassified the non-adenoma lesions as adenomas.

In Table-III, there is a more detailed stratification of diagnostic results on the background of demographic variables and clinical variables with p-values. The age and the diagnostic performance were statistically significantly correlated ($p = 0.007$) with younger subjects (50-65 years) showing a higher false-negative occurrence. There was no significant influence of gender, smoking status, diabetes mellitus, and hypertension on the diagnostic accuracy of the participants as their non-significant p-values ($p > 0.05$).

The laterality of the lesions showed the borderline relationship ($p = 0.063$), which implies that the false outcomes were higher among the right-sided lesions than the left-sided lesions. This trend can be attributed to the difference in anatomy or technical aspects influencing the CT performance. In general, it is evident that stratification proves that age and side of lesion are the main variables affecting diagnostic variability but other patient factors are not evident in influencing CT accuracy.

The results of the calculated diagnostic accuracy measures of contrast-enhanced CT with the gold standard of histopathology are provided in Table-IV. The sensitivity was found to be 52.0 which showed that CT was able to accurately identify a little bit more than half of the real cases of adenoma. Specificity on the other hand was high at 93.8 which is the high capability of CT to rule out non-adenoma lesions. A positive predictive value (PPV) of 96.2 percentage indicates that a CT that declared one lesion as an adenoma was nearly correct. On the contrary, the negative predictive value (NPV) was low (39.0%), which implies that negative CT did not rule out adenoma with high accuracy. The general diagnostic quality of CT was 62.3%. All these indicators confirm that contrast-enhanced CT has a high confirmatory value of adenoma (high PPV and specificity) but a poor exclusion of adenoma (low sensitivity and NPV) as it is corroborated by the high false-negative rate in Table-II.

TABLE-I

Frequency distribution of demographic and clinical variables (N = 130)

Variable	Category	Frequency (n)	Percent (%)
Age	50-65 years	98	75.4
	66-80 years	32	24.6
Gender	Male	54	41.5
	Female	76	58.5
Smoking	Yes	37	28.5
	No	93	71.5
Diabetes	Yes	43	33.1
	No	87	66.9
Hypertension	Yes	92	70.8
	No	38	29.2
CT Adenoma	Positive	53	40.8
	Negative	77	59.2
Histopathology Adenoma	Positive	98	75.4
	Negative	32	24.6

TABLE-II

Diagnostic classification using histopathology as gold standard

Classification	Frequency (n)	Percent (%)
True Positive	51	39.2%
True Negative	30	23.1%
False Positive	2	1.5%
False Negative	47	36.2%

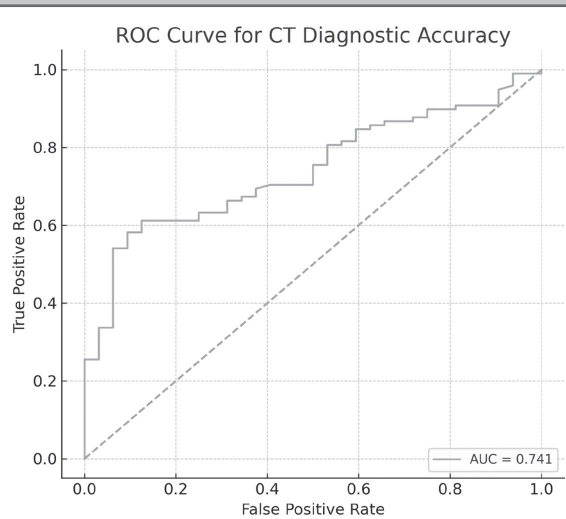
ROC curve for CT diagnostic accuracy

The ROC curve below depicts the diagnostic ability of the APW% as derived in contrast-enhanced CT in differentiating the adrenal adenoma and non-adenoma. The sum of the discriminatory abilities of the test is called the Area Under the Curve (AUC).

TABLE-III							
Stratified diagnostic outcome across variables With P-Values							
Variable	**Category**	**TP n (%)**	**TN n (%)**	**FP n (%)**	**FN n (%)**	**Total**	**P-Value**
Age	50-65 years	36 (36.7%)	28 (28.6%)	0 (0%)	34 (34.7%)	98	0.007
	66-80 years	15 (46.9%)	2 (6.3%)	2 (6.3%)	13 (40.6%)	32	
Gender	Male	22 (40.7%)	12 (22.2%)	1 (1.9%)	19 (35.2%)	54	0.983
	Female	29 (38.2%)	18 (23.7%)	1 (1.3%)	28 (36.8%)	76	
Smoking	Yes	12 (32.4%)	8 (21.6%)	2 (5.4%)	15 (40.5%)	37	0.114
	No	39 (41.9%)	22 (23.7%)	0 (0%)	32 (34.4%)	93	
Diabetes	Yes	15 (34.9%)	10 (23.3%)	0 (0%)	18 (41.9%)	43	0.598
	No	36 (41.4%)	20 (23.0%)	2 (2.3%)	29 (33.3%)	87	
Hypertension	Yes	37 (40.2%)	24 (26.1%)	2 (2.2%)	29 (31.5%)	92	0.261
	No	14 (36.8%)	6 (15.8%)	0 (0%)	18 (47.4%)	38	
Lesion Side	Right Adrenal	28 (41.2%)	10 (14.7%)	2 (2.9%)	28 (41.2%)	68	0.063
	Left Adrenal	23 (37.1%)	20 (32.3%)	0 (0%)	19 (30.6%)	62	

TABLE-IV		
Diagnostic accuracy of contrast-enhanced CT		
Accuracy Measure	**Description**	**Value**
Sensitivity	Ability of CT to correctly detect adenoma (TP/(TP+FN))	52.0%
Specificity	Ability of CT to correctly detect non-adenoma (TN/(TN+FP))	93.8%
Positive Predictive Value (PPV)	Probability a CT-positive case truly has adenoma (TP/(TP+FP))	96.2%
Negative Predictive Value (NPV)	Probability a CT-negative case truly has no adenoma (TN/(TN+FN))	39.0%
Overall Accuracy	Correct CT diagnoses out of all cases ((TP+TN)/Total)	62.3%

FIGURE-1



DISCUSSION

The present study evaluated the diagnostic value of contrast-enhanced CT (CECT) in differentiating adrenal adenoma and non-adenomatous lesions with the use of histopathology as the reference standard. The main results reveal that though CECT had high specificity and PPV, its sensitivity, NPV, and general accuracy were significantly lower with a high percentage of false-negative outcomes. These findings reflect the natural shortcomings of attenuation- and washout-based CT criteria particularly in lipid-poor adenoma and lesions that exhibit unusual enhancement appearance. The research meets its aim by resolving these diagnostic ambiguities by re-evaluating the effectiveness of CECT in a modern clinical cohort.

Comparison to the extant literature indicates both agreement and disagreement with the previous results. In an almost identical study, Qurat-ul-Ain et al. showed significantly greater sensitivity (86.7%), and diagnostic accuracy (92.4) with CECT in detecting adrenal adenoma, but specificity parallels ours (93.2%).[12] It is possible that the improved sensitivity is due to more rigorous lesion selection (>1 cm, >10 HU), and possibly a more homogeneous patient population, indicating that sensitivity to adenomas increases with tightly controlled imaging regimes and patient populations. In the same manner, 196 cases of adrenalectomy were studied by Yip et al[13] who established that the CT and MRI specific criteria such as HU less than 10, absolute washout greater than 60 percent and loss of chemical-shift signal reveals a specificity of 100 percent and sensitivity of 57 percent, which are significantly close to our specificity and sensitivity trends. Their findings support the idea that CECT is quite accurate to prove the presence of benign adenoma in the presence of typical criteria, but can still be susceptible to the missing adenoma that does not have characteristic features of washout or low attenuation.

Our results are also contextualized by the greater biological and imaging issues that are related to adrenal lesions. According to Viétor et al., the heterogeneity of tumors, radiologic appearance overlap and lipid variation significantly make it difficult to characterize adrenal tumors correctly.[14] Our data supports these limits with the high false-negative burden of our data, which suggests the theory that lipid-poor adenoma and the indeterminate lesion are many times beyond the conventional CT washout limit. The existing observations are thus in line with the known pathophysiological principles that indicate that the dependence on attenuation values and percentage washout is only potentially able to represent the entire range of adenoma morphology.

The multidimensionality of the adrenal mass evaluation is also emphasized by the advanced imaging research. Systematic review and meta-analysis by Zhang et al. has shown that radiomics of CT could have pooled sensitivity and specificity of 0.80 and 0.83, respectively, in differentiating between benign and malignant adrenal tumors.[15] Although radiomics is superior in certain situations compared to regular CT, a significant amount of heterogeneity and methodological constraints restricts applicability. However, the new function of the quantitative analysis of texture highlights the possibility of the future diagnostic instruments to defeat the shortcomings of the traditional washout-based analysis, especially with the ambiguous lesion or lipid-poor lesion located at the center of the false-negative cases in our cohort.

Despite the fact that CECT is the preferred modality when it comes to the characterization of adrenal masses, alternative imaging modalities can be used to supplement or refine diagnosis in a few cases. Radha et al. reported in a study comparing adrenal lesions in the oncology patients that PET/CT was also able to distinguish between benign and malignant nodules with a 89.7 and 88.6 percent sensitivity and accuracy, respectively.[16] The sensitivity of the latter exceeds that of CECT in our experiment and indicates the usefulness of metabolic imaging in high-risk or uncertain cases. Nevertheless, PET/CT is still more expensive and is not used regularly in incidentalomas, which only restricts its application to selective clinical findings.

Combined, the current research study confirms the larger literature that CECT has high specificity and poor sensitivity in detecting adrenal adenoma. To the extent that the high PPV in our cohort supports the utility of the tool as a confirmatory one, the low NPV requires that the negative CT result cannot be a reliable indicator of adenoma exclusion. Clearly, this has serious clinical consequences: patients with indeterminate or non-diagnostic CT results need to undergo adjunct MRI, functional imaging, or multidisciplinary review to prevent misclassification. We also found in our stratified analysis that the issue of age and lesion laterality affected diagnostic performance indicating that technical and anatomical differences could have subtle effects on the washout behavior.

The study strengths comprise the use of histopathology as the ultimate gold standard, standardized CT method and the extensive stratification of the population based on the demographic and clinical variables. Limitations: The sample size is relatively small, there are no special MRI or PET/CT comparison groups, the study was single-centered, and this could narrow the scope of generalizability. The radiomics-based models and multiparametric imaging and external validation in a variety of population should be considered in the future research to enhance diagnostic accuracy.

CONCLUSION

Although contrast-enhanced CT continues to serve as a useful first line test with good specificity and confirmatory accuracy, its low sensitivity points to the fact that this test must be interpreted with caution in the absence of classic washout. The incorporation of the changing imaging strategies, especially quantitative radiomics and functional modalities, can contribute to the diagnostic confidence and better-focused patient management.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Saba Jahangir:** Data collection, paper writing.
2	**Amna Rehan:** Data collection.
3	**Awais Ahmed:** Literature review, data entry.
4	**Zonaira Shabbir:** Data analysis.
5	**Asim Shaukat:** Review of manuscript.
6	**Muhmmad Zohaib Asgher:** Discussion writing.