

Diagnostic Accuracy of Tc^{99m}-Sestamibi in Differentiating Benign vs Malignant Renal Masses

Zeeshan Sikandar, Fida Hussain, Zaigham Salim Dar, Rebecca Sharoon, Aleena Tariq*, Muhammad Usman Ibrahim

Department of Nuclear Medicine, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan,

*Department of Nuclear Medicine, Rawalpindi Medical University (RMU), Rawalpindi Pakistan

ABSTRACT

Objective: To assess the role of pre-operative Tc-99m sestamibi scintigraphy in Differentiating Benign vs Malignant Renal Masses.

Study Design: Cross-sectional study

Place and Duration of Study: Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Jun 2022 to Jun 2023.

Methodology: A total of 41 patients with T1 solid renal tumours who were eligible for undergoing surgery or suitable for biopsy underwent Tc-99m sestamibi scintigraphy during study duration. Tc-99m sestamibi scintigraphy findings were correlated with post-operative histopathology results to determine accuracy of scintigraphic study.

Results: Out of forty-one patients, 24(58.5%) were men and 17(41.5%) were women with a mean age 54.39±13.28 years. Among total patients, 24(58.5%) had clear cell RCC, 5(12.2%) had papillary RCC, 3(7.3%) had chromophobe RCC, 2(4.9%) had oncocytic papillary RCC, 5(12.2%) had oncocytoma and 2(4.9%) had lipid poor angiomyolipoma variant on histopathology. Overall, 7(17.07%) patients had benign pathology. Tc-99m Sestamibi SPECT/CT correctly identified all benign lesions (oncocytoma and lipid poor angiomyolipoma) and two variants of malignant pathology (chromophobe and oncocytic papillary RCC) yielding a sensitivity of 100% while specificity of 85.29% in detecting benign lesions. There was significant correlation between positive Tc-99m sestamibi findings and benign pathology with a *p*-value <0.001.

Conclusions: Tc-99m sestamibi scintigraphy plays a significant role in pre-operative evaluation of renal masses and offers a non-invasive modality to help differentiate benign and malignant renal masses.

Keywords: Oncocytoma, Renal Cell Carcinoma, SPECT/CT, Tc-99m Sestamibi.

How to Cite This Article: Sikandar Z, Hussain F, Dar ZS, Sharoon R, Tariq A, Ibrahim MU. Diagnostic Accuracy of Tc99m-Sestamibi in Differentiating Benign vs Malignant Renal Masses. *Pak Armed Forces Med J* 2025; 75(5): 901-904. DOI: <https://doi.org/10.51253/pafmj.v75i5.10913>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Renal cell carcinoma (RCC) is on rise globally making approximately 2% of the cancer worldwide.¹ Incidence of RCC has almost doubled in last fifty years. Around the world, renal tumours are the sixth leading cause of malignant growth in men and the 10th in women, representing 5% and 3% of every oncological finding, separately.² Malignant renal tumours are also common in children representing 5% of childhood cancers.³ As the prevalence of renal tumours has increased, most cases of renal cell carcinoma are found incidentally on various imaging modalities (i.e. ultrasonography, CT and MRI).^{4,5} Most of these cancers comprises of renal cell carcinomas (RCCs). But, almost 20% of small kidney masses (<4cm) are one of a few benign growths, most commonly renal oncocytoma, angiomyolipoma (lipid poor-AML) and infected cyst.⁶ Oncocytoma comprises for almost 10% of all epithelial renal tumours.⁷ Among renal tumours, oncocytomas is unique, because their

cells have abundant, densely packed mitochondria which show significant Tc-99m sestamibi uptake. One of the technique for differentiating benign renal masses from malignant is percutaneous biopsy. Although this method has best accuracy, but it also carries poor negative predictive value, making it challenging for surgeons to have the confidence to go for surgical intervention after a negative biopsy.⁸ Renal biopsies have also a significant non-diagnostic rate, ranging from almost 8-14%. Moreover, renal biopsy is less convincing when evaluating small renal masses. Beside the invasive nature of renal biopsy, there are multiple complications like hematoma and haematuria that may occur after percutaneous biopsy.⁹

In the field of nuclear medicine and molecular imaging, Tc-99m sestamibi is broadly used as a mitochondrial agent for cardiac perfusion scintigraphy and the localizing normal and ectopic parathyroid adenomas. On the basis of this information, several studies are conducted to explore the effectiveness of Tc-99m sestamibi in differentiating benign vs. malignant renal masses. Tc-99m sestamibi is a lipophilic cation that concentrates predominantly in

Correspondence: Dr Zeeshan Sikandar, Department of Nuclear Medicine, Armed Forces Institute of Pathology, Rawalpindi Pakistan
Received: 18 Sep 2023; revision received: 19 Dec 2023; accepted: 20 Dec 2023

those cells that are rich in mitochondria. As renal oncocytoma consist of numerous oncocyctic cells having densely packed mitochondria, it shows significant Tc-99m sestamibi uptake. The objective of this study was to elucidate the diagnostic accuracy of Tc-99m sestamibi in differentiating benign vs. malignant renal masses. This study will not only help in establishing its diagnostic value but also improve patient care and clinical practice.

METHODOLOGY

This cross-sectional study was conducted at Nuclear Medical Centre Armed Forces Institute of Pathology from June 2022 to June 2023 over a period of 1 year. Study protocol was approved from Institutional Review Board (IRB) before start of the study (IRB number FC-NMC20-1/READ-IRB/22/1451). WHO sample size calculator was used for calculating sample size taking margin of error 6%, confidence interval 95% and prevalence of 0.96.¹⁰ The sample size came out to be 41. All patients were selected by convenient sampling technique. Informed written consent were taken from all the participants.

Inclusion Criteria: All patient irrespective of age and gender having T1 solid renal tumours, suitable for surgical intervention or biopsy were included in our study.

Exclusion Criteria: Patients having tumours >7 cm in maximum diameter on CT scan/MRI and those having metastatic disease on preoperative imaging i.e. visceral extension and regional lymphadenopathy were excluded from our study.

All patients were in fasting condition for at least 4-6 hours before administration of radiopharmaceutical. SPECT/CT imaging was initiated on a Siemens Symbia T6 (Siemens Healthcare, Erlangen, Germany), 60-90 minutes after the injection of 925±25 MBq (25 mCi) Tc99m-sestamibi, 1-7 days before surgery or percutaneous biopsy. Gamma camera was equipped with low energy high resolution (LEHR) collimators. SPECT scintigraphy was performed with a 128 × 128-pixel matrix size (with a zoom factor of 1.23) acquiring 32 projections in a step and shoot mode. Each projection frame was acquired for a period of 25-seconds. After the SPECT study directly, a CT scan was acquired at 130 kV tube voltage and 20 mA. 2.5-mm axial slices were reconstructed for both SPECT data and CT data. For attenuation correction and anatomical correlation CT acquisition was used.

SPECT/CT images were analysed at Siemens Symbia workstation. SPECT/CT images were

independently analysed by two well qualified nuclear medical specialists, each having almost 17 years of experience in nuclear medicine and molecular imaging. SPECT/CT images were matched with the corresponding CT/MRI images for correct identification of the renal tumour. They reached on the consensus of the location of the tumour, the degree of radiotracer uptake by the tumour, and the ipsilateral/contralateral normal renal tissue. Focal Tc99m-sestamibi accumulation in the tumoral lesion detected on SPECT/CT images was considered as Tc99m-sestamibi positive (sestamibi +), whereas that lesion having mild or absent Tc99m-sestamibi uptake was considered to be Tc99m-sestamibi negative (sestamibi -).

All data including patient demographic data, clinical & radiological data such as (tumour site and size, composition i.e. cystic/solid), type of surgery (radical nephrectomy vs. partial nephrectomy) and results of pathological consideration including tumour size, histological type & grading were collected on pre-designed proforma.

Data was entered and analysed using statistical package for social sciences (SPSS version 21). Quantitative variables were presented as Mean±SD while categorical data was presented as frequency and percentages. Chi-square test was used to compare histopathological and Tc99m-sestamibi findings and *p*-value of ≤0.05 was considered significant.

RESULTS

Out of 41 patients, 24 were men (58.5%) and 17 were women (41.5%) ranging in age between 29 and 77 years (mean age: 54.39±13.28 years). 13(31.7%) were smokers, 23(56.1%) patients were incidentally diagnosed with renal mass, while patients with clinical features had weight loss in 24(58.5%), flank pain in 31(75.6%) and haematuria in 29(70.7%). Out of 41 patients 21(51.2%) had left renal mass and 20(48.8%) had right renal mass. 14(34.1%) had tumour size <4cm while 27(65.9%) had tumour size >4cm. Majority of patients (90.2%) underwent radical nephrectomy as shown in Table-I.

Among total patients, 24(58.5%) had clear cell RCC, 5(12.2%) had papillary RCC, 3(7.3%) had chromophobe RCC, 2(4.9%) had oncocyctic papillary RCC, 5(12.2%) had oncocytoma and 2(4.9%) had lipid poor angiomyolipoma variant on histopathology as shown in Table-II. Overall, 7(17.07%) patients had benign pathology. Tc-99m Sestamibi SPECT/CT accurately identified all benign lesions (oncocytoma and lipid poor angiomyolipoma) and two variants of

malignant pathology (chromophobe and oncocytic papillary RCC) as shown in Table-II. The overall sensitivity of Tc99m-sestamibi to detect benign lesions is 100% while specificity is 85.29%. There was significant correlation between positive Tc99m-sestamibi findings and benign pathology with a p -value <0.001 .

Table-I: Baseline Characteristics, Clinical Features and Operative Findings (n=41)

Characteristics	Values
Age	54.39 $\pm$ 13.28 years
Gender	
Male	24(58.5%)
Female	17(41.5%)
Incidental findings	23(56.1%)
Clinical features	
Weight loss	24(58.5%)
Flank pain	31(75.6%)
Haematuria	29(70.7%)
Tumour size	
<4cm	14(34.1%)
>4cm	27(65.9%)
Location	
Right kidney	20(48.8%)
Left kidney	21(51.2%)
Surgery	
Radical nephrectomy	37(90.2%)
Partial nephrectomy	4(9.8%)

Table-II: Histopathological Findings and Tc99m-Sestamibi SPECT/CT Results (n=41)

Histopathological Type	Frequency	Tc-99m sestamibi SPECT/CT Findings		p -value
		Avid	Non Avid	
Clear cell RCC	24	0	24(100%)	<0.001
Papillary RCC	5	0	5(100%)	
Chromophobe RCC	3	3(100%)	0	
Oncocytic papillary RCC	2	2(100%)	0	
Oncocytoma	5	5(100%)	0	
Angiomyolipoma (lipid poor)	2	2(100%)	0	

Renal cell carcinoma=RCC

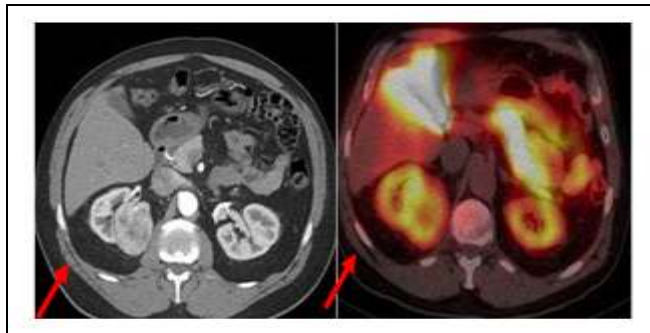


Figure: Tc-99m Sestamibi SPECT/CT Image Showing Avid Lesion (Oncocytoma)

DISCUSSION

In the present study aimed to assess the diagnostic accuracy of Tc99m-sestamibi in differentiating benign vs. malignant renal masses it was found that Tc-99m sestamibi scintigraphy plays a significant role in pre-operative evaluation of renal masses and offers a non-invasive modality to help in differentiating benign and malignant renal masses. The detection of renal masses on CT/ MRI is significantly increased, but it is still a challenging task to differentiate benign from malignant, mostly in the cases of small renal masses having size <20 mm. Among various techniques percutaneous biopsy has good accuracy in diagnosis, but it leads to a lot of complications.¹¹ In nuclear medicine Tc-99m sestamibi is extensively used as mitochondrial agent. Tc-99m sestamibi is a lipophilic monovalent cation that diffuses passively through the cell membrane and strongly binds to mitochondria in the cytoplasm. Tc-99m sestamibi is removed from the cell via multidrug resistant (MDR) pump. Among the renal tumours, oncocytoma is rich in mitochondria, so it shows significant radiotracer uptake, so it is strongly avid on Tc-99m sestamibi scan¹² and there is less MDR pump expression in oncocytoma so radiotracer remains attached for longer period of time. Lipid poor angiomyolipoma is also a benign variant of renal masses, showing variable Tc-99m sestamibi uptake, almost equal to or less than normal renal parenchyma. Tzortzakakis et al published a case of angiomyolipoma displaying increased Tc-99m sestamibi uptake alike the normal renal parenchyma.¹³ Some of the malignant variant of the renal cell carcinoma like chromophobe and oncocytic papillary RCC also show significant radiopharmaceutical uptake due to increased mitochondrial content and low MDR pump expression in these less aggressive malignant tumour.¹⁴ Chromophobe (specifically eosinophilic type) and oncocytic papillary RCC are although malignant tumours, but these tumours rarely metastasize and have indolent clinical course. In other types of renal cell carcinoma like clear cell RCC and papillary RCC, there is no significant radiotracer uptake because these tumours have high expression of multidrug resistant pumps (MDR) and low mitochondrial content, so they appear photopenic on Tc-99m sestamibi scan.^{15,16}

Literature review is limited on this study in Pakistan, so this study will not only help in establishing its diagnostic value but will also improve patient care in clinical practice. In the future we can

significantly reduce unnecessary nephrectomies in those patients having renal masses of likely benign etiology by evaluating these masses by Tc-99m sestamibi scanning. Studies with larger sample sizes is necessary for establishing a quantitative tool as important supplement to visual evaluation in order to reach the accurate diagnosis.^{17,18}

LIMITATION OF STUDY

The major limitation of our study was little sample size and also the very few cases of less frequent pathologies, such as oncocytoma, lipid poor angiomyolipoma and HOCT (hybrid oncocytic chromophobe tumour).

CONCLUSION

Tc-99m sestamibi scintigraphy plays a significant role in pre-operative evaluation of renal masses and offers a non-invasive modality to help in differentiating benign and malignant renal masses.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ZS & FH: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZSD & RS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AT & MUI: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

- Padala SA, Barsouk A, Thandra KC, Saginala K, Mohammed A, Vakiti A, et al. Epidemiology of renal cell carcinoma. *World J Oncol* 2020;11(3):79-87. <https://doi.org/10.14740/wjon1279>
- Capitanio U, Bensalah K, Bex A, Boorjian SA, Bray F, Coleman J, et al. Epidemiology of renal cell carcinoma. *Eur Urol* 2019; 75(1): 74-84. <https://doi.org/10.1016/j.eururo.2018.08.036>
- Nakata K, Colombet M, Stiller CA, Pritchard-Jones K, Steliarova-Foucher E, IICC-3 contributors. Incidence of childhood renal tumours: an international population-based study. *Int J Cancer* 2020; 147(12): 3313-3127. <https://doi.org/10.1002/ijc.33147>
- Tsili AC, Andriotis E, Gkeli MG, Krokidis M, Stasinopoulou M, Varkarakis IM, et al. The role of imaging in the management of renal masses. *Eur J radiol* 2021; 141: 109777. <https://doi.org/10.1016/j.ejrad.2021.109777>
- Ljungberg B, Albiges L, Abu-Ghanem Y, Bedke J, Capitanio U, Dabestani S, et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2022 Update. *Eur Urol* 2022; 82(4): 399-410. <https://doi.org/10.1016/j.eururo.2022.03.006>
- Schieda N, Krishna S, Pedrosa I, Kaffenberger SD, Davenport MS, Silverman SG. Active surveillance of renal masses: the role of radiology. *Radiol* 2022; 302(1): 11-24. <https://doi.org/10.1148/radiol.2021204227>
- Asi T, Tuncali MÇ, Tuncel M, Alkanat NEİ, Hazir B, Kösemehmetoğlu K, et al. The role of Tc-99m MIBI scintigraphy in clinical T1 renal mass assessment: Does it have a real benefit? *Urol Oncol* 2020; 38(12): 937. <https://doi.org/10.1016/j.urolonc.2020.07.018>
- Posielski NM, Bui A, Wells SA, Best SL, Gettle LM, Ziemlewicz TJ, et al. Risk factors for complications and nondiagnostic results following 1,155 consecutive percutaneous core renal mass biopsies. *J Urol* 2019; 201(6): 1080-1087. <https://doi.org/10.1097/ju.000000000000113>
- Bakdash K, Schramm KM, Annam A, Brown M, Kondo K, Lindquist JD. Complications of Percutaneous Renal Biopsy. *Semin Intervent Radiol* 2019; 36(2): 97-103. <https://doi.org/10.1055/s-0039-1688422>
- Zhu H, Yang B, Dong A, Ye H, Cheng C, Pan G, et al. Dual-phase 99mTc-MIBI SPECT/CT in the characterization of enhancing solid renal tumors: a single-institution study of 147 cases. *Clin Nucl Med* 2020; 45(10): 765-770. <https://doi.org/10.1097/rln.0000000000003212>
- Cooper S, Flood TA, Khodary ME, Shabana WM, Papadatos D, Lavallee LT, et al. Diagnostic yield and complication rate in percutaneous needle biopsy of renal hilar masses with comparison with renal cortical mass biopsies in a cohort of 195 patients. *Am J Roentgenol* 2019; 212(3): 570-575. <https://doi.org/10.2214/ajr.18.20221>
- Wilson MP, Katlariwala P, Abele J, Low G. A review of 99mTc-sestamibi SPECT/CT for renal oncocytomas: A modified diagnostic algorithm. *Intractable Rare Dis Res* 2022; 11(2): 46-51. <https://doi.org/10.5582/iridr.2022.01027>
- Tzortzakakis A, Gustafsson O, Karlsson M, Ekström-Ehn L, Ghaffarpour R, Axelsson R. Visual evaluation and differentiation of renal oncocytomas from renal cell carcinomas by means of 99mTc-sestamibi SPECT/CT. *EJNMMI Res* 2017; 7(1): 1-5. <https://doi.org/10.1186/s13550-017-0278-z>
- Tzortzakakis A. Differentiation of Renal Oncocytoma from Renal Cell Carcinoma by Means of 99m TC-Sestamibi SPECT/CT (Doctoral dissertation, Karolinska Institute (Sweden)). <https://doi.org/10.21203/rs.3.rs-446272/v1>
- Rowe SP, Gorin MA, Solnes LB, Ball MW, Choudhary A, Pierorazio PM, et al. Correlation of 99mTc-sestamibi uptake in renal masses with mitochondrial content and multi-drug resistance pump expression. *EJNMMI res* 2017; 7(1): 1-7. <https://doi.org/10.1186/s13550-017-0329-5>
- Sistani G, Bjazevic J, Kassam Z, Romsa J, Pautler S. The value of 99mTc-sestamibi single-photon emission computed tomography-computed tomography in the evaluation and risk stratification of renal masses. *Can Urol Assoc J* 2021; 15(6): 197. <https://doi.org/10.5489/cuaj.6708>
- Gorin MA, Rowe SP, Baras AS, Solnes LB, Ball MW, Pierorazio PM, et al. Prospective evaluation of 99mTc-sestamibi SPECT/CT for the diagnosis of renal oncocytomas and hybrid oncocytic/chromophobe tumors. *Eur Urol* 2016; 69(3): 413-436. <https://doi.org/10.1016/j.eururo.2015.08.056>
- Jones KM, Solnes LB, Rowe SP, Gorin MA, Sheikhbaheei S, Fung G, et al. Use of quantitative SPECT/CT reconstruction in 99mTc-sestamibi imaging of patients with renal masses. *Ann Nucl Med* 2018; 32(2): 87-93. <https://doi.org/10.1007/s12149-017-1222-z>