Prospective Evaluation of $^{99m}$Tc-sestamibi SPECT/CT for the Diagnosis of Renal Oncocytomas and Hybrid Oncocytic/Chromophobe Tumors


Abstract

Nuclear imaging offers a potential noninvasive means of determining the histology of renal tumors. The aim of this study was to evaluate the accuracy of technetium-$^{99m}$ ($^{99m}$Tc–)–sestamibi single-photon emission computed tomography/x-ray computed tomography (SPECT/CT) for the differentiation of oncocytomas and hybrid oncocytic/chromophobe tumors (HOCTs) from other renal tumor histologies. In total, 50 patients with a solid clinical T1 renal mass were imaged with $^{99m}$Tc-sestamibi SPECT/CT prior to surgical resection. Preoperative SPECT/CT scans were reviewed by two blinded readers, and their results were compared with centrally reviewed surgical pathology data. Following surgery, 6 (12%) tumors were classified as renal oncocytomas and 2 (4%) as HOCTs. With the exception of 1 (2%) angiomyolipoma, all other tumors were renal cell carcinomas (82%). $^{99m}$Tc–sestamibi SPECT/CT correctly identified 5 of 6 (83.3%) oncocytomas and 2 of 2 (100%) HOCTs, resulting in an overall sensitivity of 87.5% (95% confidence interval [CI], 47.4–99.7%). Only two tumors were falsely positive on SPECT/CT, resulting in a specificity of 95.2% (95% CI, 83.8–99.4%). In summary, $^{99m}$Tc–sestamibi SPECT/CT is a promising imaging test for the noninvasive diagnosis of renal oncocytomas and HOCTs.

Patient summary: We found that the imaging test $^{99m}$Tc–sestamibi SPECT/CT can be used to accurately diagnose two types of benign kidney tumors. This test may be eventually used to help better evaluate patients diagnosed with a renal tumor.

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that is commonly used for the localization of parathyroid adenomas [3] and myocardial perfusion imaging [4].

We recently carried out a pilot study evaluating ⁹⁹ᵐTc-sestamibi single-photon emission computed tomography/x-ray computed tomography (SPECT/CT) for the imaging of renal tumors [5]. In this study, we imaged three oncocytomas and three renal cell carcinomas (RCCs). Consistent with an earlier report in which a single oncocytoma was imaged with ⁹⁹ᵐTc-sestamibi [6], we observed that the three oncocytomas accumulated radiotracer at levels near or above that of the normal renal parenchyma. In contrast, the three RCCs were profoundly photopenic and thus readily distinguishable from the oncocytomas. Given these encouraging data, we next embarked on a prospective study to evaluate the accuracy of ⁹⁹ᵐTc-sestamibi SPECT/CT for the diagnosis of renal oncocytomas and HOCTs.

Patients presenting with a solid solitary clinical T1 renal mass were imaged with ⁹⁹ᵐTc-sestamibi SPECT/CT prior to surgery. SPECT/CT scans were analyzed independently by two blinded nuclear medicine attending physicians (L.B.S., M.S.J.) in two separate random orders. Readers categorized tumors as positive (ie, “hot”) (Fig. 1A–1C) or negative.
We found that \( 99m\text{Tc-sestamibi} \) SPECT/CT correctly identified 5 of 6 (83.3%) oncocytomas and 2 of 2 (100%) HOCTs, resulting in a specificity of 95.2% (95% CI, 83.8–99.4%). On post hoc analysis, a relative uptake value of 0.6 was found to be optimal for identifying HOCTs, a subtype of renal tumor that histologically resembles both oncocytoma and chromophobe RCC but behaves in a benign fashion [7]. These data demonstrate the potential utility of this nuclear imaging test for the preoperative assessment of indeterminate renal tumors, possibly sparing patients with a positive test further invasive procedures.

A concern about a test that aims to identify benign tumors is that a false-positive finding may result in inaction on the part of the physician, placing the patient at risk for undertreatment. The results of our study, however, show nearly perfect specificity of \( 99m\text{Tc-sestamibi} \) SPECT/CT, with only two tumors being incorrectly classified as positive, resulting in a specificity of 95.2%. Interestingly, both false-positive lesions were chromophobe RCCs, an RCC subtype that has a largely indolent clinical course. In fact, proposed biopsy-based treatment algorithms recommend active surveillance as the management of choice for small chromophobe tumors [8]. This is further supported by data from our institution’s own active surveillance program, in which no case of chromophobe RCC has crossed over to require an intervention [9]. Moreover, in a contemporary systematic review of the active surveillance literature, no case of chromophobe RCC has been reported to have metastasized while on surveillance [10]. Consequently, although in our study we classified these tumors as falsely positive, from a practical standpoint, a test that can identify renal oncocytomas, HOCTs, and chromophobe RCCs offers a tremendous leap forward in our current ability to noninvasively risk-stratify patients presenting with an indeterminate renal mass.

A limitation of our study is the relatively small sample size of only 50 tumors. Given this, the CIs associated with the observed values for sensitivity and specificity are fairly wide. In addition, not all RCC subtypes/variants were adequately sampled, for example, no case of clear cell RCC with eosinophilic features or any tumor type with sarcomatoid components was imaged. These tumors are potentially aggressive, and more fully evaluating their imaging characteristics with this test will be of value. Lastly, we feel it is critical to image a larger number of chromophobe RCCs so as to better understand the performance of this test with respect to these tumors.

In summary, \( 99m\text{Tc-sestamibi} \) SPECT/CT is a promising imaging test for the differentiation of oncocytomas and HOCTs from other renal tumor histologies. This test offers the potential to spare a substantial number of patients unnecessary invasive procedures such as biopsy, ablation, and surgery, each with its attendant risk of complications. Prior to clinical implementation, however, larger numbers are needed to more precisely define the sensitivity and specificity of this test and its exact place in the diagnostic armamentarium.

**Author contributions:** Mohamad E. Allaf had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Appendix A. Supplementary data

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References