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Initial Management of Indeterminate Renal Lesions in a Statewide Collaborative: A MUSIC-KIDNEY Analysis

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Study Need and Importance: Renal masses may be characterized as "indeterminate" on imaging due to a lack of differentiating characteristics. For example, some bright lesions on contrast CT are hyperdense cysts, while those that enhance (compared to non-contrast CT) are suspicious for renal cancer. Other lesions are too small to accurately characterize or are incompletely visualized on the initial imaging study. Limited data exist on the histological breakdown, natural history, and optimal management of indeterminate renal lesions.

What We Found: We assessed management of indeterminate renal lesions within the MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative—Kidney mass: Identifying and Defining Necessary Evaluation and therapY) collaborative, as well as the impact of additional imaging and biopsy on mass characterization prior to treatment. Among 2,109 patients with renal masses ≤7 cm in size, 21.1% were indeterminate on initial imaging. Of these 444 patients diagnosed with an indeterminate renal lesion, 33% underwent immediate treatment without additional imaging or renal mass biopsy, with nonmalignant pathology present in 10.1%. Reimaging led to reclassification of 79% of the indeterminate lesions as suspicious or benign, and renal mass biopsy provided a definitive pathological diagnosis in 87%. Significant practice-level variation in the performance of additional imaging was seen (see Figure), indicating an opportunity for quality improvement.

Limitations: The lack of histological data on observed indeterminate renal lesions limits our ability to comment on their oncologic potential. Additionally, heterogeneity in interpretation of imaging studies may exist due to the lack of a centralized radiology service.

Interpretation for Patient Care: Most patients with radiographically indeterminate renal lesions should be managed with surveillance; short-interval imaging can establish suspicion for renal cancer and growth rate. Prior to intervention, patients with indeterminate renal lesions should undergo additional imaging or renal mass biopsy to establish suspicion for renal cancer. This management schema will reduce the overtreatment of patients with benign renal neoplasms which do not require intervention.

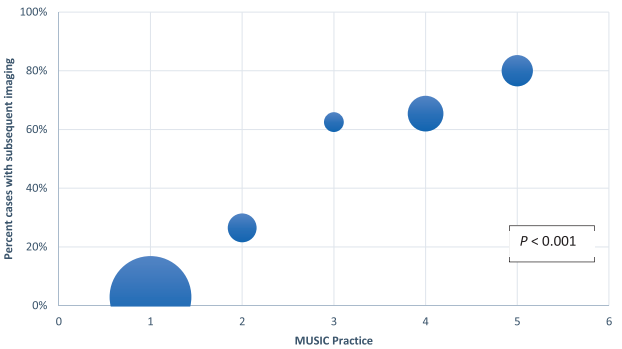

Figure. Practice variation in rates of additional imaging performed for indeterminate renal lesions. Size of bubble denotes case volume. MUSIC indicates Michigan Urological Surgery Improvement Collaborative.

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Initial Management of Indeterminate Renal Lesions in a Statewide Collaborative: A MUSIC-KIDNEY Analysis

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Ethics Statement: This study received Institutional Review Board approval (IRB No. 2011-320).

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Editor's Note: This article is the second of 5 published in this issue for which Category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 227 and 228.

Purpose: Renal masses can be characterized as "indeterminate" due to lack of differentiating imaging characteristics. Optimal management of indeterminate renal lesions remains nebulous and poorly defined. We assess management of indeterminate renal lesions within the MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative—Kidney mass: Identifying and Defining Necessary Evaluation and therapY) collaborative.

Materials and Methods: Each renal mass is classified as suspicious, benign, or indeterminate based on radiologist and urologist assessment. Objectives were to assess initial management of indeterminate renal lesions and the impact of additional imaging and biopsy on characterization prior to treatment.

Results: Of 2,109 patients, 444 (21.1%) had indeterminate renal lesions on their initial imaging, which included CT without contrast (36.2%), CT with contrast (54.1%), and MRI (9.7%). Eighty-nine patients (20.0%) underwent additional imaging within 90 days, 8.3% (37/444) underwent renal mass biopsy, and 3.6% (16/444) had reimaging and renal mass biopsy. Additional imaging reclassified 58.1% (61/105) of indeterminate renal lesions as suspicious and 21.0% (22/105) as benign, with only 20.9% (22/105) remaining indeterminate. Renal mass biopsy yielded a definitive diagnosis for 87%. Treatment was performed for 149 indeterminate renal lesions (33.6%), including 117 without reimaging and 123 without renal mass biopsy. At surgery for indeterminate renal lesions, benign pathology was more common in patients who did not have repeat imaging (9.9%) than in those who did (6.7%); for $\leq$4 cm indeterminate renal lesions, these rates were 11.8% and 4.3%.

Conclusions: About 33% of patients diagnosed with an indeterminate renal lesion underwent immediate treatment without subsequent imaging or renal mass biopsy, with a 10% rate of nonmalignant pathology. This highlights a quality improvement opportunity for patients with cT1 renal masses: confirmation that the lesion is suspicious for renal cell carcinoma based on high-quality, multiphase, cross-sectional imaging and/or histopathological features prior to surgery, even if obtaining subsequent follow-up imaging and/or renal mass biopsy is necessary. When performed, these steps lead to reclassification in 79% and 87% of indeterminate renal lesions, respectively.

Key Words: kidney neoplasms, molecular imaging, watchful waiting

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MOST renal lesions are detected incidentally due to the widespread use of abdominal imaging. While most newly diagnosed renal masses (RMs; ~80%) are renal cell carcinoma (RCC), approximately 20% will harbor benign pathology.[1-3] In cases where lesions are detected incidentally by ultrasound, single-phase, or noncontrast enhanced imaging, dedicated multiphasic, cross-sectional imaging (abdominal CT or MRI, with and without contrast) is recommended to optimally characterize renal lesions.[4,5] Although some renal lesions are classified as suspicious for RCC and others as likely benign (Bosniak I-IIF cysts or angiomyolipomas), still other lesions are initially characterized as "indeterminate."

An indeterminate renal lesion (IRL) may be difficult to conclusively characterize as enhancing without additional imaging sequences, or it may be too small to fully characterize even with dedicated imaging. While patients with benign renal lesions are almost universally managed conservatively unless symptomatic, and treatment algorithms and guidelines exist for management of suspicious RMs,[4-7] patients with IRLs are faced with an added layer of complexity in selecting between diagnostic and therapeutic options available. Some of these lesions might benefit from additional imaging and renal mass biopsy (RMB) to better characterize these lesions and consequently direct the patient to a more appropriate management plan. The histological breakdown, natural history, and optimal management for IRLs are not well defined, with limited data available in the literature. We hypothesized that IRLs may be managed like suspicious RMs, resulting in overtreatment of benign lesions. We assessed the current incidence, pattern of subsequent testing, and management of IRLs within the MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative—Kidney mass: Identifying and Defining Necessary Evaluation and therapY) statewide quality improvement (QI) collaborative.

METHODS

MUSIC-KIDNEY

The MUSIC-KIDNEY program seeks to standardize and improve care for patients with RMs.[8] The MUSIC-KIDNEY data registry collects information on all patients newly presenting to urologists for RMs up to 7 cm in size.[8] Trained data abstractors at each clinical site review the primary medical record at fixed intervals and enter pertinent clinical, radiographic, and laboratory parameters. Fourteen community, academic, and hospital-based practices contributed data to this analysis. All participating sites obtained exemption or approval from local Institutional Review Boards for participation.

Study Sample

We identified patients with radiographic IRLs identified on studies (CT, MRI, or ultrasound) from May 2017 to November 2020. Data registrars are instructed to examine medical records of patients presenting to a MUSIC urologist with an "RM" or "complex renal cyst" and extract data for any patient with 1 or more renal lesions $\leq$7 cm. RMs are then classified into 3 categories: (1) suspicious for RCC, which includes solid, enhancing RMs and complex cysts (Bosniak III-IV); (2) benign, which include simple cysts, Bosniak I-IIF cysts, and angiomyolipomas; or (3) indeterminate, which includes all lesions not classified as suspicious or benign on each radiographic study. We also collect data regarding the clinical impression of the urologist regarding the RM. All lesions read as indeterminate by the radiologist were included in this analysis. Data abstraction was performed at least 4 months (120 days) after the initial office visit to capture the patient demographics, tumor characteristics, initial workup, plan, and treatment decision at 90 days (immediate intervention vs initial observation) for each patient. Patients with <4 months of follow-up were excluded from analysis.

Objectives

Our primary objective was to assess the initial management strategy selected by patients with IRLs. This includes the initial imaging utilized and the primary treatment selected. Our secondary objective was to assess the impact of additional imaging and RMB on better characterizing these lesions prior to treatment.

Statistical Analysis

To assess initial management strategy selected by patients with IRLs compared those with non-IRLs (ie, suspicious or benign), clinical and demographic characteristics of all patients were compared by initial tumor type (suspicious vs indeterminate vs benign), and by the receipt of subsequent imaging (yes vs no) among patients with IRLs. The comparison was performed using χ^2 test for categorical variables and Wilcoxon rank-sum test for continuous measures. To assess the impact of additional imaging and/or RMB on characterization of IRLs and subsequent treatment, type of subsequent imaging studies, biopsy pathology, treatment modality, and surgical pathology for patients with IRLs were also summarized. Practice-level variation in the receipt of subsequent imaging for practices with at least 10 cases was assessed. All the analyses were performed using SAS 9.4, and statistical significance was set at .05.

RESULTS

Patient and Lesion Characteristics Prior to Urology Evaluation

We identified a total of 2,109 patients with newly diagnosed RM at 14 MUSIC-KIDNEY practices after excluding patients who did not have adequate follow-up or had missing information. Of these, 189 patients (9.0%) had >1 lesion. Of the patients 21.1% (444/2,109) were recorded as having an IRL at their initial imaging study. Details regarding the patient and lesion characteristics stratified by suspicious, indeterminate, or benign on initial imaging are highlighted in Table 1. Patients with IRLs tended to

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Table 1. *Baseline Characteristics of Patients Referred for Management of cT1 Renal Mass Stratified by Classification at Initial Imaging*

Variable	Suspicious		Indeterminate		Benign		*P* value
No. patients	1,554		444		111		
Age, median (IQR), y	65.0 (54.0-73.0)		66.0 (57.0-75.0)		64.0 (56.0-70.0)		.034
Gender, No. (%)							
Male	930	(59.8)	253	(57.0)	48	(43.2)	.002
Female	624	(40.2)	191	(43.0)	63	(56.8)	
Race, No. (%)							
White	1208	(77.7)	369	(83.1)	83	(74.8)	< .001
Black	184	(11.8)	59	(13.3)	18	(16.2)	
Other/unknown	162	(10.4)	16	(3.6)	10	(9.0)	
Initial imaging type, No. (%)							
Noncontrast CT	110	(7.1)	74	(16.7)	18	(16.2)	< .001
Contrast CT	1005	(64.7)	240	(54.1)	43	(38.7)	
Noncontrast MRI	37	(2.4)	17	(3.8)	2	(1.8)	
Contrast MRI	232	(14.9)	43	(9.7)	9	(8.1)	
Nonaxial imaging (ultrasound)	170	(10.9)	70	(15.8)	39	(35.1)	
Tumor size, median (IQR), cm	2.7	(1.8-4.1)	2.2	(1.5-3.2)	2.1	(1.5-3.9)	< .001
Tumor size, No. (%), cm							
≤1.0	62	(4.0)	38	(8.6)	14	(12.6)	< .001
1.1-2.0	429	(27.6)	174	(39.2)	40	(36.0)	
2.1-3.0	400	(25.7)	117	(26.4)	21	(18.9)	
3.1-4.0	265	(17.1)	52	(11.7)	13	(11.7)	
4.1-5.0	189	(12.2)	32	(7.2)	15	(13.5)	
5.1-6.0	134	(8.6)	18	(4.1)	5	(4.5)	
6.1-7.0	75	(4.8)	13	(2.9)	3	(2.7)	
Chest imaging performed, No. (%)	759	(48.8)	114	(25.7)	26	(23.4)	< .001

Abbreviations: CT, computerized tomography; IQR, interquartile range; MRI, magnetic resonance imaging.

be slightly older than patients with suspicious or benign lesions. IRL and suspicious RMs were both more common in men, while benign renal lesions were more common in women. IRLs were smaller in size (2.2 cm, IQR: 1.5-3.2) compared to suspicious lesions (2.7 cm, IQR 1.8-4.1, $P < .001$). Three-quarters of IRLs (74.1%) were ≤3 cm, compared with 57.3% of suspicious and 67.8% of benign lesions.

Imaging of Indeterminate RMs

Of the 444 IRLs based on initial radiographic study, 36.3% were identified on noncontrast imaging, 54.1% on contrast CT, and 9.7% on contrast MRI (uniformly performed for other indications). Prior to their initial urology visit, 370 patients had 1 study and 74 (16.7%) underwent more than 1 radiographic study. At the consultation, the urologist classified 228 lesions as indeterminate, 202 as suspicious, and 14 as benign.

As the next step in management after the IRL was identified, 20.0% (89/444) underwent additional imaging, 8.3% (37/444) underwent RMB without additional imaging, and 3.6% (16/444) underwent both additional imaging and RMB within 3 months of initial consultation, while 302 patients (68.0%) had no further testing. Among practices with at least 10 cases (representing 415/444 cases), significant practice-level variation was seen in the performance of additional imaging (2.9% to 80%, $P < .0001$). Of those obtaining additional imaging, the pattern of imaging studies performed following identification of the IRL is indicated in Table 2. The total number of imaging studies was 2 in 77 patients, 3 in 24 patients, 4 in 3 patients, and 5 in 1 patient. Following these studies, 58.1% (61/105) of the lesions initially characterized as IRL were reclassified as suspicious lesions and 21.0% (22/105) as benign lesions, with only 21.0% (22/105) remaining IRLs. Patients who had subsequent imaging within 3 months had similar characteristics to those who did not, other than being found to be younger (median age 63 vs 67 years, $P = .008$; Supplementary Table 1, https://www.jurology.com).

Initial Management of Indeterminate RMs

Surveillance was the most common approach for IRLs (66.4%), particularly for those <4 cm in size (70%). The average size of surveilled vs treated IRLs was 2.2 and 3.0 cm, respectively ($P < .05$). Immediate intervention was performed in 145 patients (32.6%), including 43 radical nephrectomies, 88 partial nephrectomies, and 14 ablations. Partial nephrectomy was the most common intervention for T1a lesions (79/114, 69%), while radical nephrectomy was more common for T1b lesions (23/35, 66%). Of these 149 patients, 117 (78.5%) did not have additional imaging prior to intervention and 123 did not undergo RMB (82.6%). Subsequent imaging in the 30 patients who underwent surgery determined 27 IRLs to be suspicious, with 2 indeterminate and 1 benign lesion. Of the 131 patients who underwent surgery, 119 (90.8%) had malignancy (Supplementary Table 2, https://www.jurology.com). Benign surgical pathology was more common in patients who did not have

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Table 2. *Subsequent Imaging Type for Indeterminate Renal Lesions Stratified by Initial Imaging Type*

Imaging study	No. (%)
Nonaxial imaging (ultrasound)	
Initial	70 (15.8)
Subsequent[a]	
None	56 (80.0)
Nonaxial imaging (ultrasound)	0 (0.0)
Noncontrast CT	0 (0.0)
Contrast CT	9 (12.9)
Noncontrast MRI	0 (0.0)
Contrast MRI	5 (6.6)
Noncontrast CT	
Initial	74 (16.7)
Subsequent[a]	
None	51 (68.9)
Nonaxial imaging (ultrasound)	3 (4.1)
Noncontrast CT	0 (0.0)
Contrast CT	12 (16.2)
Noncontrast MRI	2 (2.7)
Contrast MRI	6 (8.1)
Contrast CT	
Initial	240 (54.1)
Subsequent[a]	
None	179 (74.6)
Nonaxial imaging (ultrasound)	5 (2.1)
Noncontrast CT	2 (0.8)
Contrast CT	21 (8.8)
Noncontrast MRI	0 (0.0)
Contrast MRI	33 (13.8)
Noncontrast MRI	
Initial	17 (3.8)
Subsequent[a]	
None	14 (82.4)
Nonaxial imaging (ultrasound)	0 (0.0)
Noncontrast CT	0 (0.0)
Contrast CT	3 (17.6)
Noncontrast MRI	0 (0.0)
Contrast MRI	0 (0.0)
Contrast MRI	
Initial	43 (9.7)
Subsequent[a]	
None	39 (90.7)
Nonaxial imaging (ultrasound)	0 (0.0)
Noncontrast CT	0 (0.0)
Contrast CT	2 (4.7)
Noncontrast MRI	0 (0.0)
Contrast MRI	2 (4.7)

Abbreviations: CT, computerized tomography; MRI, magnetic resonance imaging.
[a] One hundred five of 444 patients underwent >2 imaging studies within 120 days of diagnosis. Indicated are the most informative subsequent tests when >2 were performed.

repeat imaging (9.9%) than in those who did (6.7%); for IRLs ≤4 cm, these rates were 11.8% and 4.3%. The histological breakdown for the indeterminate lesions is provided in Supplementary Table 3 (https://www.jurology.com).

Table 3 highlights the treatments selected based on the clinical impression of the treating urologist. For these 444 radiographic IRLs, initial observation was utilized in 66.4% overall. For IRLs regarded by the urologist as "suspicious," observation was only used in 40.1%, with much higher rates for lesions regarded as "indeterminate" (88.6%) or benign (85.7%). In total, 53 of 444 patients with IRLs (11.9%) underwent RMB to guide the initial management decision. Biopsy findings in these patients included 37 malignancies, 9 benign neoplasms, and 7 indeterminate findings. Of the 105 patients with IRLs who underwent repeat imaging within 3 months of diagnosis, 16 masses were biopsied (14 malignant, 1 benign, 1 indeterminate). Eight of the 15 patients with cancer/indeterminate biopsy results underwent treatment, with the remaining 8 patients continuing on surveillance.

DISCUSSION

More than 1 in 5 patients presenting to a urologist with a cT1RM had a lesion classified as indeterminate on initial imaging (21.1%, 444/2,109). Most of these patients (68%, 302/444) had no further testing following initial classification, including 33% (145/444) who had immediate intervention. More than 1 fourth of patients diagnosed with an IRL underwent immediate treatment without subsequent imaging or RMB, with nonmalignant pathology being present in 10% (10/101) of these surgeries. Among those patients having subsequent dedicated imaging, ~80% (83/105) of IRLs were reclassified as suspicious for RCC or benign. In addition, a definitive pathological diagnosis (malignant or benign neoplasm) was provided to 87% (46/53) of patients who underwent RMB prior to intervention. Our study provides one of the largest assessments of the pattern of management performed after identification of an IRL. The true incidence of these lesions is not well understood, as prior research has focused only on the incidence of suspicious or confirmed renal malignancies.

Current guidelines, including those of the American College of Radiology and the AUA, recommend high-quality, multiphase, cross-sectional abdominal imaging to fully evaluate renal lesions,[4,9] and recent research has suggested multiparametric MRI may allow for more accurate differentiation between benign and malignant masses.[10] However, a significant number of studies may not be adequately characterizing lesions to the best of our current imaging technology. In our study, no more than 60% of initial imaging studies met the guideline-recommended criteria. Repeat imaging is commonly needed to obtain information necessary for proper evaluation of cT1RM. For example, some lesions do not meet criteria for enhancement with dedicated imaging, because they do not enhance by >20 HU from noncontrast to contrasted studies, such as with a hyperdense cyst. Other patients undergo imaging for unrelated reasons with a finding of an incompletely visualized or not definitively characterized renal lesion on a CT thorax or MRI spine study. These patients may benefit from additional up-front multiphase imaging to better guide treatment.

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Table 3. *Treatment of Indeterminate Renal Lesions*

	IRLs per radiologist			
	All	Suspicious per urologist	IRLs per urologist	Benign per urologist
Treatment of T1RM, No. (%)[a]	N = 444	N = 202	N = 228	N = 14
Initial observation	295 (66.4)	81 (40.1)	202 (88.6)	12 (85.7)
Immediate intervention	149 (33.6)	121 (59.9)	26 (11.4)	2 (14.3)
Radical nephrectomy	43 (9.7)	34 (16.8)	9 (3.9)	0
Partial nephrectomy	88 (19.8)	73 (36.2)	14 (6.1)	1 (7.1)
Tumor ablation	14 (3.2)	11 (5.4)	3 (1.3)	0
Other	4 (0.9)	3 (1.5)	0	1 (7.1)
Total patients undergoing surgery	131 (29.5)	107 (53.0)	23 (10.1)	1 (7.1)
Benign surgical pathology	12 (9.2)	9 (8.4)	3 (13.0)	0
Treatment of T1aRM, No. (%)[a]	N = 381	N = 170	N = 200	N = 11
Initial observation	267 (70.1)	73 (42.9)	184 (92.0)	10 (90.9)
Immediate intervention	114 (29.9)	97 (57.1)	16 (8.0)	1 (9.1)
Radical nephrectomy	20 (5.2)	17 (10.0)	3 (1.5)	0
Partial nephrectomy	79 (20.7)	68 (40.0)	10 (5.0)	1 (9.1)
Tumor ablation	14 (3.7)	11 (6.5)	3 (1.5)	0
Other	1 (0.3)	1 (0.6)	0	0
Total patients undergoing surgery	99 (26.0)	85 (50.0)	13 (6.5)	1 (9.1)
Benign surgical pathology	10 (10.1)	7 (8.2)	3 (23.1)	0
Treatment of T1bRM, No. (%)[a]	N = 63	N = 32	N = 28	3
Initial observation	28 (44.4)	8 (25.0)	18 (64.3)	2 (66.7)
Immediate intervention	35 (55.6)	24 (75.0)	10 (35.7)	1 (33.3)
Radical nephrectomy	23 (36.5)	17 (53.1)	6 (21.4)	0
Partial nephrectomy	9 (14.3)	5 (15.6)	4 (14.3)	0
Tumor ablation	0	0	0	0
Other	3 (4.8)	2 (6.3)	0	1 (33.3)
Total patients undergoing surgery	32 (50.8)	22 (68.8)	10 (35.7)	0
Benign surgical pathology	2 (6.2)	2 (9.1)	0	0

Abbreviations: IRL, indeterminate renal lesion; RM, renal mass.
[a] Treatment was determined at 3 months after initial consultation.

Our data suggest additional dedicated renal imaging can lead to reclassification of about 80% of lesions characterized as "indeterminate" at initial radiographic evaluation. A substantial number of patients can be reassured by benign radiographic findings (of a Bosniak I-IIF cyst, for example) or confidently directed to RMB or intervention based on suspicious imaging features. Not all patients with IRLs may benefit from additional imaging: some elderly and infirm patients may be surveilled appropriately for a cT1RM felt to be indeterminate or suspicious by the managing urologist. Additional imaging in this scenario is best performed outside of the initial 3-month window as a short-term surveillance study to better characterize the IRL and permit assessment for interval growth (at 3-6 months).[6,7] For the average patient with a cT1RM, however, our study indicates a clear QI opportunity, namely to perform additional up-front multiphase imaging to optimize IRL management.

Our findings also suggest a second QI opportunity for patients with IRLs, namely the use of an initial period of surveillance, with follow-up imaging, to avoid a potentially unnecessary invasive procedure. Approximately 25% of patients with IRLs in the MUSIC registry underwent immediate treatment without subsequent imaging, while AUA guidelines suggest all masses <2 cm can be managed with surveillance, with early repeat imaging in 3-6 months to assess for interval growth and consideration of an RMB in patients where the risk/benefit analysis for treatment is equivocal.[6] There would appear to be strong motivation to avoid immediate intervention in IRLs of any size, as the likelihood of malignancy is unclear. With multiple reports in the literature of benign final histology at partial nephrectomy in up to a third of patients, and favorable oncologic outcomes in patients on surveillance for cT1RM, this strategy may still be underutilized in wider urological practice.[11,12] Given 60% of all lesions and over 70% of IRLs are ≤3 cm in the MUSIC registry, the overall likelihood of metastasis is very low in this group. An initial period of surveillance seems to be most appropriate in these individuals, with subsequent imaging providing the opportunity to better characterize any IRLs. Subsequent imaging findings will either provide reassurance, if benign findings are present, or suggest continued surveillance (or RMB) if a suspicious mass is identified and has not demonstrated rapid growth. Our data demonstrate that a high proportion of patients with lesions felt to be indeterminate by the urologist were placed on surveillance, suggesting that MUSIC urologists do tend to avoid immediate intervention in this situation (when compared to lesions they find suspicious for RCC).

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A third QI opportunity in patients with IRLs is the use of RMB, which has been shown to be a safe and effective strategy to characterize suspicious RMs as benign or malignant. RMB is being increasingly utilized to characterize renal lesions and has been shown to decrease surgery rates and the rate of benign histology at the time of surgery in other series.[13,14] Meta-analyses have reported a high sensitivity (97.5%-99.7%), specificity (96.2%-99.1%), and positive predictive value (99.8%) associated with RMB.[15,16] Our data with regard to RMB, similarly, showed its utility and effect on management of the selected patients in whom it was performed.[17] There was a definitive reclassification to benign or malignant histology in 87% of patients with IRLs, with only 5.6% of radiographically IRLs continuing to be categorized as indeterminate after RMB. The overall RMB utilization rate with IRLs was 11.9%, which is lower than the overall rate of 15.5% across all cT1RM in the registry and other reported rates in the literature, further reinforcing the fact that urologists might be underutilizing a tool that can help reduce overtreatment and rates of nonmalignant pathology at surgery. [13,17,18]

The economic impact of the management of IRLs has not been studied, and few data exist comparing the true cost of immediate treatment to surveillance for cT1RMs. However, hypothetical models have demonstrated active surveillance with the possibility of delayed intervention to be a cost-effective approach in managing small RMs when compared to immediate intervention.[19] Likewise, previous research has demonstrated additional evaluation (via RMB) to be cost-effective when compared to immediate intervention.[20] The population-level burden of surgical overtreatment is substantial, [21] warranting more research regarding the economic impact of improving diagnostic accuracy for nonextirpative management. However, currently available data would suggest initial surveillance or additional workup (via dedicated reimaging and/or RMB) for IRLs to be a cost-effective management strategy.

Our primary goal with this manuscript was to assess initial urologist actions in response to the presence of an IRL on imaging performed prior to consultation. These findings can help our discipline work toward improving the quality of care provided to each cT1RM patient. We hope the data in this report will provide an impetus to standardize and improve the pathway for management of IRLs. This may provide opportunity for multidisciplinary collaboration (eg, with radiology) to identify best practice in the evaluation of an IRL. Additionally, patient anxiety and distress have been previously shown to be a driving force in the decision for patients who are on active surveillance to progress to surgical treatment.[22] Additional data regarding the nature of a given IRL, from subsequent imaging and/or RMB, may improve the counseling and care for patients on surveillance. The availability of better data will strengthen the shared decision-making process.

This study does have several limitations worth noting. Although patients are enrolled in MUSIC-KIDNEY prospectively, clarifying the data elements in patients with IRLs was performed retrospectively. This leads to the limitations of any observational study, including selection biases both recognized and unrecognized, and confounding. We do not have histological correlates for all IRLs (as many patients did not undergo RMB or surgery), which limits our ability to comment on the oncologic potential of every lesion. Additionally, there is no centralized radiology service to standardize review. While the duration of follow-up is limited, continued collection of patient data over longer periods will help better define how surveillance is carried out for lesions confirmed, suspicious, or indeterminate for malignancy. There is always a risk of missing or inaccurate data collection; we have minimized this risk with targeted re-review to ensure high fidelity of data.

CONCLUSIONS

More than 1 in 5 RMs in the MUSIC-KIDNEY registry were indeterminate on initial imaging. More than one-quarter of patients diagnosed with an IRL underwent immediate treatment without subsequent imaging or RMB, with nonmalignant pathology being present in 10% of these surgeries. Among those patients having subsequent dedicated imaging, ~80% of IRLs were reclassified as suspicious for RCC or benign. In addition, a definitive pathological diagnosis (malignant or benign neoplasm) was provided to 87% of patients who underwent RMB prior to intervention. This highlights a QI opportunity for patients with cT1RM: confirmation that the lesion is suspicious for RCC based on high-quality, multiphase, cross-sectional imaging and/or pathological features prior to surgery, even if obtaining subsequent follow-up imaging and/or RMB is necessary. When performed, these steps lead to improved characterization of IRLs, often resulting in a change in subsequent management.

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EDITORIAL COMMENTS

A third of renal masses are labeled as "indeterminate" at initial imaging due to insufficient features to differentiate between malignant and benign pathology. The MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative–Kidney mass: Identifying and Defining Necessary Evaluation and therapY) collaborative provided granular data on 444 patients diagnosed with indeterminate lesions after initial imaging (21% of analyzed cohort).[1] Up-front treatment was performed in 33% of patients, while 89 patients (20%) underwent additional imaging, 37 patients (8.3%) biopsy, and 16 patients (3.6%) both. Additional imaging reclassified 79% indeterminate lesions as either suspicious or benign, with only 21% remaining indeterminate. As a result, benign pathology was more common in patients who did not repeat imaging (9.9% vs 6.7%). This was more pronounced when focusing on cT1a masses (11.8% vs 4.3%).

It is an open secret that indeterminate lesions are often managed like suspicious masses, resulting in overtreatment (up to 30% of resected small renal masses are ultimately found benign). On one hand, "anatomical" imaging cannot reliably discriminate benign vs malignant (specificity for CT enhanced scan is around 60%); on the other hand, adding biopsy can be invasive and/or nondiagnostic.

While the baseline classification of renal masses as suspicious, benign, or indeterminate might have been nuanced, Butaney et al must be commended because they did the math of these issues on their database.[1] A posteriori of the analysis, we must admit that although additional imaging reclassified 80% of the masses, the differences in terms of number of benign lesions "overoperated" was not that impressive.

In this scenario, the cost-effectiveness of additional "triage" tests such as molecular imaging (eg, ^{99m}Tc-sestamibi single photon emission computerized tomography/CT and positron emission tomography/CT imaging with radiolabeled girentuximab) or biopsy is still controversial and needs to be investigated.

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Notably, the latest WHO classification of urogenital tumors cautioned against a definitive diagnosis of oncocytoma from a needle core biopsy, adding uncertainty to the EAU Guidelines' recommendation to "offer active surveillance to patients with biopsy-proven oncocytoma or other oncocytic renal tumors as an acceptable alternative to surgery or ablation."[2,3] Yet, similar uncertainty remains after virtual biopsy tests.

Initial diagnosis and risk stratification of renal masses remains an unmet need within the field. Radiomics and artificial intelligence might improve the diagnostic ratios; however, novel approaches should bring to the table a lot more certainty on diagnosis than current statements.

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The MUSIC (Michigan Urological Surgery Improvement Collaborative) group publishes another impactful study addressing trends concerning management of indeterminate renal lesions (IRLs).[1] This study reports only 32% of patients with IRLs had additional workup with repeat imaging, renal mass biopsy (RMB), or both. With further imaging, only 21% of these masses continued to be labeled as IRL. Of all patients with IRL who went on to have intervention, over 25% had no additional workup, and of these 10% showed benign tumors. Given these data, ample opportunity for quality improvement likely exists.

The authors do well to highlight potential room for improvement, suggesting use of additional imaging and/or RMB to optimize IRL management to avoid overtreatment and provide timely care. One area of clear benefit to initial surveillance is decreased intervention. Treatment of IRL carries risk, and mitigating the removal of benign masses significantly benefits our patients and health care system. Removing the risk of surgical complications is obvious, and the potential for significant costs savings is also present. Previous work has found the average insurance claims submitted over the 12 months post-radical nephrectomy for benign renal masses totaled $23,951.[2] Given previous estimates of approximately 10,000 nephrectomies being performed for benign tumors annually, there is a potential for $230 million in health care spending in a time when rising health care spending continues to pose a serious concern in this country.[3,4] Beyond the cost to our health care system, there are additional data showing the cost to patients is also significant with robotic radical nephrectomy.[5] These data, published by Butaney et al from the MUSIC group,[1] highlight an important area for quality improvement for patients and the health system with pertinent actionable data toward further imaging and/or RMB to increase the likelihood of removing a cancerous lesion.

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