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Renal Mass Biopsy Is Associated With Fewer Radical Nephrectomies for Benign or Indolent Disease, Particularly for T1b Renal Masses

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Study Need and Importance: Deciding whether active surveillance (AS), partial nephrectomy (PN), or radical nephrectomy (RN) is appropriate for a patient with a localized renal mass ≤ 7 cm (T1RM) can be challenging. Some patients undergo renal mass biopsy (RMB) to assist in decision-making. We examined associations between RMB and selection of AS, PN, and RN for T1RM patients.

What We Found: We analyzed data regarding 4062 T1RMs; the initial plan was RMB for 18%, 42% of patients were treated, and 40% were started on AS without RMB. Factors associated with RMB included younger age, higher comorbidity, tumor size > 2.0 cm, and higher tumor complexity. AS was selected by 88%, 68%, and 27% of patients with benign, indeterminate, and malignant RMB findings, respectively. Nonmalignant pathology at surgery was significantly ($P < .0001$) more common without RMB (vs after RMB): 14.8% vs 7.2% of PN and 10.2% vs 1.7% of RN. Patients with 4- to 7-cm tumors (T1bRM) elected AS (22% vs 34%), nephron-sparing intervention (31% vs 35%), and RN (47% vs 32%) without vs with RMB ($P = .0027$; Figure). In multivariable analyses accounting for practice-level variation and other confounding variables, AS was utilized more after RMB in T1bRM patients. The risk-adjusted RN rate for T1bRM was 41.4% without RMB vs 27.8% with RMB; 7.4 RMBs are needed to avoid 1 RN for benign or indolent disease.

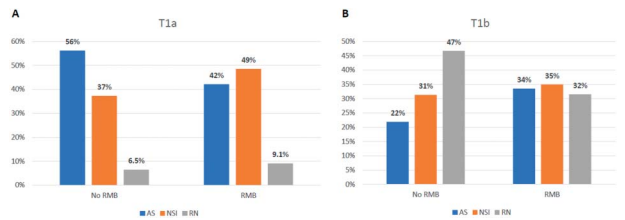

Figure. Treatment of patients with T1 renal masses according to performance of renal mass biopsy (RMB). Bars indicate the percentage of patients with T1a renal masses (A) and T1b renal masses (B) who pursued active surveillance (AS), nephron-sparing intervention (NSI), or radical nephrectomy (RN).

Limitations: Our analysis was an observational, retrospective assessment of treatment patterns across the state of Michigan. Observed practice patterns may not be representative of those in other regions of the US or worldwide. Long-term oncologic data regarding patients managed conservatively following RMB are lacking at present.

Interpretation for Patient Care: Patients undergoing RMB receive different treatments than when RMB is omitted. T1RM patients benefit from reduction in intervention for nonmalignant disease, particularly when RN is planned. For every 7 biopsies of T1bRM performed, 1 RN can be avoided.

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Renal Mass Biopsy Is Associated With Fewer Radical Nephrectomies for Benign or Indolent Disease, Particularly for T1b Renal Masses

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Introduction: How renal mass biopsy (RMB) impacts patient management with T1 renal masses (T1RMs) is unclear. We explore the association between RMB and utilization of active surveillance (AS), nephron-sparing interventions, and radical nephrectomy (RN).

Methods: Data were analyzed retrospectively using the MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative Kidney Mass: Identifying and Defining Necessary Evaluation and Therapy) registry. Treatment received was analyzed using a fitted mixed-effects multinomial logistic-regression model.

Results: Of 4062 patients, 19.6% underwent RMB. Factors associated with RMB included younger age, higher Charlson comorbidity score, tumor size $>$ 2.0 cm, and higher complexity tumors. AS was selected by 88%, 68%, and 27% of patients with benign, indeterminate, and malignant RMB findings. Nonmalignant pathology at surgery was significantly ($P < .0001$) more common without RMB (vs after RMB), ie, 14.8% vs 7.2% of PN and 10.2% vs 1.7% of RN. In patients with T1bRM managed without vs with RMB, AS was chosen by 22% vs 34%, nephron-sparing interventions by 31% vs 35%, and RN by 47% vs 32% ($P = .0027$). An interaction between tumor stage (T1a vs T1b) and RMB remained in multivariable analyses accounting for practice-level variation and other confounding variables. The risk-adjusted RN rate for T1bRM was 41.4% without RMB vs 27.8% with RMB; 7.4 RMBs are needed to avoid 1 RN (number needed to treat) for benign or indolent disease.

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Ethics Statement: Each practice in MUSIC obtained exemption or approval for collaborative participation from a local Institutional Review Board.

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Conception and design: Lane, Seifman, Rogers, Mirza, Butaney, Noyes.
Critical revision of the manuscript for scientific and factual content: Lane, Seifman, Rogers, Boynton, Ghani, Mirza, Jafri, Butaney, Van Til, Noyes.
Drafting the manuscript: Lane, Rogers, Boynton, Butaney.
Data analysis and interpretation: Rogers, Boynton, Ghani, Mirza, Jafri, Butaney, Van Til.
Mentor to medical student—oversaw data integrity and progress: Lane, Seifman, Rogers, Boynton, Ghani, Mirza, Jafri, Butaney, Van Til, Noyes.
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Conclusions: Treatments received by T1RM patients undergoing RMB are different than when RMB is omitted, based on RMB results and several confounders. T1RM patients benefit from reduction in intervention for nonmalignant disease, particularly when RN is planned. For every 7 biopsies of T1bRM performed, 1 RN was avoided.

Key Words: diagnosis, kidney cancer, management

Renal cell carcinoma (RCC) is one cancer commonly treated surgically without obtaining a definitive pathologic diagnosis.[1,2] Recent studies indicate that 13.5% to 30.9% of surgeries performed for suspected RCC reveal nonneoplastic findings.[3,4] Prior estimates of the lowest achievable/acceptable rate of benign pathology at surgery were 1.9% and 5.4%, respectively.[5] Despite strong recommendations from both the European Association of Urology and the AUA on the benefits of renal mass biopsy (RMB) in clinical decision-making, utilization is variable among practicing urologists.[6-8]

Prior studies have reported RMB outcomes from single academic centers.[4,9-12] Prior work has focused on localized renal masses (RMs) $\leq$ 4.0 cm (T1aRM),[13,14] with limited data regarding use or outcomes for localized RMs 4.1 to 7.0 cm (T1bRM).[4,15,16] Although benign histopathology is less common, radical nephrectomy (RN) is more common for T1bRM than T1aRM, so costs are higher for patients, especially if RN is performed for a benign renal neoplasm.

The Michigan Urological Surgery Improvement Collaborative (MUSIC), established in 2011, is a community that partners to improve patients' lives by inspiring high-quality care through data-driven best practices, education, and innovation. MUSIC investigates practice patterns within community, hybrid, and academic urology practices across Michigan, with patient-level data collected prospectively from initial consultation. In this study, we explore initial therapeutic plans and chosen management strategies for patients based on whether they underwent RMB. We assessed RMB utilization and clinical decision-making for T1aRM and T1bRM.[6] We hypothesize that RMB may have greater associations with management of T1bRM patients than with T1aRM.

Methods

The MUSIC Kidney Mass: Identifying and Defining Necessary Evaluation and Therapy (known as MUSIC-KIDNEY) initiative prospectively enrolls all T1RM patients beginning at diagnosis. Trained data abstractors at each site record standardized data in a web-based registry at least 120 days after the initial urology visit.[17] Twenty-one participating practices obtained exemption or approval from local Institutional Review Boards.

Eligible patients were newly diagnosed with T1RM (May 2017-February 2023); cystic RM patients were unlikely to undergo RMB (9/271, 3.3%) and thus were excluded. Patients with higher-stage (>cT1) RM, nodal or distant metastases, Bosniak I to IIF cysts, or angiomyolipoma; younger than 18 years; or missing treatment data were excluded. Initial therapeutic plan is recorded as either (1) specific intervention such as RN or a nephron-sparing intervention (NSI) (partial nephrectomy [PN], tumor ablation, or stereotactic body radiation therapy), (2) noninterventional approach (active surveillance [AS] with a plan for repeat imaging in >90 days), or (3) additional imaging within 90 days, RMB, or second opinion. After excluding 88 patients referred for second opinion and considering the results of repeat imaging, patients were categorized according to (1) initial plan for RN, NSI, AS, or RMB; (2) whether RMB was performed within 90 day; and (3) actual treatment received within 90 days.

Patient data included tumor type (solid or indeterminate), tumor size (T1a or T1b), preoperative estimated glomerular filtration rate ($\geq$60 mL/min/1.73 m^2 or <60 mL/min/1.73 m^2), RMB, and surgical pathology (benign, favor benign, indeterminate, favor malignancy, or malignant).

Primary outcome of interest was treatment type (AS, NSI, RN) in T1aRM and T1bRM patients managed without vs with RMB. Secondary outcomes included treatment type according to RMB results, practice-level variation in RMB, and identifying factors associated with NSI and RN relative to AS.

Comparisons across RMB/no RMB cohorts used χ^2 tests for categorical variables, Jonckheere-Terpstra tests for ordinal variables, and Wilcoxon rank sum tests for continuous variables. Logistic regression was used to model intervention received with main effects for initial plan, RMB, and an interaction between the two. A mixed-effects multinomial logistic regression model for treatment received (AS, NSI, or RN) was fit to adjust for confounding and tested for interaction between RMB and tumor size. The factors were adjusted based on the infrequent use of RMB for tumors < 1 to 2 cm and because patients with higher age and/or comorbidity are commonly managed without intervention (or RMB).

Results

For 4062 T1RM patients, the initial plan was intervention (n = 1706), RMB (n = 655), or no intervention (AS; n = 1612). In patients not undergoing RMB, treatment within 90 days matched the initial plan for intervention in 93% and

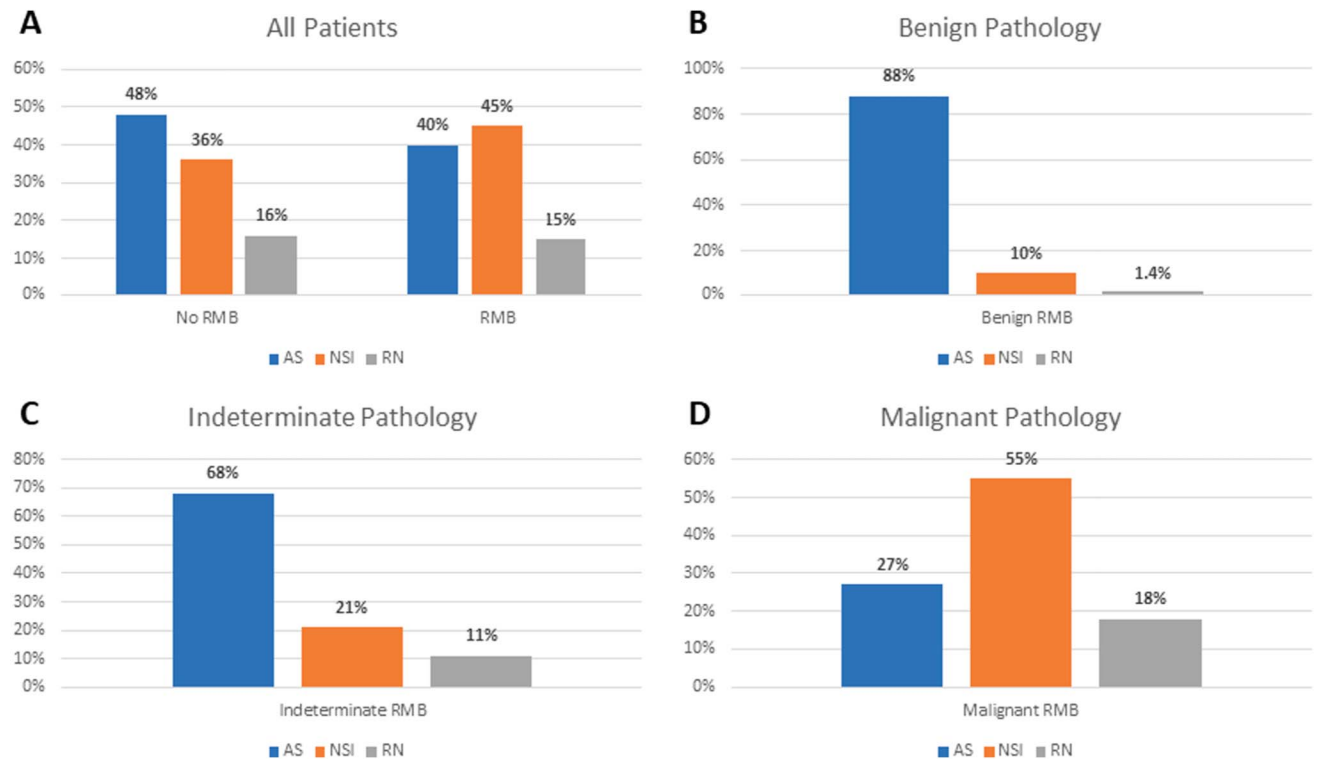

Figure 1. Management of patients with T1 renal masses stratified according to use and results of renal mass biopsy (RMB). A, Two sets of bars indicate percentage of patients who pursued active surveillance (AS), nephron-sparing intervention (NSI), or radical nephrectomy (RN) as initial management after evaluation without or with RMB. The group that underwent RMB is then subdivided according to the results of RMB. These sets of bars indicate the management of patients with benign findings (B), indeterminate histopathologic findings (C), or malignant findings (D).

nonintervention in 90% (Supplementary Table 1, https://www.urologypracticejournal.com). Of 655 patients with a plan for RMB, 632 (96%) underwent RMB, of whom 366 (58%) received intervention within 90 days, while 23 patients did not undergo RMB with 22 proceeding directly to intervention. The association between initial plan and treatment received differed ($P < .001$) by RMB (Figure 1). Sensitivity analysis was performed with assignment of patients with initial plan for RMB to intervention for masses > 3 cm and nonintervention for masses ≤ 3 cm (Supplementary Table 2, https://www.urologypracticejournal.com). After this assignment, of 405 patients planned for intervention, 29% elected AS after RMB. RMB complications included emergency department visits for 25 patients (3.1%) at a median of 6 days after RMB (interquartile range: 1-10) with 7 hospital admissions (0.9%).

The 3267 patients managed without RMB and 795 with RMB differed (Table 1). Patients without RMB more commonly had low comorbidity (Charlson Comorbidity Index [CCI] = 0 in 51% vs 45%) and tumors that were smaller (2.6 vs 3.0 cm), of low complexity (RENAL [for radius, exophytic/endophytic, nearness of tumor to collecting system, anterior/posterior, location relative to polar line] nephrometry score 4-6 in 46% vs 36%), and indeterminate (17% vs 8.6%). RMB was used less commonly for tumors ≤ 2.0 cm (12%) and in patients > 75 years (16%; Supplementary Table 3, https://www.urologypracticejournal.com). Differences between the cohorts persisted in multivariable analyses (MVAs; Supplementary Table 4, https://www.urologypracticejournal.com); RMB use was associated with younger age, CCI ≥ 1, and larger tumor size ($P < .005$ for each). There were some differences in treatment types between the cohorts (Table 1), with minimally invasive PN (81%) and minimally invasive RN (95%) most common overall.

AS was the most common treatment in patients not undergoing RMB vs NSI for RMB patients ($P < .0001$; Figure 1, A). Examination of the treatments in various subgroups revealed clinically meaningful differences according to RMB status (Supplementary Table 3, https://www.urologypracticejournal.com). For example, AS was chosen by < 38% of patients ≤ 65 years regardless of RMB, but for patients 66 to 75 years, AS was chosen by 51% and 37%, and for patients > 75 years, by 78% and 67% without vs with RMB ($P < .001$). AS was less commonly selected with increasing tumor size. Tumor size was associated with treatment choice after RMB, with AS less common in the no RMB vs RMB subgroups having tumors ≤ 2.0 cm (74% vs 48%) and more common for tumors > 4.0 cm (22% vs 34%; Supplementary Table 4, https://www.urologypracticejournal.com). T1aRM patients were more likely to receive

Table 1.
Demographic and Clinical Characteristics of Patients With Clinical T1 Renal Masses Subdivided Into Those Who Did or Did Not Undergo Renal Mass Biopsy

	All patients		No RMB		RMB		*P* value
No. of patients (%)	4062	(100)	3267	(80)	795	(20)	
Age, median (IQR), y	65	(56-74)	66	(56-74)	65	(55-73)	.06
Race, No. (%)							.14
White	3125	(77)	2510	(77)	615	(77)	
Black	526	(13)	412	(13)	114	(14)	
Other	140	(3.5)	121	(3.7)	19	(2.4)	
Unknown	271	(6.7)	224	(6.9)	47	(5.9)	
Sex, No. (%)							.4
Male	2444	(60)	1956	(60)	488	(61)	
Female	1618	(40)	1311	(40)	307	(39)	
Charlson Comorbidity Index, No. (%)							< .001
0	2015	(50)	1659	(51)	356	(45)	
1	818	(20)	658	(20)	160	(20)	
≥2	1228	(30)	949	(29)	279	(35)	
Baseline eGFR, median (IQR), mL/min/1.73 m^2	77	(58-91)	76	(59-91)	77	(56-91)	.8
CKD at baseline (eGFR <60 mL/min/1.73 m^2), No. (%)	963	(27)	756	(26)	207	(28)	.030
Tumor type, No. (%)							< .001
Solid	3434	(85)	2707	(83)	727	(91)	
Indeterminate	628	(15)	560	(17)	68	(8.6)	
Tumor size, median (IQR), cm	2.7 (1.8-4.0)		2.6 (1.7-3.9)		3.0 (2.2-4.1)		< .001
Clinical tumor stage, No. (%)							.010
T1a	3115	(77)	2523	(77)	592	(74)	
T1b	947	(23)	744	(23)	203	(26)	
Tumor complexity (RENAL nephrometry score), No. (%)							< .001
4-6	807	(44)	665	(46)	142	(36)	
7-9	779	(42)	598	(41)	181	(46)	
10-11	261	(14)	189	(13)	72	(18)	
Nephron-sparing intervention type, No. (%)							< .001
Minimally invasive PN	1240	(81)	1006	(86)	234	(65)	
Open PN	72	(4.7)	54	(4.6)	18	(5.0)	
Thermal ablation	179	(12)	89	(7.6)	90	(25)	
Radiation therapy	42	(2.7)	25	(2.1)	17	(4.7)	
RN type, No. (%)							.6
Minimally invasive	596	(95)	483	(95)	113	(96)	
Open	33	(5.3)	28	(5.5)	5	(4.2)	
Practice type, No. (%)							< .001
Academic	943	(23)	718	(22)	225	(28)	
Hybrid	2801	(69)	2271	(70)	530	(67)	
Private/community-based	318	(7.8)	278	(8.5)	40	(5.0)	

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PN, partial nephrectomy; RENAL, radius, exophytic/endophytic, nearness of tumor to collecting system, anterior/posterior, location relative to polar line; RMB, renal mass biopsy; RN, radical nephrectomy. Data were not available for Charlson Comorbidity Index in 1 patient, baseline eGFR in 446 patients, or RENAL nephrometry score in 2215 patients.

intervention if they underwent RMB (Figure 2, A). Conversely, T1bRM patients were less likely to receive intervention, specifically RN (Figure 2, B).

Histopathologic findings at RMB were 147 benign (18%), 38 indeterminate (4.8%), and 610 malignant (77%). Benign etiologies included 83 oncocytoma/oncocytic tumors, 17 angiomyolipomas, and 47 others. Cancer subtypes included 358 clear cell RCC (59%), 128 papillary RCC (21%), 46 chromophobe RCC (7.5%), and 78 unclassified RCC/other cancer (13%). For T1aRM patients, 19% were benign, 5.1% indeterminate, and 76% malignant; for T1bRM, 16% were benign, 3.9% indeterminate, and 80% malignant. A total of 162 RCC patients at RMB elected AS, including 86 with clear cell RCC, 32 with papillary RCC, 11 with chromophobe RCC, and 33 with other subtypes. Twelve indeterminate RMB patients had surgery, 8 had PN (pathology revealed 5 had RCCs, 3 were benign), and 4 had RN (3 RCC, 1 benign). Three patients classified with malignancy at RMB (unclassified RCC or favor chromophobe RCC) had oncocytoma, and 1 with a low-grade renal cell neoplasm had only chronic inflammation at PN. Seventeen patients with benign findings at RMB underwent PN (n = 15) or RN (n = 2) with final pathologic diagnosis of RCC in 4 (3 papillary, 1 chromophobe).

When examining treatment choice in the RMB group according to pathology, differences were noted ($P < .0001$). AS was pursued for 88% of patients when RMB results showed benign pathology, 68% with indeterminate

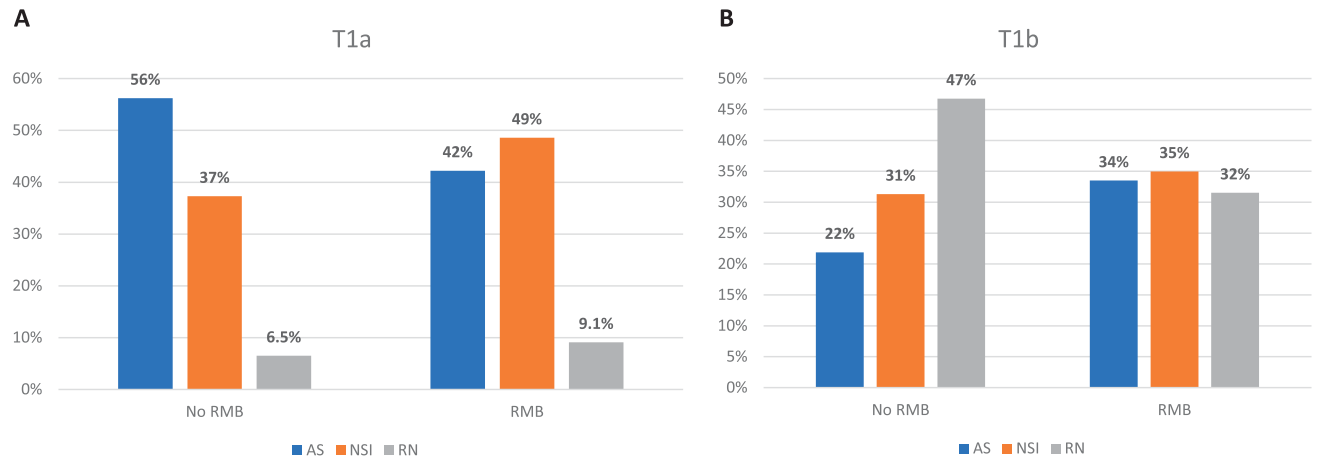

Figure 2. Treatment of patients with T1 renal masses according to performance of renal mass biopsy (RMB). Bars indicate the percentage of patients with T1a renal masses (A) or T1b renal masses (B) who pursued active surveillance (AS), nephron-sparing intervention (NSI), or radical nephrectomy (RN). *P* value is .0027, indicating significant differences between the 2 cohorts.

pathology, but only 27% with biopsy-proven malignancy (Figure 1). Median follow-up in 314 patients who pursued AS after RMB was 7 months (CI: 4-27). The cumulative incidence of delayed intervention was 20% (CI: 14%-27%) at 36 months. Intervention was more common with malignant pathologic findings (Supplementary Figure 1, https://www.urologypracticejournal.com).

The rate of nonmalignant pathology at surgery was 13.3% without RMB and 5.4% with RMB ($P < .0001$). For patients undergoing PN without vs with RMB, rates were 14.8% vs 7.2%, and for patients undergoing RN, rates were 10.2% vs 1.7% (each $P < .0001$). For T1aRM patients, rates were 15.7% and 5.6%, and T1bRM rates were 9.0% and 5.0%, respectively (each $P < .0001$).

There was significant variation in the frequency with which RMB was utilized across practices for T1RM (Figure 3, A), T1aRM, and T1bRM (Figure 3, B). For most practices, RMB rates were similar in T1aRM and T1bRM patients, but some practices more commonly biopsied T1aRM and some more commonly biopsied T1bRM.

After adjusting for confounders in the mixed-effects multinomial regression model (Table 2), the association of RMB with treatment depended on T1a vs T1b ($P < .0001$). Factors associated with patients receiving NSI (vs AS) included larger tumor size (odds ratio [OR]: 1.50, CI: 1.17-1.92, $P < .0001$), younger age (OR: 0.95, CI: 0.94-0.96, $P < .0001$), and less comorbidity ($P < .0001$ for CCI score 1 and ≥ 2 vs 0). Factors associated with patients receiving RN (vs AS) included larger tumor size (OR: 8.33, CI: 6.28-11.06, $P < .0001$), younger age (OR: 0.96, CI: 0.95-0.97, $P < .0001$), and intermediate or high RENAL nephrometry score (vs low, $P < .0001$).

After adjusting for the aforementioned factors in the mixed-effects model, T1aRM patients obtaining an RMB had higher likelihood of NSI (OR: 1.60, CI: 1.28-1.99, $P < .0001$) and RN (OR: 1.64, CI: 1.15-2.35, $P < .0001$). Conversely, cT1bRM patients with RMB had a lower likelihood of RN (OR: 0.47, CI: 0.31-0.72, $P < .0001$). Using this multivariable model, we obtained the risk-adjusted treatment rates for T1aRM and T1bRM (Table 3). The 13.5% decrease in the risk-adjusted RN rate between the RMB and no RMB groups (41.4%-27.9%) translates to a number needed to treat of 7.4.

Discussion

The impact of RMB on management of T1RM patients is unclear at present, so we explored this across Michigan. Accounting for the significant practice-level variation in RMB use in a mixed-effects MVA, the relationship between RMB and treatment depended on tumor size (T1a vs T1b); RMB in T1bRM patients was associated with significantly fewer RNs. We found 7 completed biopsies were needed to avoid 1 RN for benign/indolent disease. Conversely, we found lower AS utilization in T1aRM patients undergoing RMB than in those where RMB was omitted. We believe these results clarify which groups may benefit most from RMB.

T1bRM patients appear to be ideal candidates for RMB in many circumstances. Few T1bRM patients are directed to AS without RMB (22%); most proceed directly to surgery. In T1bRM patients who underwent RMB, there was greater use of AS and NSI and lesser use of RN. Only 32% of T1bRM patients underwent RN following RMB, which compares quite favorably with prior literature demonstrating RN use in 52% to 65% of T1bRM patients.[18,19] Moreover, based on the 13.6% decrease in the risk-adjusted RN rate, our data show that for every 7.4 biopsies obtained for T1bRM one kidney was saved from RN. The odds of undergoing RN were 53% lower in MVA accounting for patient- and practice-related factors.

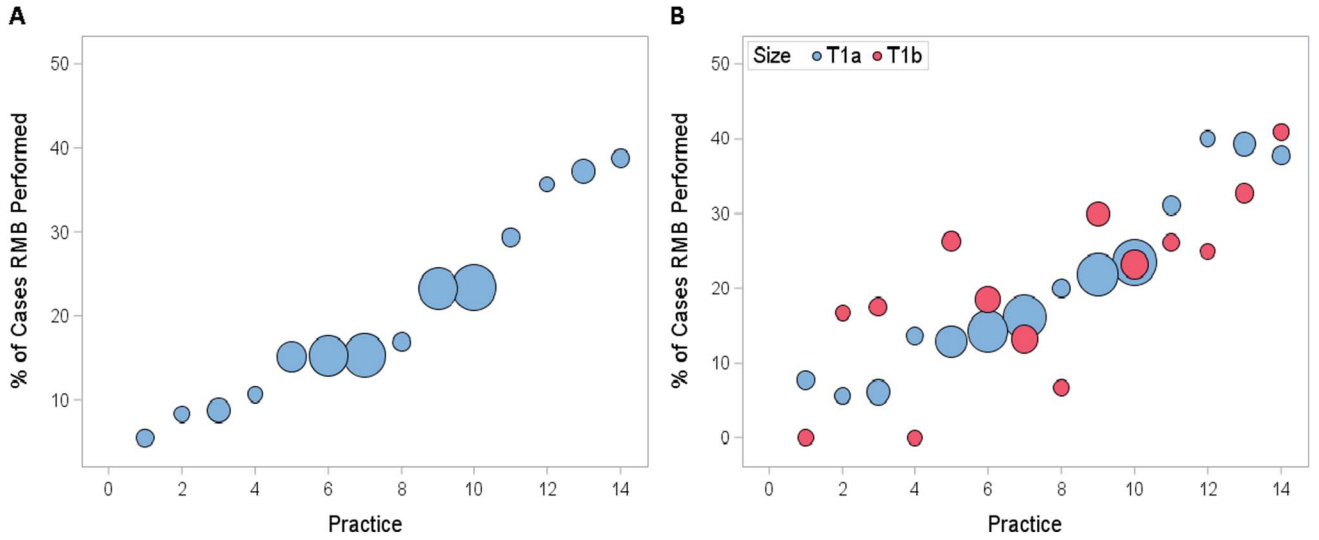

Figure 3. Practice-level variation in the use of renal mass biopsy (RMB) across the Michigan Urological Surgery Improvement Collaborative. Each bubble represents a single practice, with the size of the bubble indicating the number of patients evaluated. A, Overall use of RMB for T1 renal masses in 14 practices with at least 10 T1 renal masses. RMB rates range from 5.6% to 39% across these practices. The *P* value by χ^2 test is $< .001$, indicating statistically significant practice variation in RMB rates. B, Use of RMB for T1a and T1b renal masses ordered by the overall use of RMB. There was significant practice-level variation in both RMB for T1a renal masses (range: 5.6%-39%, $P < .001$) and for T1b renal masses (range: 0%-41%, $P < .001$). Logistic regression models were used for each of these bubble plots; the model for B included practice, tumor size, and the interaction between them. Practice variation did not significantly differ by tumor stage ($P = .16$).

RMB was utilized in the diagnostic evaluation of < 20% of T1RM patients, with wide variability across MUSIC practices (5.6%-39%). Intervention for benign renal neoplasms is not indicated when pathology is known beforehand.[5] Management with AS was more common with biopsy-proven benign (88%) or indeterminate (68%) pathology when compared to patients without RMB (48%). Moreover, nonmalignant pathology was present in 5.4% of patients who received RMB before surgery compared with 14.8% PN and 10.2% RN specimens from patients not undergoing RMB. All NSIs, including PN and thermal ablation, are associated with procedure-related morbidity that exceeds RMB. Avoidance of RN is key for patients without renal malignancy, due to a significantly increased risk of developing chronic kidney disease and all-cause mortality when compared to NSI or AS.[5,20,21]

Given increased AS use with nonmalignant RMB findings, we expected to find less intervention in both T1aRM

Table 2.
Multinomial Regression Model Indicating Factors That May Influence a Provider to Pursue Either Nephron-Sparing Intervention or Radical Nephrectomy Over Active Surveillance

	Nephron-sparing intervention (ref = active surveillance)			Radical nephrectomy (ref = active surveillance)			
Variable	Odds ratio	95% Confidence limits		Odds ratio	95% Confidence limits		*P* value
Tumor size: T1b vs T1a	1.50	1.17	1.92	8.33	6.28	11.06	< .0001
RMB	1.12	0.88	1.42	0.88	0.66	1.16	.23
Patient age	0.95	0.94	0.96	0.96	0.95	0.97	< .0001
Tumor type: solid vs indeterminate	2.60	2.03	3.33	2.43	1.69	3.49	< .0001
CCI: 1 vs 0	0.77	0.63	0.94	0.87	0.65	1.16	< .0001
CCI: 2+ vs 0	0.54	0.44	0.65	0.81	0.62	1.06	
RENAL nephrometry score: intermediate vs low	1.36	1.07	1.73	3.52	2.22	5.57	< .0001
RENAL nephrometry score: high vs low	0.64	0.42	0.97	8.47	4.97	14.42	
RENAL nephrometry score: unknown vs low	0.47	0.38	0.59	2.22	1.45	3.39	
RMB * tumor size							< .0001
RMB * T1a	1.60	1.28	1.99	1.64	1.15	2.35	
RMB * T1b	0.78	0.51	1.20	0.47	0.31	0.72	

Abbreviations: CCI, Charlson Comorbidity Index; ref, reference; RENAL, radius, exophytic/endophytic, nearness of tumor to collecting system, anterior/posterior, location relative to polar line; RMB, renal mass biopsy.
Both nephron-sparing intervention and radical nephrectomy were compared to active surveillance, and odds ratios were generated for the factors analyzed. After adjusting for the listed covariates, we found that the effect of RMB on intervention depended on tumor size ($P < .0001$).

Table 3.
Risk-Adjusted Rates of Treatment With Active Surveillance, Nephron-Sparing Intervention, and Radical Nephrectomy for T1a and T1b Renal Masses Based on the Multivariable Model

	T1aRM (%)		T1bRM (%)	
	No RMB	RMB	No RMB	RMB
AS	48.2	36.7	19.4	28.0
NSI	45.3	55.1	39.2	44.1
RN	6.6	8.2	41.4	27.9

Abbreviations: AS, active surveillance; NSI, nephron-sparing intervention; RM, renal mass; RMB, renal mass biopsy; RN, radical nephrectomy.

and T1bRM patients undergoing RMB. Indeed, prior studies have shown that obtaining RMB increases AS for T1RM.[12,22,23] Others argue RMB does not alter management.[24] Surprisingly, we found RMB was associated with lower rates of AS and concomitantly higher rates of NSI and RN in T1aRM patients. We attribute this to confounding factors that lead to the selection of patients for RMB by the managing urologist; for example, RMB was used more commonly in patients $\leq$ 75 years, in patients with greater comorbidity (CCI $\geq$1), and for tumors $>$ 2.0 cm and of intermediate/high complexity. Across MUSIC practices, 56% of T1aRM patients initiate AS without RMB. Therefore, T1aRM patients undergoing RMB are more commonly those in whom intervention may or will be performed if malignancy is identified. This practice pattern helps explain why more T1aRM patients undergo intervention after RMB, as 74% of these patients had malignant findings at RMB. Current guidelines support AS in selected T1aRM patients,[6,7,25] based on limited risk of progression to metastases.[26] In MUSIC, we found that ideal patients for AS (those $>$75 years, with tumors $\leq$2 cm) were least likely to undergo RMB and more often received intervention than those without RMB (Supplementary Table 1, https://www.urologypracticejournal.com). Our data suggest that not all T1aRM patients are ideal candidates for RMB, specifically those already deemed appropriate for AS.

There are benefits to RMB for patients when immediate intervention is planned. As indicated in the AUA guidelines, RN should be performed when PN will be challenging and adverse features suggestive of high-risk RCC are present on RMB.[6] Assessing such features is a clear benefit of pretreatment RMB, but the likelihood of such an outcome is low. More beneficial is the decreased incidence of benign surgical pathology in patients undergoing RMB when compared to patients without RMB.[4,5] This sizable reduction in nonmalignant pathology persisted for patients with T1aRM and T1bRM, and for those undergoing PN and RN. We conclude that, though the rate of intervention was higher in the T1aRM RMB cohort, surgery was more appropriately utilized as it was performed for a mass known to harbor potentially aggressive cancer. Some investigators have cautioned that cases identified as oncocytoma at RMB may harbor tumors with malignant potential, and several emerging/provisional entities of oncocytic tumors now exist in the 2022 WHO kidney tumor pathology guidelines (5th edition).[27] We would argue AS is reasonable for many patients with indolent RCC, not just those with confirmed benign lesions. Whatever terminology is employed for the range of oncocytic renal neoplasms with low malignant potential, they have malignant potential ranging from 0 to very low.[28,29] We acknowledge the limitation that long-term oncologic data regarding patients managed conservatively following RMB are lacking. RMB pathology reports indicating oncocytic tumor or other benign neoplasms are distinct from reports indicating normal renal parenchyma or inflammation; the latter should be viewed with skepticism, as the tumor may not have been adequately sampled.

Additional limitations include those inherent to any observational study. Practice patterns in Michigan may not be representative of those in other regions of the US. Based on observations of the interaction between RMB and tumor stage (T1a vs T1b) on management type, we hypothesized that unmeasured confounding and/or practice-level variation in RMB utilization might play a dominant role. Our analyses suggest this is the case; there are unmeasured factors associated with providers' decisions to perform RMB and how the patient is managed afterward. The finding of a lower RN rate following RMB persisted in MVA accounting for practice-level factors and other potential confounders. After a random-effects multinomial regression model accounting for practice variation, the effect of RMB on management of T1bRM and T1aRM persisted. Nevertheless, this observational study was not designed to investigate the impact of RMB on treatment decisions, and therefore must be viewed as hypothesis-generating in the absence of clinical trial data.

Future directions include initiation of a randomized clinical trial exploring RMB and decision-making for T1RM examining patient-reported outcomes and other quality of life measures. We also intend to explore the relationship between RMB and cancer-specific and all-cause mortality as there is limited evidence currently.[12] We believe collection and analysis of data regarding conservative management of T1bRM will prove valuable for physicians uncertain regarding RMB. MUSIC has prioritized avoidance of RN for benign renal neoplasms as a primary objective for quality improvement.[5] In MUSIC, we instituted a value-based reimbursement incentive to prioritize RMB use before RN for T1RM to achieve benign pathology rate below 6% at RN across our collaborative. We plan to revisit practice-level RMB utilization following the institution of the value-based reimbursement to see if it has both increased and

standardized. This information could prove valuable for other payers worldwide interested in achieving a similar goal.

Conclusions

RMB is associated with treatment choice for T1bRM differently than for T1aRM. Utilization of RMB in patients with T1bRM was associated with both lower rates of nonmalignant pathology and higher rates of NSI and AS. For every 7.4 RMBs performed in T1bRM patients, one kidney was spared from RN. We recommend that RMB be strongly considered for T1RM patients in whom intervention is being considered, particularly if RN might be performed.

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Editorial Commentary

Managing cT1 renal tumors—particularly small renal masses (SRM, cT1a)—varies from the most conservative strategy (active surveillance) to the most radical option (radical nephrectomy [RN]) and everything in between (partial nephrectomy, ablation). There often is not a right or wrong approach, as most SRM are not imminently threatening; however, when intervention is pursued, the AUA recommends prioritizing nephron-sparing approaches whenever possible.[1]

The decision to offer partial nephrectomy vs RN is multifactorial and driven by perceived technical feasibility (tumor complexity, surgeon experience) and patient factors (age, comorbidities, renal function, heritable conditions). While these variables can be difficult to capture retrospectively, Boynton et al leveraged the robust MUSIC-KIDNEY (Michigan Urological Surgery Improvement Collaborative—Kidney mass: Identifying and Defining Necessary Evaluation and therapY) registry and found that renal mass biopsies (RMB) may influence management for cT1 renal masses, including surgical approach.[2]

Localized kidney cancer is uniquely one of the few malignancies for which a biopsy is not routinely obtained to inform management. The role of RMB has evolved with variability across practices. RMB can be subject to false-negatives, undersampling, diagnostic uncertainty, or limited value added. Furthermore, RMB are invasive with inherent risks. Nevertheless, RMB can be valuable in certain scenarios, and as Boynton et al observed, RMB may even help avoid unnecessary RN for cT1b renal masses, which would offer considerable long-term benefits.

Although RMB may help reduce overtreatment for some, RMB were also associated with lower utilization of active surveillance for SRM—arguably leading to unnecessary interventions. In forgoing RMB, we assume that the majority of SRM are malignant; however, if RMB are pursued and confirm malignancy, there is seemingly a greater push—perhaps driven by the patient, clinician, or both—to pursue treatment.

Looking forward, imaging techniques (eg, sestamibi single photon emission CT/CT, girentuximab positron emission tomography/CT, multiparametric MRI) will likely provide noninvasive options to more accurately characterize renal masses for diagnostic, prognostic, and therapeutic guidance.[3]

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