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Utilization of Renal Mass Biopsy for T1 Renal Lesions across Michigan: Results from MUSIC-KIDNEY, A Statewide Quality Improvement Collaborative

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Abstract

Background: Renal mass biopsy (RMB) has had limited and varied utilization to guide management of renal masses (RM).

Objective: To evaluate utilization of RMB for newly diagnosed cT1 RMs across diverse practice types and assess associations of outcomes with RMB.

Design, setting, and participants: MUSIC-KIDNEY commenced data collection in September 2017 for all newly presenting patients with a cT1 RM at 14 diverse practices. Patients were assessed at ≥ 120 d after initial evaluation.

Outcome measurements and statistical analysis: Demographics and outcomes were compared for patients undergoing RMB versus no RMB. Clinical and demographic characteristics were summarized by RMB status using a χ^2 test for categorical variables and Student *t* test for continuous variables. A mixed-effects logistic regression model was constructed to identify associations with RMB receipt.

Results and limitations: RMB was performed in 15.5% ($n=282$) of 1808 patients with a cT1 RM. Practice level rates varied from 0% to 100% ($p=0.001$), with only five of 14 practices using RMB in $>20\%$ of patients. On multivariate analysis, predictors of RMB included greater comorbidity (Charlson comorbidity index ≥ 2 vs 0: odds ratio [OR] 1.44; $p=0.025$) and solid lesion type (cystic vs solid: OR 0.17; $p=0.001$; indeterminate vs solid: OR 0.58; $p=0.01$). RMB patients were less likely to have benign pathology at intervention (5.0% vs 13.5%; $p=0.01$). No radical nephrectomies were performed for patients with benign histology at RMB. The limitations include short follow-up and inclusion of practices with low numbers of RMBs.

Conclusions: Utilization of RMB varied widely across practices. Factors associated with RMB include comorbidities and lesion type. Patients undergoing RMB were less likely to have benign histology at intervention.

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Patient summary: Current use of biopsy for kidney tumors is low and varies across our collaborative. Biopsy was performed in patients with greater comorbidity (more additional medical conditions) and for solid kidney tumors. Pretreatment biopsy is associated with lower nonmalignant pathology detected at treatment.

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1. Introduction

Increasing detection of small renal masses (SRMs), partly driven by greater use of abdominal imaging, has resulted in increases in the rates of detection and intervention for presumed renal cell carcinoma (RCC). No clinical or conventional radiographic features are able to accurately predict histology, so contemporary series of surgical interventions report a benign final pathology rate of 20–30% for cT1a tumors [1].

It has been shown that renal mass biopsy (RMB) is safe and accurate, with low rates of adverse events [2] and reported sensitivity of 97.5–99.7%, specificity of 96.2–99.1%, and a positive predictive value of 99.8% in two large meta-analyses [2,3]. When an RMB-based management approach was applied to a large partial nephrectomy (PN) data set, it was felt that almost half of the surgeries were potentially avoidable [4]. However, adoption of RMB has been limited, with a recent survey showing that 31.8% of urologists would never consider a biopsy for a cT1a renal mass [5]. Opponents argue that the results do not influence management substantially and that novel imaging modalities can provide as useful information as RMB via a noninterventional study [6,7].

The Michigan Urological Surgery Improvement Collaborative (MUSIC) established Kidney Mass: Identifying and Defining Necessary Evaluation and Therapy (MUSIC-KIDNEY) as a quality improvement initiative for patients with a renal mass ≤ 7 cm (cT1 RM). The aim of our study was to assess the use of RMB for newly diagnosed cT1 RM across a range of practice types, using data collected through a statewide quality improvement collaborative.

2. Patients and methods

The MUSIC-KIDNEY conception and data collection methods have been previously outlined [8]. The MUSIC coordinating center is responsible for overall administration and management of collaborative activities. One urologist per practice serves as the clinical champion, with responsibilities that include oversight of local data collection and leadership around local implementation of quality improvement activities. Data abstractors recorded 122 data points at a single time point (≥ 120 d after initial consultation).

2.1. Study population

Our data set consisted of patients presenting to a urologist for the first time with a renal lesion measuring ≤ 7 cm. Exclusion criteria for the analysis included age < 18 yr, documented Bosniak I, II, and IIF cysts, and imaging-determined angiomyolipoma.

2.2. Patient characteristics and outcomes

For each patient, the following variables were extracted: age, gender, Charlson comorbidity index (CCI), race (white vs black vs others), insurance category (private vs public [Medicare, Medicaid] vs uninsured vs unknown), estimated glomerular filtration rate (eGFR), body mass index (BMI), tumor size, tumor position (anterior vs posterior), polar location (upper vs mid vs lower pole), tumor nephrometry score (RENAL score), tumor characteristics (solid vs cystic), tumor management, and final histology if available. For patients who underwent treatment with or without RMB, additional information was extracted from the data set, including biopsy histology, treatment, and surgical pathology, where available. Patients with biopsy results indicating malignancy or favoring malignancy were grouped, results with a benign diagnosis or favoring a benign diagnosis were grouped, and patients undergoing biopsy and ablation at the same time were assigned to a no-RMB group, as it was assumed that the biopsy result did not aid in decision-making regarding treatment. RMB results were classified as indeterminate if there was insufficient information to determine the probability of malignant versus benign histology or no tumor tissue was sampled.

2.3. Statistical analysis

Patient clinical and demographic characteristics were summarized by RMB status using a χ^2 test for categorical variables and Student *t* test for continuous variables. Practice-level variation in the utilization of RMB for cT1 RM patients was examined. A mixed-effects logistic regression model was constructed to identify factors associated with RMB versus no RMB. The model included patient-level characteristics as predictors, and random intercepts for each practice/hospital to account for within-practice correlation. All the analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and statistical significance was set at $p = 0.05$.

3. Results

3.1. Predictors of RMB utilization

Among 1808 patients with a cT1 RM, 282 (15.5%) underwent RMB to assist in management. The patient and tumor characteristics associated with RMB (Table 1) included increasing comorbidity ($p = 0.001$), academic practice ($p = 0.001$), higher BMI ($p = 0.025$), posterior tumor location ($p = 0.033$), and tumor type ($p < 0.001$). The rate of RMB utilization was 17.9% for solid masses, 10.3% for indeterminate lesions, and 3.5% for Bosniak III/IV cysts. The RMB utilization rate was much lower for the smallest tumors (1.2% for tumors ≤ 1 cm) than for tumors of 1.1–7.0 cm. For tumors between 1.1 and 7.0 cm, rates were similar (Fig. 1). In particular, for tumors of 1.1–4.0 cm and 4.1–7.0 cm (T1b) in

Table 1 – Patient, physician, and tumor characteristics for RMB versus no RMB

Variable	All patients	RMB	No RMB	p value
Patients (n)	1808	282	1526	
Mean age, yr (SD)	64.0 (13.3)	63.7 (13.1)	64.0 (13.4)	0.724
Mean BMI, kg/m ² (SD)	31.2 (8.0)	32.1 (8.1)	31.0 (8.0)	0.025
Race, n (%)				0.684
White	1389 (76.8)	224 (79.4)	1165 (76.4)	
African American	257 (14.2)	35 (12.4)	222 (14.5)	
Other	43 (2.4)	7 (2.5)	36 (2.4)	
Unknown	119 (6.6)	16 (5.7)	103 (6.7)	
Sex, n (%)				0.218
Male	1062 (58.7)	175 (62.1)	887 (58.1)	
Female	746 (41.3)	107 (37.9)	639 (41.9)	
Insurance, n (%)				0.344
Private	953 (52.7)	151 (53.5)	802 (52.6)	
Public	826 (45.7)	130 (46.1)	696 (45.6)	
None	27 (1.5)	1 (0.4)	26 (1.7)	
Unknown	2 (0.1)	0	2 (0.1)	
eGFR, n (%)				0.237
>60 ml/min/1.73 m ²	1111 (70.7)	169 (67.6)	942 (71.3)	
≤60 ml/min/1.73 m ²	460 (29.3)	81 (32.4)	379 (28.7)	
CCI, n (%)				0.001
0	942 (52.1)	121 (42.9)	821 (53.8)	
1	341 (18.9)	55 (19.5)	286 (18.7)	
≥2	525 (29.0)	106 (37.6)	419 (27.5)	
Multiple lesions, n (%)				0.869
No	1596 (89.0)	249 (89.2)	1347 (88.9)	
Yes	198 (11.0)	30 (10.8)	168 (11.1)	
Tumor type, n (%)				<0.001
Solid	1355 (74.9)	243 (86.2)	1112 (72.9)	
Indeterminate	339 (18.8)	35 (1.4)	304 (7.2)	
Complex cyst	114 (6.3)	4 (12.4)	110 (19.9)	
Tumor size, n (%)				0.004
0–1.0 cm	85 (4.7)	1 (0.4)	84 (5.5)	
1.1–2.0 cm	508 (28.1)	71 (25.2)	437 (28.6)	
2.1–3.0 cm	472 (26.1)	82 (29.1)	390 (25.6)	
3.1–4.0 cm	295 (16.3)	56 (19.9)	239 (15.7)	
4.1–5.0 cm	211 (11.7)	36 (12.8)	175 (11.5)	
5.1–6.0 cm	155 (8.6)	21 (7.4)	134 (8.8)	
6.1–7.0 cm	82 (4.5)	15 (5.3)	67 (4.4)	
Practice type, n (%)				<0.001
Academic	353 (19.5)	82 (23.2)	271 (76.8)	
Private	1455 (80.5)	200 (13.7)	1255 (86.3)	
Practice location, n (%)				0.070
Southeast Michigan	1396 (77.2)	206 (29.1)	1190 (17.8)	
Elsewhere	412 (22.8)	76 (70.9)	336 (82.2)	
Tumor location, n (%) ^a				0.033
Anterior	154 (45.8)	16 (32.0)	138 (48.3)	
Posterior	182 (54.2)	34 (68.0)	148 (51.7)	
Tumor location, n (%) ^a				0.217
Upper, upper/mid	513 (33.5)	79 (32.4)	434 (33.7)	
Mid	476 (31.1)	87 (35.7)	389 (30.2)	
Lower, lower/mid	543 (35.4)	78 (31.9)	465 (36.1)	
RENAL, n (%) ^a				0.779
Low	337 (41.3)	63 (39.6)	274 (41.8)	
Intermediate	358 (43.9)	70 (44.0)	288 (43.9)	
High	120 (14.7)	26 (16.4)	94 (14.3)	

BMI = body mass index; CCI = Charlson comorbidity index; eGFR = estimated glomerular filtration rate; RMB = renal mass biopsy; RENL = radius, exophytic/endophytic, nearness, and location items from the RENAL score; SD = standard deviation.

^a Analysis performed on available data as indicated in the “All patients” column.

size, there was no difference in the RMB utilization rate (15.9% vs 16.3%; $p = 0.87$).

There was substantial variation in utilization across the 14 urology practices evaluated. The median practice-level utilization of RMB was 11.3% (IQR 2–24%), with a wide range from 0% to 100% ($p = 0.001$). Only five of the 14 practices used RMB in >20% of cT1 RM cases. Provider-level

differences in utilization of RMB were also noted, but the data are somewhat limited by the small number of evaluable patients for a provider-by-provider analysis (data not shown).

In multivariable analysis (Table 2), the factors associated with RMB utilization were CCI and tumor type. Patients with CCI of ≥ 2 were more likely to undergo RMB (odds ratio

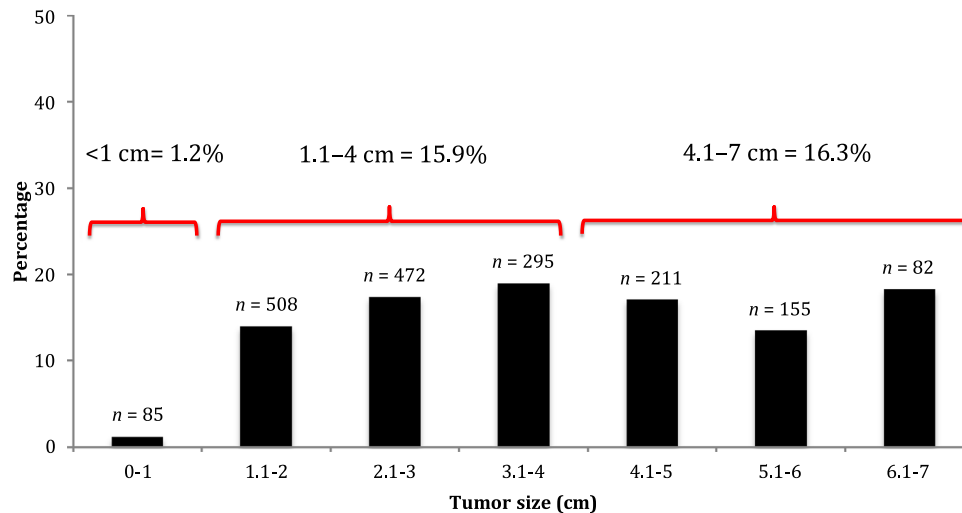


Fig. 1 – Utilization of renal mass biopsy according to tumor size in 1-cm increments.

[OR] 1.44; $p=0.025$) compared to those without comorbidity. Patients with complex cystic (OR 0.17; $p=0.001$) and indeterminate lesions (OR 0.58; $p=0.01$) were less likely to undergo RMB compared to patients with solid tumors.

3.2. Outcomes according to RMB utilization and biopsy results

The results for RMB before treatment for cT1 RMs include 70.6% with malignant pathology, 20.6% with benign pathology, and 9.8% with indeterminate results. The sensitivity and specificity of RMB were 98.1% and 60.0%, respectively, for the 119 patients undergoing surgical treatment. Five patients with indeterminate results on RMB underwent surgical intervention, four with RCC and one patient with benign histology. Two patients were classified as having malignant disease at RMB (oncocyctic neoplasm favoring chromophobe RCC) but pathology at

surgery revealed benign (oncocytoma) findings. The four patients with benign RMB histology who underwent surgery all had confirmation of oncocytoma on final surgical pathology.

The proportion of patients receiving the three main treatment choices (observation, nephron-sparing intervention, or radical nephrectomy [RN]) did not significantly differ between the RMB and no-RMB groups ($p=0.13$). However, in the cohort undergoing RMB, treatment choice was dramatically different (Fig. 2). If a benign histology outcome was obtained at RMB, patients were far more likely to undergo observation than with a malignant RMB result (94.7% vs 30.2%; $p<0.001$). Of note, no patients with a benign RMB result underwent RN. A total of 64 patients underwent ablation during the study time period. Twenty-eight of these patients had a biopsy with suspicion of malignancy before ablation. It is possible that the RMB results may have influenced management by either helping to justify treatment decisions or changing treatment decisions after RMB.

The rate of nonmalignant pathology (NMP) at surgical intervention was 5.0% with RMB and 13.4% without RMB ($p=0.01$). The NMP rate at RN was 2.7% ($n=1$) with RMB and 9.0% without RMB ($p=0.20$). Of note, the NMP RN performed in the RMB group involved an RMB result indicating unclassified RCC. The rate of emergency room visits after biopsy was 2.5% and the readmission rate was 1.8%.

4. Discussion

The MUSIC-KIDNEY initiative allows insight into the current management of newly presenting T1 RMs across the state of Michigan. Although the utility and efficacy of RMB have been championed by several thought leaders and institutions in Michigan [4,9,10], RMB utilization in our cohort was limited at 15.5%, with wide variability across MUSIC practices. In the context of prior rates

Table 2 – Multivariable logistical regression analysis to identify factors associated with undergoing RMB versus no RMB

Comparison	OR (95% CI)	p value
Age	1.00 (0.99–1.01)	0.561
Body mass index	1.01 (0.99–1.03)	0.196
African American vs White	1.01 (0.67–1.53)	0.955
Other vs White	0.85 (0.34–2.10)	0.718
Unknown vs White	1.02 (0.57–1.83)	0.953
Female vs male	0.87 (0.66–1.14)	0.307
Public vs private insurance	1.08 (0.81–1.45)	0.611
None/unknown vs private insurance	0.24 (0.03–1.90)	0.176
Academic vs community practice	1.85 (0.79–4.33)	0.156
Southeast Michigan vs elsewhere in Michigan	1.17 (0.55–2.47)	0.687
Charlson comorbidity index 1 vs 0	1.25 (0.87–1.80)	0.233
Charlson comorbidity index ≥ 2 vs 0	1.44 (1.05–1.98)	0.025
Multiple lesions vs single lesion	0.88 (0.57–1.35)	0.546
Bosniak III/IV cyst vs solid lesion	0.17 (0.06–0.46)	0.001
Indeterminate vs solid lesion	0.58 (0.38–0.88)	0.010
T1b vs T1a tumor size	1.01 (0.75–1.37)	0.933

CI = confidence interval; OR = odds ratio; RMB = renal mass biopsy.

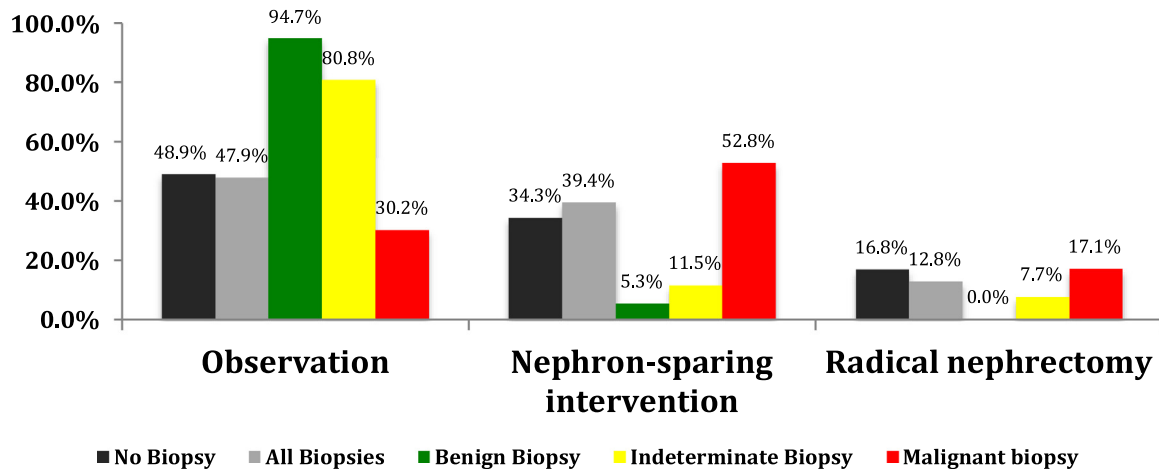


Fig. 2 – Treatment rates for patients with a cT1 renal mass evaluated with or without renal mass biopsy and according to biopsy histology result.

reported in multiple academic series [11,12] and systematic reviews [2,13,14], this rate may appear to be surprisingly low. Previous analysis of the National Cancer Data Base (NCDB) and Surveillance, Epidemiology and End Results (SEER) database reported RMB utilization rates of 15.3–30.1% [15,16]. However, a major limitation of the NCDB reporting is that it only includes patients with known malignancy. In addition, the published data from 2015 focused on T1a RMs alone. The SEER data set also has inherent issues regarding the study population, such as inclusion of only those aged >66 yr, elimination of negative RMB results, and exclusion of patients with private insurance. Similarly, a study on RMB in the Clinical Research Office of the Endourological Society (CROES) renal mass registry reported incidence of 11.8%, but investigated only T1a RMs [17]. Our study is the only multicenter report to date that includes all T1 renal masses (up to 7 cm) and is not limited by the inclusion of only malignant histology. Our study is also unique in that the collaborative includes diverse academic and private groups, giving a “real world” look at RMB utilization. Although RMB rates were higher in academic practices, this was not a predictor of utilization on multivariate regression, in contrast to previously published data [5].

The only patient factor associated with RMB use was greater comorbidity, which has previously been reported [16]. Age and renal function appeared to have no impact on RMB rates in MUSIC-KIDNEY. One might expect that older patients and those with lower renal function would be more likely to undergo RMB since they are less likely to proceed straight to intervention. Our findings do not support this assumption and might be attributable to the high rate of initial observation in our cohort of almost 50% [8], which is frequently offered to such patients without up-front RMB [28]. The high rate of observation is an important feature of the treatment pattern for cT1 RM within MUSIC-KIDNEY, with predictors of noninterventional management including lesion type (Bosniak III–IV > solid; $p=0.017$), tumor stage (T1a vs T1b; $p<0.001$), and higher age ($p<0.001$) [28].

With regard to the decision to perform RMB, tumor size played a role, as tumors of <1 cm were seldom managed with RMB, while tumors of 1.1–7.0 cm in size had similar rates of RMB utilization. This is intriguing considering the significant literature regarding the use of RMB for SRMs, but not for larger, localized suspected RCCs. The low rates of biopsy for lesions of <1.0 cm in size is probably because these lesions pose almost negligible metastatic potential [18], are benign in almost 50% of cases on surgical removal [19], and pose a greater technical challenge for RMB. In MUSIC-KIDNEY, 77% of 0.1–1.0-cm cT1 RMs are managed with observation, even without RMB [8]. Interestingly, RMB was carried out for 16.3% of T1b lesions, of which 12.5% were benign, which is similar to previously reported data at surgery [19]. We suggest that the T1b population might be the most suitable for RMB, as these patients have the most to gain (or lose) with diagnosis of nonmalignant pathology. RN was performed for almost 40% of T1b lesions in our cohort. It has been shown that RN is associated with lower non-RCC survival [20] and lower eGFR is strongly associated with risk of death, cardiovascular events, and hospitalization [21]. It is therefore important to reduce unnecessary decreases in renal function. In addition, although prior studies observed associations of race and gender with RMB utilization [16], we did not observe such an association.

We recently published the MUSIC-KIDNEY experience with cT1 RMs to identify potential improvement opportunities to reduce overtreatment, including nephrectomy [22]. Our data showed that 11% of cT1 RMs treated with surgery had NMP, which is a lower rate than in most published reports. Moderate to major quality improvement opportunities were identified in nearly half of these cases, most notably cases with the unintended outcome of RN for NMP. NMP rates can be reduced by ensuring that dedicated imaging is performed before any decision on surgery, considering observational strategies, when appropriate, and RMB. Our previous publication suggests a potential role for RMB in reducing unnecessary treatment for NMP cases, especially for patients for whom RN is planned or likely on the basis of tumor complexity or size.

As might be expected, patients in our study with cystic tumors and anterior tumors were less likely to undergo RMB. Other reports have shown lower diagnostic rates for cystic RMBs (83.6% vs 99.1%) [2,23] and there is controversy regarding the appropriateness of RMB for cystic tumors given the inherent challenges of adequate tumor sampling and some concerns regarding tumor spillage [24–26]. RMB might be less likely for anterior tumors because of closer proximity to the bowel and visceral organs and a perceived risk of injury. No difference in RMB rates by polar location was observed despite presumed higher risks associated with upper-pole tumor biopsy. Tumor complexity was not associated with RMB utilization (although data were unavailable for just under half of the patients). Although it has been shown that nephrometry scoring can predict surgical complications and renal function decline [27], no evidence is currently available on defining suitability for RMB.

Our finding of sensitivity of 98.1% for RMB is similar to that reported in a prior meta-analysis [2]. Specificity is, however, lower than in prior reports, perhaps impacted by the 95% of patients with a benign biopsy who underwent surveillance with no surgical pathology for correlation. Overall, the benign, malignant, and nondiagnostic rates were similar to those previously reported [2,14].

RMB was associated with a significantly higher rate of benign pathology at intervention, with no patients with a benign RMB undergoing nephrectomy and almost all of these patients opting for observation. Patients with a malignant RMB were less frequently assigned to observation, in contrast to a prior report [15]. It is frequently argued by opponents that RMB rarely changes management, but our findings indicate that inclusion of RMB in an assessment algorithm could avoid unnecessary intervention and better select patients for treatment.

The study limitations include limited follow-up and inclusion of practices with low numbers of RMBs. If treatment occurred beyond the follow-up period, patients could have been misclassified to observation. With ongoing collection of data within the MUSIC-KIDNEY registry, there will be opportunities to further assess RMB utilization and patient outcomes. Our statewide quality improvement database does not contain granular data to determine indications for RMB, patient preferences during this period, and how RMB ultimately affected decision-making. However, we did find that patient comorbidities and tumor factors were associated with a higher rate of RMB, and these factors were probably an important part of the shared decision-making process on whether to perform RMB. In addition, data for nephrometry scores and tumor position, which could be useful in determining suitability for RMB, were unavailable for up to half of the patients. Collecting and recording tumor nephrometry data has been one quality improvement goal for our collaborative.

5. Conclusions

RMB utilization within a statewide quality improvement collaborative (MUSIC KIDNEY) was low overall, with wide practice variation. Predictors of RMB include greater

comorbidity and solid lesion type. The results for RMB performed before treatment greatly impact management, particularly when a benign histological diagnosis was made. More widespread use of RMB could further reduce the number of radical nephrectomies with findings of only benign pathology.

Author contributions: Amit K. Patel 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.

Study concept and design: Patel, Lane, Rogers.

Acquisition of data: Johnson, Qi.

Analysis and interpretation of data: Patel, Lane, Rogers, Johnson, Qi.

Drafting of the manuscript: Patel, Chintalapati, Fouad, Butaney, Budzyn, Lane, Rogers.

Critical revision of the manuscript for important intellectual content: Patel, Schervish, Rogers, Lane.

Statistical analysis: Patel, Qi.

Obtaining funding: Lane, Rogers, Johnson.

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Other: None.

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