HHS Public Access

Author manuscript

Int J Urol. Author manuscript; available in PMC 2021 June 08.

Published in final edited form as:

Int J Urol. 2019 February ; 26(2): 260–265. doi:10.1111/iju.13854.

Urinary Aquaporin-1 and Perilipin-2: Can These Novel Markers Accurately Characterize Small Renal Masses and Help Guide Patient Management?

Joseph B. Song, M.D.[1], **Jeremiah J. Morrissey, Ph.D.**[2,3], **Jonathan M. Mobley, M.D.**[1], **Karen G. Figenshau**[1], **Joel M. Vetter, M.S.**[1], **Sam B. Bhayani, M.D.**[1,3], **Evan D. Kharasch, M.D., Ph.D.**[2,3,4], **Robert Sherburne Figenshau, M.D.**[1,3]

[1]Division of Urology, Washington University School of Medicine, St. Louis, MO, USA

[2]Department of Anesthesiology, Division of Clinical and Translational Research, Washington University School of Medicine, St. Louis, MO, USA

[3]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA

[4]Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, St. Louis, MO, USA and The Center for Clinical Pharmacology, St. Louis College of Pharmacy and Washington University School of Medicine, St. Louis, MO

Abstract

Objective: Small renal masses (SRMs) ≤4cm are malignant in the majority of cases. Renal mass biopsy (RMB) can prevent resection of benign lesions but are often followed by a second procedure if malignancy is found. Urine aquaporin-1 (AQP1) and perilipin-2 (PLIN2) have been identified as potential biomarkers for renal cell carcinoma. Here, we evaluate their role as a complimentary adjunct to RMB in guiding management of patients with SRMs.

Methods: Preoperative AQP1 and PLIN2 levels in 57 patients with SRMs undergoing partial nephrectomy were analyzed and compared to postoperative tumor histology. An algorithm was created utilizing AQP1 and PLIN2 in conjunction with RMB. Cutoff values were implemented to maximize biomarker sensitivity and specificity. RMB utilization and intervention were then compared to rates in traditional RMB algorithms.

Results: All clear cell and papillary RCCs were correctly identified and assigned to the treatment path. All benign lesions were correctly sorted to a confirmatory RMB path. Two chromophobe masses did not have elevated AQP1 and PLIN2 and would require RMB. Compared to protocols that call for all SRMs to be biopsied, confirmatory RMB could have been safely avoided in 74% of patients with elevated AQP1 and PLIN2. Compared to protocols that do not utilize RMB, surgical intervention would have been avoided in 23% of patients with benign masses.

Corresponding Author: Robert Sherburne Figenshau, Address: 4921 Parkview Pl, Suite 11c, Saint Louis, Missouri 63110, figenshaur@wustl.edu, Phone: 314-454-2235 Fax: 314-367-5016.

CONFLICTS OF INTEREST:

Washington University has a US and a European patent for the use of urinary AQP1 to diagnose kidney cancer.

Conclusions: AQP1 and PLIN2 possess high sensitivity and specificity for detecting clear cell and papillary renal cell carcinoma. Use of these markers may compliment RMB in the characterization of SRMs.

Keywords

Urine biomarkers; Renal cell carcinoma; Small renal mass; Aquaporin-1; Perilipin-2

INTRODUCTION

Incidentally found small renal masses (SRMs), defined as stage T1a renal masses ≤4cm, are detected with greater frequency as a result of more widespread use of modern cross-sectional abdominal imaging.[1–2] Most solid enhancing masses without fat are renal cell carcinomas (RCC). However, recent literature suggests higher rates of benign pathology in small lesions.[2–3] Indeed, malignancy directly relates to tumor size. Lesions under 1 cm are benign in 46% of cases; lesions under 2 cm are benign in 22%.[1] There are a wide range of clinical options in managing patients with a SRM. Some centers routinely biopsy all SRMs while others perform almost no renal mass biopsies prior to treatment. Furthermore, depending on patient characteristics and regional practice patterns, providers may recommend active surveillance, image-guided ablation, or surgical resection. Among patients who do receive resection, 13–28% have benign pathology.[2–3] Therefore, non-invasive testing is an important tool in differentiating benign from malignant masses and can benefit patients by preventing overtreatment of their nonmalignant SRMs.

Renal mass biopsy (RMB) is an adjunct which can differentiate malignant papillary, chromophobe, and clear cell renal cell carcinomas (RCC) from benign lesions such as oncocytoma and angiomyolipoma.[5] In cases where ablative treatments are performed, RMB is typically done concomitantly to provide tissue diagnoses. Currently, some physicians avoid RMB due to patient factors, for fear of false negatives, or worry about nondiagnostic results and tumor seeding. However, modern RMB has been proven safe and effective with sensitivities and specificities reaching 80–92% and 83–100%, respectively.[5–6] A recently published RMB-based algorithm distinguishes benign from malignant pathology and directs management between active surveillance and surgical treatment.[7] One disadvantage of RMB, however, is that it is a purely diagnostic procedure. The majority of patients with malignant lesions will likely receive a recommendation for an additional therapeutic procedure.

Urine aquaporin-1 (AQP1) and perilipin-2 (PLIN2) concentrations are elevated in patients with clear cell and papillary RCC compared to patients with chromophobe RCC, oncocytoma, cystic nephroma, plasmacytoma, hemangioma, angiomyolipoma, non-renal urinary tract cancers, non-cancer renal disease, and healthy controls.[8–11] When used in conjunction, the two markers are able to achieve very high positive and negative predictive values.[11] As a result, AQP1 and PLIN2 have been proposed for use in screening for clear cell and papillary RCC, and for the characterization of imaged renal masses. However, these markers are not elevated in chromophobe RCC and therefore would need to be used in combination with RMB to identify these lesions of low malignant potential. Here, we

explore the utility of these biomarkers in conjunction with RMB to characterize SRMs in the least invasive way.

METHODS

PATIENTS

The Washington University Institutional Review Board approved the study. Written informed consent was obtained from all patients. Preoperative urine samples were collected between November 2009 and November 2012 from 57 patients with CT or MRI imaged renal masses ≤ 4.0cm. There was pre-surgical concern for RCC in all 57 patients. Post-surgical pathology of the resected masses showed 34 clear cell RCC, 8 papillary RCC, 2 chromophobe RCC, 6 angiomyolipoma, and 7 oncocytoma. All of the urine AQP1 and PLIN2 concentrations for these patients have been reported previously.[9,10] The present dataset is a subset of these patients.

CLINICAL AND PATHOLOGICAL DATA

Demographic and medical histories were recorded including age, sex, past medical history, and body mass index (BMI). Serum creatinine levels were obtained and the estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation.[13] Pathology reports provided the histological diagnosis and tumor size.

AQP1 AND PLIN2 MEASUREMENT

Urine biomarker concentrations were determined by Western blot and normalized to urinary creatinine concentration as previously described.[8–10] Quality control samples evaluated gel-to-gel reproducibility. Results are reported as Absorbance Units per mg urine creatinine.

STATISTICAL ANALYSIS AND SRM ALGORITHM

Clinical parameters and urine concentrations were compared among the five tumor subtypes. Analysis was performed using R statistical software (R Development Core Team, 2010). Descriptive statistics compared continuous variables using the t-test assuming non-equal variance. Categorical variables were compared using the Chi-square test of independence. The Mann-Whitney U Test was used to differentiate AQP1 and PLIN2 among the five subtypes. Tests were performed two-sided with statistical significance set at the 0.05 level. Based on retrospective data from these cohorts, receiver operating characteristic (ROC) analysis was used to determine optimum cut-off values each for AQP1 and PLIN2. Two sets of cut-off values for the biomarkers were established to maximize either sensitivity or specificity. A third set of cut-off values were then established to combine the markers into a single test maximizing both sensitivity and specificity. Using these cutoffs, we devised and tested an algorithm using both markers to evaluate the ability to accurately distribute patients with clear cell and papillary RCC into a treatment path and those with chromophobe RCC, oncocytoma, and angiomyolipoma into a biopsy path.

The algorithm was thus constructed so that the combined elevation of urinary AQP1 and PLIN2 would indicate a true positive test for clear cell and papillary RCC and a true negative test for chromophobe RCC, angiomyolipoma, or oncocytoma. The algorithm would

then assign patients with positive results to a treatment path, and those with negative results to a RMB path to confirm benign pathology and find the rare chromophobe RCC.

RESULTS

Table 1 lists the patient characteristics. Patients in all groups were statistically similar, with the exception of patients with clear cell and chromophobe RCC having a higher BMI than other patients (p=0.046). Figure 1 provides the AQP1 and PLIN2 values for all patients. The median AQP1 and PLIN2 values for clear cell and papillary RCC were significantly higher than those of chromophobe RCC, oncocytoma, and angiomyolipoma.

Combining AQP1 and PLIN2, the sensitivity and specificity were maximized for 100% specificity, sensitivity, positive predictive value, and negative predictive value (Figure 2). In this combined biomarker algorithm, any patients with AQP1 ≥ 5 or PLIN2 ≥ 16 would be assigned to intervention for presumed clear cell or papillary RCC. Patients with AQP1 <5 and PLIN2 <16 would go to RMB. Using these cut-offs, our algorithm would correctly sort patients into RMB or treatment path in every case. This would result in a 74% reduction in confirmatory biopsies that show clear cell and papillary RCC from conventional RMB algorithms where all SRMs undergo RMB. Also, 23% of patients with benign pathology would have been directed to RMB and avoided resection or ablation. Two patients (3%) with chromophobe RCC did not have elevated AQP1 or PLIN2 and would have undergone RMB.

DISCUSSION

Incremental decreases in renal function raise the risk of hospitalization, cardiovascular events and death.[14] Two publications examined the effects of radical and partial nephrectomy on renal function and overall survival of patients with unanticipated benign renal lesions. Both series found greater post-operative renal function and survival in patients that underwent partial versus radical nephrectomy.[15–16] Additionally, patients' postoperative eGFR was an independent predictor of cardiac-specific survival as well as overall survival, with lower eGFR portending less favorable outcomes.[15] These observations provide evidence that renal preservation should be considered when treating patients with SRMs.

The most "nephron sparing" approach to managing benign SRMs is to diagnose the lesion as benign and avoid unnecessary treatment. Several series document that cross-sectional imaging fails to diagnose benign masses in 13–28% of lesions less than 4cm in size.[1–3] A needle-acquired RMB directed treatment algorithm that detects benign pathology and stratifies management of malignant lesions based on histological characteristics and tumor size has been reported.[7] In that study, preoperative RMB distinguished malignant from benign pathology with 100% accuracy for masses under 4cm. Although this algorithm can be used to prevent the resection of benign renal lesions, there continues to be wide variation in clinical practice.[5,17] A simple, relatively inexpensive diagnostic urine test to identify which patients are most likely to benefit from RMB could aid in the adoption of RMB and lead to more widespread adoption and standardization of the evaluation of SRMs.

In 2009, the American Urological Association polled 759 active urologists regarding management of SRMs. Regarding the use of RMB, 37% of urologists reported that RMB

was never ordered in the evaluation of SRMs. Furthermore, 63% occasionally obtained a RMB, while only 8% performed a RMB on more than 20% of SRMs.[17] Similar practice patterns were observed in the United Kingdom; 43% of urologists surveyed never used RMB and only 23% occasionally used RMB.[5] The risks of false negative results, tumor seeding, intra-tumor heterogeneity and complications were common reasons for avoiding RMBs. The belief that a RMB would not affect final patient management was also cited as a reason to avoid ordering RMBs.[5] Recent literature, however, does not support these beliefs and suggests that RMB has a low rate of false negative results and rarely results in severe complications or tumor seeding.[6]

Avoiding resection of benign SRMs could significantly decrease patient morbidity, loss of productivity, and risk of developing chronic kidney disease from nephron loss. However, there are hurdles to widespread adoption of a RMB based treatment algorithm. Factors such as patient preference or suitability for surgery may preclude RMB. Furthermore, 72–87% of patients with SRMs have malignant disease and will require some form of further treatment after their biopsy.[1–3] Biopsy of these masses increases healthcare costs and exposes these patients to some degree of risk with little or no benefit.

The water channel protein AQP1 has been shown to be involved in multiple cellular mechanisms, including angiogenesis,[18] cell adhesion,[19] and cellular proliferation.[20] While AQP1 is abundantly expressed in the apical membrane of proximal tubule cells,[21] it is also known to be upregulated in lung and brain tumors.[22,23] On the other hand, PLIN2 is involved in lipid metabolism, transport, and cellular signaling,[24] and has been shown to be elevated in multiple malignancies which demonstrate clear cell pathology,[24,25] including ccRCC.[26] The exact mechanisms by which these markers are passed into the urine are unclear. While the association of RCC with the proximal tubule provides a mechanism for these markers to be expressed in the urine, it is unclear whether they are secreted or merely shed into the urinary system. However, we have previously demonstrated that elevated AQP1 and PLIN2 are not associated with other urologic malignancies such as prostate or bladder cancer, and that renal tumor size is positively correlated with levels of AQP1 and PLIN2.[8,9]

The high sensitivity and specificity of AQP1 and PLIN2 are promising as a primary means of characterizing renal masses. Within the subset of patients with SRMs, these biomarkers can potentially decrease the need for RMB. Modifying existing algorithms to include urine AQP1 and PLIN2 may prevent the unnecessary resection of benign SRMs and reduce the number of RMBs required to differentiate benign from malignant lesions.

By combining the two markers, we were able to maximize the sensitivity and specificity of both to detect clear cell and papillary RCC. Patients with AQP1 ≥ 5 or PLIN2 ≥ 16 were deemed likely to have clear cell or papillary RCC and were sorted directly to the treatment path of the algorithm (Fig 2). Patients assigned to the treatment path would then be counseled on appropriate management strategies, including observation, ablative therapies, and surgical resection. Patients with lower levels would be assigned to the biopsy path. Patients with biopsy confirmed oncocytoma, angiomyolipoma or other benign lesion would be counseled favoring observation. Importantly, AQP and PLIN2 do not detect chromophobe RCC. In the rare cases where the biopsy finds chromophobe RCC not detected by AQP1 and

PLIN2, these patients would be counseled on treatment options. Using the combined biomarker and RMB algorithm developed here, RMB would have been avoided in the majority of patients, potentially reducing cost and morbidity in 74% of patients with SRMs.

On a national basis, where RMB has not been widely implemented, the need for differential diagnosis of SRMs is compelling. About 45,000 partial and radical nephrectomies were performed in the United States alone in the year 2015.[27] It is estimated that 18% of these would involve nephron reduction for a benign tumor (extrapolation of SEER 18 Data Base). While utilization of RMB could potentially have prevented unnecessary treatment in these 8,000 cases, RMB has not been widely adopted. By adding a noninvasive biomarker test to select patient who would benefit most from a RMB, this algorithm may be able increase the utilization of these tools in avoiding overtreatment of SRMs.

One limitation of this study is that patients with chromophobe RCC have normal AQP1 and PLIN2 concentrations.[8,10] Indeed, only 1 chromophobe RCC was detected when PLIN2 was used at the highest sensitivity. By performing a RMB as a second screening tool in patients with normal markers, the algorithm would prevent missed chromophobe RCCs. Fortunately, chromophobe RCC accounts for only 5% for all cases of RCC and has a better prognosis than clear cell RCC. [28] A multi-institutional review of 291 patients with chromophobe RCC found that only about 2% of patients presented with distant metastasis. In their series, 5 and 10-year cancer-specific survival was 93% and 89%.[29] Among 203 patients with chromophobe RCCs, all 132 patients with lesions less than 7cm lacked metastasis at initial presentation. Only two patients with lesions less than 4cm in size developed local recurrence or metastasis following primary tumor resection.[28]

Furthermore, as previously reported, urinary AQP1 and PLIN2 correspond with tumor size and stage, but not with grade.[30] As a result, aggressive tumor subtypes with high grade may be missed with the use of these markers alone and the decision to proceed with active surveillance in the setting of positive urinary markers must be taken with this point in consideration.

Other limitations of our current study are its retrospective nature and the small sample size. While our results suggest that the sensitivity and specificity of AQP1 and PLIN2 approach 100%, we recognize that this is influenced by our small sample size. Future prospective studies are warranted to validate the algorithm and determine if current cut-off values accurately direct patient care. In addition, current quantifications of AQP1 and PLIN2 are done via Western blot, which makes large scale investigation and clinical implementation difficult. Further work will need to be done to create scalable ways to quantify these markers.

Despite these considerations, it is clear that urine AQP1 and PLIN2 are elevated in clear cell and papillary RCC subtypes when compared to chromophobe RCC, oncocytoma, and angiomyolipoma. By combining the two markers, we can establish a test that with high sensitivity and specificity for clear cell and papillary RCC. Using these non-invasive markers to prescreen patients with SRMs, we may be able to more appropriately select patients for

RMB, significantly reducing both the number of surgeries done for benign renal masses and the number of renal biopsies needed to diagnose malignant renal lesions.

ACKNOWLEDGMENTS

We thank anesthesiology clinical coordinators Megan Kalin, CCRP, and Karen Frey, CCPR, as well as urology clinical coordinators Alethia Paradis, MS, Janise Webb, CTR for help during the study.

REFERENCES

1. Frank I, Blute ML, Cheville JC, et al.: Solid renal tumors: an analysis of pathological features related to tumor size. J Urol. 2003; 170: 2217 [PubMed: 14634382]
2. Schachter LR, Cookson MS, Chang SS, et al.: Second prize: frequency of benign renal cortical tumors and histologic subtypes based on size in a contemporary series: what to tell our patients. J Endourol. 2007; 21: 819 [PubMed: 17867935]
3. Kutikov A, Fossett LK, Ramchandani P, et al.: Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. Urology. 2006; 68: 737 [PubMed: 17070344]
4. Wang R, Wolf JS, Wood DP, et al.: Accuracy of percutaneous core biopsy in management of small renal masses. Urology. 2009; 73: 586 [PubMed: 19118884]
5. Khan AA, Shergill IS, Quereshi S, et al.: Percutaneous needle biopsy for indeterminate renal masses: a national survey of UK consultant urologists. BMC Urol. 2007; 7: 10 [PubMed: 17610739]
6. Lane BR, Samplaski MK, Herts BR, et al.: Renal mass biopsy--a renaissance? J Urol. 2008; 179: 20 [PubMed: 17997455]
7. Halverson SJ, Kunju LP, Bhalla R, et al.: Accuracy of determining small renal mass management with risk stratified biopsies: confirmation by final pathology. J Urol. 2013; 189: 441 [PubMed: 23253955]
8. Morrissey JJ, London AN, Luo J, et al.: Urinary biomarkers for the early diagnosis of kidney cancer. Mayo Clin Proc. 2010; 85: 413 [PubMed: 20375178]
9. Morrissey JJ and Kharasch ED: The Specificity of Urinary Aquaporin 1 and Perilipin 2 to Screen for Renal Cell Carcinoma. J Urol. 2012; 189: 1913 [PubMed: 23154208]
10. Morrissey JJ, Mobley J, Figenshau RS, Vetter J, Sam Bhayani S, Kharasch ED: Urine Aquaporin 1 and Perilipin 2 Differentiate Renal Carcinomas from Other Imaged Renal Masses and Bladder and Prostate Cancer. Mayo Clin. Proc. 2015; 90(1):35–42. [PubMed: 25572193]
11. Morrissey JJ, Mellnick VM, Luo J, et al. Evaluation of Urine Aquaporin-1 and Perilipin-2 Concentrations as Biomarkers to Screen for Renal Cell Carcinoma. JAMA Oncol. 2015;1093:1–9.
12. Rini BI, Campbell SC: Urinary Biomarkers for the Detection and Management of Localized Renal Cell Carcinoma. JAMA Oncol. 1:212–3, 2015 [PubMed: 26181026]
13. Levey AS, Bosch JP, Lewis JB, et al.: A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999; 130: 461 [PubMed: 10075613]
14. Go AS, Chertow GM, Fan D, et al.: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004; 351: 1296 [PubMed: 15385656]
15. Weight CJ, Lieser G, Larson BT, et al.: Partial nephrectomy is associated with improved overall survival compared to radical nephrectomy in patients with unanticipated benign renal tumours. Eur Urol. 2010; 58: 293 [PubMed: 20546991]
16. Kaushik D, Kim SP, Childs MA, et al.: Overall Survival and Development of Stage IV Chronic Kidney Disease in Patients Undergoing Partial and Radical Nephrectomy for Benign Renal Tumors. Eur Urol. 2012; 64: 600 [PubMed: 23280319]
17. Breau RH, Crispen PL, Jenkins SM, et al.: Treatment of patients with small renal masses: a survey of the American Urological Association. J Urol. 2011; 185: 407 [PubMed: 21168170]
18. Nico B, Ribatti D. Aquaporins in tumor growth and angiogenesis. Cancer Lett. 2010 8 28;294(2):135–8. [PubMed: 20199845]

19. Galán-Cobo A, Ramírez-Lorca R, Echevarría M. Role of aquaporins in cell proliferation: What else beyond water permeability? Channels (Austin). 2016;10(3):185–201. [PubMed: 26752515]
20. Galán-Cobo A, Ramírez-Lorca R, Toledo-Aral JJ, Echevarría M. Aquaporin-1 plays important role in proliferation by affecting cell cycle progression. J Cell Physiol. 2016 1;231(1):243–56 [PubMed: 26081645]
21. Borgnia M, Nielsen S, Engel A, Agre P. Cellular and molecular biology of the aquaporin water channels. Annu Rev Biochem. 1999;68:425–58. [PubMed: 10872456]
22. Saadoun S, Papadopoulos MC, Davies DC, Bell BA, Krishna S. Increased aquaporin 1 water channel expression in human brain tumours. Br J Cancer. 2002 9 9;87(6):621–3. [PubMed: 12237771]
23. López-Campos JL, Sánchez Silva R, Gómez Izquierdo L, Márquez E, Ortega Ruiz F, Cejudo P, Barrot Cortés E, Toledo Aral JJ, Echevarría M. Overexpression of Aquaporin-1 in lung adenocarcinomas and pleural mesotheliomas. Histol Histopathol. 2011 4;26(4):451–9. [PubMed: 21360438]
24. Zhang XD, Li W, Zhang N, Hou YL, Niu ZQ, Zhong YJ, Zhang YP, Yang SY. Identification of adipophilin as a potential diagnostic tumor marker for lung adenocarcinoma. Int J Clin Exp Med. 2014 4 15;7(4):1190–6. [PubMed: 24955208]
25. Matsubara J, Honda K, Ono M, Sekine S, Tanaka Y, Kobayashi M, Jung G, Sakuma T, Nakamori S, Sata N, Nagai H, Ioka T, Okusaka T, Kosuge T, Tsuchida A, Shimahara M, Yasunami Y, Chiba T, Yamada T. Identification of adipophilin as a potential plasma biomarker for colorectal cancer using label-free quantitative mass spectrometry and protein microarray. Cancer Epidemiol Biomarkers Prev. 2011 10;20(10):2195–203. [PubMed: 21828233]
26. Tolkach Y, Lüders C, Meller S, Jung K, Stephan C, Kristiansen G. Adipophilin as prognostic biomarker in clear cell renal cell carcinoma. Oncotarget. 2017 4 25;8(17):28672–28682. [PubMed: 28404922]
27. Johnson DV, Vukina J, Smith A, Meyer A-M, Wheeler SB, Kuo T-M, Tan H-J, Woods ME, Raynor MC, Wallen EM, Pruthi RS, Nielsen ME, Preoperatively misclassified, surgically removed benign renal masses: A systematic review of surgical series and United States population level burden estimate. J. Urol (2015) 193; 30–35. [PubMed: 25072182]
28. Przybycin CG, Cronin AM, Darvishian F, et al.: Chromophobe renal cell carcinoma: a clinicopathologic study of 203 tumors in 200 patients with primary resection at a single institution. Am J Surg Pathol. 2011; 35: 962 [PubMed: 21602658]
29. Volpe A, Novara G, Antonelli A, et al.: Chromophobe renal cell carcinoma (RCC): oncological outcomes and prognostic factors in a large multicentre series. BJU Int. 2012; 110: 76 [PubMed: 22044519]
30. Morrissey JJ, Mobley J, Song J, Vetter J, Luo J, Bhayani S, Figenshau RS, Kharasch ED. Urinary concentrations of aquaporin-1 and perilipin-2 in patients with renal cell carcinoma correlate with tumor size and stage but not grade.Urology. 2014 1;83(1):256.e9–14

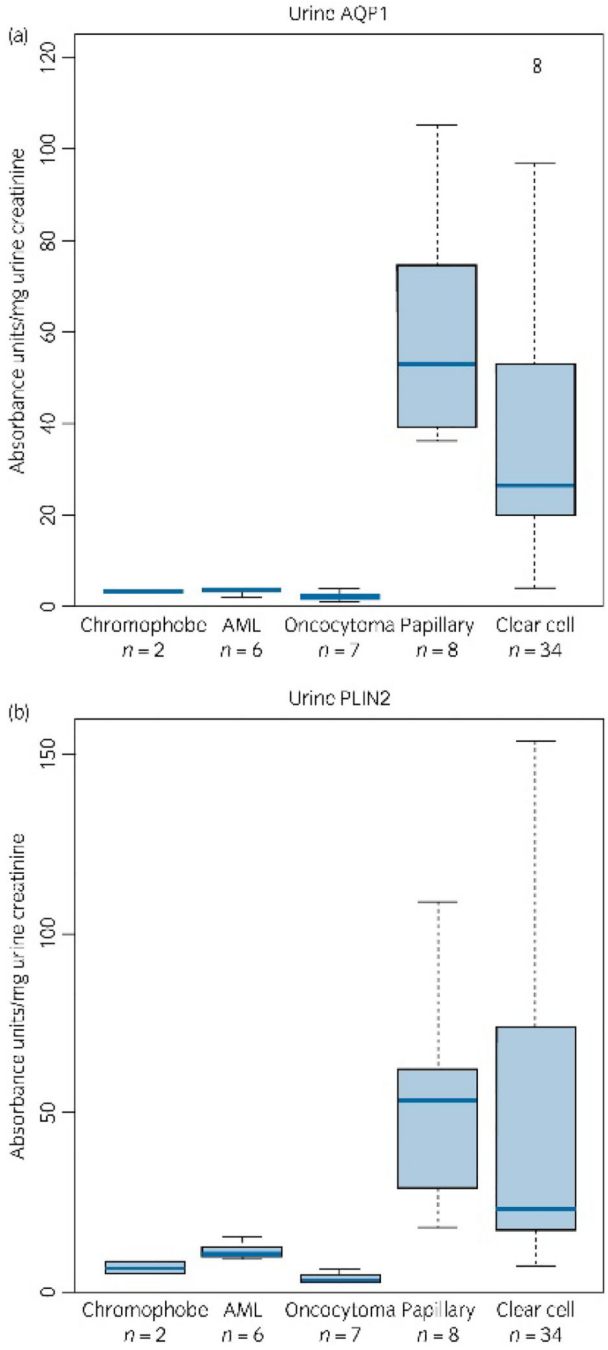

Figure 1.

Box plot showing the urine concentrations of (a) AQP1 and (b) PLIN2 for patients with clear cell RCC, papillary RCC, chromophobe RCC, oncocytoma and AML. The box represents the interquartile range of values, with the solid line representing the median value. The dotted lines extend to the maximum and minimum vales of each biomarker.

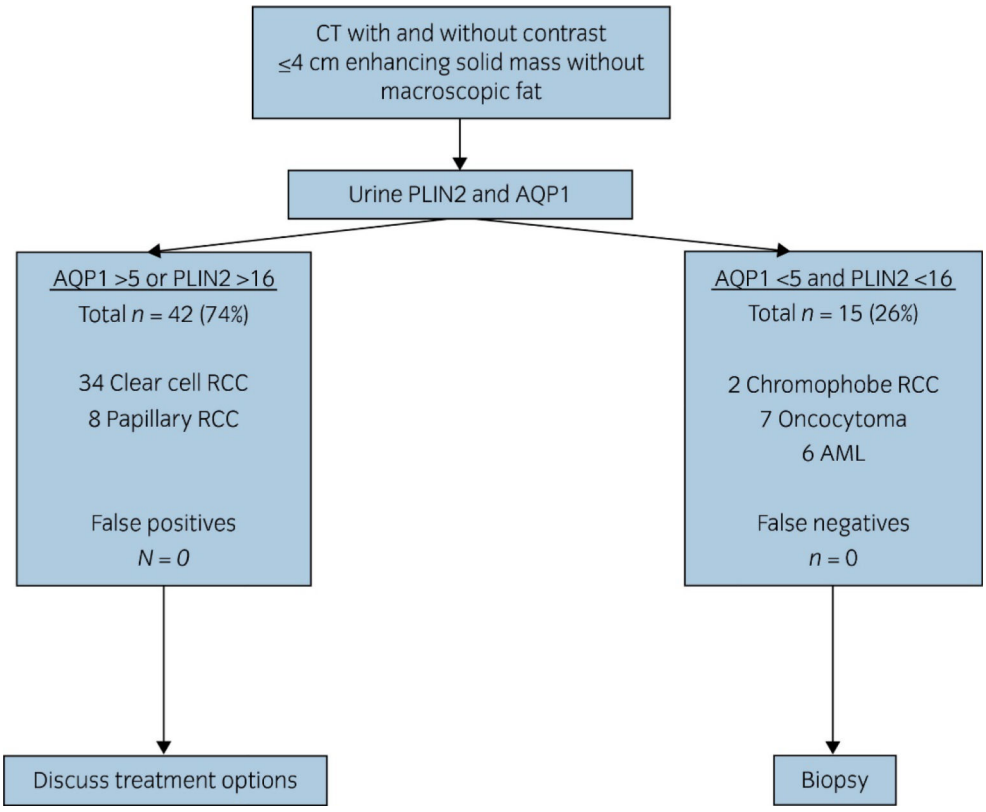

Figure 2.
SRM algorithm.

Table 1.

Clinical and laboratory features of all patients

Characteristics	Clear cell	Papillary	Chromophobe	Oncocytoma	AML	*P*-value
n	34	8	2	7	6	
Age, years (mean ± SD)	56 ± 2	56 ± 5	60 ± 7	60 ± 2	54 ± 2	0.781
Male, *n* (%)	18 (53)	5 (63)	2 (100)	2 (29)	2 (33)	0.394
Hypertension, *n* (%)	14 (41)	4 (50)	1 (50)	5 (71)	2 (33)	0.623
Diabetes, *n* (%)	6 (18)	0 (0)	0 (0)	3 (38)	1 (17)	0.714
BMI, kg/m^2 (mean ± SD)	31 ± 1	28 ± 2	32 ± 1	26 ± 2	25 ± 2	0.046
eGFR (mean ± SD)	85 ± 4	71 ± 12	74 ± 34	79 ± 6	95 ± 9	0.326
Tumor size (mean ± SD)	2.3 ± 0.2	2.9 ± 0.3	2.7 ± 1.1	2.2 ± 0.3	1.6 ± 0.3	0.093
Nephrometry score (mean ± SD)	7.4 ± 0.3	7.9 ± 0.6	6.5 ± 1.5	8.5 ± 0.8	6.5 ± 0.9	0.302