


Biomarkers to Screen for Renal Cell Carcinoma

ORIGINAL INVESTIGATION

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Purpose: To assess the diagnostic and predictive potential of urinary AQP1 and PLIN2 in renal cell carcinoma (RCC).

Methods: Two separate urinary markers, aquaporin 1 (AQP1) and perilipin 2 (PLIN2), were measured in a total of 720 patients with small renal tumors, among whom were a screening group of 30, a treatment group of 274, and a control group of 416.

Results: Of these patients, 58 patients with RCC had raised urinary AQP1 and PLIN2 levels compared with healthy controls, and 19 patients with pathologically confirmed RCC. Patients with known RCC had significantly higher AQP1 and PLIN2 levels than the controls or the screening population, with sensitivities and specificities in the 90% range compared with the screening population and approaching 100% compared with healthy controls. Notably, the sensitivity and specificity of the combination of biomarkers was not different from those of the individual markers. In addition, of the 720 screened patients who had elevated AQP1 and PLIN2 levels and on computed tomography were found to have a renal mass, 2 of which were confirmed RCC.

Morrissey et al2 are to be commended for their efforts to validate clinically meaningful biomarkers in this setting. There are 2 separate but equally important aspects to this work. The first is whether these biomarkers can be applied to a general population to screen for RCC, and the second is whether these biomarkers could be used in the management of SRMs. Regarding the first, the important question for any biomarker to be used in a screening setting is whether it can detect clinically meaningful cancers. Several decades after the introduction of prostate-specific antigen (PSA), the utility of this biomarker to detect lethal prostate cancer is still debated, and overtreatment of nonlethal prostate cancer is a significant clinical issue. Of note, of the 3 screening patients discovered to have a renal mass in the setting of high urinary biomarker levels, 2 had small, low-grade clear cell tumors (grade 2, pathologic stage T1a) and 1 patient died, presumably of non-RCC-related causes. Thus, the lethality of RCC tumors detected by these urinary biomarkers is not supported by the current data. Another overriding issue with any screening modality for RCC is the relatively low incidence in the general population (20-25 new cases per 100,000 population per year) and obligatory concerns about cost-effectiveness. In this setting, any proposed test must be almost 100% specific to avoid an unacceptably high false-positive rate, which would lead to unnecessary, expensive, and potentially harmful diagnostic or therapeutic procedures. The utility of these biomarkers may be enhanced by application to target populations at higher risk for RCC, such as those with a known or suspected inherited RCC syndromes, smokers, or patients with acquired renal cystic disease associated with end-stage renal failure. Renal ultrasonography could be complementary in these settings as a secondary screening modality for patients with elevated urinary biomarker levels.

The second and perhaps more immediately clinically relevant application of these urinary markers would be in the care of patients with known SRMs. Such patients can present a dilemma regarding which masses will be potentially lethal in the patient’s lifetime and which can be safely observed, since no current clinical features are associated with aggressive growth kinetics. Previous work from Morrissey and colleagues6 demonstrated that urinary AQP1 and PLIN2 levels were significantly higher in patients with clear cell and papillary RCC compared with benign renal tumors including oncocytoma and angiomyolipoma. However, while current and previous data show a correlation with renal tumor size, there is no association of these markers with tumor grade, which is equally if not more important in determining risk of progression and metastases.7 It is conceivable that information regarding 1 or both of these markers could be used in conjunction with imaging characteristics and potentially renal mass biopsy findings to guide SRM management. This will require prospective study but is potentially valuable, especially if AQP1 and PLIN2 measurement are able to obviate the need for biopsy or reduce the frequency of imaging in certain cohorts of patients.

In conclusion, elevated urinary AQP1 and PLIN2 levels are associated with the presence of RCC and have potential utility in both general population screening and SRM management settings. Further investigation, however, with more robust numbers of patients with SRMs and independent, prospective evaluation will be required to validate these findings and define the ultimate utility of these biomarkers.

References:


ARTICLE INFORMATION

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Conflict of Interest Disclosures: None reported.