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Title

Plasma glycosaminoglycan scores in early stage renal cell carcinoma

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Introduction & Objectives

No diagnostic blood biomarker for RCC is currently used in the clinical routine. Using a systems biology approach, we previously developed a score based on circulating glycosaminoglycans (GAGs) that detected metastatic clear cell renal cell carcinoma (RCC) with 92.6%, 93.7%, and 100% accuracy vs. healthy subjects using either plasma, urine, or combined measurements in a validation cohort (Gatto et al., 2016, Cell Reports). It is still unknown if this test is accurate in early stage RCC or other RCC histologies. The primary endpoint of this study was the area-under-the-curve (AUC) in the use of plasma GAG scores to detect pre-operative RCC, any stage and any histology, versus healthy individuals.

Materials & Methods

Sample collection was retrospective. Eligibility criteria were: patients with radiographic finding of renal mass; healthy volunteers without any history of malignancy. Participants were enrolled as a consecutive series at the Memorial Sloan Kettering Cancer Center, New York City, United States between 2011 and 2014. Plasma samples were collected in EDTA-coated tubes up to 4 weeks before nephrectomy. A convenience sub-cohort was followed longitudinally and samples were collected during follow-up visits up to 12 months after nephrectomy. A group of samples from healthy subjects was formed using plasma collected among relatives of cancer patients or available in previously stored samples. Laboratory measurements of GAGs was performed using capillary electrophoresis with laser induced fluorescence. Samples were scored according to the previously published formula to compute plasma GAG scores. Pre-specified variations of this formula were: omission of total chondroitin sulfate concentration; omission of heparan sulfate terms; omission of both.

Results

In total, we collected 470 samples from 237 subjects with a radiographic finding of renal mass and 44 samples from as many healthy volunteers. We report interim analysis of GAGs in the 25 stored samples from healthy volunteers and in 195 randomly selected samples from subjects with a renal mass. Of these, 71 were obtained pre-operatively from patients with subsequent pathologic diagnosis of RCC. Fifty had clear cell RCC (25 Stage I, 1 Stage II, 21 Stage III, and 3 Stage IV), while 21 had non-clear cell RCC (14 Stage I, 3 Stage II, 2 Stage III, and 1 Stage IV, 1 NA). The AUC in the detection of RCC, any stage, any histology, versus healthy was 0.866 (95% CI: 0.796-0.937), 0.883 (CI: 0.814-0.954), 0.999 (CI: 0.996-1), and 0.947 (CI: 0.903-0.991) using, respectively, the original plasma GAG score, or the variations without total chondroitin sulfate concentration, without any heparan sulfate terms, or without either.

Conclusions

Interim analyses revealed that plasma GAG scores have the potential to differentiate samples from RCC versus healthy subjects with remarkable AUC, ranging 0.866 to 0.999 depending on the different formula variations.