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Detection of urothelial carcinoma using selected urine-DNA methylation biomarkers in patients with gross hematuria: A prospective, single-center study





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Background

- Hematuria is the most common symptom of urothelial carcinomas (UC) but is often idiopathic.
- Cystoscopy is expensive which involves considerable patient discomfort, and conventional urine cytology for non-invasive UC detection and disease monitoring suffers from poor sensitivity.
- Previously, we identified that the methylation status of CDH1, HSPA2, RASSF1A, GDF15, BRCA1, THBS1 and TMEFF2 in tissue samples was associated with tumor stage, grade and lymph node status in upper tract urothelial carcinomas (UTUC).

Objective

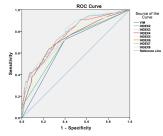
 We aim to evaluate the performance of genes selected from a previous study in detecting UC especially among patients with gross hematuria, as well as UTUC and bladder carcinoma separately, in voided urine samples.

Methods

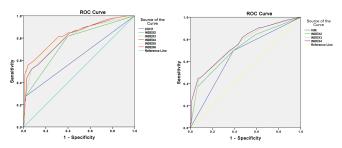
 Using methylation-sensitive PCR, we examined the promoter methylation status of ten genes in voided urine samples among 473 patients at our institution, including 217 UC patients and 256 control subjects.

Results

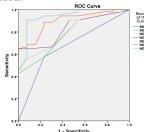
 The final combination of VIM, CDH1, SALL3, TMEFF2, RASSF1A, BRCA1, GDF15 and ABCC6 identified UC with a sensitivity of 0.83 and a specificity of 0.60.



- · Receiver operating characteristic curves for the urinary biomarkers in urothelial carcinomas
- · A panel of selected genes (CDH1, HSPA2, RASSF1A, TMEFF2, VIM and GDF15) identified UTUC with a sensitivity of 0.82 and a specificity of 0.68.
- A panel of selected genes (VIM, RASSF1A, GDF15 and TMEFF2) identified bladder carcinoma with a sensitivity of 0.82 and a specificity of 0.53.



 Receiver operating characteristic curves for the urinary biomarkers in upper tract urothelial carcinomas (left) and bladder carcinoma (right). Remarkably, a different panel (CDH1, SALL3, THBS1, TMEFF2, VIM and GDF15) identified UC in patients with gross hematuria with 0.89 sensitivity and 0.74 specificity, and sensitivity (0.91) and specificity (0.92) could be achieved when cytology was included.



 Receiver operating characteristic curves for the urinary biomarkers among patients with gross hematuria.

Conculusions

 The selected urine-DNA methylation biomarkers are reliable, non-invasive, and cost-effective diagnostic tools for bladder carcinoma and UTUC, especially among patients with gross hematuria.

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