Urinary tissue inhibitor of metalloproteinase 1 as a novel biomarker to identify men with clinically significant prostate cancer.

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Background: The overdetection and overdiagnosis of low-risk prostate cancer (PCa) has become a major clinical consideration. In this study, we evaluate the ability of urinary tissue inhibitor of metalloproteinase 1 (uTIMP1) to discriminate between men with low-risk or no PCa from those with clinically-significant disease.

Methods: 159 urine samples were collected from men with PCa, along with 41 samples from men with no PCa. These samples were subjected to ELISA for quantification of uTIMP1. Western blots were performed to visualize uTIMP1 levels. Immunohistochemistry was done to observe TIMP1 expression in human prostate tissue. Results were compared between age- and sex-matched groups through univariate and multivariate analyses.

Results: uTIMP1 is significantly decreased in men with PCa Gleason score ≥7 compared to men with Gleason score 6 or no PCa. The median value of uTIMP1 in men with Gleason ≥7 PCa was 0.95 ng/mL, and that for men with Gleason 6 or no PCa was 1.65 ng/mL ($P < 0.0001$). This decrease was observed by Western blotting and immunohistochemistry. Receiver operating characteristic analysis for uTIMP1 showed an area under the curve (AUC) of 0.727, which was significantly higher than that for PSA (AUC = 0.677).The addition of PSA to uTIMP1 improved the model's predictive ability with an AUC of 0.807.

Conclusions: We report the ability of uTIMP1 to identify men with clinically-significant PCa, and discriminate them from men with low-risk or no PCa. The application of uTIMP1 as a biomarker may help reduce the number of low-risk PCa cases detected in the clinic.

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