

Urinary MMP-9 activity is an independent marker of poor survival in bladder cancer

Offersen BV, Knap MM, Horsman MR, Verheijen J, Hanemaaijer R, Overgaard J. (2010). Matrix metalloproteinase-9 measured in urine from bladder cancer patients is an independent prognostic marker of poor survival. *Acta Oncol.* 49(8):1283-7. <http://www.ncbi.nlm.nih.gov/pubmed/20184870>

Abstract

INTRODUCTION: Matrix metalloproteinase 9 (MMP-9) is an endopeptidase involved in various cellular processes, such as tumour development and metastatic spread. In biological samples, MMP-9 can occur as pro-MMP-9 and active MMP-9, or these factors complexed with the inhibitor TIMP-1. An assay, which can measure active and total MMP-9 in biological samples, has been used on the urine from bladder cancer patients and demonstrated a significant correlation between MMP-9 and clinical parameters. The prognostic value of these measurements has never been investigated. Using this assay we have investigated the prognostic influence of total and active MMP-9 in urine from bladder cancer patients.

MATERIAL AND METHODS: Fresh voided urines from 188 consecutive patients diagnosed with bladder cancer were collected and frozen at diagnosis. After 15 years follow-up 13 patients were still alive, and 175 patients had died. MMP-9 was measured with an immunocapture activity assay.

RESULTS: Median MMP-9(total) was 173.7 units/10 g creatinine (range 0-34 792), and median MMP-9(active) was 14 units/10g creatinine (range, 0-294 757). The two factors were correlated (Spearman's rho 0.74, $p < 0.0001$). High MMP-9(total) and MMP-9(active) were significantly correlated with large tumour size and poor malignancy grade. Increasing tertiles of MMP-9(total) and MMP-9(active) were associated with poor overall survival ($p < 0.0001$ and $p = 0.003$, respectively). A Cox multivariate analysis using death as endpoint identified high tertiles of MMP-9(total) as independent prognostic markers with a relative risk 2.25 (95% confidence interval, 1.53-3.30).

CONCLUSION: MMP-9 measured in urine from bladder cancer patients was a strong independent prognostic marker of poor survival. This is the first time high levels of MMP-9 measured in urine from bladder cancer patients have been linked to poor prognosis. This may reflect MMP-9 playing a role in tumour invasion and metastasis. It may be possible to non-invasively measure tumour response to therapy and identify possible tumour recurrence in an early phase.