Letter to the Editor


In looking for new urinary markers for bladder cancer (1, 2), an article on MMP-2 and -9 published in this journal is of great interest. Using recently introduced commercially available MMP-2 and MMP-9 specific activity assays, Sier et al. (3) studied urine MMP-2 and MMP-9 excretion of superficial bladder carcinoma patients compared with patients with high-invasive tumors and healthy controls. The authors found increased concentrations of MMP-2 and MMP-9 in urine of bladder cancer patients. According to their results, urinary MMP-9 was elevated even in the early-stage bladder carcinoma. Because we have carried out similar measurements, we would like to add some comments on their findings to complement the data and conclusions of Sier et al. (3).

In our investigation, we used similar activity assays for MMP-2 and MMP-9 (Amersham Pharmacia Biotech, Little Chalfont, United Kingdom; cat. no. RPN 2630 and RPN 2631). In contrast to Sier et al. (3), we measured only the total MMP-2 and MMP-9 and did not distinguish between active and latent forms of both enzymes. The study population included a group of 71 bladder cancer patients, 42 healthy controls, and a group of 14 cystitis patients. MMP values were corrected for urine creatinine concentration. Fig. 1 summarizes the results.

The upper reference limits were determined as nonparametric 95% percentiles. The corresponding limits were 3.0 μg/g creatinine for MMP-2 and 9.2 μg/g creatinine for MMP-9.

In accordance to Sier et al. (3), urinary MMP-2 and MMP-9 were increased in bladder cancer patients compared with controls (Fig. 1). However, our data give additional information that in part differ from the results of Sier et al. (3): (a) in comparison with the controls, MMP-9 excretion was significantly increased in urine of cystitis patients (P < 0.05), whereas MMP-2 was not elevated in these patients (Fig. 1). Sier et al. (3) preferred MMP-9 instead of MMP-2, but, as our data have shown, inflammation should be considered as determinant of increased MMP-9 excretion. (b) MMP-2 and MMP-9 excretions were mainly elevated in bladder cancer patients with muscle-invasive tumors (stages T2–T4) but not with noninvasive tumors (stages Ta and T1). With regard to the tumor grade, only 1 of 11 patients with tumor grade G1, but 8 of 28 with tumor grade G2, and 16 of 32 with tumor grade G3 showed MMP-2 excretions values above the cutoff. For MMP-9, 3 of 11 patients with G1 tumors, 10 of 28 patients with G2 tumors, and 20 of 32 with G3 tumors had increased excretion rates.

In conclusion, we draw the clinician’s attention to these two aspects for utilizing urinary MMPs in bladder cancer diagnosis in order avoid false hopes in these new markers.

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References

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2 The abbreviation used is: MMP, matrix metalloproteinase.

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Fig. 1. Excretion of MMP-2 (A) and MMP-9 (B) in urine of controls, cystitis patients, and bladder cancer patients. All of the values were corrected for urine creatinine concentration. The study included 43 controls, 14 cystitis patients, 43 bladder cancer patients with stage Ta and T1, 18 patients with stage T2, and 10 patients with stage T3 and T4. Median values of the respective groups are shown as horizontal lines. The nonparametric 95% upper percentile as cutoff is given as dotted line. Significant differences between patient groups and controls (Kruskal-Wallis nonparametric ANOVA) are indicated: a, \( P < 0.05 \); b, \( P < 0.001 \). Significant differences between carcinoma patients are marked with brackets.

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