Null Results in Brief

Serum Macrophage Migration Inhibitory Factor Is Not Elevated in Patients with Prostate Cancer

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Introduction
Prostate cancer (PCa) is the most common neoplasia in men in the Western world. There have been many efforts to detect this malignancy in early stages. Prostate-specific antigen (PSA) has been established as the most valuable tool for that purpose. Because PSA is an organ but not a tumor-specific marker, increased serum PSA is also found in benign prostatic hyperplasia (BPH). Using the conventional PSA cutoff of 4 μg/liter as discrimination limit between cancer and nonmalignant prostatic diseases, false-positive findings of 65% are observed. Thus, new biomarkers and multivariate evaluation procedures of data are needed to facilitate the differentiation between PCa and BPH to prevent unnecessary biopsies (1).

Recently, serum macrophage migration inhibitory factor (MIF) has been recommended as potential biomarker of PCa (2). On the basis of these hopeful results, we conducted a case-control study testing the possibility to include this variable (2). On the basis of these hopeful results, we conducted a case-control study testing the possibility to include this variable into our recently developed artificial neural network with free PSA (3).

Materials and Methods
This study was carried out from a population of 511 men who was initially selected between 1999 and 2002 for a study on the diagnostic usefulness of artificial neural network in PCA diagnostics and was described in detail previously (3). It included 175 patients with PCa (cases; mean age ± SD, 64.0 ± 6.4 years), 250 patients with BPH (67.8 ± 7.6 years), and 86 men with no prostatic pathology (56.4 ± 12.9 years) as controls. Archived (at −80°C) and unthawed serum samples were used. The study was performed in accordance with the ethical standards of the Helsinki Declaration and was approved by the local ethical board of the hospital.

Serum MIF was determined by using an ELISA (R&D Systems, Minneapolis, MN). The interassay coefficient of variation was 12.5%. Total and free PSA were measured with the IMMULITE PSA kits (Diagnostic Products Corp., Los Angeles, CA).

Results
The serum MIF concentrations of both control groups, of healthy men and BPH patients, were Gaussian distributed and did not differ (Table 1). In contrast to the results of Meyer-Siegler et al. (2), we found a decreased mean value of MIF in PCa patients compared with the BPH control group. The concentrations extremely overlapped between the two groups. Taking into account the stage and grade of the PCa, subgroup analyses of the cases were performed in comparison with the BPH control group (Table 1).

Statistical Power.
With 175 cases (PCa patients) and 250 controls (BPH patients), there is ~85% power at a 5% significance level to detect a mean MIF difference of 300 ng/liter. The power to detect differences between the subgroups and the BPH controls is given in Table 1.

Study Limitations.
Both analytical problems and the limited sample size in some subgroups were potential limitations of this study. As we used the same ELISA as Meyer-Siegler et al. (2) and obtained comparable MIF concentrations, analytical problems could be excluded as reasons for the discrepancies between the two studies. In addition, there is little reason to expect that a higher sample size of some subgroups would lead to increased values as observed by Meyer-Siegler et al. (2) in opposite to the rather decreased MIF values found in our study.

Discussion and Conclusions. MIF is an ubiquitously expressed cytokine with varied functions, including induction of cell proliferation, angiogenesis, and inhibition of tumor suppressor genes (4). In prostatic cancer tissue, MIF mRNA is overexpressed, whereas MIF protein levels are decreased (2, 5). Meyer-Siegler et al. (2) found increased MIF concentrations in patients with PCa compared with controls and BPH patients. In contrast to that data, we were not able to document increased values. We found decreased MIF values. Because the MIF concentrations overlapped between the PCa and BPH patients, there was no support for the hypothesis that the use of serum MIF as a single marker could improve the differentiation between PCa and BPH. At the moment, we could not yet explain...
these discrepancies between the two studies. However, before a final answer regarding any lack of association between increased MIF in prostatic cancer tissue and decreased serum MIF in PCa patients can be given, other studied should be carried out.

References


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