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European Association of Urology

Words of Wisdom

Re: The Metabolites Citrate, Myo-Inositol, and Spermine Are Potential Age-Independent Markers of Prostate Cancer in Human Expressed Prostatic Secretions

Serkova NJ, Gamito EJ, Jones RH, O'Donnell C, Brown JL, Green S, Sullivan H, Hedlund T, Crawford ED

Prostate 2008;68:620–8

Expert's summary:

Using nuclear magnetic resonance (NMR) spectroscopy, metabolite profiles of expressed prostatic secretions (EPS) from patients with prostate cancer were compared with those from healthy controls. Among the metabolites measured, citrate, spermine, and myo-inositol showing 2–3 times lower concentrations in patients were most predictive of prostate cancer. The areas under the receiver operating characteristic (ROC) curves were 0.89, 0.87, and 0.79 with specificities of 74%, 51%, and 34%, respectively, at the cut-off points for 90% sensitivity. The authors suggested the analytes as potential markers of prostate cancer.

Expert's comments:

The areas under the ROC curves for the metabolites were higher than those for prostate-specific antigen (PSA) and corresponding derivatives generally reported in the literature. Thus, the conclusion of the authors concerning the diagnostic potential of those analytes seems to be justified, although they did not compare metabolites and PSA. Otherwise, since EPS is a rather unsuitable specimen for routine use, I believe that more important than these results is the forward-looking approach of metabolite profiling to discover new analytes characteristic of prostate cancer and to use them for improving the diagnostic range beyond PSA measurements.

Several aspects for future research in this field should be considered. First, it would be necessary to examine whether the mentioned metabolites are also discriminative markers in urine after digital rectal examination (DRE). For that purpose, a standardized DRE protocol as applied in recent studies on prostate cancer antigen 3 (PCA3) would be necessary [1]. Second, a more detailed metabolite profiling of prostate cancer tissue samples should be established for better selecting specific metabolites for prostate cancer. More sensitive mass-spectrometry methodologies, rather than the NMR technology as employed in this study, should be applied [2]. Through use of a combined liquid and gas chromatography-based mass-spectrometry approach, about 600 metabolites were recently identified in the prostate cancer tissue and about 300 of those were also detected in urine of these patients (AM Chinnaiyan, personal communication). That study proved that sarcosine in post-DRE urine discriminated between positive and negative prostate cancer biopsies and might be an indicator of aggressive forms of prostate cancer. Third, in post-DRE urine, potential discriminative metabolites should be simultaneously measured and compared with markers on mRNA or DNA bases that were recently recommended because of their outperformance against serum PSA [2–4].

In conclusion, cancer-related metabolites alone or combined with other markers measured in post-DRE urine can be expected to become promising tools to avoid unnecessary biopsies in prostate cancer diagnostics.

Conflicts of interest: The author has nothing to disclose.

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Re: A 5-Year Follow-Up Study of Asymptomatic Men with Testicular Microlithiasis

DeCastro BJ, Peterson AC, Costabile RA

J Urol 2008;179:1420–3

Expert's summary:
In 2001, this group published a 5.6% prevalence (84 patients) of testicular microlithiasis (TM) within an ultrasound screening population of 1504 healthy volunteers between the ages of 18–35. The recent paper reports the incidence of testis cancer (TC) during further follow-up. Only one TC occurred 64 mo after the screening round among the 63 TM patients who could be followed for >5 yr and who had no risk factors for TC (1.6%). Seventy percent, or 1.4 million euro, of the money spent for treating urological diseases in the United States per year would be necessary to identify one TC by screening TM patients. Follow-up was estimated as not cost-effective with questionable outcome. The authors recommend improving education in testicular self-examination for men with TM or who are at risk for TC.

Expert's comments:
This paper is the only one on screening for TM with long-term follow-up in the age group at risk for TC. TM as an incidental finding increases secondary to advances in ultrasound technology and causes anxiety among patients and confusion among physicians. Coincidence of TC and TM and testicular cancer risk is of major concern. Recommendations on management of TM and intensity and usefulness of follow-up are controversial. Furthermore, TM is not mentioned in any of the testicular cancer guidelines.

Data on follow-up are given in nine studies reporting on a total number of 23 100 patients of all ages. Incidence of TM in these mainly referred patients was 2.8% worldwide, with regional differences: 1.26% in Europe, 6.2% in the United States, and 6.75% in Asia. Only six tumours were observed in 343 TM patients followed for approximately 40 mo (1.75%) [1–4]. An additional 800 sonograms were performed in children in the United Kingdom. TM was found in 1.3%, and no tumours occurred during follow-up [5]. TC with concomitant TM was found in 15% (6–46%) and testicular intraepithelial neoplasia (TIN) with bilateral TM in 20%. TM is frequently seen in association with cryptorchism, inflammation, torsion, small testes, and infertility [1], probably as part of the testicular dysgenesis syndrome (TDS), as defined by Skakkebek and coworkers.

Arguments against TM as an independent risk factor for TC include the fact that tumours and surrounding TM were only found within the typical tumour ages and associated with other predisposing factors. African Americans showed the highest prevalence of TM (14%) but the lowest prevalence of TC. Only a few TM patients will develop tumours, mostly Stage I with excellent cure rates.

Regular self-examination seems to be most effective to identify TC. Recommendations on TM should be part of the guidelines.

Conflicts of interest: The author has nothing to disclose.

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