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Correspondence

CORRESPONDENCE

RE: Risk of Prostate Cancer in Men Treated With 5α-Reductase Inhibitors—A Large Population-Based Prospective Study

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I read with interest the recent Journal article by Wallerstedt et al. (1) analyzing the influence of 5α-reductase inhibitors (5-ARI) on prostate cancer risk in men treated for lower urinary tract symptoms. After six to eight years of treatment, there was a 69% reduction in the overall risk of prostate cancer, a 74% reduction in Gleason 7 disease, but no statistically significant change in the risk of Gleason 8–10 disease. These results are certain to attract the attention of many physicians who have been reluctant to use 5-ARI because of concerns about high-grade cancers.

I write to express concern about the interpretation of these results and question whether these findings truly represent a decrease in the risk of prostate cancer. The Prostate Cancer Prevention Trial was a large, seven-year, randomized placebo-controlled trial that evaluated the effect of finasteride 5 mg/day on the prevention of prostate cancer (2). During the first seven years, men who had an abnormal digital rectal examination or PSA (corrected for the effect of the drug) underwent annual biopsies. In the initial report, after seven years of these annual biopsies there was a 25% reduction in the prevalence of the disease (2). However, when the FDA reanalyzed the data, they reduced that estimate to 14% (3). Furthermore, there was no reduction in Gleason 7–10 disease. Why are these results so different from the findings in the article under discussion? The authors hint at the reason—"there was no predefined indication for prostate biopsy"—but do not discuss it.

There is no 5α-reductase enzyme in normal or malignant prostatic epithelial cells; it is located in the stroma. Because higher-grade cancers (Gleason >6) have little stroma, 5-ARI have no effect on Gleason 7–10 disease. Treatment with a 5-ARI reduces the production of PSA by the stroma in benign prostatic hyperplasia. To correct for this effect, men treated with a 5-ARI must multiply their level by 2.0 for the first two years, by 2.3 for years 2 to 7, and after year 7 by 2.5 (4). If patients do not know this, they do not realize they may need a biopsy and will not be diagnosed with cancer, even high-grade disease. Furthermore, a recent study reported that Swedish men with elevated PSA levels are unlikely to undergo further testing (5). This would explain why the results in this study are so different: Treatment with a 5-ARI prevented biopsies, but not cancer.

If my concerns are true, this means that the 74% "reduction" in Gleason 7 disease indicates that three-quarters of men with clinically significant cancers do not know about their risk. In the last paragraph of the article the authors correctly stated that "men treated with 5-ARI had a reduced risk of being diagnosed with prostate cancer" but elsewhere in the article, including the title, only the words "risk of prostate cancer" were used. In my opinion, this is misleading and dangerous advice to give to readers who should understand the severe limitations inherent in this study. I sincerely believe this should be rectified.

Notes

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The author has no conflicts of interest to disclose.

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