Conclusions: The currently used AS criteria performed significantly better for patients aged < 70 years. The authors concluded that the current results should be taken into account when deciding whether to offer active surveillance to patients with low-risk PCa.

Editorial Comment

The major issue related to an initial surveillance policy is the possibility of losing the window of curability of the disease, and this is directly related to patients' life expectancy according to their comorbidity profile and disease natural history that are very heterogeneous and unpredictable, in part due to the misclassification of patients regarding these variables.

Previous studies suggest an association between age and prostate cancer aggressiveness, this study though retrospective and not including patients under active surveillance, highlights that older patients are affected more frequently by more aggressive disease at final pathology compared with their younger counterparts, even when they are affected by very-low-risk disease according to the criteria proposed by van den Bergh et al. and Carter et al..

In this context, mortality should be considered as the main outcome in future confirmatory studies and while older patients are typically encouraged to undergo active surveillance due to virtually shorter life expectancy, better tools predicting life expectancy and disease natural history are warranted.

Dr. Leonardo Oliveira Reis
Assistant Professor of Urology
University of Campinas, Unicamp
Campinas, São Paulo, Brazil
E-mail: reisleo@unicamp.br

Association of Clinical Benign Prostate Hyperplasia with Prostate Cancer Incidence and Mortality Revisited: A Nationwide Cohort Study of 3 009 258 Men

Orsted DD, Bojesen SE, Nielsen SF, Nordestgaard BG
Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, Faculty of Health Sciences, University of Copenhagen, Denmark

Background: Although benign prostate hyperplasia (BPH) and prostate cancer (PCa) share features such as hormone-dependent growth and response to treatment with antiandrogen therapy, BPH is generally not considered a premalignant lesion.

Objective: To determine whether clinical BPH is associated with an increased risk of PCa incidence and mortality.

Design, Setting, and Participants: Using designs with individual participant data from five national registries, we studied the entire Danish male population from 1980 through 2006, a total of 3 009 258 Danish men. We collected PCa diagnoses (n = 53 315), information on PCa mortality (n = 25 459), and ascertained clinical BPH (not histologically proven BPH) through hospitalization (n = 187 591) and/or surgery (n = 77 698) from 1980 to 2006 and the use of α-adrenergic receptor antagonists (n = 143 365) and/or the use of 5α-reductase inhibitors (5-ARIs) (n = 47 465) from 1995 to 2006.

Measurements: PCa incidence and mortality was assessed for each category of clinical BPH using Kaplan-Meier plots of cumulative incidence and Cox proportional hazard ratios (HRs) adjusted for potential confounders.

Results and Limitations: For the entire cohort studies, multivariate-adjusted HRs for PCa incidence were 2.22 (95% confidence interval, 2.13-2.31) in men hospitalized and 3.26 (3.03-3.50) in men operated on for clinical BPH versus general population controls. Corresponding HRs for PCa mortality were 2.00 (1.91-2.08) for hospitalization and 7.85 (7.40-8.32) for surgery. For age-matched cohort studies, corresponding HRs for PCa incidence were 3.04 (2.96-3.13) for hospitalization, 2.60 (2.47-2.73) for surgery, 4.49 (4.33-4.65) for α-adrenergic receptor antagonist use, and 2.54 (2.40-2.68) for 5-ARI use. Each category of clinical BPH has limitations, but limitations differ between the categories and therefore are unlikely to explain the results.

Conclusions: In Danish men followed for up to 27 yr, clinical BPH was associated with a two- to three-fold increased risk of PCa incidence and with a two- to eight-fold increased risk of PCa mortality. These data should not be used to infer causality.

Editorial Comment

This is a provocative study focusing on diagnosis and mortality, drawn from multiple nationwide registries including local causes of civil death registry and register of medicinal products statistics. All included patients have in common the final diagnosis through hospitalization and/or prescription for treatment, both utilized for registration only, all the previous heterogeneous circumstances are ignored. General population tends to be under diagnosed and under treated compared to medicated and hospitalized patients.

Selection and surveillance biases due to increased disease awareness and co-diagnosis are impossible to be excluded in this scenario of population-based study, which should not be used to infer causality as stated by authors. There are lots of similar examples of possible misinterpretations of huge collected data. The same phenomenon occurs to the risk of prostate cancer that increased markedly after the introduction of PSA testing, with a concurrent elevation in total mortality after prostate cancer diagnosis. Is PSA test related to prostate cancer incidence and mortality? Or is it related to awareness, diagnosis, and registry?

As well recognized by authors, due to the possible effect of other factors, additional studies with detailed information on PSA testing, analysis of biopsies, number of biopsies, number of visits to a urologist, number of digital rectal examinations, familial risk of prostate cancer, and staging of prostate cancer, among others are warranted and the current type of study does not allow us to use the word "risk" which should be avoided and changed by "diagnosis", "awareness", "report" or "registry" to prevent misinterpretations - rendering the dispassionate final title: "Association of Clinical Benign Prostate Hyperplasia with Prostate Cancer Diagnosis Report and Mortality Registry Revisited: A Nationwide Cohort Study of 3 009 258 Men".

Dr. Leonardo Oliveira Reis

Assistant Professor of Urology
University of Campinas, Unicamp
Campinas, São Paulo, Brazil
E-mail: reisleo@unicamp.br