Atrophy in prostate needle biopsy cores and its relationship to prostate cancer incidence in screened men

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Objectives: To evaluate whether the incidence of atrophy reported on sextant biopsies is associated with subsequent prostate cancer detection and to obtain a more thorough analysis of the different categories and extent of atrophy, we performed a review of benign biopsy cores.

Methods: In the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer, 4117 and 1840 men underwent sextant biopsy in the first and second screening round (4-year interval), respectively. Sextant biopsy was prompted by elevated prostate-specific antigen levels. For review, randomly taken benign sextant biopsies (n = 202) with a follow-up of at least 8 years were chosen.

Results: Before review, atrophy was reported in the biopsies of 11.4% and 8.7% of the first and second round, respectively. The prostate cancer incidence during 8 years of follow-up after an initial diagnosis of atrophy was 10.4%, which was not significantly different than the 12.3% of cancers detected after a benign diagnosis without reference to atrophy. After review, the incidence of simple atrophy, post-atrophic hyperplasia, and sclerotic atrophy in sextant biopsies was 91%, 47%, and 9%, respectively. Extensive atrophy was observed in 5% of biopsies. Only 2 men (4.7%) in the reviewed group had a subsequent diagnosis of prostate cancer in the 8 years of follow-up. Additionally, prostatic intraepithelial neoplasia was diagnosed in 3 men (7.0%) in the second screening round.

Conclusions: Atrophy, especially its simple form, is a very common lesion in prostate biopsy cores (94%). Atrophy in an asymptomatic population undergoing screening was not associated with a greater prostate cancer or prostatic intraepithelial neoplasia incidence during subsequent screening rounds.

Editorial Comment
Prostatic atrophy is one of the most frequent histologic mimics of prostatic adenocarcinoma. It occurs most frequently in the posterior lobe or peripheral zone and gained importance with the increasing use of needle biopsies for the detection of prostatic carcinoma. Chronic inflammation of longstanding duration has been linked to the development of carcinoma in several organ systems. In the prostate, chronic inflammation is associated with both hyperplastic atrophy (or postatrophic hyperplasia) and simple atrophy. De Marzo et al. (1) from Johns Hopkins propose combining these lesions into a category called proliferative inflammatory atrophy (PIA). The authors suggest that there are morphological transitions within the same acinar/duct unit, between high-grade prostatic intraepithelial neoplasia (HGPIN) and PIA which occur frequently. This finding supports a model whereby the proliferative epithelium in PIA may progress to GHPIN and subsequently to adenocarcinoma of the prostate.

This hypothesis is contested by others. In an autopsy study done by us, no association was found between atrophy and either HGPIN or histologic carcinoma (2). In a subsequent study also in autopsies, we did not find any association between atrophy with inflammation (PIA) and either HGPIN or histologic carcinoma (3). Anton et al. (4) studying radical prostatectomies concluded that hyperplastic atrophy (or postatrophic hyperplasia) is a relatively common lesion present in about one-third of prostates, either with or without carcinoma. The authors found no association between the presence of postatrophic hyperplasia and the likelihood of cancer and no topographic association between postatrophic hyperplasia and prostate foci.
The findings of Postma et al. of the present survey, are similar to Bakshi et al. (5). The latter authors studied 79 consecutive prostate biopsies: 54% of initial biopsies were benign, 42% of the cases showed cancer, and 4% HGPIN or atypia. Postatrophic hyperplasia was seen in 17% of benign initial biopsies with available follow-up. Of these, 75% had associated inflammation. There was no significant difference in the subsequent diagnosis of prostate cancer for groups with postatrophic hyperplasia, partial atrophy, atrophy, or no specific abnormality. The authors conclude that the subcategories of atrophy do not appear to be associated with a significant increase in the risk of diagnosis of prostate cancer subsequently.

References

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Incidence and follow-up of patients with focal prostate carcinoma in 2 screening rounds after an interval of 4 years
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Background: Focal carcinoma detected by needle biopsy has been a common finding since prostate-specific antigen (PSA)-based screening was introduced. Clinicopathologic features in patients with focal prostate carcinoma who underwent radical prostatectomy (RP) or who were treated with watchful waiting (WW) were analyzed to detect clinical predictors for disease progression during follow-up.

Methods: Patients were selected from the European Randomized Screening study for Prostate Cancer. Focal carcinoma on sextant biopsy was defined as ≤ 3.0 mm involvement by tumor in 1 biopsy core lacking Gleason pattern 4 or 5. PSA doubling time was used in the WW group as a marker of disease progression.

Results: The proportion of patients with focal prostate carcinoma increased significantly from 16% in the first screening round to 29% in the second screening round. One hundred eighteen men underwent RP, and 108 men were treated with WW. The median tumor volume was 0.13 mL. PSA level and prostate volume were predictive for tumor volume in a multivariate regression analysis. A PSA density cut-off level of ≤ 0.1 ng/mL/cm³ predicted organ-confined tumor (< 0.5 mL) in 94% of patients.
Positive surgical margins were predictive for PSA recurrence. Four patients in the RP group had PSA recurrence at follow-up. PSA doubling times < 2 years, < 3 years, and < 4 years were noted in 4.9%, 14.6%, and 22.0% of patients in the WW group, respectively.

Conclusions: The median tumor volume was small (0.13 mL). A comparison between PSA recurrence in the RP group and PSA doubling time in the WW group showed a significantly more favorable outcome after RP if a PSA doubling time of < 3 years or < 4 years was chosen as a marker for disease progression in the WW group. A WW policy with delayed curative intent may be recommended in patients ages 55-75 years with focal carcinoma and PSA density < 0.1 ng/mL/cm³.

Editorial Comment

“Minimal” or “insignificant” refers to a low-grade, organ confined cancer < 0.5 mL in a surgical specimen of radical prostatectomy. It must be emphasized that it does not mean “latent”, “dorment” or “indolent” cancer but a low-volume incipient neoplasia that can progress either as an latent or clinical carcinoma. Unfortunately there is no known marker for biologic behavior of prostatic cancer.

Postma et al. propose some criteria on needle biopsies to predict these minimal cancers: focal carcinoma on sextant biopsy defined as ≤ 3 mm in length in only one core, no Gleason grade (pattern) 4 or 5, and PSA density cut-off level of ≤ 0.10 ng/mL. Using these criteria, the authors predicted 94% of patients harboring low-grade, organ confined < 0.5 mL tumors.

We have used the criteria proposed by Epstein et al. (1): needle biopsies with prostate carcinoma in fewer than 3 cores (from a 6-core biopsy sample), absence of Gleason grade (pattern) 4 or 5, no more than 50% prostate carcinoma involvement in any of these cores, stage T1c and PSA density < 0.15 ng/mL. Using these criteria, in 1994, the authors found that 79% of tumors with volume ≤ 0.5 mL were organ confined and did not qualify as high-grade lesions at the time of radical prostatectomy. Bastian et al. (2) from Johns Hopkins, applied these criteria in a series of 237 men with extended needle biopsies who had undergone radical prostatectomy for T1c disease between December 2000 and August 2003. According to the Epstein needle biopsy criteria, low-grade, organ-confined prostate carcinoma was detected in 91.6% of all patients.

The histologic criteria used by Bastian et al. and Postma et al. differ in two aspects: number of cores with carcinoma and the extent of core involvement. Postma et al. are more restrictive considering just one core involved and report the linear length of cancer. Epstein et al. consider a maximum of 2 cores involved and the percentage of involvement of the core. It seems to us that linear length is superior to the percentage of involvement: percentage varies according to the length of the core, unless is established a minimum length of the core for percentage evaluation.

References


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