Analysis of T1c prostate cancers treated at very low prostate-specific antigen levels
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Background: The Prostate Cancer Prevention Trial (PCPT) has challenged the validity of recommended prostate-specific antigen (PSA) thresholds for prostate biopsy (> 2.5 ng/ml) given the 17% prostate cancer (pCA) detection rate at PSA of 1.1-2.0. The outcome of patients treated at PSA < or = 2.5 is poorly defined, and advantages associated with such an early diagnosis are uncertain.

Objective: Compare the outcome of patients with T1c pCA with pretreatment PSA < or = 2.5 and 2.6-4.0.

Design, Setting, And Participants: Since 1998, 351 patients with clinical stage T1c and PSA < or = 4.0 have been treated at our institution; 84 (24%) of those patients had PSA < or = 2.5. Clinical information was obtained from a prospective database. Treatment was radical prostatectomy (RP), brachytherapy, and external-beam radiotherapy (EBRT) in 261 (74%), 67 (19%), and 23 (7%) patients, respectively.

Intervention: Definitive therapy for clinically localized pCA.

Measurements: Progression-free probability and pathologic end points.

Results and Limitations: No significant differences between the groups were observed in terms of biopsy (18% vs 22%) or specimen Gleason score 7-8 (44% vs 56%), non-organ-confined cancer (11% vs 13%), indolent cancer (34% vs 24%), or 5-yr progression-free probability (89% vs 93%; p>0.1 for all). More biologically unimportant cancers (defined as pathologically organ-confined and Gleason < or = 6) were identified among patients with PSA < or = 2.5 (55% vs 41%, p=0.050), and indolent cancers were three times more frequent than non-organ-confined cancers among these patients (p=0.003).

Conclusions: The pathologic features and outcome of patients treated at low PSA levels are favorable and similar for patients with PSA < or = 2.5 versus 2.6-4.0. However, > 50% of the former have potentially biologically unimportant cancer. We failed to identify a therapeutic benefit to the diagnosis of cancers below accepted PSA thresholds for biopsy.

Editorial Comment
The debate of lowering the threshold for biopsy in patients with a low PSA is still active and gets some support from this paper. The authors compare the results from two cohorts of patients with low PSA, namely < 2.5 ng/ml and 2.5-4 ng/ml. They did not find any significant differences between these groups but further data in this paper are of interest. Taken together both groups, 21% of these patients had biopsy Gleason sum scores 7 or 8, whereas 53% had specimen Gleason scores 7-8, again suggesting undergrading in biopsies. 12% had non-organ confined cancers and 12 % had positive surgical margins.

Altogether these and other data (e.g. from the PCPT trial) suggest that the threshold for performing biopsies is rather low and should include more factors than PSA alone.

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