Some investigators consider active surveillance (AS) a solution to the problem of overdiagnosis and overtreatment in men undergoing screening for early prostate cancer (PCa) [1]. Other authorities are less optimistic and emphasize the continuing uncertainties in this context [2]. In a study appearing in this issue [3], Wong and coworkers retrospectively studied 186 men who received at least two follow-up biopsies after being scheduled for AS. In this study, patients were eligible for AS when they fulfilled the following criteria: prostate specific antigen (PSA) ≤10 ng/ml, clinical tumor stage T2a or lower, no Gleason grade 4 or 5, three or fewer biopsy cores involved, and no biopsy core containing >50% cancer tissue. The median follow-up after the first follow-up biopsy was 41 mo. The authors found that an absence of cancer on the first follow-up biopsy during AS was associated with a decreased risk of volume-related disease progression but was not related to grade-related progression. They expressed the opinion that this fact must be considered during counseling of patients undergoing AS [3].

It is not surprising that patients selected by a negative first follow-up biopsy harbor lower-volume tumors, which are less likely to increase in volume considerably during a limited observation time period than those cancers that are detectable on first follow-up biopsy. The facts that grade-related progression was not predictable from the absence of cancer tissue in the first follow-up biopsy and that age was the only predictor of grade progression [3] may indicate that follow-up biopsies are of limited clinical significance in patients undergoing AS and do not sufficiently reflect the tumor biology.

Currently available data demonstrating the relative safety of watchful waiting or AS strategies are derived from highly selected samples with limited follow-up [4–7]. Selection affected not only the tumor-related risk criteria (enrichment of good risks) but also the risk of competing mortality (enrichment of poor risks). In series investigating deferred treatment in low-risk early PCa, competing mortality rates after 10 yr were twice [7] or even three times [3,5] as high as those seen in contemporary radical prostatectomy series [8–10]. The currently available data [4–7] allow AS to be considered relatively safe only in well-selected men with low-risk PCa (Gleason score <7 and PSA <10 ng/ml) and a high risk of medium-term competing mortality. With the currently available prognostic tools, it is impossible to reassure healthy patients or patients with non-low-risk disease, even if the latter were older or had moderate comorbidity putting them at an increased risk of medium-term competing mortality.

Primary strict and careful selection is the presupposition of the relative safety of AS strategies in men with early PCa. The study by Wong and coworkers [3] underscores this fact. Currently available surveillance strategies like PSA monitoring and follow-up biopsies do not work sufficiently well for discriminating long-term stable tumors from dangerously progressing tumors even in the first years of follow-up. No data are available for the very long time periods, counted in decades, that are in question for healthy and younger men diagnosed with early PCa.

Wong et al. [3] recommended consideration of the absence of cancer in the first follow-up biopsy during AS when counseling patients undergoing this treatment option. The way in which this counseling should be performed remains open. Probably the main message of this study [3] for the patient is the uncertain predictive value of early follow-up biopsies. This uncertainty should be communicated to patients prior to treatment decision.
making and preferably during counseling on undertaking PSA determination for early detection of PCa.

The differentiation between volume- and grade-related progression introduced by the authors of this study [3] certainly requires further investigation before use in daily practice. With the extremely short follow-up available, it is currently impossible to estimate whether such differentiation could be of clinical significance. In PCa in general, the prognostic impact of grade is clearly greater than that of tumor volume [11,12]. The clinical implications of this fact for the management of patients undergoing AS have been unknown. The 2013 update of the European Association of Urology guidelines [11] does not mention volume progression as a criterion to move from AS to active treatment. In contrast, the German S3 guidelines (updated in 2011 [12]) considered volume progression (involvement of ≥2 of 10–12 follow-up biopsy cores or ≥50% tumor involvement in 1 follow-up biopsy core) as a contraindication for further surveillance.

The study by Wong and coworkers [3] underscores the continuing uncertainties surrounding AS because of the lack of sufficiently powered prospective long-term studies. Enrolling patients selecting AS as a treatment option into multicentric follow-up databases and standardizing the follow-up regimens could fill some of this knowledge gap.

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References