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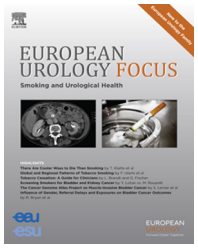

Review – Prostate Cancer

Approaches for Initial Prostate Biopsy and Antibiotic Prophylaxis

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Abstract

Context: Debate on the optimal technique to use as an initial prostate biopsy (PB) strategy is continually evolving.
Objective: To review recent advances and current recommendations regarding initial PB and antibiotic prophylaxis.
Evidence acquisition: A nonsystematic review of the literature was performed up to October 2014 using the PubMed and Embase databases. Articles were selected with preference for the highest level of evidence in publications within the past 5 yr.
Evidence synthesis: The decision to perform PB is still based on an abnormal digital rectal examination or increased prostate0specific antigen (PSA) level without clear consensus about the absolute cutoff. Several biomarkers have been suggested to improve PSA-based PB decision-making and minimize overdiagnosis and overtreatment. The random 12-core transrectal (TR) ultrasound-guided approach remains the standard-of-care technique for PB. A >12-core scheme may be considered as an alternative in a single patient given his clinical features (large volume, low PSA levels). Transperineal biopsies may only be considered as an alternative to the TR route in special situations. Nevertheless, given the increase in antimicrobial resistance, the impact on the post-biopsy sepsis rate should be assessed in well-designed clinical trials. Imaging-guided targeted PB strategies, combined or not with random PBs, may represent the future of prostate cancer diagnosis by reducing the number of PBs and improving decision-making.
Conclusions: The 12-core TR scheme remains the standard of care for initial PB. The actual trend for PB strategy, with the aim of avoiding overdiagnosis of very low-risk cancers, could rapidly change our current indications and techniques through new biomarkers and imaging-guided targeted strategies. Nevertheless, the cost-benefit balance of these techniques should be closely assessed in the setting of initial PB strategy.
Patient summary: This review highlights current recommendations for prostate biopsy and possible advances in the near future.

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1. Introduction

Despite recent advances in prostate imaging, a prostate biopsy (PB) is the only way to establish a cancer diagnosis and is the most important predictor for clinical decision-making in men suspected of prostate cancer (PCa). The optimal initial PB strategy remains a controversial and timely topic. Since its introduction by Hodge et al [1], random, systematic, ultrasound (US)-guided transrectal (TR) needle biopsy has significantly improved PCa diagnosis in terms of the detection rate and pathologic characterization before treatment decisions [1]. Studies have demonstrated that a

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traditional sextant technique could miss substantial numbers of PCas, and that additional sampling of the lateral peripheral zone increases the diagnostic yield [2–4]. The will to increase the detection rate and to improve pathologic characterization has led to new biopsy approaches, including TR saturation biopsy, the transperineal (TP) approach, and image-guided targeted PBs. Importantly, during the last decades, the role of PB has evolved from purely PCa detection to investigating how PB results can assist clinical management for patients. Thus, concerns about overdetection leading to overtreatment of low-risk PCa have greatly modified our clinical perception and the indications for PB.

This review focuses on evidence-based initial PB strategies and preventive antibiotic prophylaxis.

2. Evidence acquisition

A nonsystematic review of the literature was performed up to October 2014 using the PubMed and Embase databases. Articles were selected with a preference for the highest level of evidence in articles published within the past 5 yr. When available, articles with level 1 evidence were included. The search strategy included various algorithms and the following MeSH terms: prostate biopsy, prostate cancer, detection, transrectal ultrasound, diagnosis, imaging-guided, MRI, elastography, contrast-enhanced ultrasound, histoscanning, and transperineal. The search results were restricted to the English language without a year limit. Abstracts were reviewed for relevance to the defined review question, and the corresponding full papers were then assessed.

3. Evidence synthesis

3.1. Current recommendations for initial PB strategy

3.1.1. Indications

The decision to perform PB is usually based on an abnormal digital rectal examination (DRE) or increased prostate-specific antigen (PSA) level. While abnormal DRE necessarily indicates an initial PB irrespective of PSA level, debate regarding the pros and cons of PSA-based screening continues and there is no consensus on the absolute cutoff for performing PB.

The updated European Association of Urology (EAU) guidelines do not recommend widespread mass screening for PCa, but do strongly recommend early detection with PSA and biopsy in well-informed men [5]. The recent EAU recommendations suggest that the PSA level should be considered as a continuous parameter: the higher the value, the more likely the existence of PCa. A baseline PSA determination at 40–45 yr of age has been suggested, on which the subsequent screening interval can then be based. It has been demonstrated that baseline serum PSA $\geq$1.0 ng/ml at 45 yr of age and baseline serum PSA $\geq$2.0 ng/ml at 60 yr of age are associated with a significantly increased risk of PCa-related mortality and diagnosis of advanced or metastatic disease, even 25 yr after the initial PSA was obtained [5]. The EAU guidelines do not use a specific chronological age as a threshold for screening (Tables 1 and 2).

Table 1 – European Association of Urology recommendations for early detection of PCa

(1) Early detection of PCa reduces PCa-related mortality
(2) Early detection of PCa reduces the risk of being diagnosed and developing advanced and metastatic PCa
(3) A baseline serum PSA level should be obtained at 40–45 yr of age
(4) Intervals for early detection of PCa should be adapted according to the baseline PSA serum concentration
5) Early detection should be offered to men with a life expectancy $\geq$10 yr
(6) In the future, multivariate tools to predict clinical risk need to be integrated in the decision-making process

PCa = prostate cancer; PSA = prostate-specific antigen.

By contrast, the 2014 National Comprehensive Cancer Network (NCCN) guidelines suggest a cutoff value of 3 ng/ml in association with percentage free PSA (fPSA) and PSA kinetics in PB decision-making [6]. Moreover, risk calculators can be used and predictive models such as nomograms that include more variables have been developed to improve the ability to counsel patients on the need for PB [7,8]. Since they have not been tested in randomized controlled trials (RCTs), the cut-point for risk associated with a reduction in PCa mortality remains unknown [6].

Currently, increasing age, ethnicity, and family history are established risk factors for PCa. Individuals with a positive family history of PCa are at twofold higher risk of having PCa [9]. While the recently revised guidelines of the EAU and the British National Institute for Health and Care Excellence do not comment on the management of men with a hereditary high risk of PCa, the Swedish 2014 guidelines recommend PB for men $<$50 yr who have two close relatives with PCa (at least one relative should be diagnosed at $<$75 yr), and for men with *BRCA2* mutations and a suspicious DRE, PSA of 3 ng/ml, or PSA of 2–2.9 ng/ml with a doubling time of $<$2 yr [10].

Given the pitfalls of PSA testing, several new biomarkers have been suggested to improve PB or treatment decision-making and to minimize overdiagnosis and overtreatment. The Progensa PCA3 test is an FDA-approved test that has been commercially available since 2012. This test is generally used in men who had previous negative PBs, and may help in repeat PB decision-making. The exact PCA3 cutoff score that should be taken into account (25 or 35) is debatable. Recent studies have demonstrated a significant correlation between PCA3 and PCa significance [11–13]. The consensus in most papers is that PCA3 is often negative in patients with indolent cancer. In a recent multi-institutional study in a clinical setting, Scattoni et al [14] added PCA3 to a multivariate base model consisting of total PSA, percentage fPSA, and prostate volume, but could not show a significant increase in predictive accuracy at initial PB [14].

Besides PCA3, the most promising biomarker in the last 2 yr is [−2]proPSA (p2PSA), a serum isoform of PSA, and its derivatives, namely percentage p2PSA (p2PSA as a proportion of fPSA) and the Beckman Coulter (La Brea, CA, USA) prostate health index (PHI; p2PSA/fPSA $\cdot \sqrt{}$tPSA, where tPSA