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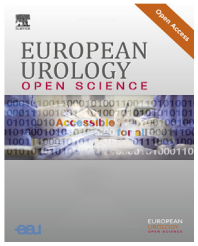

European Association of Urology

Brief Correspondence

Screening for Prostate Cancer with Prostate-specific Antigen

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In Europe and elsewhere, there is no consensus on population-based prostate cancer (PC) screening [1]. The controversy arises from uncertainty about the benefits and harms of population-based screening. There is strong evidence that cancer-specific mortality is significantly lower in a prostate-specific antigen (PSA)-screened population [2,3], but overdiagnosis of indolent PCs is of concern [4]. Clinical trials are under way to improve on the specificity of organized PSA screening. PSA is the most established biomarker (STHLM3 and 4K are others) and is integral to most approaches, and has recently been combined with prostate magnetic resonance imaging (MRI) to increase specificity [5]. Age, family history, and genetic testing might also play a role in risk-adapted screening recommendations, as early-onset PC is genetically inherited [6]. More recently, the screening performance of DRE alone proved to be poor and showed no benefit in combination with PSA [7]. Therefore, DRE should no longer be part of national statutory programs for early PC detection.

Currently, there is no nationally organized PC screening program in almost all European countries and the USA. However, opportunistic PSA screening is widespread and leads to numerous cases of overdiagnosis and overtreatment of indolent PC [1].

The focus of the current debate is whether PSA or MRI alone, or a combination of both, is sufficient to adequately fulfill the demands of a comprehensive screening strategy for PC.

The European Union recommended the introduction of a smart Europe-wide screening strategy by 2022 [4].

Following the ongoing PROBASE study, the future strategy should be risk-adapted PSA-based screening (Fig. 1) [8]. Using a baseline PSA threshold of ≥3 ng/ml at the age of 45 yr and confirmation of suspicious PSA levels, only 1% of all men were assigned to a high-risk category with subsequent need for prostate biopsy. Most men (89%) had low PSA and did not need any further interventions for at least 5 yr. A further 10% of men had PSA between 1.5 and 3 ng/ml (intermediate risk) and underwent PSA control tests after 2 yr [8]. Among 186 men with PSA ≥3 ng/ml, targeted and systematic biopsies were performed in 120 and multiparametric MRI in 147, with biopsy performed regardless of the MRI result. Of the men who underwent MRI, 20% had a negative result (Prostate Imaging-Reporting and Data System [PI-RADS] 1–2) and 80% had suspicious findings (PI-RADS 3–5). The PROBASE screening pathway detected 48 PC cases (overall prevalence 0.2%), of which 15 were International Society of Urological Pathology grade 1, 29 were grade 2, and four were grade ≥3 PCs [8].

Such a PSA-based screening strategy is simple and applicable everywhere. As it has been shown that DRE is ineffective for screening, this strategy does not initially require physicians. This makes it more objective and feasible and very cost effective. It should be acknowledged that PROBASE is an ongoing trial and the primary endpoint of metastasis-free survival at the age of 60 yr has not been reached yet.

The IP1-PROSTAGRAM study (n = 408 patients) showed that in comparison to PSA ≥3 ng/ml, MRI alone with a Likert score of 3 as the threshold for biopsy led to a twofold higher biopsy rate (40 vs 72) and an increase in the detection of clinically insignificant PC (6 vs 7). The MRI-only pathway with Likert 3–5 was associated with an increase in detection of clinically significant cancer (7 vs 14). An MRI Likert score of 4 or 5 alone as the definition of a positive test in comparison to PSA ≥3 ng/ml resulted in more clinically significant

https://doi.org/10.1016/j.euros.2024.01.010

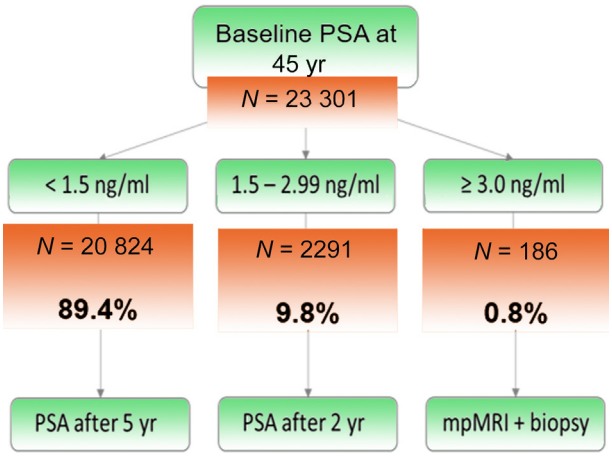

Fig. 1 – Risk stratification in PROBASE. Adapted from Arsov et al [8]. PSA = prostate-specific antigen; mpMRI = multiparametric magnetic resonance imaging.

PC cases (11 vs 7) and even fewer clinically insignificant PC cases (5 vs 6). However, MRI alone with a Likert sore of 4–5 missed 3/14 clinically significant PCs [9]. It should be noted that the median age for men in IP1-PROSTAGRAM was 57 yr.

In contrast to prostate cancer screening based on PSA alone, the combination of MRI and PSA reduces the number of unnecessary biopsies and is more specific [5]. Thus, in regions with excellent health care systems and widespread access to at least biparametric MRI, the combination of MRI and PSA could be discussed. However, widespread use of MRI in screening is currently unrealistic and too expensive. Furthermore, MRI scans for young screening populations are difficult to read [10]. Expert reading (>10 000 scan per expert) resulted in significantly better MRI accuracy [10]. Thus, expert reading or artificial intelligence might be required for further screening programs. In the context of this debate, it should be noted that radiologists with such experience are rare and not available for a Europe-wide screening program.

PSA-based risk-adapted screening is easily feasible around Europe and elsewhere. This screening strategy had a high acceptance rate in PROBASE [11]. For men with suspicious PSA results, high-quality MRI could serve as reflex test to increase the efficiency of future screening pathways. The availability of highly qualified radiologists and MRI scanners is an obstacle. Widespread use of MRI in a fixed combination or as a stand-alone measure for screening does not seem feasible or reasonable at this time.

Conflicts of interest: The authors have nothing to disclose.

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