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Updates to Early Detection of Prostate Cancer: AUA/SUO Guideline (2026)

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Purpose: The recommendations discussed on the early detection of prostate cancer provide a framework to facilitate clinical decision-making in the implementation of prostate cancer screening and follow-up.

Materials and Methods: The Early Detection of Prostate Cancer Guideline was reviewed in 2025 and updated through the AUA amendment process. This process involved reviewing and integrating newly published literature into the previously established Guideline. The methodologist updated the original Guideline search strategy to systematically search Ovid MEDLINE and Embase for new evidence published between November 2022 and December 2024.

Results: The Early Detection of Prostate Cancer Amendment Panel updated evidence- and consensus-based Guideline statements to provide guidance on prostate cancer screening, imaging and biomarker use, initial and repeat biopsies, and biopsy technique.

Conclusions: This update provides several new insights, including revised strength of evidence based on recently published literature on the use of MRI in biopsy-naïve patients and biopsy techniques, updates on available biomarkers, and revised recommendations for atypical small acinar proliferation. This Guideline will require future review and updates, as early detection and diagnostic strategies in this space continue to evolve.

Abbreviations and Acronyms

5-ARI = 5-alpha reductase inhibitors
95% CI = 95% confidence interval
ACR = American College of Radiology
aOR = adjusted odds ratio
ASAP = atypical small acinar proliferation
AUA = American Urological Association
AUC = area under the curve
CDR = cancer detection rate
DRE = digital rectal examination
ERSPC = European Randomized Study of Screening for Prostate Cancer
GG = grade group
LATP = local anesthetic transperineal prostate biopsy
mpMRI = multi-parametric magnetic resonance imaging
MPS = MyProstateScore
MPS2 = MyProstateScore 2.0
MRI = magnetic resonance imaging
NNS = numbers needed to screen
NND = numbers needed to diagnose
NPV = negative predictive value
PCA3 = Prostate Cancer Antigen 3
PHI = prostate health index
PI-RADS = Prostate Imaging Reporting and Data System
PPV = positive predictive value
PRS = polygenic risk score
PSA = prostate-specific antigen
PSAD = prostate-specific antigen density
RCT = randomized controlled trial
RR = relative risk
SDM = shared decision-making
SNP = single nucleotide polymorphism
STHLM-3 = Stockholm-3
SUO = Society of Urologic Oncology
TRUS = transrectal ultrasound
U.S. = United States
UTI = urinary tract infection

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BACKGROUND

Prostate cancer is the most commonly diagnosed noncutaneous malignancy in American men. It is estimated that 333,830 patients will be diagnosed with prostate cancer, and 36,320 deaths from prostate cancer will occur in the United States (U.S.) in 2026.[1] There was an estimated 1,414,259 new cases of prostate cancer and 375,304 deaths worldwide in 2020.[2] Significant advances have been made in early detection, especially with the increasing availability and usage of biomarkers and multiparametric MRI (mpMRI). This Guideline is based on a systematic review of the recently published literature and addresses early detection with an emphasis on PSA-based screening, considerations for imaging and biomarker use, initial and repeat biopsy, and biopsy technique, with the goal of identifying clinically significant prostate cancer. Updates to the specific Guideline statements are summarized herein.

This guideline is intended for all patient populations with a prostate gland. For consistency purposes, this guideline refers to these individuals as "people" or "patients" throughout this document.

GUIDELINE STATEMENTS

PSA Screening

When screening for prostate cancer, clinicians should use PSA as the first screening test. (*Strong Recommendation; Evidence Level: Grade A*)

The PSA blood test remains the first-line screening test of choice based on randomized trials of PSA-based screening showing reductions in metastasis and prostate cancer death.[3,4] At the time of this evidence review, limited evidence has emerged regarding other candidates for first-line biomarkers or imaging.

The digital rectal examination (DRE) should not be used as a first-line screening test prior to PSA or a replacement for PSA in otherwise asymptomatic patients. In symptomatic patients, DRE can be considered as a diagnostic tool rather than a screening test for cancer. It can be used as a complement to screening with PSA testing and is discussed in greater detail below.

For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy. (*Expert Opinion*)

The definition of an elevated PSA has changed over time. The commonly cited threshold of 4 ng/mL is based on very early studies that identify the highest levels typically observed among patients thought to be free of prostate cancer. Another cited threshold of 3 ng/mL is taken from the Finnish European Randomized Study of Screening for Prostate Cancer (ERSPC) trial of prostate cancer screening that showed a significant reduction in prostate cancer deaths among patients who entered the trial between ages 55 to 69 years and were referred to biopsy based on that threshold. Typically, 5-alpha reductase inhibitors (5-ARIs) decrease PSA levels after at least 6 months of use, with some older studies suggesting serum PSA should be doubled for patients using 5-ARIs as an adjusted baseline.[5] However, PSA kinetics vary from patient to patient, with 1 trial suggesting only one-third of patients on 5-ARI therapy experience a 40% to 60% decline in PSA at 1 year.[6]

Clinicians may personalize the re-screening interval, or decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following shared decision-making (SDM). (*Conditional Recommendation; Evidence Level: Grade B*)

Patients With Low PSA. Amongst patients 60 years of age with a PSA < 1 ng/mL (age-specific median), the 25-year risk of metastases or death from prostate cancer in a largely *unscreened* population (Malmö Preventive Project) is extremely low (0.5% and 0.2%, respectively).[7] Although modeling data suggest a higher likelihood of death from prostate cancer if screening were discontinued in these patients (5%-13.1% fewer lives saved compared with continuing screening to 69 years of age),[8] the absolute number of lives saved by continuing screening is small; therefore, it may be reasonable to significantly lengthen the re-screening interval or discontinue screening based on SDM provided there are no other risk factors, such as strong family history of prostate cancer.[7-9]

In comparison of regularly screened patients in the Goteborg-1 trial vs unscreened people 60 years of age in the Malmö Preventive Project with PSA < 2 ng/mL, continued screening every 2 years for 15 years found an increase in prostate cancer incidence (7.7%) without a decrease in prostate cancer mortality.[9] For patients with PSA ≥ 2 ng/mL, the reduction in cancer mortality for screened patients was large with 23 patients being screened (numbers needed to screen) and 6 diagnosed (numbers needed

to diagnose) to prevent 1 prostate cancer death at 15 years.[9] In long-term follow-up from ERSPC, the actuarial probability of clinically significant prostate cancer at 16 years was 1.2% to 1.5% for patients aged 55 to 69 years with baseline PSA < 1.0 ng/mL, while for those initially screened at age 60 to 61 years with baseline PSA < 2 ng/mL, further continuation of screening is unlikely to be beneficial after the age of 68 to 70 years if PSA is still < 2 ng/mL.[10]

Older Patients. The decision to screen patients should be an SDM conversation predicated upon a person's prior PSA levels and general health. A flexible age to discontinue screening may be based on individualized decision-making to balance detection of aggressive cancers and overdiagnosis. This is particularly important in people between the ages of 70 to 80 years where there is a higher risk of competing mortality.[11] In the Baltimore Longitudinal Study of Aging, patients 75 years or older with a PSA < 3 ng/mL were unlikely to be diagnosed with aggressive prostate cancer, and no patients between the ages of 75 to 80 years with a PSA < 3 ng/mL died of prostate cancer during their remaining lifetime.[12] In ERSPC Rotterdam, patients aged 70 to 74 years who have previously undergone PSA-based screening without receiving a prostate cancer diagnosis had a cumulative incidence of prostate cancer-specific mortality of 0.54% (95% CI: 0.40-0.70) in all patients, 0.11% (95% CI: 0.05-0.27) in patients with PSA < 2 ng/mL, and 0.85% (95% CI: 0.47-1.5) in patients with PSA 2 to 3 ng/mL, by age 85, suggesting that discontinuation of screening could be considered in patients with PSA < 3.0 ng/mL.[13]

Clinicians may use DRE alongside PSA to establish risk of clinically significant prostate cancer. (*Conditional Recommendation; Evidence Level: Grade C*)

The primary screening modality recommended for the early detection of prostate cancer is a PSA blood test. Clinicians should not use DRE as the sole screening method in otherwise asymptomatic patients. This statement does not apply to symptomatic patients where a DRE could be considered a diagnostic exam.

There is insufficient evidence to support adding DRE to PSA-based prostate cancer screening. The positive predictive value (PPV) of DRE as a screening method to detect prostate cancer is low. A recent meta-analysis demonstrated that adding DRE to PSA screening did not significantly improve the PPV compared to PSA screening alone for detection of prostate cancer.[14] The study reported a pooled PPV of 0.21 (95% CI: 0.13-0.33) for DRE, which was similar to the PPV of PSA (PPV: 0.22; 95% CI: 0.15-0.30; $P = .9$), and no difference in PPV with the combination of DRE and PSA (PPV: 0.19; 95% CI: 0.13-0.26; $P = .5$).[14]

There are also practical considerations for performing DRE in clinical practice, and it may not be acceptable to all patients as compared to a blood draw. Survey data suggest nearly a quarter of patients may forego prostate cancer screening when it includes up-front DRE with PSA testing.[15]

Initial Biopsy

Clinicians may use MRI prior to initial biopsy to increase the detection of Grade Group (GG) 2+ prostate cancer. (*Conditional Recommendation; Evidence Level: Grade A*)

Studies have demonstrated the clinical value of mpMRI and its use in guiding biopsy decision-making to increase the likelihood of detecting clinically significant prostate cancer while lowering detection of insignificant disease. While this is particularly true in patients with a prior negative prostate biopsy, more recent studies suggest that the mpMRI may have benefit in the screening setting.

The PRECISION trial was a randomized noninferiority study that sought to compare the effectiveness of MRI-targeted vs systematic biopsy in detecting clinically significant prostate cancer in biopsy-naïve patients.[16] This 500-patient trial was performed at 25 centers in 11 countries. There was no central reading of the MRI prior to biopsy, and biopsies were performed by transrectal or transperineal route, using a cognitive or ultrasound fusion technique. Of patients who underwent an MRI, nearly 70% had a lesion targetable for biopsy (Prostate Imaging Reporting and Data System [PI-RADS] score ≥3). Clinically significant prostate cancer was detected in 38% of the patients undergoing mpMRI and 26% of patients undergoing systematic biopsy. Patients undergoing MRI-targeted biopsy also had fewer insignificant cancers detected (9% vs 22%). The agreement between a local and a central read for MRI was 78%, which was considered moderate.

The MULTIPROS trial was a prospective, multicenter randomized study in the United Kingdom enrolling 413 biopsy-naïve patients with clinical suspicion for prostate cancer between 2015 and 2020. All participants underwent prebiopsy mpMRI, and those with suspicious lesions (PI-RADS ≥ 3) were randomized to systematic biopsy alone or combined MRI-targeted plus systematic biopsy. The study found that the combined approach significantly improved detection of clinically significant prostate cancer compared with systematic biopsy alone (adjusted odds ratio [aOR]: 1.79; 95% CI: 1.14-2.79; $P = .01$). These results underscore that

mpMRI guides lesion detection and augments biopsy strategy by increasing the yield of clinically significant cancers.[17]

Subsequent prospective trials in both initial diagnosis and screening settings provide evidence on outcomes among biopsy-naïve patients with negative MRI findings. In a follow-up report of the Göteborg-2 screening trial, a PSA + MRI strategy allowed those with negative MRI to avoid biopsy, leading to more than a 50% reduction in detection of clinically insignificant cancer without an excess of advanced or metastatic disease after a relatively short follow-up of 4 years. The relative risk (RR) of detecting clinically significant prostate cancer in the targeted biopsy group compared with the systematic biopsy group was modestly lower (RR: 0.84; 95% CI: 0.66-1.07) and not statistically significant.[18]

Similarly, the PROKOMB trial prospectively evaluated an MRI-informed biopsy strategy in biopsy-naïve patients with elevated PSA across multiple German centers. All participants underwent prebiopsy MRI; those with PI-RADS $\geq$ 3 lesions were recommended for targeted plus systematic biopsy, while those with negative MRI (PI-RADS 1-2) were advised to defer biopsy and instead undergo structured surveillance with serial PSA, DRE, and repeat MRI or biopsy only if risk indicators emerged. A total of 593 patients underwent mpMRI with 286 (48%) having negative MRI results, 261 (44%) avoiding biopsy initially, and 242 (41%) avoiding biopsy over 3 years. Of the 286 patients with a negative MRI, 25 (9%) underwent immediate biopsy with detection of 7 (28%) prostate cancers, of which 4 (57%) were GG2+. During 3 years of structured follow-up, an additional 44 (15%) patients from the negative-MRI group underwent biopsy, and clinically significant prostate cancer was detected in 7 (16%). No cases of metastatic disease were reported over a short monitoring period of 3 years.[19]

The PROBASE trial, a large German population-based, risk-adapted screening study, enrolled approximately 46,000 patients aged 45, who were randomized to immediate or delayed PSA testing as part of a long-term prostate cancer early-detection strategy. In the first screening round, of 186 participants with elevated PSA ($\geq$3 ng/mL), 114 (61%) underwent mpMRI, followed by a combined targeted plus systematic biopsy if the PI-RADS score was $\geq$ 3. Among these 114 patients, 47 (41%) were diagnosed with prostate cancer, with 33 (29%) having clinically significant disease. For scans interpreted centrally by experienced reference radiologists, using PI-RADS $\geq$ 4 as the biopsy threshold yielded 79% sensitivity, 91% negative predictive value (NPV), and 85% accuracy for clinically significant cancer. In contrast, local MRI reads performed substantially worse using the same PI-RADS $\geq$ 4 threshold: only 55% sensitivity, 80% NPV, and 68% accuracy in identifying clinically significant prostate cancer. Furthermore, interobserver agreement between local and expert readings was moderate (κ = 0.41), indicating only modest consistency in MRI interpretation across settings. These results emphasize that the oncologic safety of avoiding biopsy in patients with negative MRI (PI-RADS 1-2) depends heavily on high-quality imaging and expert interpretation.[20]

While it is reasonable to routinely obtain an mpMRI in biopsy-naïve patients, the dependance of the outcomes on image quality and expert interpretation tempers the enthusiasm for a stronger recommendation. Recognizing this challenge, multiple U.S. initiatives—particularly those led by the American College of Radiology—have sought to enhance and standardize prostate MRI through structured quality-improvement collaboratives, education efforts, and accreditation programs that promote high-quality acquisition, interpretation, and reporting across diverse practices.[21]

For patients with both absence of suspicious findings on MRI and elevated risk for GG2+ prostate cancer, clinicians should proceed with a systematic biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)

Among the factors to predict clinically significant prostate cancer in patients with negative (PI-RADS 1-2) or equivocal (PI-RADS 3) results, PSA density (ie, serum PSA divided by gland volume) has been the most extensively investigated. Haj-Mirzaian et al conducted a systematic review and meta-analysis of 72 studies including 36,366 patients to determine the optimal prostate biopsy decision-making strategy for avoiding unnecessary biopsies and minimizing the risk of missing clinically significant cancers by combining MRI PI-RADS scores and clinical data. In patients with negative MRI (PI-RADS 1-2), adding PSA density significantly improved the ability to exclude clinically significant prostate cancer. Using a PSA density threshold of 0.15 ng/mL/cc, biopsy could be avoided in up to 67% of patients with GG2+ prostate cancer while maintaining a 94% NPV. Similarly, in those with equivocal MRI (PI-RADS 3), using a PSA density threshold of 0.10 ng/mL/cc, biopsy could be avoided in up to 43% of patients while maintaining a 93% NPV. The strategy to forego biopsy in those with PI-RADS 3 or less and PSA density less than 0.10 ng/mL^2 or less than 0.15 ng/mL^2 would avoid 30% or 48% of unnecessary biopsies, respectively, while maintaining sensitivity of 97% or 95%, respectively. Across analyses, PSA density was consistently the strongest predictor of clinically significant disease in MRI-negative or equivocal cases,

outperforming total PSA and other clinical factors. These findings suggest that incorporating PSA density could guide biopsy decisions in patients with negative or equivocal MRI findings, reducing unnecessary procedures.[22]

Clinicians may use adjunctive urine or serum markers when further risk stratification would influence the decision regarding whether to proceed with biopsy. (*Conditional Recommendation*; *Evidence Level: Grade C*)

It is debatable which of the newer biomarkers (alone or in combination) is best, and comparative studies are sparse. A list of available tests for an initial biopsy cohort is summarized in Table. With this update, Table now includes additional references describing studies of previously included biomarkers for biopsy-naïve patients. In general, the tests are calibrated such that avoiding biopsy in the setting of a sub-threshold test reduces biopsies by about one third, resulting in delayed detection or non-detection of 5% to 10% of clinically significant prostate cancers.[74]

In addition to the biomarkers in Table, polygenic risk scores (PRSs) that are based on single nucleotide polymorphisms measured in saliva or blood are genetic tests used to predict a person's risk of developing prostate cancer. The endpoint of the majority of studies on PRS has mainly focused on any detection of prostate cancer, not clinically significant or metastatic/lethal prostate cancer. Few PRS scores have been shown to discriminate between aggressive and indolent prostate cancer risk.[75] Calculating a PRS based on genotypes of 66 known prostate cancer loci for 4967 patients in the ERSPC, the rate of overdiagnosis (eg, detection of GG1) of screen-detected cancers was 42%, with 58% of these found in the lower PRS risk group and 37% in those with higher PRS risk.[76] Adding single nucleotide polymorphisms to Stockholm-3 (STHLM-3) added 1% to the area under the curve (from 0.75 to 0.76) for GG2+ (Gleason Score $\geq$ 7) after the clinical information and protein biomarkers.[50] The ongoing large-scale BARCODE-1 trial invited individuals to obtain prostate cancer screening using PRS and recently published the primary outcome. The participation rate was low (22%), which limits generalizability.[77] Of over 40,000 patients invited, 6393 participated and had a PRS calculated, of whom 745 (12%) were in the top 10% of PRS (ie, elevated risk). Among those, about half (n = 468) underwent an MRI and prostate biopsy, irrespective of PSA, and 40% (187/468) had prostate cancer, half of which were considered clinically significant. However, whether PRS testing without PSA improves risk stratification of early detection strategies and favorably balances the risks of unnecessary biopsy, overdiagnosis and detection of clinically significant prostate cancer as compared to other currently available strategies, is unclear.[77] It is also important to note that PRS has largely been developed from European-ancestry genome-wide association studies, and their performance across other ancestries remains variable, underscoring the need for careful cross-ancestry calibration and multi-ancestry research. At present, PRS should not independently dictate prostate imaging or biopsy decisions outside of structured screening programs, as their clinical utility in isolation remains limited. Ongoing research efforts focus on the role of PRS in distinguishing aggressive vs indolent prostate cancers.

Repeat Biopsy

After a negative biopsy, clinicians may use blood-, urine-, or tissue-based biomarkers selectively for further risk stratification if results are likely to influence the decision regarding repeat biopsy or otherwise substantively change the patient's management. (*Conditional Recommendation; Evidence Level: Grade C*)

Blood-, urine-, or tissue-based biomarkers may provide additional information for risk stratification in patients with a prior negative biopsy and with ongoing suspicion for GG2+ prostate cancer. Several blood-, urine-, and tissue-based biomarkers have been developed and reported in several studies with varying performance characteristics. These tests generally present percentage risk of biopsy-detectable disease (and/or GG2+), and it is up to the clinician and patient to decide on the threshold for proceeding with a biopsy with consideration given to the performance metrics of the test. For example, the proportion of GG2+ prostate cancer missed by 4Kscore at $\geq$ 10%, 15%, and 20% threshold were 5%, 16%, and 16%, respectively, which might impact a patient's decision to pursue a repeat prostate biopsy.[23] In another example, a validation study showed that using a threshold of 40 for MyProstateScore (MPS) would result in 95% NPV and avoid 67% of biopsies among those considering repeat prostate biopsy.[78] The MyProstateScore 2.0 (MPS2) urine-based biomarker may help avoid half of biopsies while maintaining 95% sensitivity for GG2 cancer detection. Additionally, there is significant heterogeneity in the outcomes reported for these biomarkers. It is imperative clinicians are familiar with biomarkers, understand what information or data each test provides, and consider whether additional information will impact management decisions before ordering a test. As in the PSA screening setting, the use of SDM is highly recommended given the uncertainty involved.

Table. *Available Biomarker Assays*

Test	Biomarker component	Clinical variable	Biopsy population
Serum			
4Kscore[23-29]	PSA, fPSA, iPSA, hK2	Age, prior biopsy status, DRE (optional)	Initial biopsy[24-27] Repeat biopsy[23] Mixed[28,29]
IsoPSA[30-33]	All PSA isoforms	None	Mixed[30-33]
Proclarix[34-36]	THBS1, CTSD, PSA, fPSA	Age, prostate volume (optional)	Mixed[34-36]
PHI[26,37-49]	p2PSA, fPSA, PSA	None	Initial biopsy[26,37-40,44-47] Repeat biopsy[41-43] Mixed[48,49]
STHLM-3[50-53]	232 genetic polymorphisms SNPs, PSA, fPSA, iPSA, hK2, MSMB, MIC1	Age, family history, previous biopsy, DRE (optional)	Initial biopsy[52] Mixed[50,51,53]
Urine			
PCA3[40,54-60]	PCA3	Some studies add age, PSA, prostate volume	Initial biopsy[40,54-58] Repeat biopsy[59,60]
SelectMDx[61-63]	HOXC6, DLX1 mRNA	Age, PSA, prostate volume, DRE	Initial biopsy[61-63]
TMPRSS2:ERG[58]	TMPRSS2:ERG	None	Initial biopsy[58]
ExoDx Prostate Intelliscore[64-69]	PCA3, ERG, SPDEF mRNA	None	Initial biopsy[64-66,68,69] Repeat biopsy[67]
MyProstateScore 2.0 (MPS2)[70]	TMPRSS2:ERG, SCHLAP1, OR51E2, APOC1, PCAT14, CAMKK2, PCA3, NKAIN1, B3GNT6, TFF3, SPON2, PCGEM1, TRGV9, TMSB15A, ERG, KLK4, HOXC6, KLK3	Age, race, DRE, PSA, family history, previous biopsy	Initial biopsy[70] Repeat biopsy[70] Mixed[70]
MiR Sentinel[71]	Small non-coding RNAs	None	Mixed[71]
Tissue			
Confirm MDx[72,73]	Hypermethylation of GSTP1, APC, RASSF1	None	Repeat biopsy[72,73]

Abbreviations: DRE, digital rectal examination; PHI, prostate health index; SNPs, single nucleotide polymorphisms.

In patients with ASAP, clinicians should perform additional testing, which may include repeat biopsy. (*Moderate Recommendation; Evidence Level: Grade C*)

In routine pathology reports, ASAP is synonymous with a small focus (or foci) of atypical glands suspicious, but not definitive, for a diagnosis of carcinoma.[79,80] An ASAP finding alone on needle biopsy is associated with a 30% to 50% risk of prostate cancer detection on repeat biopsy,[79-86] with approximately 10% to 20% of these being GG2+.[85,86] A recent meta-analysis reported that following a diagnosis of ASAP on initial biopsy, the pooled incidence rate of GG2+ cancer detection on repeat biopsy was 12%.[87] MRI guidance was rarely used for the initial biopsy for many patients in this study. Nevertheless, based on this study, the previous Expert Opinion can now be considered a Moderate Recommendation, and now includes repeat biopsy among options for repeat testing. Less information is available on the risk of prostate cancer detection following an ASAP diagnosis in patients for whom MRI-targeted biopsy was included in the initial biopsy. Given these risks, additional testing should be considered following an ASAP diagnosis, which may include repeat systematic needle biopsy with consideration of mpMRI ± targeted biopsy, PSA, as well as urine, serum, or tissue-based biomarkers. Evidence is limited regarding the optimal tests to use in this setting. Regarding repeat testing, including biopsy, there is limited evidence on optimal timing following an ASAP diagnosis. Patients with a diagnosis of ASAP in the setting of other biopsy cores showing invasive prostate cancer should be managed in accordance with the definitive carcinoma component.

Biopsy Technique

Clinicians may use either a transrectal or transperineal biopsy route when performing a biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)

In patients with a suspicion for GG2+ prostate cancer who are undergoing biopsy, the cancer detection rates associated with transrectal vs transperineal biopsy route are not significantly different.[88,89] Prior data from case series was suggested that transperineal biopsy may detect anterior and apical cancers at a higher rate or yield longer cancer core length and percentage of core involvement.[90-92] However, 2 subsequent meta-analyses, 1 of 11 retrospective series[90] and another of 3 randomized controlled trials (RCTs)[93] do not suggest a difference in the overall detection rates of clinically significant prostate cancer between the transperineal or transrectal biopsy approaches. Data from the pre- and post-MRI guided biopsy era suggest that similarity in cancer detection rates is consistent regardless of the use of MRI imaging.[94] In the PERFECT trial, Ploussard et al[95]

found that transrectal biopsies may have a higher rate of detection for peripheral zone cancers, while transperineal biopsies may be better at detecting anterior zone cancers. The most recently reported randomized trial on this topic, the TRANSLATE study, fell outside the search range for the updated search conducted in 2024.[96] Data from the TRANSLATE suggest that the study was powered to demonstrate a difference of 10% in detection rate of Gleason GG2+ prostate cancer between those undergoing local anesthetic transperineal prostate biopsy (LATP) vs transrectal ultrasound (TRUS) guided biopsies. The actual difference detected was 6%. Almost all the differences between the groups favoring LATP biopsy was from a higher level of detection of GG2 cancer (52.8% vs 45.7%) with no differences between groups for detection of GG3+ prostate cancer. There was no difference in overall complication rates between the groups including infection requiring hospital admission. Local pain was higher among those undergoing LATP. All patients undergoing TRUS biopsy received antibiotic prophylaxis compared to only 11% in the LATP group. Per prespecified subgroup analysis, lesion site did not seem to affect detection rates, and the only significant variable was prostate volume with detection rate by LATP being higher in those with prostate volume < 50 cc. Prior meta-analyses and retrospective reviews of single center data suggest a lower risk of infections with the transperineal approach; however, these data are not entirely substantiated by recently reported RCTs (0.8%-2.6% vs 0%-2.7%; transperineal vs TRUS biopsies, respectively) including the recently reported TRANSLATE study (<1% vs 2%; transperineal vs TRUS biopsies, respectively).[95-99] One has to acknowledge, however, that the usage of antibiotic prophylaxis is significantly lower to none in those undergoing transperineal biopsies.

The 3 RCTs comparing transperineal and transrectal prostate biopsy had different primary endpoints and trial designs. The PREVENT trial[99] and the PROBE-PC trial[97,98] were superiority trials aiming to demonstrate a difference in infectious complication rates of 0.4% vs 5% or 0.8% vs 4%, respectively, in the 2 trials, between the transperineal and the transrectal biopsy arms.[97,99] The PERFECT trial was a noninferiority trial aimed at demonstrating equivalence in detection of clinically significant prostate cancer between transperineal and transrectal biopsy arms.[95] It is noted that 2 of the 3 (PREVENT and PERFECT trials) and many of the recent studies on this subject have used patients exclusively undergoing MRI-guided prostate biopsies.[93] Antibiotic regimen also varied between the 2 trials aimed at demonstrating differences in infection rates (PREVENT and PROBE-PC trials).[93] In the PREVENT trial, patients undergoing transperineal biopsy did not receive any antibiotics, whereas those undergoing transrectal biopsy received prophylactic antibiotics based on prebiopsy rectal swab culture. In the PROBE-PC study, those undergoing transperineal biopsy received prophylactic antibiotics based on surgeon assessment of high risk (4/367 patients) while all patients undergoing transrectal biopsy received either 1 day of oral antibiotics or a combination of oral antibiotics and intramuscular antibiotics. The incidence of infection was not statistically significantly different between the 2 arms in any of the 3 randomized trials. It is also unclear if the administration of routine prophylactic antibiotics vs rectal swab directed antibiotics significantly impacts the occurrence of infectious complications.[100,101] There was one episode of sepsis in the PERFECT trial in the transrectal biopsy arm. The overall incidence of infectious complications of any kind was approximately 2% in either the transperineal or transrectal biopsy group.[93] Some cohort studies do indicate a higher rate of UTI even with antibiotic prophylaxis in the transrectal biopsy patients.[102] It is to be noted that the other potential complication of urinary retention was not statistically different between the transrectal or transperineal biopsy groups; rectal bleeding was more common among those undergoing transrectal biopsies, as was the incidence of prolonged hematospermia. Pain, particularly persistent pain, was more common among those undergoing transperineal biopsy vs transrectal biopsy.[99,103] Use of transperineal biopsies may have specific value in patients who have experienced infectious complications with a prior biopsy, are at higher risk for biopsy-related infection, or have anterior lesions that may not be as easily accessible transrectally. There are multiple RCTs listed in clinicaltrials.gov that address these and other questions[104-106] and the results are pending.

Given the concern surrounding the rising rate of sepsis and antibiotic resistance, using transperineal biopsy to mitigate these concerns is a reasonable approach and is gaining traction. The lack of definitive results supporting the superiority of the transperineal biopsy approach either for clinically significant cancer detection or for reduction of infection rates render it difficult to exclusively emphasize the transperineal approach over the transrectal approach at this time. The transperineal approach requires specific equipment such as a biplanar linear side firing probe, precise delivery of local anesthetic, training in localization and other accessories which can facilitate the procedure. On the other hand, use of transrectal approach may be appropriate in certain situations (eg, patient preference/comfort, patient cannot be placed into the lithotomy position, clinician training/experience or lack of appropriate equipment for the transperineal approach). Moreover, use of adjunctive measures (eg, rectal swab cultures, augmented antibiotic

approaches) to reduce sepsis for a transrectal biopsy approach have also been shown to reduce sepsis and have been effective in the randomized trials as well as in several retrospective studies, with lower than expected cases of infection complications including sepsis.[107]

FUTURE DIRECTIONS

While this update extensively reviewed emerging data surrounding MRI imaging of the prostate, other imaging technologies, such as micro-ultrasound, have shown similar promise in the detection of clinically significant prostate cancer in patients with elevated PSA.[108] Furthermore, no imaging technique has been shown to impact meaningful long-term outcomes such as cancer-specific mortality. Even with growing clinical experience with mpMRI and fusion biopsies, there remain some cases concerning GG2+ cancer where the targeted biopsy either did not detect cancer or only detected GG1 disease. While this may be due to false positive mpMRI reading, it is also possible that the lesion was undersampled (eg, small target in a difficult to access location), and the use of perilesional + lesion-only biopsies is being investigated in retrospective data. On a practical level, the impact of interobserver variability and reliance on high-quality imaging and expert interpretation have been highlighted by recent studies. As such, the future directions in the imaging domain will focus on evolving MRI protocols, such as biparametric MRI, and the use of computer-aided and artificial intelligence-enhanced interpretation of MRI-acquired prostate anatomic and radiomic imaging.[21,109]

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