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RECENT PROGRESS IN NEW BIOMARKERS FOR PROSTATE CANCER DETECTION

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ABSTRACT

Since prostate cancer is still the most frequent cancer in males, extensive research has been done to improve detection techniques, diagnosis, and treatment options. When combined with MRI targeted biopsies, PSA-based screening has shown encouraging results in improving diagnostic quality and lowering overdiagnosis. Current research on screening for prostate cancer Recent advancements in prostate cancer screening are reviewed here, with an emphasis on new genomic and molecular markers that may be useful for early detection, prognosis, and therapeutic targeting, such as circulating tumor cells (CTCs) and exosomal miRs. Research on immunotherapy strategies to enhance immune responsiveness is still underway. One such strategy is the use of DNA-based vaccines in conjunction with sipuleucel-T to treat patients with advanced or metastatic prostate cancer. Molecular markers like PCA3 and TMPRSS2. These markers hold great promise to enhance the specificity of diagnosing the condition in urines. In their advances, there remains the challenge of improved sensitivity of the biomarker; less overtreatment of patients, and promoting non-invasive diagnosis. They would alter prostate cancer practice in as much as these markers are instituted in clinical practices promising a more precise, focused approach to managing cases of prostate cancer and increasing better outcomes among the patient groups.

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INTRODUCTION

Prostate cancer is one of the most common cancers in men worldwide. The World Health Organization reported a new case of around 1.4 million cases and nearly 375,000 deaths in 2020 (World Health Organization, 2020). In the United States alone, it is projected to cause 34,700 deaths in 2023, ranking as the second leading cause of death due to cancer among men (American Cancer Society, 2023). Although PSA-based screening has helped improve early detection and reduced prostate cancer-specific mortality, controversies about overdiagnosis and overtreatment have adversely affected a patient's quality of life (de Vos et al., 2023).[1]

Recent advances such as MRI-targeted biopsies appear promising for an improvement in diagnostic accuracy, along with potential risks for overdiagnosis (Hugosson et al., 2022).[2]The future hope lies for the identification of biomarkers that will clearly differentiate aggressive from indolent diseases. CTCs and Exo-miRs are molecular markers that hold promise for advancing early detection, prognosis, and treatment selection in prostate cancer.

The review will discuss the current updates on prostate cancer biomarkers, mainly PSA-based screening, MRI-targeted biopsy, and emerging molecular markers. This review should indicate how important identifying and validating new biomarkers is to increase screening accuracy and thus reduce unnecessary treatments and direct targeted therapeutic approaches. It will contribute to changing the management of prostate cancer by making the treatment more personalized and ultimately leading to better outcomes in the patient.

In light of this, the improvement of early detection and individualized treatment plans by assessing the current developments in prostate cancer screening, diagnosis, and treatment with a focus on PSA-based screening, MRI-targeted biopsies, and newly developed molecular markers such as CTCs and Exo-miRs shall form part of this review.

METHODS

The article was based on new studies on prostate cancer screening, diagnosis, and treatment published between 2019 and 2024. The author sourced papers from a number of databases, including Google Scholar and PubMed.

RESULTS AND DISCUSSION

Established Tumor Markers

A number of studies have evaluated techniques in prostate cancer screening and detection with particular emphasis on higher accuracy and lesser overdiagnosis. Among them was a 2022 study conducted by Hugosson et al.,[2] in which the authors found that MRI-directed targeted biopsy decreased the risk of overdiagnosis by 50% compared to systematic biopsy in PSA-based screening, with minimal delay in identifying some intermediate-risk tumors.

Promising results of PSA-based screening have also been documented in the long-term follow-up studies. There was a reduction in PCSM and metastatic disease in the Rotterdam part of the ERSPC 21 years into PSA-based screening. According to de Vos et al. (2023), [1] the NND and NNI to end one prostate cancer mortality were at 246 and 14, respectively.

The Cluster Randomised Trial of PSA testing for Prostate Cancer-CAP found that compared with usual care an invitation for PSA screening from a single invitation reduced deaths due to prostate cancer at a follow-up time of median 15 years. However, the deaths from all causes were modestly reduced only by Martin et al., 2024.[3]

There is hope that immunotherapy methods may promise treatment. A pilot study in patients with metastatic castration-resistant prostate cancer (mCRPC) suggested that combining a DNA vaccine (pTVG-HP) with sipuleucel-T, which is an FDA-approved anti-tumor vaccination targeting prostatic acid phosphatase, was promising in potentially enhancing and broadening immunity. It proved the capability to improve humoral and T cell immunity by the utilization of prime boost vaccination techniques despite not finding appreciable differences in advancement between arms (Wargowski et al., 2018).[4]

There was another study on the use of APC8015 (sipuleucel-T) and bevacizumab on patients with biochemically recurrent prostate cancer. This regimen, by Rini et al., 2006,[5] caused an immunologic response and changed PSA levels so some of the patients experienced drops in PSA and increases in PSA doubling time.

Further advances in diagnostic technology have finally made it possible to detect prostate cancer. Its prostatic acid phosphatase (PAP) can be detected with great sensitivity using the Delfia PAP kit that uses a time-resolved fluor immunoassay with europium as the tracer, especially in advanced stages of prostate cancer.

Table 1 : Comparative Analysis of Markers

Marker	Sensitivity	Specificity	Clinical Utility
PSA Test	Moderate	Moderate	Commonly used; risk of overdiagnosis; limited specificity alone
MRI-Targeted Biopsy	High	High	Reduces unnecessary biopsies; improves detection of significant cancers
CTCs	Moderate	Variable	Prognostic in advanced disease; useful for monitoring treatment response
Exo-miRs (e.g., miR-205-5p)	High	High	Non-invasive; potential to identify aggressive cancers
PCA3/TMPRSS2	High	High	Adds specificity to PSA; useful in risk calculators
DNA Methylation (utMeMA)	High	High	Promising for non-invasive detection; further validation required

The most intuitive understanding of their clinical utility comes from the organized review of established markers, genomic markers, and new diagnostic technologies. This comparison provides insight into how these markers can complement one another toward the goal of a more accurate and individualized diagnosis and management of prostate cancer.

Genomic and Molecular Markers

For patients with non-small-cell lung cancer (NSCLC), an adaptive umbrella trial (CTONG1702) and a real-world observational research (CTONG1705) is reported by Liu et al.[6] The focus of the umbrella trial seems to be on the assessment of the biomarker-driven drugs tyrosine kinase inhibitors and PD-1 inhibitors in the treated patients who have stage IIIB to IV NSCLC. Enrolment of patients is based on the response of PD-L1 IHC analysis and next-generation sequencing (NGS). Conjugate observational study means the development of a complete genomic data base and the exploration of the correlation between clinical outcomes and genetic variants in patients with non-small cell lung cancer.

Udar et al. validated the Extended RAS Panel assay as an NGS-based companion diagnostic, identifying 56 RAS mutations in samples of metastatic colorectal cancer (mCRC), using samples from the PRIME trial, which compared panitumumab + FOLFOX4 to FOLFOX4 alone. [7]The authors are able to detect patients who might appropriately be selected for panitumumab treatment and found that agreement with Sanger sequencing is very good. The Extended RAS Panel had identified almost 13% more patients to carry RAS mutations compared to the KRAS exon 2 testing alone.

Genuardi et al. applied the EuroClonality-NGS IGH approach to detect immunoglobulin heavy chain rearrangements in 20 MCL patients enrolled in the Italian phase III trial.[8] The pilot study showed that the approach could be feasible for the MCL setting because, among the 20 cases, it was capable of identifying a molecular IGH target in 19 patients, which may enable the monitoring of MRD in patients without genetic markers available for the classical screening techniques.

Table 2: Key Genomic and Molecular Markers in Prostate Cancer

Marker	Role in Prostate Cancer	Clinical Validation Status	Relevant Studies/Trials
CTCs	Prognostic and treatment response marker in mCRPC	Moderate; sensitivity varies by disease stage	Zapatero et al., 2020[11]; Goldkorn et al., 2021[11]
Exo-miRs (e.g., miR-205-5p)	Non-invasive diagnostic and prognostic marker for aggressive disease	Early; promising for stratification; further validation needed	Marin et al., 2022[3]
DNA Methylation Panels (e.g., utMeMA)	Epigenetic detection of high-risk cancers	Early; high sensitivity and specificity reported	Chen et al., 2020[22]

These genomic and molecular markers show strong potential for enhancing diagnostic accuracy, treatment monitoring, and prognostication in prostate cancer. Large-scale clinical trials and standardization efforts will be essential for these biomarkers to become routine tools in clinical practice, ultimately facilitating more personalized and effective patient care.

Circulating Tumor Cells (CTCs)

Pancreatic Cancer CTCs: Patients with pancreatic cancer who were clinically recurrence-free for up to 12 months post-resection were assessed in this study regarding the levels of their CTCs. The investigators reviewed whether persistent CTCs correlate with a higher probability for recurrence. The researchers compared individuals bearing transitional CTCs-trCTCs-to those with no existence of these transitional CTCs. They concluded that more significantly, those bearing trCTCs saw a higher recurrence rate and a shorter time to recurrence than those without them. It was also determined that positive trCTC status one year after the surgery was related to a distinct recurrence pattern and a higher risk of late recurrence, which may aid CTCs in functioning as a useful biomarker in the prognosis and management of patients affected by this form of cancer (Javed et al., 2023).[9]

Colorectal Cancer CTCs (Sastre et al., 2020): Here, a large cohort study was conducted in metastatic colorectal cancer patients to identify the association of clinical characteristics with tumor molecular profiling and baseline CTC count. The study researchers found that 41% of the patients had ≥3 baseline CTCs. The higher baseline CTCs were associated with poorer performance status, multiple metastatic sites, higher carcinoembryonic antigen levels, and stage IV at diagnosis. Curiously enough, microsatellite instability and RAS or BRAF mutations are not associated with baseline CTC count. Additionally, correlations of different genetic variants-BRAF, RAS, and PIK3CA-and a range of clinicopathological features are reported (Sastre et al., 2020).[10]

CTCs in Prostate Cancer (Zapatero et al., 2020): A prospective phase II study analyzed the kinetics and detection of CTCs in patients with high-risk prostate cancer who were receiving radiation and hormone therapy. The absolute rate of CTC detection was rather low, at 7.5% at diagnosis, and 18.6% at the end of radiation therapy. Neither overall survival nor clinical or pathological factors were correlated with a positive CTC status. The T3 and N1 stages, however, were correlated with the change of CTC status. To establish the prognostic and therapeutic applicability of CTCs in non-metastatic prostate cancer, the researchers emphasized that further studies with more substantial samples and improved techniques to detect CTCs need to be conducted (Zapatero et al., 2020).[11]

Exosomes and MicroRNAs

Yu et al. has carried out the research in most about renal cell carcinoma (RCC) and exosomal miRs or exo-miRs. According to them, among all urological malignancies, RCC is the deadliest due to its origin from the nephron tubular epithelial cells. [12]The crux of the matter presented by the authors is that Exo-miRs can be potential non-invasive markers for prognosis and diagnosis with a chance to become new therapeutic targets in RCC. Thus, such Exo-miRs can be regarded as a sort of "signature" or "fingerprint" of the donor cell, indicating its biological origin and pathophysiological condition.

Kok and Yu (2020) also present an expanded overview of exosomes of cancer. According to them, exosomes are defined as small extracellular vesicles that range from 30 to 100 nm in size, produced by all cells, and found in all bodily fluids. Exosomes have been taken over by cancer cells to facilitate the rapid growth of tumors and to avoid being eliminated by their hosts, say the authors.[13] It emphasizes the control of paracrine trafficking, which exosomes affect the circulatory and tumor microenvironment. It covers the capability of exosomes as a target for therapy in cancer and its use in the development of a diagnostic biomarker with the writers.

Aboutalebi et al. (2020) focused their research on ovarian cancer (OC) and circulating microRNAs. [14]They pointed out that the late onset of symptoms in OC usually results in the advanced diagnosis and hence raises the death rate of the disease. The authors revealed the role played by aberrant miRNA expression in the process of tumor initiation and progression. They highlight serum miRNAs as potential predictors of response to OC treatment and prognostic markers. This paper forms an overview of circulating miRNAs as new biomarkers in the development of OC.

In 2022, Marin et al. discuss the microRNAs present in exosomes prepared from the plasma of Brazilian patients with pancreatic cancer. [15]The study emphasizes the fact that pancreatic cancer is aggressive and thus would be best diagnosed early. The authors report that some of the miRNAs were significantly over-expressed in the exosome of the plasma of the pancreatic cancer patients compared to the healthy controls: specifically, miR-125b-3p, miR-122-5p, and miR205-5p. Such patients had a significant overexpression of miR-205-5p, and this gene presented high diagnostic capacity with a ROC curve at 0.86. The study thereby emphasizes how demographic-specific factors become crucial for consideration during research into biomarkers.

Urinary Biomarkers

Ankerst et al. (2019) studied the Prostate Cancer Prevention Trial Risk Calculator in relation to the incorporation of urinary prostate cancer antigen 3 (PCA3) and TMPRSS2:ERG. [16]The inclusion of PCA3 but not of TMPRSS2:ERG increased the ability to predict the model significantly.

For patients on androgen-deprivation therapy with advanced and metastatic prostate cancer, Martínez-Piñeiro et al. tested the PCA3 and TMPRSS2-ERG scores. The results indicated that these urine markers were not reliable for staging purposes of the cancer or to determine the effectiveness of treatment in advanced prostate cancer.[17]

Fernandez-Perez et al. (2023) studied patients with metastatic castration-resistant prostate cancer on enzalutamide therapy; among the most important biomarkers were plasma Androgen Receptor copy number increase and circulating tumor cells (CTCs). Conversely, their results did not associate TMPRSS2-ERG detection with differential efficacy of enzalutamide.[18]

Ahearn et al. studied the expression of IGF/insulin receptor in prostate cancer tissues in 2018. High expression of IGF1R is slightly increased in the risk of lethal prostate cancer, particularly in the risk of tumors that are positive for ERG.[19]

An open-label study investigated whether three months of treatment with finasteride altered prostate cancer biomarkers. The investigators reported that while short-term finasteride treatment substantially changed widely used prostate cancer biomarkers, it did not improve their accuracy.

In 2021, Lee et al reported a study on CYP3A activity using urinary metabolic markers. They observed that such markers in healthy individuals reflect the activity of CYP3A in the liver, not in the intestine.[20]. Using measurements of urinary markers of hydration when water was restricted and then introduced in graded amounts, Johnson et al. (2020) determined that approximately 1500 mL of excess water would be necessary to achieve the urine color corresponding to an acceptable intake after three days of water restriction.[21]

Chen et al. in 2020 developed a urine DNA methylation test called utMeMA for early diagnosis of bladder cancer and follow-up of its recurrence. Results in the current test were even more precise, sensitive and specific as compared to cytology and FISH in tumors detected at the early stages, with minimal and residual content or recurrence.[22]

Shrestha et al. (2020) evaluated breath, plasma, and urine markers for diagnosing lactase non-persistence. They observed that in the absence of lactose or milk as a substrate, the most reliable marker to identify lactose malabsorption was breath H2.[23]

Nata et al in 2023 assessed whether febuxostat affects markers of endothelial dysfunction and renal progression in chronic kidney disease. Febuxostat reduced blood uric acid levels without changing endothelial function markers; however, it showed promise for maintaining renal function in some individuals whose serum uric acid concentrations decreased after treatment.[24]

Clinical Applications

Fahrmann et al. (2021) identified the biomarker potential of CA19-9 for the early detection of pancreatic cancer. They reported that the levels of CA19-9 started to increase dramatically even two years before diagnosis, with as high as 60% sensitivity at 99% specificity in as short a time as 0-6 months. According to the study, CA19-9 can be used as an anchor marker for applications such as the early diagnosis of pancreatic cancer.[25]

The study by Bidard et al. (2022), also called PADA-1, is an experiment which tested the hypothesis of transferring advanced breast cancer patients with an ESR1 mutation that started to

increase during therapy with aromatase inhibitors and palbociclib to therapy with fulvestrant and palbociclib. The switch yielded a significant gain in progression-free survival, indicating that the therapeutic intervention with ESR1 mutations in the blood occurs early enough to offer clinical benefit.[26]

Singh et al. evaluated the possible marker for diagnosing non-invasive urinary bladder urothelial carcinoma: the HMGB-1 associated with autophagy (2022). The given study disclosed an increase in serum levels of HMGB-1 among patients with UBC and correlated the same with the severity of the disease. Hence, the above candidate is recommended as a potential candidate for the early identification of UBC, provided that further validation in larger cohorts of patients can be made.[27]

By classifying two distinct cohorts namely the favorable cohort characterized by some patients harboring low tumor mutational burden that showed robust intratumoral CD8 T cell density and antigen-specific T cell responses and also shorter survival or progression periods, they scrutinized those characteristics that translated into clinical benefit. Immunological correlates and neoantigen responses in patients receiving ipilimumab for prostate cancer were analyzed by Subudhi et al.[28]

The baseline circulating tumor cell count has now been found to have prognostic value in metastatic castrate-sensitive prostate cancer by Goldkorn et al, who demonstrated that undetectable CTCs were associated with both progression-free survival and better PSA response, implying that CTC count may be a useful prognostic biomarker in this scenario.[29]

Emmett et al conducted a phase 2 pilot study of therapy with 177Lu-PSMA-617 in metastatic castration-resistant prostate cancer in 2019. They showed that, during the screening of PSA on PSMA PET, standardized uptake value predicted a PSA response; therefore, PSMA PET is useful for the foresight of treatment outcome and failure patterns.[30]

Roh et al. studied the combination of EBV status, microsatellite instability (MSI) and single patient classifier (SPC) as biomarkers for prognosis in stage II/III gastric cancer. The author reported that this combination may serve as a marker for prognostic purposes and prediction in response to adjuvant treatment.[31]

In 2021, de Deus et al. studied the effects of blood flow-restricted resistance exercise on redox balance and cardiac autonomic function in patients with chronic renal disease. Both training models increased heart autonomic function, decreased oxidative stress, and enhanced antioxidant defences.[32]

Immune microenvironment in small HER2-positive breast cancers from APT trial: Barroso-Sousa et al. (2019) have described the immunological microenvironment of small HER2-positive breast cancers in the APT trial.[33] They found immune profiles to vary based on hormone receptor status, histological grade, and molecular subtype. Some tumour features, however, were found to be associated with high levels of tumor-infiltrating lymphocytes and PD-L1 expression.

Shore et al. (2019) studied a new 3-month formulation of leuprolide acetate for androgen deprivation therapy in the patient diagnosed with prostate cancer.[34] Outcomes of study showed that this product safely elevated and maintained castrate testosterone levels without a safety and tolerability profile different from what had already been established with known androgen deprivation therapies.

Future Research Directions

To facilitate the clinical translation of these biomarkers, future research should focus on several key areas:

1. These need multibackground large scale validation studies: across varied populations to demonstrate sufficient test sensitivity, specificity and to ensure clinical utility with proper multicenter trial research.
2. Cost-Effective Assay Development: The research agenda should include more cost-effective biomarker assays, and most particularly, such strong biomarkers as CTCs and Exo-miRs. Such techniques as microfluidic devices or simplified molecular assays would cut costs and make these tests available across healthcare settings.

3. Standardized Protocols: Consistency in standardized protocols for detecting and analyzing biomarkers guarantees reproducibility. Stabilized standardized workflows and especially in the assays aimed at identifying Exo-miRs as well as those related to DNA methylation patterns are needed to obtain reliability in their clinical introduction.
4. Multiplex Biomarker Panels: Multiplexing of PSA, CTCs, and Exo-miRs in one panel increases the likelihood of obtaining proper risk stratification and treatment planning. Investigations on multi-modal diagnostics may then be able to empower clinicians in tailoring individual patient profiles in the clinic.
5. Biomarker-Guided Combination Therapies in Advanced or Treatment-Resistant Prostate Cancer: A combination therapy guided by a biomarker that includes hormonal, immunologic, and targeted treatment may be best for advanced or treatment-resistant prostate cancer patients. The study of using biomarkers as guides for combination therapy may be one of the best areas to be explored since it will help improve survival and quality of life for patients with advanced or resistant prostate cancer.

Addressing these research priorities can help the prostate cancer field make significant strides in the integration of emerging biomarkers into clinical practice. This will enable more personalized, efficient, and effective management of prostate cancer, improving patient outcomes and quality of life.

Challenges and Considerations

The study of Fendler et al. was a prospective single-arm clinical study to evaluate the sensitivity of the 68Ga-PSMA-11 PET for the diagnosis of recurrent prostate cancer. Results: It was reported that higher detection rates were associated with higher levels of PSA, which were accompanied by a very high positive predictive value of 0.84-0.92. This procedure has been highly accurate in localizing prostate cancer that has recurred and is widely agreed upon by most experts.[35]

A 22-gene genomic classifier (Decipher) was validated in individuals with recurrent prostate cancer by Feng et al. in 2021. According to the study, the classifier had an independent relationship with overall survival, mortality specific to prostate cancer, and distant metastases. The findings showed that the benefits of hormone therapy in combination to salvage radiation may not be uniform for all men with biochemically recurrent prostate cancer.[35]

Tagawa et al. enrolled patients with metastatic castration-resistant prostate cancer into a phase I dose-escalation study utilizing the alpha emitter 225Ac-J591 targeting PSMA. Many of those patients experienced a fall in PSA and control of circulating tumor cells, markers both for safety and preliminary efficacy demonstrated by the study.[36]

Greenwood et al tested intradialytic exercise within a 6-month program in the randomized controlled PEDAL study on quality-of-life effects. The authors report that this intervention did not, as compared with standard care, result in any statistically improved primary outcome, which is the physical component summary score for the Kidney Disease Quality of Life Short Form.[37]

McManus et al conducted a randomized controlled trial with the aim to explore the computerized intervention for hypertension management, called HOME BP. The intervention that incorporated guided self-management together with self-monitoring improved control of systolic blood pressure at one-year follow-up at a lower cost than standard care.[38]

Lai et al. assessed the cost-effectiveness of salt substitutes and salt supply restrictions in the DECIDE-Salt experiment among older adults in Chinese elder care facilities. The authors concluded that replacement of ordinary salt with salt substitute will result in cost savings from reductions in mean systolic blood pressure and prevalence of hypertension and, cumulatively, in number of major adverse cardiovascular events.[39]

Wang et al (2023) reported on the design and challenges of an online randomized controlled study assessing the dissemination of cancer genetic research findings to Black women in the United States. The study threw up a number of moral, legal and societal issues that the study methodology needed to take into account.[40]

Makhnoon et al. conducted the FamilyTalk randomized controlled study to evaluate the effects of an online teaching tool on family communication on risk and colorectal cancer screening.

Results: No significant differences were observed between the intervention and control groups with respect to their colorectal cancer screening rates or privacy concerns.[41]

Beri et al. investigated the preferences for in-person disclosure of genetic test results in a multicenter study. 18% of patients refused random allocation as they wanted to receive the disclosure in person. Such patients also manifested greater levels of anxiety and distress, were tested for multigene panels, and were older in age. [42]

Future Directions

In the ROAR trial of patients with nonmetastatic, hormone-sensitive prostate cancer bearing the "BRCAness" genotype, rucaparib monotherapy was assessed. Although results were prematurely stopped for changes in standards of care, rucaparib established acceptable toxicity and efficacy as an ADT-sparing strategy to biochemically recurrent nonmetastatic prostate cancer.[43]

Using metabolomic analysis, Deng et al. (2021) discovered putative urine biomarkers for the diagnosis of latent tuberculosis infection (LTBI) and tuberculosis (TB). Histamine and glutathione (GSH) have been found to be promising molecular markers with excellent diagnostic precision.[44]

In a subgroup analysis of participants with sickle cell disease who were not asthmatic, Langer et al, suggested that inhaled mometasone was associated with decreased markers of macrophage activation. This effect may have contributed to the therapeutic benefits noted in an earlier randomized controlled trial.[45]

Hou et al. (2021) characterized the alteration of TCR repertoires in COVID-19 patients. Further, a panel of TCRβ clones may be well able to distinguish COVID-19 patients from controls. Identification of such a panel of TCRβ clones opens avenues for further development of immunodiagnosis and treatment.[46]

In the ENZA-p study by Emmett et al. (2024), a radio-doucherapy enzalutamide + [177Lu]Lu-PSMA-617, enzalutamide was compared against patients who had metastatic castration-resistant prostate cancer. This therapy came with tolerable tolerability and resulted in an important increase in progression-free survival of PSA (HR 0.43; 95% CI 0.29-0.63, p <0.0001).[47]

In the STHLM3-MRI trial, Nordström et al. (2024) will assess the results of the secondary prostate cancer screening by integrating PSA testing and MRI. They achieve low-grade tumor detection and limited cancer detection in the second round of the screening test, which in turn outlines potential ways for reducing the resource utilization associated with MRIs.[48]

Chi et al, in their 2020 study, demonstrated the metabolomic impact of ADT on prostate cancer patients and recognized changes in fatty acid metabolism, a decrease in steroid production, and ketogenesis. The researchers focused on the microbial synthesis of indoles related to immunological pathways and even suggested the possibility of a limited ketogenic diet.[49]

Gilbert et al 2024 provided an overview of results from PATCH and STAMPEDE studies that evaluate the value of transdermal oestradiol patches as a side-stream alternative to conventional ADT for prostate cancer. Preliminary data suggested that there was no increase in cardiovascular events with these approaches, similar suppression of androgens, improvements in metabolic parameters, and quality of life and bone health.[50]

CONCLUSION

This could become one of the major pathways toward bettering the treatment of patients. Integration of these emerging biomarkers in routine prostate cancer diagnostics and treatment has enormous potential. Improvement in molecular and genomic markers might enable the possibility of better risk stratification, improved early detection, and thus become a base for tailoring approaches for treatments. Adding these biomarkers along with the established PSA-based screening and the MRI-targeted biopsies may reduce the concerns of overdiagnosis and overtreatment, which plague prostate cancer management for far too long.

Further research is needed to fully realize the clinical benefits of these emerging markers. Large-scale, multicenter clinical trials are needed to validate the sensitivity and specificity of these biomarkers in diverse patient populations, providing the rigorous data needed to support regulatory

approval. Furthermore, future research should include the development of combination diagnostic panels that integrate multiple biomarkers, potentially offering a more comprehensive assessment of disease risk and progression.

Finally, the area for combination therapies based on information provided by biomarkers-particularly in metastatic or treatment-resistant cases-offers a promising avenue to potentially enhance therapeutic outcomes. Determination of cost-effective assays that are accessible, standard protocols, and efforts into widespread adoption of markers shall also be crucial in enabling such markers. Therefore, focusing on these areas should take the prostate cancer field of care closer to personalized medicine with better therapeutic options-a quality of life for and survival of patients.

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