

## EDITORIAL



## Best of 2023 in Prostate Cancer and Prostatic Diseases

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*Prostate Cancer and Prostatic Diseases*; <https://doi.org/10.1038/s41391-024-00790-7>

In recent years, several authors have focused on the role of social determinants of health (SDOH) in prostate cancer (PCa), which may have a significant impact on access to treatment and survival rates. The notable advancements in surgical and medical treatments for PCa have, however, exacerbated disparities due to the high costs associated with new diagnostic pathways and therapies. The present clearly represents a gap which needs to be filled. As a result, urologist and oncologist are actively fighting to reduce these disparities and the emerging literature is identifying areas where the most significant discrepancies exist [1, 2].

Regarding prostate cancer diagnosis, the best strategy to perform prostate biopsy is still a great matter of debate. Although we are slowly abandoning the transrectal (TR) route, the number of unnecessary biopsies and insignificant cancers detected still represent an unmet need. Consequently, an increasing interest in evaluating different biopsy schemes is clearly gaining momentum across the PCa panorama. However, for the time being the transperineal (TP) route including target and random biopsies still represents the gold standard [3–7].

Treatment of localized PCa involves several lacks which need to be addressed too. The efficacy of focal therapy in PCa treatment remains questionable. Despite various publications on the topic, its application is only advised within the context of well-designed clinical trials.

Besides, authors are focusing on identifying patients at risk of relapse after localized treatment in order to refine their management [8–10]. The introduction of genomic classifiers and new-generation imaging is clearly improving the ability to better classify and stage PCa patients; however, the absence of these diagnostic tools in historical clinical trials complicates their implementation.

In the past few years, the introduction of minimally invasive techniques (MISTs) has opened new scenario for the treatment of benign prostatic hyperplasia (BPH). Based on the current evidence, MISTs are a viable option between medical and definitive surgical treatment. The best candidates for each MIST still represent a great area of debate and studies are providing new evidence to tailor the right treatment to the right patient. Indeed, recent studies are proposing patient reported outcomes and perspectives as a proxy of surgical success [11–13].

Finally, the introduction of natural language processors has unlocked a new reality in the field of artificial intelligence. After an initial skepticism from the scientific community with the fear of being replaced by complex algorithms, several authors are exploring the millions of different applications of this new technology. Although the most recent evidence suggests that a fundamental landmark has been achieved, significant improvements are warranted before its clinical use [14–17].

In 2023 hundreds of manuscripts were evaluated by our editorial team. In this commentary, we present the best articles

selected to highlight the hot topics of this year for “*Prostate cancer and prostatic diseases*”.

**PROSTATE CANCER DISPARITIES**

The impact of race on survival in the metastatic prostate cancer (mPCa) setting has been evaluated by Freedland et al. in a systematic review including 51 studies. Main results showed Black and White patients to have similar survival outcomes in terms of metastasis free survival (MFS) and overall survival (OS). A secondary analysis demonstrated a better OS for Black patients on mPCa treatments. Similarly, no differences were recorded when comparing White and Hispanic patients. Finally, the Asian cohort presented better survival outcomes when compared to White patients. Certainly, the most intriguing finding of this study is the lower degree of disparities observed in metastatic stages rather than in earlier stages of the disease. Overall, continuous efforts to minimize such disparities in localized PCa diagnosis and management are needed [18].

**PROSTATE BIOPSIES: WHERE DO WE STAND?**

Novara et al. explored the role of perilesional biopsies in patients on active surveillance (AS). The authors enrolled 112 patients with very low and low risk PCa and evaluated the detection rate of random biopsies, targeted biopsies and perilesional biopsies. A detection rate of 19% for ISUP > 2 cancer was gained using only targeted biopsies. By adding 4 perilesional, 14 random or 24 random biopsies, the detection rate was 30%, 39% and 49% respectively. Hence, the present study adds further evidence to the field of targeted biopsies in patients on AS. At this stage, performing only target or target and perilesional biopsies represents a suboptimal strategy for the detection of clinically significant cancer. Although several different strategies to avoid unnecessary biopsies are available, the use of standard plus targeted biopsies still represents the gold standard in the management of patients at risk of PCa [19].

Biopsy's approach was evaluated by Hogenhout et al. in a retrospective cohort of 712 men undergoing either the TR approach or the TP approach without antibiotic prophylaxis. The authors recorded no differences in terms of PCa detection while a higher risk of infectious complications was observed in the TR arm (5% vs 1%;  $p < 0.05$ ). In doing so, further evidence for the TEXIT movement was added. However, even though the TR approach should be avoided when possible, additional studies should confirm the safety of the TP approach without antibiotic prophylaxis and its clinical implementation outside of clinical trials [20].

**LOCALIZED PROSTATE CANCER: HOW TO DEFINE OUTCOMES?**

A systematic review on functional and patient reported outcomes was performed by Nicoletti et al. in patients undergoing focal therapy for PCa. The authors retrieved 107 studies including high

intensity focal ultrasound, focal cryotherapy, irreversible electroporation, focal brachytherapy, focal laser ablation, photodynamic therapy, microwave ablation, robotic partial prostatectomy, bipolar radio frequency ablation and prostatic artery embolization. The most important outcome observed was pad-free rate which reached 92–100%. Overall erectile function results were very heterogeneous, ranging from 0% to 94%. Regarding complications, hematuria, infections, and urethral strictures were the most commonly reported issues. The present review clearly underlines the advantages of focal therapy in terms of patient reported outcomes. In any case, the key to success is selecting the appropriate patients for personalized treatment strategies. However, it still remains unclear which specific focal therapy technique is the most effective and moreover, how many different focal therapy approaches should be available in every center [21].

Sood et al. analyzed the oncological outcomes of patients undergoing radical prostatectomy (RP) in a PSA screened cohort. Overall, 1807 men with a median follow-up of 14 years were analyzed. The 15-year rates of biochemical failure, metastasis rate, adjuvant therapy adoption, positive surgical margin (PCSM), and OS were 28.1%, 4.0%, 16.3%, 2.5%, and 82.1%, respectively. These findings clearly differed based on the D'Amico classification and Diaz classification, confirming the strong role of these tools in predicting survival and oncological outcomes [22].

The role of genomic classifier in patients with localized PCa was analyzed by Boyer et al. More specifically, they assessed Decipher, GPS and Prolaris ability to predict biochemical recurrence, MFS and cancer specific mortality (CSM) compared to standard classification schemes. According to their results, all the new classifiers improved the accuracy of the standard schemes, although the benefit was modest and the certainty of evidence low. In the past years, the use of genomic classifiers has undoubtedly improved the management of PCa, particularly in the diagnostic setting. Nowadays, however, prognostic models are severely challenged by the introduction of different imaging modalities and treatment regimens. Therefore, integrating genomic classifiers with artificial intelligence models may be a possible path to streamline, reducing the complexity of predicting outcomes in localized PCa [23].

### RECURRENT PROSTATE CANCER: IS NEXT GENERATION IMAGING CHANGING THE GAME?

Preisser et al. evaluated the importance of persistent PSA after salvage RP. The authors identified 580 patients undergoing salvage RP, of whom 42% presented a persistent PSA. At 84 months after salvage RP, BCR-free, MFS, and OS was 6.6% vs. 59%, 71% vs. 88% and 77% vs. 94%, respectively for patients with persistent vs. undetectable PSA (all  $p < 0.01$ ). At multivariable Cox models, persistent PSA was an independent predictor for BCR (HR: 5.47,  $p < 0.001$ ) and death (HR: 3.07,  $p < 0.01$ ). The present study, even using exclusively conventional imaging, represents one of the widest cohorts of patients undergoing salvage RP, opening new insights on the possible role of adjuvant treatments in these patients with poor prognosis [24].

The role of NGI in biochemically recurrent PCa was summarized in a systematic review by Moul et al., evaluating nuclear medicine imaging modalities and MRI. According to their analysis, the detection rates of these new imaging range between 46% and 50%. While International Guidelines suggest the use of NGI for detecting recurrences and metastatic disease only, this study remarks that not enough evidence exists up to date to define how NGI affects treatment choices and patient outcomes. Indeed, the primary limitation of introducing NGI is its application in clinical practice. In fact, clinical trials supporting the use of systemic therapies for PCa at various stages, even in this setting used conventional imaging methods. Hence, the impact of NGI on clinical use is still to be defined [25].

### BLADDER OUTLET OBSTRUCTION: BACK TO PHYSIOPATHOLOGY



Cash et al. highlighted new perspectives on the physiopathology of bladder neck obstruction in men. In fact, a new model of obstruction involving inflammation was proposed. According to their findings, an initial prostatitis might lead to a chronic inflammation of the bladder neck and consequently to a sclerosis with collagen deposition, continuous inflammatory processes, and neuromuscular dysfunction. Overall, the possible different clinical scenarios associated with primary bladder neck obstruction clearly suggest a non-homogeneous and non-continuous remodeling of the bladder neck. Therefore, it is pivotal to investigate physiopathology to better understand different clinical conditions. The authors' hypothesis should be confirmed through in vitro or in vivo studies to definitively rule out the idea of a direct consequence of anatomical dysfunction [26].

Zhu et al. performed a real-world analysis of functional and surgical outcomes of Rezum surgery comparing younger vs elderly patients. The authors enrolled 256 patients of whom 110 (43%) were defined as elderly patients (>65 years). No significant differences in terms of IPSS, QoL and Qmax improvements were observed between groups. Likewise, no differences in terms of AEs and regret scores were recorded. Retreatment rates at 4 years were comparable (between 4–4.4%). In summary, the present study offers new insights into the management of elderly patients and those with comorbidities [12].

### PERSPECTIVES IN BASIC RESEARCH AND ARTIFICIAL INTELLIGENCE

Liang et al. investigated the possible role of omega 3 acid diet on PCa by using cancer mouse models. More specifically they evaluated the antitumoral effect on mice with GPR120 receptors. According to their results, only GPR120+ animals responded to omega 3 effects. Therefore, they concluded that host bone marrow cells with functional GPR120 are essential for the anticancer effects of dietary omega-3 fatty acids, and that a key target of the omega-3 diet are the M2-like CD206+ macrophages. This study confirms the role of lipid metabolism in PCa and possibly open new insights in evaluating the role of diet and metabolic factors in PCa management [27].

Cocci et al. evaluated the quality of information and appropriateness of ChatGPT outputs for urology patients. The authors retrieved case studies of 100 patients and asked ChatGPT to answer the question: "According to the patient data presented, what are the most likely diagnosis, what examinations do you propose, and what are the treatment suggestions?". The authors assessed accuracy, comprehensiveness, and clarity of ChatGPT. According to their results, 52% of all responses were deemed appropriate. Indeed, ChatGPT provided more appropriate responses for non-oncology conditions (58.5%) compared to oncology (52.6%) and emergency urology cases (11.1%) ( $p = 0.03$ ). Although ChatGPT's enthusiasm is rapidly growing, the present study clearly focuses on the significant limitations of the 3.5 version. Artificial intelligence will likely change our practice and research capabilities; however, as physicians, urologists, and researchers, we still need to identify and investigate its capabilities and safety [28]. Future studies should evaluate the best strategy for AI training and its future applications.

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#### AUTHOR CONTRIBUTIONS

CDN: Writing, Editing, Review, Data Collection, Intellectual Concept, Final Approval.  
 RL: Writing, Editing, Review, Data Collection, Intellectual Concept, Final Approval.

#### COMPETING INTERESTS

The authors declare no competing interests.