EDITORIAL

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"Quality: a parallel priority to quantity in prostate cancer focal therapy"

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There is little doubt about the effectiveness of radical prostatectomy (RP) and radiation therapy (RT) as the standard of care for prostate cancer management, particularly in intermediate and high-risk disease. In line with the "do not harm" tenet, the evolution of surgery has consistently advanced towards less invasive procedures with reduced pain and complications. The adoption of active surveillance (AS) in the US serves as a noteworthy illustration, with the proportion of low-risk men opting for AS escalating from 29.6% in 2014 to 49.5% in 2019, while for intermediate-risk men, rising from 10.4% to 20.4% over the same period [1]. Now that we are in the era of "treatment de-escalation" by reasonably trading off between exposing the oncologic outcomes and preserving the quality of life (QoL), focal therapy (FT) could be an option to bridge the gap between AS and radical treatments, namely RP or RT. Nicoletti and colleagues wisely identified a controversial yet exciting topic focusing on the oncological outcomes of different available modalities of partial-gland ablation. They contributed an important overview of FT, highlighting the shortcomings of the existing practice while maintaining hope through the promising outcomes aligned with preserving QoL. Several points should be considered regarding this valuable systematic review.

First, FT is a cancer management strategy rather than a definitive cure. It is an extension of AS with periodic measured intervention, aligning better genitourinary functions than RP [2]. The main driving force behind FT lies in preserving potency and urinary function while providing the patient a chance for rescue, if needed, and achieving a no-evidence-of-disease (NED) state. It is of utmost importance for younger men with unfavorable intermediate-risk prostate cancer, who are more likely to take risks to preserve their sexual and urinary functions. Pad-free rates could be as high as 98%, and erections sufficient for intercourse could likely be preserved [3]. The success of FT relies on the precision of imaging techniques that have seen remarkable advancements in recent years, particularly in prostate MRI. As technology continues to evolve, the landscape ahead of FT will look more promising, especially with the genomic analysis tests and incorporation of artificial intelligence in pathology and imaging.

Second, repeating FT could also be offered in case of residual or de novo localized disease, as it has been shown to preserve QoL. Repeatability is an advantage of FT. Of 271 men who required retreatment after primary FT, 71% chose to repeat focal HIFU in the study of *Stabile* and colleagues, which might be considered a satisfaction indicator, although not a perfect measure [4]. Repeat FT could induce NED in half of the men with residual clinically significant prostate cancer with only 7% treatment regret, although the sample size of this study was small [5].

Third, FT does not burn bridges regarding secondary treatment if necessary. It requires close follow-up to detect failure early, and patients can fall back on additional FT, RP, RT, or even full-gland ablation if necessary. Comparing primary robot-assisted radical prostatectomy (RALP) versus post-FT RALP revealed no significant increase in toxicity levels [6]. Salvage RP post RT versus post FT showed higher non-organ-confined disease and positive surgical margins in FT with better urinary function and similar biochemical recurrence, potency, and overall survival [6, 7].

Fourth, a significant hurdle in assessing the oncological results of FT is the absence of a standardized definition for cancer control. In practice, many randomized clinical trials face challenges in achieving adequate statistical power to detect potential improvements in overall survival (OS) due to the necessity for large sample sizes and extended follow-up periods. Consequently, alternative event-driven endpoints have been suggested as potential predictive indicators of OS in light of these limitations. These heterogeneous measures include progression-free survival (PFS), recurrence-free survival, metastasis-free survival, cancer-specific survival, retreatment-free survival, and freedom from radical treatment. In diseases characterized by slow progression and long-term survival expectations, the utility of overall survival OS is restricted [8]. Although metastasis-free survival might be superior to PFS due to the long post-progression period and the lack of a precise definition for biochemical recurrence in this setting, the best outcome measure is yet to be determined for assessing FT outcomes.

Finally, the acceptance and implementation of FT have experienced a significant uptick in recent years [9, 10]. However, the lack of randomized clinical trials and long-term follow-up has limited the acceptance of FT. Unfortunately, studies comparing RT and other FT modalities are scarce. Although RT is an accepted primary treatment, patients deserve to be counseled about all available options in a multidisciplinary fashion. Additionally, contemporary clinical practice moves toward precision medicine, which entails educating patients and involving them in shared decision-making to deliver personalized treatments that are aligned with their values. The goal is to address each patient's specific needs to enhance clinical outcomes and minimize side effects. Collaboration and data sharing among prostate cancer experts are pivotal in fostering a comprehensive understanding of the benefits and limitations of FT modalities compared to the traditional radical approaches. This synergy will enable the comparison of outcomes and ensure the delivery of evidence-based, patient-centered care that could optimize treatment management.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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