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Open to Debate: Con

Primary Tumor Treatment in Oligometastatic Prostate Cancer: Radiotherapy Versus Radical Prostatectomy

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The primary tumor in prostate cancer (PCa) can remain a major source for metastatic spread, even once metastases are evident and treated systemically [1]. In 2018, level 1 evidence from the STAMPEDE trial showed that patients with low metastatic burden (LMB) experienced a survival benefit with local treatment comprising radiotherapy (RT) plus standard systemic therapy compared to standard systemic therapy alone [2]. However, there are no data from randomized trials for other local treatment modalities such as radical prostatectomy (RP) [3]. Nonetheless, numerous retrospective studies investigating RP for oligometastatic PCa were also able to demonstrate an advantage of local therapy [4–6]. Thus, the choice of local treatment in patients with oligometastatic PCa remains a controversy of general importance to urology practice.

In this Open Debate, we address this controversy that concerns all PCa patients with LMB. The main outcomes of interest are overall survival (OS) and quality of life in this patient cohort. Our arguments are underlined by both prospective and retrospective data sources.

Since both RP and RT are equally effective in curing localized PCa [7], it is not unreasonable to expect comparable outcomes in the oligometastatic setting. Indeed, several series have pioneered the feasibility of RP in patients with oligometastatic PCa [4,5]. However, the pretreatment characteristics and outcome measurements varied widely. Therefore, we analyzed data for men treated with RP using the same inclusion criteria and endpoints as STAMPEDE in a retrospective series in 2019 [6] and found 3-yr OS of 91%, while STAMPEDE reported 3-yr OS of 81% [2,6]. Even though the patient characteristics might have differed between the two cohorts, the results at least suggest no major oncologic disadvantage may be expected with RP as local treatment compared to RT in patients with LMB.

Tumors need to be locally resectable to benefit from RP as a local treatment option. For tumors that are resectable, RP may prevent local symptomatic progression, underlining its high efficacy with respect to local disease control [6,8]. In addition, both the complication rates and continence rates with RP are acceptable. By contrast, RT showed no advantage regarding symptomatic local events when compared to systemic treatment alone [2]. Moreover, a relevant number of men experience lower urinary tract symptoms due to prostate enlargement. For these cases, RT may not be the optimal treatment approach, especially if de-obstruction is necessary, since patients treated with RT after transurethral resection have a higher risk of severe genitourinary toxicity [9].

Lastly, an advantage of the surgical approach is the potential to harvest larger amounts of pathologic tissue for genetic testing. Indeed, genetic profiling is increasingly recommended by international guidelines to guide treatment decisions for patients with metastatic disease [10].

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Nonetheless, several limitations of our study, as well as previous retrospective series, are evident. First are the limitations inherent to retrospective analyses, which preclude a direct and valid comparison to randomized controlled trial data. Second, since some of the RP cohort received additional adjuvant RT to the prostate bed or pelvis, the oncologic results may not exclusively be achieved by RP alone, as adjuvant RT may have also contributed. In addition, no quality-of-life evaluation was available, which could have provided further details regarding patients' general wellbeing after RP in this setting. However, this lack of quality-of-life data also applies to the RT setting.

The major counter point to all arguments is the lack of randomized data to support our position. Unfortunately, one of the earliest randomized controlled phase 3 trials (the RAMPP trial) examining RP as a local treatment option for patients with oligometastatic PCa was stopped after the STAMPEDE results were published because of ethical concerns regarding the failure to offer local treatment to these patients [11]. Further randomized data are expected from a Chinese trial (NCT03988686) as well as several phase 2 and feasibility studies within the next few years [12].

In conclusion, for valid comparisons of oncologic, functional, and quality-of-life outcomes between RP and RT, including pelvic lymphadenectomy versus pelvic lymph-node radiation, properly controlled randomized trials are needed. However, since local treatment in patients with LMB is now considered the new standard, RP should be further explored as a local treatment option for these patients. This is emphasized by the equal efficacy of RP and RT demonstrated for the treatment of localized disease [7].

Conflicts of interest: The authors have nothing to disclose.

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