Local Treatment of the Prostate in Metastatic Prostate Cancer: Need to Change the Concept?

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Potential benefits of a definitive local treatment for the prostate itself in metastatic prostate cancer (mPCa) patients has been discussed recently [1]. Several reports showed that local treatment at the original prostate site could have a survival benefit for patients with this disease [2–4].

Locoregional therapy is not usually suggested for metastatic cancer in which tumor cells have already spread into systemic circulation and metastasis has developed; however, several studies focusing on other metastatic tumors demonstrated that a reduction in the primary tumor burden resulted in a survival benefit and a better response to systemic therapy. Among urogenital cancers, cytoreductive nephrectomy is a standard therapy for metastatic renal cell carcinoma because radical nephrectomy improves survival in patients treated with interferon for metastatic disease [5,6].

The current standard treatment for mPCa is androgen deprivation therapy (ADT); however, a definitive local treatment can be used when it reduces significant local symptoms, improves the response of systemic treatment, and leads to an overall survival (OS) benefit. A retrospective study from the Surveillance Epidemiology and End Results (SEER) database showed OS and cancer-specific survival (CSS) benefits when radical prostatectomy (RP) or brachytherapy was added to ADT in mPCa patients [2]. Data from the Munich cancer registry reproduced these results [3]. A small cohort study showed that cytoreductive prostatectomy for low-volume skeletal mPCa patients was feasible and associated with better outcome for both clinical progression-free survival (PFS) and CSS; however, these studies were nonrandomized and/or conducted retrospectively, and the data cannot direct the current management of patients with mPCa. The patients’ baseline condition and selection bias would affect the outcome. Local therapy (including RP, brachytherapy, and external radiation therapy [RT]) can potentially harm urinary and sexual functions. The role of definitive local treatment for mPCa patients needs to be confirmed in randomized prospective clinical trials or further retrospective studies.

In this issue of European Urology, Lüppenberg et al. [7] reported the impact of local treatment on OS in mPCa patients using a national cancer data base. There are 15,501 mPCa patients identified in the database, and 9.5% (n = 1470) of these patients received definitive local treatment (RP or RT targeting the prostate). The mPCa patients with local treatment showed better OS. The survival benefit of local treatment was demonstrated in a propensity score–matched cohort with 2924 patients. In the matched cohort analysis, the 3-yr OS rate was 69% for patients who received local therapy compared with 54% for those without local treatment. Using a multivariate risk model for OS, the patients with relatively low risk of mortality received the most potential benefit from the definitive local treatment.

To minimize the risk of selection bias, a propensity score–matched analysis was performed in this nonrandomized retrospective study. The matched cohort analysis demonstrated the OS benefit of local treatment for mPCa patients in the adjusted cohort. The outcome in advanced mPCa disease can be affected by baseline risk factors for OS.
In this matched cohort, the metastatic status was adjusted using only the M stage (M1a, M1b, and M1c) and not using the extent of disease or the number of metastatic sites, which are predictors of survival in patients with mPCa. Because survival of mPCa patients with a limited number of metastases (typically up to three or five sites), which is called oligometastasis, is better than survival in patients with a high volume of metastases [8], it would be interesting to evaluate the impact of local prostate treatment for patients with mPCa using the cohort adjusted by the extent of metastasis.

The role of local prostate treatment for mPCa patients should be defined in randomized prospective trials; however, some patients may benefit from local treatment, as shown in this study [7]. The paper shows that patients with lower mortality risk benefit from local therapy. The lesion-targeted stereotactic body radiotherapy was associated with prolonged PFS in oligometastatic PCa patients [9], thus local prostate treatments would be beneficial for patients who may have better survival. Adding to the survival benefit, quality of life is also an important issue because RP and RT targeting the prostate affect urinary and sexual function.

As shown in this and previous studies [7,10], identification of patients who would benefit from local treatment would be an important issue. This might represent a paradigm shift in the management of patients with mPCa. A survival benefit was recently shown when ADT was combined with initial docetaxel chemotherapy, as chemohormonal therapy, particularly in patients with high-volume disease [11,12]. Multimodal treatment with chemotherapy has been shown to be effective for high-volume metastatic hormone-sensitive prostate cancer. Conversely, local treatment seems to benefit mPCa patients with low-volume metastasis or oligometastasis. Consequently, the current interest is in the appropriate selection for intensive systemic therapy comprising chemohormonal therapy or definitive local prostate treatment. Until the ongoing prospective trial is completed, local prostate treatment could be suggested in the management of appropriately selected mPCa patients.

Conflicts of interest: The author has nothing to disclose.

References