Clinical Considerations and Challenges in Treating Patients With Oligometastatic Prostate Cancer

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One of the most challenging aspects of caring for patients with prostate cancer remains the heterogeneity of their disease. Patients invariably ask about prognosis and curability of their cancer. Use of nomograms and clinical trial data help to provide some relevant information in various disease states. For many situations, the answer to such a question still remains difficult. A particularly difficult situation arises with patients with hormone-sensitive prostate cancer with oligometastatic disease. The excellent review by Clement and Sweeney\(^1\) sheds light on this clinically relevant population.

What exactly is oligometastatic disease in patients with prostate cancer? There has not yet been a consensus definition, and this highlights the difficult nature of this disease state. Some studies have considered patients with one to three metastases as having oligometastatic disease,\(^2\) whereas other studies have an expanded definition allowing one to five lesions.\(^3\) Current studies have tried to stratify disease as high volume versus low volume to tease out subgroups of patients with hormone-sensitive metastatic prostate cancer that would benefit from more aggressive therapy.\(^4\) Clinical outcomes and data show that patients with limited metastatic disease often do better than patients with high-volume metastases, regardless of treatment modality.\(^5\) This clinical phenomenon may account for the larger benefit of the chemohormonal therapy of androgen deprivation and docetaxel in high-volume disease but lack of a benefit in patients with low-volume disease.\(^4\) Multiple studies highlighted in the accompanying article by Clement and Sweeney\(^1\) are testing different initial androgen-deprivation therapy–based combination therapies in patients with oligometastatic disease. Unlike with docetaxel, an intense combinatorial approach may take advantage of the unique biology of patients with low-volume oligometastatic prostate cancer.

There are challenging logistics and factors in caring for patients with oligometastatic prostate cancer. The role of definitive therapy for the primary site of disease in patients with metastatic prostate cancer is unclear. Retrospective data show some clinical benefit with definitive therapy of the primary site of disease, both in men with lymph node–positive disease\(^6\) and in those with low-volume M1b disease.\(^\) This included a longer period until castration resistance.\(^7\) Prospective studies are ongoing to help determine the role of local control by radiation or surgery in addition to androgen-deprivation therapy. Patients who have poor prognostic factors such as initial unresponsiveness to androgen-deprivation therapy or other adverse prognostic factors may not be candidates for local definitive therapy. General consensus from our group would not support routine local intervention with curative intent in patients with metastatic...
disease, pending trial results. Special consideration may be given to young, fit, and well-informed men regarding localized therapy for their oligometastatic disease.

Another challenge is providing care in this era of more sensitive imaging modalities, which may detect more patients with metastasis. Historic data obtained by study of patients with metastasis has often relied on computed tomography or magnetic resonance imaging and traditional technetium-based bone scans. Some data and novel clinical trials highlighted by Clement and Sweeney use imaging modalities that are not uniformly available, such as recently approved 18F-fluciclovine–based imaging, choline-11 positron emission tomography imaging, and gallium-68 prostate-specific membrane antigen–based imaging. These newer modalities should eventually become more widely available, but immediate care will require extrapolation and careful interpretation to treat patients evaluated by standard less sensitive imaging. Disease uncovered by enhanced imaging may actually be early distant micrometastases versus true oligometastatic disease and may represent different biologic behavior.

Prospective data are limited with regard to treatment of recurrent nodal disease and directed treatment of distant oligometastatic sites, but some small series have shown biochemical control, notable periods of cancer-specific survival, and delay in androgen deprivation with salvage lymphadenectomy. Stereotactic body radiotherapy (SBRT) has also been used in a small series of patients presenting with up to three bone metastases or lymph nodes. Androgen deprivation in these patients was delayed a median of 38 months, potentially sparing the adverse effects of castration. A few retrospective analyses show increased progression-free survival with focused SBRT to metastases, and several prospective studies are ongoing for limited bone disease treated by SBRT. The choice of imaging and appropriate end point in these studies will be important given future systemic therapies that may affect an overall survival end point.

In summary, when patients present with oligometastatic or potentially curative M1 disease, it is necessary to use available data to develop a treatment plan that correlates with the goal for each patient, especially when considering non–standard-of-care, local definitive therapy in the setting of metastatic disease. Participation in clinical trials pertinent to these patients should be encouraged. Moreover, care within multidisciplinary clinics and tumor boards is vital to optimize outcomes. Whereas patients with any amount of metastatic disease traditionally only receive androgen deprivation, an exciting new frontier of enhanced imaging techniques, surgical and radiotherapeutic options, and more aggressive first-line systemic therapies suggests that we may be able to do better for our patients with oligometastatic disease. The review presented by Clement and Sweeney highlights many of the key points to consider in our practices and reminds us of the challenges to attaining optimal outcomes.
AUTHOR’S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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