



Local Ablative Treatment in Oligometastatic Prostate Carcinoma

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Editorial

Aggressive local treatment approaches in oligometastatic prostate carcinoma is one of today's most important topic in prostate cancer treatment algorithm. Hellman and Weichselbaum were first to define the notions oligometastases and oligo-recurrence [1,2] which are now widely accepted by oncologists. Hellman and Weichselbaum also differentiate 'true oligometastases' which has limited metastatic potential from 'induced oligometastases' occurring mostly after systemic treatment with extensive malignant capacities and resistant [3]. In prostate cancer, induced oligometastases includes patients with a rising PSA after primary therapy that has oligometastases on imaging or castrate resistant patients with a rising PSA level and image detected oligometastases [4]. Radical local treatment interventions like surgery or radiotherapy in oligometastatic patients is rationalized through the sentiments that disease with 1–5 metastasis is at the beginning of progression shows an attitude between localized and extensive stage. Consequently, long-term survival or cure can be achieved with definitive local therapy in such selected cases [5].

Another important mechanism to explain this unexpected outcome in patients who are treated with curative local radiotherapy is the abscopal effect. This is defined as vanishing of tumor outside the radiation portal without systemic therapy. Abscopal effect is also reported in uterine cervical cancer [6], hepatocellular cancer [7], malignant melanoma [8], and lymphoma [9]. This phenomenon is reported to occur with surgery, as well radiation therapy [10]. Lussier et al. [11] proposed tumour microRNA expression to differentiate the patients expected to live with stable disease (≤ 5 lesions) or patients who have potential of developing polymetastatic progression. Patient selection is the main issue in treatment decision of oligometastatic disease. Number and location of lesions (single metastasis, 2-5 metastasis, multiple metastases in a single organ or multiple organ metastases) are the most important means of selection. This warrants some featured imaging modalities like Multi parametric MRI, Ga-68 Prostate specific membrane antigen PET/CT (PSMA PET/CT) other conventional ones. A retrospective series of radical prostatectomy and extended pelvic lymphadenectomy in men with metastatic prostate cancer by Sooriakumaran and colleagues reported overall survival of 88.7% after a median follow-up of 22.8 months. Authors concluded that radical prostatectomy for men with distant metastatic but locally resectable prostate cancer appear safe in expert hands for selected patients [12].

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Cho et al. [13] evaluated the efficacy and toxicity of curative local radiotherapy in metastatic prostate cancer patients. In this study metastatic sites were divided into 4 groups: a) solitary bone, b) 2-4 bones, c) ≥ 5 bones, and d) visceral organs. Overall Survival (OS) and Biochemical Failure-Free Survival (BCFFS) were improved in radiotherapy patients (3-year OS: 69% vs. 43%, $p=0.004$; 3-year BCFFS: 52% vs. 16%, $p=0.002$). ECOG performance status, metastatic site, disease extent, and prostate radiotherapy were significant factors for OS in univariate analysis. Multivariate analysis confirmed significance of prostate radiotherapy as a predictor for OS ($p=0.046$). For BCFFS, only prostate radiotherapy was found to be significant ($p<0.001$) in univariate analysis. Conclusively, authors suggested that radiotherapy to the primary tumor was associated with improved OS and BCFFS in metastatic prostate cancer however they also impressed on the necessity of prospective controlled clinical trials to encourage this approach in prostate cancer patients with limited extent of bone metastasis and good performance status.

Culp et al. [14] evaluated men with documented stage IV (M1a-c) Prostate carcinoma at diagnosis using Surveillance Epidemiology and End Results (SEER) (2004-2010). Totally 8185 patients were investigated for definitive treatment of the prostate (Radical Prostatectomy (RP) or Brachy Therapy (BT)) or no local therapy. The 5-yr OS and predicted DSS were each significantly higher in patients undergoing RP or BT compared with no local treatment (Table 1)). RP or BT were

Table 1: The 5-yr OS and predicted DSS for patients with Radical Prostatectomy (RP) or Brachy Therapy (BT)) or no local therapy.

	5-yr OS %	5-yr DSS %	P<0,001
RP	67.4	75.8	
BT	52.6	61.3	
No local therapy	22.5	48.7	

also independently associated with decreased cause specific mortality CSM ($p < 0.01$). This study also confirmed the survival benefit of local therapy in metastatic prostate carcinoma however could not tease out that prospective trials are essential to recommend this approach in daily practice. In another SEER database analysis metastatic prostate cancer patients treated with radical prostatectomy, intensity modulated radiation therapy, conformal radiation therapy or no local therapy were identified. Decrease in the risk of prostate cancer specific mortality was 52% and 62% for radical prostatectomy and intensity modulated radiation therapy respectively. However conformal radiation therapy did not improve survival compared to no local therapy. As a conclusion authors suggested local therapy with radical prostatectomy and intensity modulated radiation therapy but not with conformal radiation therapy in metastatic prostate cancer [15].

Substantial amount of retrospective data encourages focal ablative treatment oligometastatic prostate carcinoma while it is a unique clinical state with indolent tumor biology. However, the basic question is who will benefit most. In their study Yao et al. [16] suggested that patients with fewer comorbidities, longer life expectancy, and lower Eastern Cooperative Oncology Group performance status are suitable for radical local treatment. Also, patients with target lesion in a suitable location with a reasonable size and patients with metastasis in organ composed of parallel functioning subunits with considerable organ reserve (e.g. bone, lymph node, and lung, liver) should preferably be considered for ablative local treatment.

Conclusion

1. Further prospective data are needed to select patients with oligometastatic prostate cancer most likely to benefit from a radical therapeutic approach. Highly sensitive imaging technology and some molecular markers may be helpful to differentiate the suitable patients.

2. Metastasis-directed approaches, such as stereotactic body radiotherapy, are associated with minimal toxicity and excellent local control; however, their effect on oncological outcomes is not proved yet.

3. A multimodal approach to patients with oligometastatic disease is warranted.

4. Local ablative therapies, such as prostatectomy and radiotherapy, are reported to be safe and seem to reduce the need for palliative treatment; however there is no level 1 evidence to support its effect on survival outcomes and to suggest it as standard of care yet [17].

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