

The role of radical prostatectomy in the management of oligometastatic prostate cancer



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Increasingly with the advent of newer hormonal manipulative strategies, and other novel agents in the treatment of metastatic prostate cancer, the clinical future for these patients is trending towards chronicity. With this in mind, one emerging clinical question is to identify; "which patient cohort may benefit from local surgical treatment of the primary prostate cancer (LTP), along with the loco-regional lymphatics, in the setting of metastatic disease". The corresponding clinical question is; "what exactly constitutes acceptable metastatic disease", now termed oligometastatic disease (OMD).

It is accepted that older and comorbid patients, with limited life expectancy, and a high burden of metastases, would be unsuitable for local treatment. However, urologists are increasingly concerned with the high rate of local problems at long term follow-up, when the primary tumour is not excised. These would include; urethral obstruction by tumour in-growth, haematuria, ureteric obstruction at the trigonal level causing renal failure, and catheter dependence, most of which require repeat admission for hospital-based management.

The conventional treatment of metastatic prostate cancer is androgen deprivation therapy (ADT), followed by secondary or novel hormonal manipulation, as well as chemotherapy. The latent local problems are dealt with as required, either by endoscopic means, or palliative radiotherapy (RT). However these local palliative therapies often come too late in the disease course, and are associated with toxicities that impair quality of life.

The scientific rationale for LTP in OMD is;

- (i) removal of the source of cytokines that

would otherwise facilitate further metastases, (ii) cytoreduction of the primary may improve response to systemic therapies, (iii) removal of more aggressive sub-populations that subsequently metastasise^{1,2}. There is speculation that the OMD patient with limited nodal and/or axial skeletal metastases is at an earlier biologic stage, or represents a more indolent cancer cell sub-type, than the patient with multiple distant and visceral metastases. In other malignancies (eg, renal cell, ovarian) there is evidence that treatment of the primary in addition to systemic therapies improves cancer survival.

One study analysed 11 patients with OMD, defined as ≤ 5 bone metastases and/or pelvic or retroperitoneal nodal disease (by bone scan, MRI, CT), who had RP with extended pelvic lymph node dissection (ePLND) – median nodal yield $n=27$. The 7-year clinical progression-free survival (PFS) was 45%, and the cancer specific mortality-free survival was 82%. Adjuvant ADT was required in 91%, and adjuvant RT in 64%³. Therefore this entailed a multimodal approach and appeared safe and feasible in this small cohort.

Multicentre randomised studies out of the US and Europe have shown improved 10-yr PFS in pT3 N0 M0 prostate cancer in patients in whom RP is followed by immediate adjuvant RT (60-64 Gy). The 10-yr PFS in RP + RT is 56-61%, versus 38-35% with RP alone^{4,5}. It is accepted that one reason for this is the multimodal treatment of occult pelvic nodal disease. These patients often have micrometastatic disease at diagnosis that is not able to be detected on routine pre-operative staging scans.

There exist several retrospective studies

demonstrating an improved biochemical-PFS, cancer specific survival and overall survival to 10-years, in patients who received LTP, in pelvic node positive OMD, followed by early ADT plus RT, versus any of these therapies alone⁶. Again confirming the benefit of LTP, in combination with other modalities, in OMD.

There are several post hoc analyses of patients presenting with metastatic prostate cancer, requiring commencement of systemic ADT. They demonstrate that patients who had LTP by RP at their initial diagnosis were conferred a significant reduction in the risk of death at long term follow-up, compared to those who did not have LTP^{7,8}.

A SEER (Surveillance Epidemiology and End Results, US) population-based study analysed 8185 patients who had LTP in OMD. The 5-yr overall survival and predicted cancer specific survival were both significantly higher in patients who underwent RP (67%, 76% respectively) versus those who did not have LTP (53%, 61% respectively)⁹.

The mentioned studies have varying methodological problems which impact applicability.

In conclusion, LTP in the setting of OMD lacks level 1 evidence. However, in the robotic era, routine surgical prostate excision with pelvic lymphadenectomy provides excellent long term local control, removes the ongoing source of cancer cells, and disrupts loco-regional lymphatics. This may translate into a survival benefit. Surgery in OMD is part of a multimodal approach which includes ADT and RT as additional therapies. Randomised trials are required.

References available on request.

