

An Update on the Treatment Options for Localized Prostate Cancer



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With an estimated 192,280 new cases in the US in 2009 and 27,360 prostate cancer deaths, prostate cancer continues to place a large burden on healthcare in the Western world.¹ Up to 15% to 20% of men will be diagnosed with prostate cancer in their lifetime.² Fortunately, the disease is curable when the tumour is localized to the prostate gland and when treated at an early stage of the disease.

Diagnosis and risk stratification

Once a patient is diagnosed with prostate cancer, most clinicians use a risk stratification system based on serum PSA, clinical stage (*i.e.*, digital rectal examination [DRE] findings) and histological Gleason score that correlate with risk of metastases, pathological outcomes, as well as success of treatment. Patients that are considered "high risk" are staged clinically with a bone scan and pelvic CT or MRI before treatment option is decided.

Treatment options

In localized disease, treatment can be categorized either into those with curative intent (*i.e.*, "radical" therapies) or active surveillance. Treatments

designed to offer curative intent comprise:

- radiotherapy, including interstitial prostate brachytherapy or external beam therapy and
- surgery, including open retropubic prostatectomy, minimally invasive laparoscopic prostatectomy and robotic-assisted laparoscopic prostatectomy.

Primary androgen deprivation therapy is used primarily in those patients with either locally advanced or metastatic cancers.

Active surveillance

Active surveillance is a treatment program that actively monitors the course of disease with expectation of a curative treatment if the cancer progresses. Active surveillance is an attractive treatment option for patients with low-risk prostate cancers, in which a significant proportion of men will not have further disease progression. The approach of active surveillance is supported by the discrepancy between incidence and mortality of prostate cancer. Furthermore, autopsy studies show an incidence of prostate cancer of up to 70% in men > 60-years-old, who have not died of prostate cancer.^{4,5}

Thus, active surveillance may allow for the avoidance of side-effects of treatments in patients in which treatment may not be beneficial.

Table 1
Risk of recurrence after treatment³

Risk of recurrence	Low	Intermediate	High
Serum PSA (ng/mL)	≤ 10	> 10 to 20	> 20
Clinical stage	T1c, T2a	T2b	T3
Gleason Score	2-6	7	8-10

Unfortunately, no serum test, molecular markers or pathological tests accurately predict those patients that may progress. As such, all patients must be closely monitored with serum PSA testing and DRE at regular intervals (six months) and repeat prostate biopsies to ensure clinical or pathological progression does not occur.⁶ Current evidence suggests that this is a safe option in low-risk patients and long-term outcomes do not appear to be compromised in patients in this type of treatment protocol. In the University of Toronto active surveillance experience with a median follow-up of 4.5 years, Klotz, *et al* show in a total number of 500 low-risk patients a disease-specific survival of 99.5%. While 65% of surviving patients remain on surveillance, 35% of the patients have been treated. Indication for treatment was a rapid PSA doubling time in 19% and grade progression in 7% of patients. In 9%, treatment was the patient's choice.⁷

Patients most suitable for active surveillance include "low risk" (Table 1) and low volume prostate cancer (*i.e.*, less than three positive cores of cancer found on biopsy and < 50% of each core having prostate cancer).

Radiotherapeutic approaches

Radical radiotherapy may be performed as brachytherapy or external beam therapy.

Brachytherapy is the transperineal, ultrasound or MRI-guided implantation of radioactive sources into the prostate gland. Usually these seeds are made of Iodine-125 or Palladium-103 with a half-life time of 59 and 17 days respectively. The benefit of brachytherapy is

the short range of irradiation emitted from these radioactive sources, resulting in adequate dose levels within the prostate and avoidance of excessive irradiation of surrounding organs such as the bladder and rectum.⁶

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Brachytherapy can be used as mono-therapy in low-risk patients, preferably with a PSA < 15 ng/mL, a Gleason score < 7 and small tumour volume (≤ cT2a). Treatment alternatives including other isotopes in combination with hormonal therapy and/or external beam radiotherapy can be used in intermediate or high-risk cases.

Relative contraindication for brachytherapy are severe lower urinary tract syndromes, large prostate volume and previous prostate surgery,

while urinary retention, previous pelvis irradiation and locally advanced disease are absolute contraindications.

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For patients with larger prostate volumes or more extensive localized disease, external beam radiation therapy might be preferable. Common doses are between 70 Gy to 79 Gy in low-risk patients and 75 Gy to 80 Gy in intermediate- and high-risk patients.⁶ Since intermediate- and high-risk patients have a higher risk for lymph node metastasis, an additional radiation of the pelvic lymph nodes in combination with an androgen deprivation therapy is indicated in high-risk patients and has to be considered in patients with an intermediate risk of recurrent disease.

Surgical approaches

While the open radical prostatectomy has been the gold standard for years in the surgical treatment of prostate cancer, new techniques such as minimal invasive, laparoscopic approaches or robotic-assisted procedures have been developed. The goal of all surgical approaches is to radically

remove the prostate and perform a lymphadenectomy in cases where indicated.

The different techniques have similar short- and intermediate-term outcomes in hands of experienced surgeons.⁸ Studies have shown a long-term oncological outcome in organ-confined disease after open radical prostatectomies with a PSA-free survival between 52% and 75%.⁹⁻¹¹

Benefits of minimally-invasive approaches include reduced blood loss,⁸ reduced hospitalization and a shorter time to recover, as well as the postoperative pain after laparoscopic prostatectomy, while the postoperative continence recovery may be faster following open surgical procedures.⁸ However, both procedures show comparable results for recovery of potency.⁸

Biochemical outcome after treatment

Studies comparing the biochemical outcome after radical prostatectomy, brachytherapy or external beam radiotherapy have shown similar results for the different treatment modalities in patients with a localized prostate cancer disease (\leq cT2a)¹² over an intermediate follow-up




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interval. Further studies will show if the different treatments have comparable long-term oncological outcomes.

Conclusion

In summary, in a localized, early stage of prostate cancer, many treatment options are available. The choice of treatment is dependent on patient factors (*i.e.*, risk stratification of patient, anxiety level, acceptance of long-term monitoring, prostate size, voiding symptoms, *etc.*) as well as patient preference relative to the side-effect profile of each treatment modality. Fortunately, excellent biochemical recurrence-free rates exist between treatment alternatives; however, evidence from direct comparative studies through randomized control trials is limited. 

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