Treatment options for localised prostate cancer

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The first article in this new clinic on men's health provides a brief overview of the treatment options available to men with localised prostate cancer.

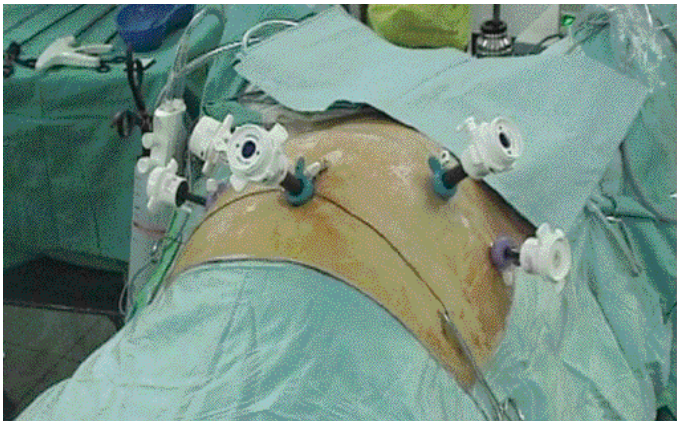

Figure. Intraoperative image of laparoscopic radical prostatectomy.

A diagnosis of prostate cancer is a shock for both the patient and his family. Not only do those affected have to come to terms with a diagnosis of cancer but soon after receiving this life-changing information patients are presented with an array of treatment options to select from.

Patients can be influenced in their decision-making by thoughts of imminent death rather than considering the efficacy and side effect profiles of available treatments. In addition, the information provided to the patient may only reflect the treatments a particular surgeon has skill and expertise in, rather than the full range of options.

It is of upmost importance to ensure that patient priorities are effectively matched with specific treatments, all of which have different efficacies, treatment durations and side effect profiles. This will clearly have a profound effect on how patients perceive their choice of treatment.

Although the lifetime risk of receiving a diagnosis of prostate cancer is 16%, the lifetime risk of death from the disease is only 3%.[1] As a result, significant debate exists over the most appropriate treatment for patients with prostate cancer.

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About 60 to 70% of men presenting with prostate cancer have localised disease. For this group, the treatment options include:

- radical prostatectomy
- radiation therapy (low dose rate brachytherapy, external beam radiotherapy or dose escalation radiotherapy)
- active surveillance
- experimental or emerging treatments (high-intensity focused ultrasound or cryotherapy).

Not all treatment options are available in all locations, particularly in rural areas. This can affect the decision-making process because some patients will choose options that are locally available rather than those that involve travelling significant distances.

Treatment selection

Treatment selection can be a difficult process for many men. The exact options available to a particular individual will depend on several factors, including:

- prostate characteristics: size, urinary symptoms, International Prostate Symptom Score
- patient characteristics: age, life expectancy, body mass index, sexual function, priorities in life
- tumour characteristics: Gleason score on biopsy, prostate specific antigen (PSA) level, clinical stage
- local: prior pelvic radiotherapy, ulcerative colitis, proctitis.

The most important factors to be considered are the grade and stage of the disease and the risks versus benefits of treatment. Patients with prostate cancer are stratified into one of three risk groups (Table 1) to provide prognostic information and to aid the decision-making process.[2] Different treatments are more appropriate for each risk group.

Radical prostatectomy

Radical prostatectomy can be performed via a number of surgical approaches including open, perineal and, more recently, laparoscopic (Figure) or robotic approaches. The cure rate for localised disease treated by radical prostatectomy is in the

Table. Risk stratification of patients with prostate cancer[2]

Low risk	Intermediate risk	High risk
PSA <10 ng/mL	PSA 10 to 20 ng/mL	PSA >20 ng/mL
Gleason score <7	Gleason score 7	Gleason score 8 to 10
Clinical stage <T2b	Clinical stage T2b/2c	Clinical stage T3

order of 95% but varies depending on risk group. Open radical prostatectomy is the established method of performing the surgery and has proven oncological efficacy. Indeed, for localised prostate cancer surgery was the only treatment option that had a demonstrable survival advantage when assessed in a randomised controlled trial.[3]

The main complications of radical prostatectomy include urinary incontinence and erectile dysfunction. The incidence of urinary incontinence is between 5 and 42%. Reported continence rates for laparoscopic radical prostatectomy are 95% at 12 months, equal to standard reference rates with open radical prostatectomy.[4] Sexual dysfunction after surgery ranges from 22 to 77%. This variation is due in part to preoperative potency, patient age, differences in potency definition and whether nerve-sparing surgery is performed.

In comparison with the open approach, the benefits of laparoscopic radical prostatectomy include improved magnification, reduced blood loss, shorter hospital stay (from about five days for the open approach to one to two days for the laparoscopic approach) and reduced convalescence.[5-7]

Touijer and colleagues have recently published a retrospective nonrandomised review of 1430 men treated with either laparoscopic radical prostatectomy or open radical prostatectomy for localised prostate cancer.[8] Rates of positive surgical margin, biochemical-free survival and sexual function were similar between the two groups. There was, however, a quicker return to continence in the group that underwent open radical prostatectomy but the group who underwent laparoscopic radical prostatectomy had less blood loss, fewer transfusions and shorter hospital stays.[8]

The advantages of the robotically assisted approach are similar to those that are offered by laparoscopic radical prostatectomy.

Until more evidence is available it would so far appear that it is the training and experience of a particular surgeon with a particular technique that is a key determinant of outcome from radical prostatectomy. Eden and colleagues demonstrated the oncological and functional outcomes from laparoscopic radical prostatectomy.[9] In their series of 1000 patients, the PSA level was 0.1 mg/L or less at three months in 99.1% of patients. At a mean follow-up of 27.7 months (range three to 72 months), 96.1% of patients were free of biochemical recurrence.

Radiation therapy

High dose rate brachytherapy

Radiation therapy can be delivered in a variety of differing modalities; however, there is an increasing body of evidence supporting improved oncological outcomes with the use of dose escalation, with the dose of radiation being increased periodically.[10-12] One such treatment that aims to increase the delivered dose of radiation to the prostate while minimising bladder and bowel toxicity is high dose rate brachytherapy. This involves the temporary placement of iridium cores into the prostate (for 24 hours to facilitate three treatment sessions), followed by a six-week course of external beam radiotherapy.

Low dose rate brachytherapy

Low dose rate brachytherapy is the placement of radioactive seeds into the prostate via a transperineal route. No skin incision is required and hospital stay is minimal.

Sylvester and colleagues have reported 15-year data from their cohort of 223 men who had combined external beam radiotherapy and low dose rate brachytherapy using iodine-125 or palladium-103.[13] When stratified for risk group, the biochemical recurrence-free survival rates at 15 years were 88% in the group at low risk, 80% in the intermediate-risk group and 53% in the group at high risk. The overall biochemical recurrence-free survival rate was 74%. Side effects include worsening lower urinary tract symptoms, urinary incontinence, erectile dysfunction and proctitis.

In a study of patients treated with iodine-125 brachytherapy followed up for at least five years, the reported rate of incontinence was 1.2% with an increased odds ratio of transurethral resection of the prostate (8.8; p=0.008).[14] The risk of rectal bleeding was 24% for up to three years after implantation of the radioactive seeds. Potency after treatment was age dependent: reported potency rates were 100% for men under 50 years of age, 80% in those aged 51 to 60 years and 45% in men over the age of 70 years.

Active surveillance

Active surveillance was previously known as 'watchful waiting', in which patients were monitored for signs of cancer progression and then palliative therapy was commenced. It was employed more often in elderly men.

Currently, with increasing use of PSA monitoring and stage migration, small-volume low-risk cancers are being detected in men who are electing to undergo active surveillance, in which definitive treatment is deferred until the first sign of disease progression. Choo and colleagues prospectively assessed the feasibility of watchful waiting with delayed intervention in 206 men. With a median follow-up of 2.4 years, 31 (15%) patients experienced disease progression and received active treatment.[15]

Carter and colleagues reported results from a series of 98 men with nonpalpable tumours fulfilling Epstein's criteria for small-volume disease.[16] Of the patients followed up for longer than 12 months, 25 (31%) experienced disease progression. Thirteen of these 25 men with progression underwent radical prostatectomy, of which one (8%) had incurable disease. This early data suggest that in appropriately selected patients active surveillance is possible.

High-intensity focused ultrasound

Although high-intensity focused ultrasound is a relatively new procedure in both

Australia and the USA, it has been used in other parts of the world to treat thousands of men with prostate cancer. There are currently two competing high-intensity focused ultrasound technologies: Ablatherm and Sonablate. Both products involve the placement of a rectal probe for the delivery of ultrasound energy to the prostate, which results in high temperatures of about 85°C.

Although long-term data are lacking, Uchida and colleagues have published intermediate-term data of their experience treating 63 men with the Sonablate device.[17] With a median follow-up of 22 months the overall success rate was 75%, as defined according to the criteria recommended by the American Society for Therapeutic Radiology and Oncology Consensus definition (three consecutive increases in PSA after the nadir level). Side effects included 24% with urethral stricture, 3% with retrograde ejaculation, 3% with epididymitis, 2% needed transurethral resection of the prostate for prolonged retention and 2% developed a rectourethral fistula. Erectile dysfunction was reported in 25% of sexually active men.

Conclusion

There are several management decisions to be made by the patient with localised prostate cancer. As a rough guide, the treatment chosen will depend on which risk group the patient falls into and the patient's priorities in life. Radical prostatectomy is the most appropriate treatment for a man who is fully aware of all his treatment options, and has a clinically localised cancer (in the low- or intermediate-risk group) with at least 10 years of life expectancy.

Radiotherapy is most suitable for men with intermediate- or high-risk disease who are either unfit for surgery or wish to avoid surgery. The disadvantage is the difficulty of salvage surgery if radiotherapy fails; however, radiotherapy may safely follow surgery.

Low dose rate brachytherapy is only suitable for patients who have a low-risk cancer, a small prostate and minimal urinary symptoms. The most appropriate patient is a man over 60 years of age who satisfies these criteria and wishes to minimise the side effects of therapy.

High-intensity focused ultrasound is an experimental tool suitable for elderly men with low-risk disease who are keen to pursue active treatment or men who do not want to pursue conventional therapies.

It is essential that patients and their families be appropriately counselled regarding:

- disease characteristics and behaviour
- the treatment options available to them
- the efficacy of these treatments
- the side effect profiles of these treatments.

Once counselled, patients and their families can make appropriate selections and gain a degree of comfort knowing that they have matched their treatment option choice with their disease and their priorities in life. It is important that patients and families realise that prostate cancer is curable in most cases and that there is no need to rush into a decision; they have time to research their disease and their options. MT

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