

## Treatment I

### TREATMENT MODALITIES:

#### 1. Deferred treatment (active surveillance AA/watchful waiting WW)

There are two distinct strategies for conservative management that aim to reduce over-treatment: AS and WW.

|                         | Active surveillance   | Watchful waiting   |
|-------------------------|---|--|
| Treatment intent        | Curative  | Palliative   |
| Follow-up               | Pre-defined schedule  | Patient-specific   |
| Assessment/markers used | DRE, PSA, MRI at recruitment, re-biopsy                           | Not pre-defined, but dependent on development of symptoms of progression |
| Life expectancy         | > 10 years  | < 10 years   |
| Aim                     | Minimise treatment-related toxicity without compromising survival | Minimise treatment-related toxicity                                      |
| Eligible patients       | Mostly low-risk patients  | Can apply to patients with all stages                                    |

DRE = digital rectal examination; PSA = prostate-specific antigen; MRI = magnetic resonance imaging.

| Recommendations   | Strength rating |
|---|-----------------|
| No active treatment modality has shown superiority over any other active management options or deferred active treatment in terms of overall- and PCa-specific survival for clinically localised low/intermediate-risk disease. | Strong          |
| Offer a watchful waiting policy to asymptomatic patients with clinically localised disease and with a life expectancy < 10 years (based on co-morbidities and age).   | Strong          |
| Inform patients that all local treatments have side effects.  | Strong          |

#### 2. Radical prostatectomy (RP)

The goal of RP by any approach is the eradication of cancer while, whenever possible, preserving pelvic organ function.

The procedure involves removing the entire prostate with its capsule intact and seminal vesicles (SVs), followed by vesico-urethral anastomosis.

#### Pre-operative preparation:

##### Pre-operative patient education:

As before any surgery appropriate education and patient consent is mandatory prior to RP. Peri-operative education has been shown to improve long-term patient satisfaction following RP.

**Pre-operative pelvic floor exercises:** Although many patients who have undergone RP will experience a return to urinary continence, temporary urinary incontinence is common early after surgery, reducing quality of life (QoL). Pre-operative pelvic floor exercises (PFE) with, or without, biofeedback have been used with the aim of reducing this early post-operative incontinence.

**Prophylactic antibiotics:** Prophylactic antibiotics should be used; however, no high-level evidence is available to recommend specific prophylactic antibiotics prior to RP.

**Neoadjuvant androgen deprivation therapy (ADT):** Neoadjuvant ADT is associated with a decreased rate of pT3 (downstaging), decreased positive margins, and a lower incidence of positive lymph nodes (LNs). These benefits are greater with increased treatment duration (up to 8 months). Neoadjuvant ADT failed to improve either PSA relapse-free survival or cancer specific survival (CSS) and as a consequence should not be used.

**Timing of radical prostatectomy:** Oncological outcomes, including adverse pathology, additional treatment and survival, were no worse with delays of up to 3 months.

#### Surgical techniques:

Prostatectomy can be performed by open-, laparoscopic (LRP)- or robot-assisted (RARP) approaches.

In 2002, RARP was introduced. This technology combined the minimally-invasive advantages of laparoscopic RP with improved surgeon ergonomics and greater technical ease of suture reconstruction of the vesicourethral anastomosis.

No significant differences for oncological-, urinary- and sexual function outcomes, although RARP and LRP both resulted in statistically significant improvements in duration of hospital stay and blood transfusion rates over open RP.

**Robotic anterior versus Retzius-sparing dissection:** RARP has typically been performed via the anterior approach, first dropping the bladder to expose the space of Retzius. However, the posterior approach (Retzius-sparing [RS-RARP]) has been used to minimise injury to support structures surrounding the prostate.

RS-RARP improved continence at 1 week post catheter removal compared to standard RARP, however, a significant concern was that RS-RARP appears to increase the risk of positive margins. Recommendations cannot be made for one technique over another.

**Pelvic lymph node dissection (PLND):** Extended PLND includes removal of the nodes overlying the external iliac artery and vein, the nodes within the obturator fossa located cranially and caudally to the obturator nerve, and the nodes medial and lateral to the internal iliac artery. Removal of lymph nodes improves the accuracy of staging but has not been shown to improve clinical outcomes. The individual risk of patients harbouring positive LNs can be estimated based on validated nomograms. The Briganti, Partin and MSKCC nomograms have shown similar diagnostic accuracy in predicting LN invasion.

**Prostatic anterior fat pad (PAFP) dissection and histologic analysis:** The PAFP is a rare but recognised route of spread of disease. Unlike PLND, there is no morbidity associated with removal of the PAFP. The PAFP is always removed at RP for exposure of the endopelvic fascia and should be sent for histologic analysis as per all removed tissue.

**Management of the dorsal venous complex:** Given the relatively small differences in outcomes, the surgeon's choice to ligate prior to transection or not, or whether to use sutures or a stapler, will depend on their familiarity with the technique and the equipment available.

**Nerve-sparing (NS) surgery:** During prostatectomy, preservation of the neurovascular bundles (NVB) with parasympathetic nerve branches of the pelvic plexus can spare erectile function.

The quality of data is not adequate to permit a strong recommendation in favour of NS or non-nerve-sparing, but pre-operative risk factors for side-specific extraprostatic extension (EPE) such as PSA, PSA density, clinical stage, ISUP grade, and PI-RADS score, EPE and capsule contact length on MRI, should be taken into account.

**Removal of seminal vesicles:** The cavernous nerves run past the SV tips such that indiscriminate dissection of the SV tips could potentially lead to erectile dysfunction (ED). Randomized clinical trials (RCT) found no difference in margin status, PSA recurrence, continence or erectile function outcomes, whilst complete SV removal should be the default.

**Techniques of vesico-urethral anastomosis:** Although there are a variety of approaches, methods and techniques for performing the vesico-urethral anastomosis, no clear recommendations are possible due to the lack of high-certainty evidence. In practice, the chosen method should be based on surgeon experience and individual preference.

**Bladder neck preservation:** It has been proposed to improve continence recovery post-RP and should be performed routinely when the cancer is distant from the base.

**Urethral length preservation:** It is likely that preservation of as much urethral length as possible during RP will maximise the chance of early return to continence. It may also be useful to measure urethral length pre-operatively to facilitate counselling of patients on their relative likelihood of early post-operative continence.

**Urinary catheter:** It is routinely placed to enable bladder rest and drainage of urine while the vesicourethral anastomosis heals. Compared to a traditional catheter duration of around 1 week, some centres remove the transurethral catheter early (post-operative day 2-3). No higher complication rates were found.