Indian Council of Medical Research

Consensus Document for Management of Prostate Cancer

Prepared as an outcome of ICMR's Subcommittee on Prostate Cancer

Division of Non Communicable Diseases

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Categories of Evidence

Levels of Evidence

Level 1: High quality randomized controlled trials (RCTs) showing (a) a statistically significant difference or (b) no statistically significant difference with narrow confidence intervals; systematic reviews of Level I RCTs

Level 2: Lesser quality RCTs (e.g. <80% follow-up, no blinding, or improper randomization); prospective comparative studies; systematic reviews of Level II studies or of Level I studies with inconsistent results

Level 3: Case control studies; retrospective comparative studies; systematic reviews of Level III studies; retrospective studies

Level 4: Case series

Level 5: Expert opinions

The set of recommendations can be divided into 2 categories:

Desirable/Ideal: Tests and treatments that may not be available at all centres but the centres should aspire to have them in the near future.

Essential: Bare minimum that should be offered to all patients by all centres treating patients with cancer.

1 Epidemiology and Risk Factors

Prostate cancer appears to be a growing problem in males in India. The incidence of prostate cancer has been steadily increasing in recent years [1]. As per the NCDIR database, prostate cancer features amongst the top 10 cancers in urban cancer registries of Bangalore, Delhi, Bhopal and Mumbai [1]. Prostate cancer seems to be less of a menace in rural areas. It does not feature in the top 10 cancer in the rural Barshi registry. Prostate cancer has moved from being the eighth most common cancer in males in 1990s to being the third most common cancer in Delhi and Mumbai by 2014. Similarly, in Bangalore, it has become the third most common cancer from being seventh in 1990s. There were 37416 reported prostate cancer cases in 2016 in India which has increased to 41532 in 2020.Prostate cancer incidence is expected to increase to over 47000 cases by 2025 [1]. This figure constitutes about 3% of total cancer cases in the country. Mean age of incidence of prostate cancer in India is 69.7 years [2]. Metabolic syndrome has been linked to prostate cancer but the evidence is weak [3]. Testosterone supplements do not increase the risk of prostate cancer in hypo gonadal male [4]. No specific life style and dietary modifications are recommended for prostate cancer [5].

Screening

As per the available evidence population based screening cannot be recommended in Indian population in any age group (Level 1) [5]. There has been no improvement in prostate cancer specific survival and overall survival by routine population based screening [6].A person with known BRCA 2 mutation needs to be explained about increased risk of developing clinically significant prostate cancer. However, in view of limited evidence (Level 3) [7] routine screening with serum PSA cannot be recommended even for persons carrying BRCA2 mutation.

2 Diagnosis and Staging

Diagnosis

Patients presenting with clinical suspicion of prostate cancer are recommended to undergo a total serum PSA estimation.

If serum PSA <4 ng/ ml and digital rectal examination (DRE) is not suspicious: Evaluate for other causes like benign prostatic hyperplasia, prostatitis etc.

If serum PSA is 4-10 ng/mL and DRE is not suspicious: Antibiotic for 1 week with fluoroquinolones followed by repeat PSA may be considered though advantage of this practice is doubtful [8].

If serum PSA >10 or DRE is suspicious: Proceed for evaluation of prostate cancer diagnosis.

Role of mpMRI- Ideally a multi-parametric MRI (mp-MRI) of prostate is to be done prior to a systematic biopsy. If PIRADS≥3 targeted biopsies along with systematic biopsy is to be done. If mp-MRI not available or PIRADS≤2 only systematic biopsies is recommended [9, 10].

Biopsy

1st choice - Systematic 12 core biopsy by Trans-perineal route (low infection rates) [11]

2nd choice - Systematic 12 core biopsy by Trans-rectal route

In patients with strong clinical suspicion but negative biopsy -

To be kept on close follow up. Biopsy is to be repeated on rising PSA or persistently elevated PSA, only intra-ductal carcinoma in previous biopsy and positive mp-MRI findings.

Staging (AJCC Eighth edition)

Primary Tumor	
Tx T0	Primary tumor cannot be assessed No evidence of primary tumor
T1	Clinically inapparent tumor not palpable not visible by imaging
T1a	Incidental tumor in < 5% of TUR tissue
T1b	Incidental tumor in > 5% of TUR tissue
T1c	Needle biopsy prompted by elevated PSA

T2	Organ confined
T3	Tumor extends beyond the prostatic capsule
T3a	Extracapsular, unilateral and bilateral or microscopic invasion of bladder neck
T3b	Tumor invades seminal vesicles (s)
T4	Tumor invades external sphincter, rectum, pelvic side wall
Lymph Nodes	
Nx N0	Regional nodes were not assessed No regional (below level of bifurcation of common iliac arteries) nodes
N1	Regional node metastases – including pelvic, hypogastric, obturator, iliac, sacral
Distant Metastases	
Mx M0	Regional nodes not assessed No Metastases
M1 M1a M1b M1c	No distant Non-regional lymph nodes (outside true pelvis) Bone(s) Other site(s) with or without bone disease

Risk grouping (Adapted from NCCN risk stratification)

Definition			
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL	PSA 10-20 ng/mL	PSA > 20 ng/mL	any PSA
and GS < 7 (ISUP grade 1)	or GS 7 (ISUP grade 2/3)	or GS > 7 (ISUP grade 4/5)	any GS (any ISUP grade)
and cT1-2a	or cT2b	or cT2c	cT3-4 or cN+
Localised			**Locally advanced**

International society of urologic pathology grade (group) system

Gleason score	**ISUP grade**
2-6	1
7 (3+4)	2
7 (4+3)	3
8 (4+4 or 3+5 or 5+3)	4
9-10	5

Staging investigations

Staging recommendations: Staging is performed as per risk groups

Low risk prostate cancer: For treatment planning

Ideal: mpMRI Pelvis (Accurate for surgical/ radiotherapy planning)

Essential: CECT Pelvis (not as accurate for surgical planning)

Intermediate risk prostate cancer: Metastatic work up essential

Ideal: PSMA PET/CT, ± mpMRI Pelvis (If being planned for radical treatment)

Essential: CECT TAP ± Bone scan

High risk prostate cancer: Metastatic work up essential

Ideal: PSMA PET/CT ± mpMRI Pelvis (If being planned for radical treatment)

Essential: CECT TAP + Bone scan

Imaging in biochemical relapse: Metastatic work up essential

Ideal: PSMA PET/CT

Essential: mpMRI Pelvis

Summary of evidence for staging in prostate cancer

Initial Staging:

Choice of staging options depends on the availability of different diagnostic modalities and the course of treatment planned. With multiple novel and well established diagnostic options available it is imperative to understand pros and cons of each so that a well informed decision can be made for the right diagnostic test.

T-staging:

Trans-rectal ultrasound (TRUS):

Even though some single-centre studies reported good results using 3D TRUS or colour Doppler for local staging, these have not been confirmed by large scale studies [12, 13]. Thus, TRUS is no more accurate at predicting organ-confined disease than DRE [14] and NOT recommended for initial T staging.

MRI:

MRI has proven to be the most useful for local staging of prostate cancer, with T2-weighted imaging being the most reliable. For T3 stage prostate cancers, MRI has good specificity but low sensitivity for assessment of extra prostatic extension and seminal vesicle involvement as shown in a pooled data from a meta-analysis with overall sensitivity and specificity of 0.61 (95% CI: 0.54-0.67) and 0.88 (95% CI: 0.85-0.91) respectively [15] [Level 2 evidence]. In low-risk patients MRI is not recommended because of its low sensitivity in detection of focal (microscopic) extra prostatic extension. Addition of a 3T MRI or functional imaging along with T2-weighted imaging improves sensitivity for detection of extra prostatic extension and seminal vesicle involvement, but there is potentially large inter-reader variability [16]. MRI even though cannot be recommended for local staging in low-risk patients, still has a useful role in treatment planning [17-19].

N category:

CT and MRI:

Anatomical imaging modalities such as CT and MRI assess nodes based on their size and morphology. Nodes with short axis diameter >8mm in pelvis and >10mm outside pelvis are considered to be involved

with a sensitivity of less than 40 [20, 21]. Diffusion weighted MRI (DW-MRI) may detect metastases in normal sized nodes, but a negative DW-MRI cannot rule out nodal metastases [22, 23].

Choline PET/CT:

For identification of pelvic nodal metastases with choline PET/CT a meta-analysis of 609 patients revealed pooled sensitivity and specificity to be 62% (95% CI: 51-66%) and 92% (95% CI: 89-94%) respectively. The sensitivity of choline PET/CT increases to 50% in patients at high risk and to 71% in patients at very high risk, in both cases performing better than CECT [24] [Level 2 evidence]. When comparing choline PET/CT with DW-MRI, studies yielded contradictory results with sensitivity of PET/CT reported to be inferior [24], superior [25] and similar [26, 27] than that of DW-MRI. Due to its low sensitivity and poor widespread availability choline PET/CT role in regular patient workup need to be evaluated further.

PSMA PET/CT:

Prostate-specific membrane antigen (PSMA) PET/CT uses different radio-isotopes such as ^{68}Ga, ^{18}F and ^{64}Cu (including Tc99m PSMA SPECT/CT) most common being ^{68}Ga and ^{18}F. In a recent systematic review and meta-analysis no significant difference in terms of detection rate was noted among the most commonly used PSMA-radiotracers (^{68}Ga PSMA-11, ^{18}F-PSMA-1007, ^{18}F-DCFPyL), but a clear superiority to choline and fluciclovine was demonstrated [28]. In a meta-analysis comprising of 10 studies overall sensitivity and specificity was 0.84 (95% CI 0.55-0.95), specificity of 0.95 (95% CI 0.87-0.98) [29]. In a meta-analysis, the pooled sensitivity and specificity of PSMA PET/CT for nodal staging in a per node analysis was 75% and 99% respectively [30] [Level 2 evidence]. In a prospective multi-centric validation study in patients with newly diagnosed prostate cancer with a negative bone scan per patient-based sensitivity and specificity was 41.5% (95% CI: 26.7-57.8) and 91% (95% CI: 79.3-96.6) respectively, with treatment change occurring in 12.6% patients [31][Level 2 evidence]. According to a systematic review, with compared to mpMRI, ^{68}Ga PSMA PET/CT was found to have higher sensitivity 0.65 (95% CI: 0.49-0.79) compared to mpMRI sensitivity of 0.41 (95% CI: 0.26-0.57) with a comparable specificity 0.94 (95% CI: 0.88-0.97) of ^{68}Ga PSMA and 0.92 (95% CI: 0.86-0.95) [Level 2 evidence].

PET-MRI

PSMA PET/MRI has a new evolving role in work up and follow up of prostate cancer. A recent meta-analysis evaluating the role of PET/MRI for evaluation of prostate cancer revealed pooled sensitivity and specificity for primary tumour (per lesion) as 61.5% and 90.9% respectively and for lymph node metastatic (per lesion) as 64.3% and 97.4% sensitivity and specificity respectively [32] [Level 2 evidence]. Impact of better diagnosis using PET MRI on treatment and survival needs to evaluated further.

M Category:

Bone scan:

Bone scan has been the most widely used method of evaluation of bone metastases of Prostate cancer. A meta-analysis shows combined sensitivity and specificity of 79% (95% CI: 73-83%) and 82% (95% CI: 78-85%) respectively [Level 2 evidence]. ^{18}F-NaF PET/CT has superior sensitivity with a similar specificity for detecting skeletal metastases in newly diagnosed high risk prostate cancer [33, 34]. But in a prospective study, ^{18}F -NaF showed no added value over bone scintigraphy in newly diagnosed intermediate/high risk prostate cancer patients with negative bone scintigraphy [35].

Whole Body-MRI (WB MRI):

In a prospective study with 100 patients comparing diffusion weighted WB-MRI (DW-WB MRI) with conventional imaging including bone scan revealed that DW-WB MRI is more sensitive than bone scan in detecting bone metastases in high risk patients [36] [Level 2 evidence]. WB MRI is also more sensitive and specific than combined bone scan, targeted radiography and abdominopelvic CT [37]. Compared to choline PET/CT WB-MRI is more sensitive while choline PET/CT shows higher specificity [38]

PSMA PET/CT:

A recent systematic review consisting of 12 studies with a total of 332 patients evaluating the role of ^{68}Ga PSMA PET in primary staging of prostate cancer revealed high variation in sensitivity (median sensitivity on per lesion analysis of 33–92% and on per-patient analysis of 66– 91%) with good specificity (per lesion 82–100% and per patient 67–99%), with most studies demonstrating increased detection rates with respect to conventional imaging modalities (bone scan and CT) [Level 2 evidence]. A prospective multi-centric randomized study comparing Ga^{68} PSMA PET/CT to conventional imaging in 302 high risk prostate cancer patients, PSMA had higher accuracy (92% of PSMA v/s 65% of conventional imaging) and led to change in management in higher number of patients (27% with PSMA v/s 5% with conventional imaging) [39] [Level 1 evidence]. However, it is unclear if the stage shifts with more sensitive modalities (e.g. PSMA) adds to any clinical benefit and whether patients with metastases detectable only with MRI or PET/CT should be managed with systemic therapies or they should be subjected to aggressive local treatment with metastases directed therapies.

Role of imaging in relapsing and metastatic prostate cancer:

Biochemical relapse (BCR) after radical prostatectomy (RP) and radiotherapy (RT) precedes clinical metastases by 7-8 yrs. Therefore, accuracy of conventional imaging techniques (bone scans, CT and MRI) is poor in asymptomatic patients especially with low PSA. Usually in men with PSA only relapse after RP, salvage radiotherapy is offered to the patient on the basis of biochemical relapse without confirming with imaging.

A meta-analysis revealed that choline PET/CT is strongly influenced by PSA level and kinetics [40] Sensitivity is only 5-24% when the PSA level is <1ng/mL [41]. PSMA PET/CT is more sensitive than other imaging modalities especially for PSA level <1ng/mL [40, 42]. Scan positivity rate of Ga^{68} PSMA PET/CT for PSA level <1ng/mL are 33% (95%CI: 16-51), for 0.0 to 0.19ng/mL PSA, 45% (95%CI: 39-52) for 0.2-0.49ng/mL PSA, and 59% (95%CI: 50-68) for 0.5-0.99ng/mL PSA respectively.

In patients with BCR after RT, there is high morbidity of local salvage options hence its necessary to obtain a histological proof for local recurrence before offering treatment [43]. MpMRI has shown excellent results in detecting local recurrences [43]. PET has poor spatial resolution compared to MRI, a study for evaluation of a combination of PET/MR in setting of biochemical relapse could be worthwhile.

3 Management of Low Risk Prostate Cancer

Options include :

Active surveillance

Surgery

Radiotherapy

Patients with low risk are particularly at increased risk of over-treatment

Management - Active surveillance should be considered for all patients. Presently, it remains unclear if regular repeat mpMRI should be performed in the absence of any triggers (i.e. protocol-mandated). Similarly, it remains unclear if protocol-mandated, untriggered repeat prostate biopsies should be performed at regular intervals. As such, no recommendations can be made at this time regarding these issues.

Active surveillance/ watchful waiting in low risk prostate cancers:

Active surveillance - Aims to avoid unnecessary treatment in men with clinically localized prostate cancer who do not require immediate treatment, but at the same time achieve the correct timing for curative treatment in those who eventually do [44]. Patients remain under close surveillance through structured surveillance programs with regular follow-up consisting of PSA testing, clinical examination, mpMRI imaging and repeat prostate biopsies, with curative treatment being prompted by pre-defined thresholds indicative of potentially life-threatening disease which is still potentially curable, while considering individual life expectancy.

Watchful waiting - Refers to conservative management for patients deemed unsuitable for curative treatment from the outset, and patients are clinically 'watched' for the development of local or systemic progression with (imminent) disease-related complaints, at which stage they are then treated palliative according to their symptoms in order to maintain QoL.

	Active surveillance	**Watchful waiting**
Treatment intent	Curative	Palliative
Follow-up	Pre-defined schedule	Patient-specific
Assessment/markers used	DRE, PSA, mpMRI, re-biopsy	Not pre-defined, but dependent on development of symptoms of progression
Life expectancy	> 10 years	< 10 years

	Active surveillance	Watchful waiting
Aim	Minimize treatment-related toxicity without compromising survival	Minimize treatment-related toxicity
Comments	Low-risk patients	Can apply to patients with all stages

Recommendations for active surveillance

Inclusion criteria

1. For inclusion, patients must have a life expectancy of 10 years, but there is no lower or upper age limit for inclusion.
2. Evaluate life expectancy using a combination of performance status, co morbidity index, and health status screening.
3. Patients of low risk prostate cancer (NCCN criteria) to be considered. Patients with low-risk localized disease should be excluded if the extent and/or stage of disease is high based on mpMRI.
4. Patients with Gleason 3+4=7(ISUPgrade2) may be considered, if favorable characteristics are present, including PSA (<10), clinical stage (cT2a), and biopsy characteristics (low core positivity).
5. Patients with intra-ductal and cribriform histology on biopsy should be excluded automatically.

Monitoring and follow-up criteria

1. During active surveillance, men should have their PSA checked every 6 months.
2. During active surveillance, men should have a DRE every 12 months.
3. During active surveillance, repeat biopsy should be performed if there is a change in mpMRI (ie, increase in PI-RADS score, lesion volume, or radiological T stage), or by DRE progression or PSA progression.
4. If repeat biopsies are needed, they should be performed by mpMRI guided targeted biopsies (including in-bore, cognitive guidance, or mpMRI fusion) with systematic biopsies. However, it remains unclear when mpMRI should be performed during monitoring, and whether it should be performed routinely or triggered (Eg: by PSA or DRE changes)
5. Active surveillance should only be continued in patients if their life expectancy continues to be 10 years.

Reclassification criteria (i.e., leaving active surveillance for an active treatment)

1. Re-classification should apply only to patients with life expectancy of 10 years at the time of assessment.
2. Consider reclassifying patients if they develop anxiety or depression due to prostate cancer.
3. Consider reclassifying patients if they are reluctant to undergo repeat biopsies or repeat imaging.

4. Patients should not be reclassified automatically based on any one criteria of
    1. PSA progression alone in the absence of other factors.
    2. Histological changes alone (increased core positivity or % involvement of core) in absence of other factors
    3. Solely on DRE / mpMRI findings.

Consider reclassifying patients if they choose to undergo active treatment, independent of other factors.

Alternatives to active surveillance for the treatment of low-risk disease

If a patient is decided to be changed to an active treatment strategy due to any reason he may either, choose between Radical prostatectomy (RP) and radical radiotherapy. There has been no head on comparison between these 2 treatment modalities but as per the results of trials [45] both of them fare pretty similarly. The side effect profiles of both however differ. Hence it should be the patient's choice.

Surgery: Although AS should be the default management strategy in patients with low-risk disease and a life expectancy > 10 years, it would be reasonable to consider surgery as alternatives to AS in patients suitable for such treatments and who accept a trade-off between toxicity and prevention of disease progression if opting for AS.

Surgical approach in low risk prostate cancer: (Radical prostatectomy) RP can be performed via open, laparoscopic or robotic retro-pubic approach or by trans-perineal approach.

Ideal: Retro pubic RP should be performed for low risk prostate cancer. Minimal invasive techniques like robotic approach preferred where facilities and expertise available.

Essential: Open and laparoscopic RP can be performed with equally comparable outcomes.

Summary of evidence for surgery in low risk prostate cancer

The goal of radical prostatectomy (RP) is cancer control with preservation of organ function [46]. The procedure involves removal of the entire prostate with its capsule and seminal vesicles (SVs), followed by vesico-urethral anastomosis. The nerve sparing technique of RP is preferred in low risk disease [47]. Temporary urinary incontinence is common early after surgery. Pre-operative pelvic floor exercises (PFE) with, or without biofeedback may reduce the incidence of urinary incontinence. Prophylactic antibiotics should be used; however, no high-level evidence is available to recommend specific prophylactic antibiotics prior to RP.

Neoadjuvant androgen deprivation therapy

Neoadjuvant ADT is associated with a decreased rate of pT3 (i.e. down staging possible), decreased positive margins, and a lower incidence of positive lymph nodes. But neoadjuvant ADT is not associated with improvement in survival. So, it should not be considered as standard clinical practice. A small recent RCT comparing ADT vs ADT plus Abiraterone in the neo-adjuvant setting found significant reduction in tumour volume and lower biochemical relapse at > 4 years ($p = 0.0014$) [48]. Till level 1 evidences come, do not offer neoadjuvant androgen deprivation therapy before surgery.

Surgical techniques

Prostatectomy can be performed by open-, laparoscopic- or robot-assisted (RARP) approaches. The initial open technique of RP described by Young in 1904 was via the perineum [49]. The open retro-pubic approach was popularised by Walshin. It permitted a bilateral nerve-sparing procedure [50]. The first laparoscopic RP was reported in 1997 performed by trans-perineal route [51]. Most recently, robot assisted prostatectomy (RARP) was introduced using the da Vinci Surgical SystemR by Binder in 2002 [52].

In a randomised phase III trial, RARP was shown to reduce blood loss during surgery and duration of hospital stay, without improvement in early (12 weeks) or late functional or oncological outcomes compared to open RP [53, 54]. A recent Cochrane review comparing either RARP or LRP vs. open RP found no significant differences for oncological, urinary and sexual function outcomes, although RARP and LRP both resulted in statistically significant decrease in blood loss and duration of hospital stay [55]. Inform patients that no surgical approach (open-, laparoscopic- or robotic radical prostatectomy) has clearly shown superiority in terms of functional or oncological results.

A recent systematic review found with moderate certainty that retzius sparing (RS) RARP as compared to standard RARP improved continence at 1 month, 3 months as well as 12 months [56]. A single-surgeon propensity score matched analysis of 1,863 patients reached the same conclusion as the systematic review [57].

Pelvic lymph node dissection (PLND)

PLND during RP has so far failed to improve oncological outcomes, including survival [58]. It can be performed via extended (eLND) or limited approach however a RCT failed to show oncological benefit of an extended approach [59]. However, eLND provides important information for staging and prognosis [60, 61]. So, when a lymph node dissection (LND) is deemed necessary, perform an extended LND template for optimal staging. The patients with low risk disease usually do not require LND.

The individual risk of patients harbouring positive LNs can be estimated based on validated nomograms. The Briganti nomogram [62, 63], the Roach formula [64] or the Partin and MSKCC nomograms [65] have shown similar diagnostic accuracy in predicting LN invasion. These nomograms have all been developed in the pre-MRI setting based on systematic random biopsy. A risk of nodal metastases over 5% can be used to identify candidates for nodal sampling by eLND during RP [66, 67].

An updated nomogram has been externally validated in men diagnosed based on mpMRI followed by MRI targeted biopsy [68]. Based on this nomogram, patients can be spared an eLND if their risk of nodal involvement is less than 7%; which would result in missing only 1.5% of patients with nodal invasion [68].

Surgical techniques dilemmas

1. **Sentinel lymph node biopsy (SNB)** - There is insufficient high-quality evidence supporting oncological effectiveness of SNB [69, 70].
2. **Prostatic anterior fat pad (PAFP) excision** - The PAFP is always removed at RP for exposure of the endo-pelvic fascia and should be sent for histologic analysis as it contains metastatic PCa in up to 1.3% of intermediate- and high-risk patients [71, 72].

3. **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 [73, 74].

4. **Nerve-sparing surgery** - During prostatectomy, preservation of the neurovascular bundles with parasympathetic nerve branches of the pelvic plexus may spare erectile function [75, 76]. Extra-, inter-, and intra-fascial dissection planes can be planned, with those closer to the prostate and performed bilaterally associated with superior (early) functional outcomes [77 - 80]. Do not perform nerve-sparing surgery when there is a risk of ipsilateral extracapsular extension (based on cT stage, ISUP grade, nomogram, multi-parametric magnetic resonance imaging) [81, 82].

5. **Role of frozen section of lymph nodes during radical prostatectomy** - Although no RCTs are available, data from prospective cohort studies comparing survival of pN+ patients (as defined following pathological examination after RP) support that RP may have a survival benefit over abandonment of RP in node-positive cases [83]. As a consequence, there is no role for performing frozen section of suspicious LNs.

6. **Removal of seminal vesicles** - The more aggressive forms of PCa may spread directly into the seminal vesicles (SVs). For oncological clearance, the SVs have traditionally been removed intact with the prostate specimen. Whilst complete SV removal should be the default, preservation of the SV tips may be considered in cases of low risk of involvement [84, 85].

7. **Techniques of vesico-urethral anastomosis -** Several methods have been described. However, no clear recommendations are possible due to the lack of high-certainty evidence. In practice, the chosen method should be based on surgeon familiarity and preference [86, 87].

8. **Bladder neck management** - Some surgeons perform mucosal eversion of the bladder neck as its own step in open RP with the aim of securing a mucosa-to-mucosa vesico-urethral anastomosis and avoiding anastomotic stricture. A non-randomised study of 211 patients with and without bladder neck mucosal eversion showed no significant difference in anastomotic stricture rate [88]. Bladder neck preservation should be performed routinely when the cancer is distant from the base as it has shown to improve urinary continence post-operatively [89]. However, bladder neck preservation cannot be performed in the presence of a large median lobe or a previous TURP as it carries risk of margin positivity.

9. **Urethral length preservation -** The length of preserved membranous urethra is chiefly responsible for urinary continence. A systematic review and meta-analysis has found that every extra millimetre of membranous urethral length seen on MRI pre-operatively improves early return to continence post-RP [90].

10. **Cystography prior to catheter removal** - Cystogram to assess anastomotic leakage is not indicated as standard of care before catheter removal 8 to 10 days after surgery [91]. If a cystogram is used, men with LUTS, large prostate, previous TURP or bladder neck reconstruction, may benefit as these factors have been associated with leakage [92, 93]. Contrast-enhanced transrectal US is an alternative to assess leakage [94].

11. **Urinary catheter** - A urinary catheter is routinely placed during RP to enable bladder rest and drainage of urine while the vesico-urethral anastomosis heals. Compared to a traditional catheter duration of around 1 week, some centres remove the transurethral catheter early (post-operative day 2–3) [95, 96].

12. **Use of a pelvic drain** - A pelvic drain has traditionally been used in RP for potential drainage of urine leaking from the vesico-urethral anastomosis, blood, or lymphatic fluid when a PLND has been performed. Two RCTs in the robotic-assisted laparoscopic setting have been performed [97, 98]. Patients with urine leak at intra-operative anastomosis watertight testing were excluded. Both trials showed non-inferiority in complication rates when no drain was used. When the anastomosis is found to be watertight intra-operatively, it is reasonable to avoid inserting a pelvic drain. There is no evidence to guide usage of a pelvic drain in PLND.

Acute and chronic complications of surgery

Post-operative incontinence and erectile dysfunction are common problems following surgery for prostate cancer. At 1 year after surgery, approx. 20% patients have incontinence. Erectile dysfunction was observed in 70.4% after RALP and 74.7% after RRP. [99]. A RCT comparing RALP and RRP reported outcomes at 12 weeks in 326 patients and functional outcomes at 2 years [100]. Urinary function scores did not differ significantly between RRP vs. RALP at 6 and 12 weeks' post-surgery (p = 0.18). Overall complication rates of 19.8% vs. 8.2% were noted for eLND vs. limited LND, respectively, with lymphoceles (10.3% vs. 4.6%) being the most common adverse event [100]. Similar rates of lymphoceles have been observed in RALP series; however, in one subgroup analysis lymphoceles were more common with the extraperitoneal approach (19%) vs. the transperitoneal approach (0%) [101, 102].

Table: Intra-and peri-operative complications of retropubic RP and RALP

Predicted probability of event	RALP (%)	Laparoscopic RP (%)	RRP (%)
Bladder neck contracture	1.0	2.1	4.9
Anastomotic leak	1.0	4.4	3.3
Infection	0.8	1.1	4.8
Organ injury	0.4	2.9	0.8
Ileus	1.1	2.4	0.3
Deep vein thrombosis	0.6	0.2	1.4
Predicted rates of event	**RALP (%)**	**Laparoscopic RP (%)**	**RRP (%)**
Clavien I	2.1	4.1	4.2
Clavien II	3.9	7.2	17.5
Clavien IIIa	0.5	2.3	1.8
Clavien IIIb	0.9	3.6	2.5
Clavien IV	0.6	0.8	2.1
Clavien V	<0.1	0.2	0.2

RALP = robot-assisted laparoscopic prostatectomy; RP = radical prostatectomy; RRP = radical retro-pubic prostatectomy.

Non-surgical management of low risk prostate cancer:

External beam radiotherapy: Moderate hypofractionation has been shown to provide similar disease control in well conducted randomized controlled trials [103] in low risk prostate cancer. Dose fractionation of 70 Gy in 28 fractions over 5.5 weeks may be preferred (Level 1). No role of androgen deprivation therapy.

Stereotactic ablative body radiotherapy (SABR): SABR has been shown to provide similar biochemical control rates with very low gastro-intestinal and genito-urinary toxicity rates in low risk prostate cancer [104]. SABR to a dose of 36.25 Gy in 5 fractions over 1.5 weeks may be considered where in advanced radiation techniques are available (Level 2)

Role of brachytherapy: Brachytherapy may be performed with low dose rate (LDR) (Level 1) or high dose rate (HDR). The indications and proposed doses are indicated below

Indications and selection criteria for brachytherapy in low-risk prostate cancer	
Factors	Recommended (Do well)
PSA (ng/mL)	<10
Gleason score	5-6
Stage	T1c-T2a
IPSS	0-15
Prostate volume (g)	<60
Qmax (ml/s)	>15

Contraindications for brachytherapy in low risk prostate cancer	
Absolute	**Relative**
• Limited life expectancy • Unacceptable operative risks • Distant metastases • Absence of rectum, precluding the use of TRUS • Large TURP defects • Ataxia telangiectasia	• High IPSS >20 • History of prior pelvic radiotherapy • TURP defects • Large median lobes • Prostate gland >60 cm^3 at implantation • Inflammatory bowel disease

Proposed doses for brachytherapy	
^{125}I (Low dose rate)	145 Gy
^{103}Pd (Low dose rate)	125 Gy
3 – 4 fractions (HDR)	9.5 Gy to 10.5 Gy