PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

GENITOURINARY

PROSTATE CANCER

GU Site Group – Prostate Cancer

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1. INTRODUCTION

Prostate cancer is the most frequently diagnosed cancer in Canadian males accounting for 28.4% of new cases and 11% of all cancer deaths (Canadian Cancer Statistics 2008). Diagnosis is most frequently made between the ages of 60-69. The average annual change in age-standardized incidence increased by 1.2%/year from 1995-2004. This increase is attributed to the introduction of prostate cancer screening during the interval.

The natural history of prostate cancer is variable, but it is frequently indolent with an age standardized mortality rate of 23.6/100,000 in 2008 compared to 209/100,000 for all cancers. Death from prostate cancer most frequently occurs over the age of 79 (53.4% of deaths), and is uncommon before the age of 70 (14.8% of deaths).

The average annual age-standardized mortality decreased in Canada by 2.9%/year from1995-2004 and this improvement is attributed to both an artifact resulting from earlier diagnosis as well as improvement in management that occurred during this interval.

2. PREVENTION

The use of 5-α reductase inhibitors finasteride and dutasteride compared to placebo have been shown to reduce the risk of being diagnosed with prostate cancer among regularly screened men during the observation interval of two randomized control trials (Prostate Cancer Prevention Trial and the Reduction by Dutasteride of Prostate Cancer Events). No cause specific or overall survival advantage has been shown to date, and the advantages of chemoprevention with 5-α reductase inhibitors include delayed or prevented prostate cancer treatment and reduced anxiety over diagnosis. Complications of 5-α reductase inhibition include increase in sexual and erectile dysfunction and the possible induction of higher grade prostate cancer.

The routine use of chemoprevention with finasteride or dutasteride is not recommended, and the risks and benefits of chemoprevention of prostate cancer should be discussed with potential candidates before initiating a program.

3. SCREENING AND EARLY DETECTION

The practice of routine screening for prostate cancer remains controversial since supporting evidence is conflicting (NEJM editorials Nov 24, 2011). Routine screening for Ontario men is not recommended by CancerCare Ontario and not supported by the Ontario Ministry of Health and Long Term Care. If screening is considered desirable, it should only be undertaken following a discussion of the potential risks of overtreatment as well as the potential benefits of early diagnosis.

Screening is not recommended for men under 50 unless there is a family history of prostate cancer, and should not be continued beyond age 75.
Screening investigations include an annual serum Prostatic Specific Antigen (PSA) determination and a digital rectal examination (DRE).

Diagnosis of suspected prostate cancer is confirmed with a transrectal ultrasound guided needle biopsy. Sextant pattern sampling is the minimum recommended procedure**.** A 12+ sector sampling, with or without lateral horn sampling is standard at UHN.
Patients with a high suspicion of cancer and a previous negative biopsy should undergo prostate magnetic resonance imaging (MRI) to exclude the presence of an anteriorly situated tumor.

4. DIAGNOSIS

Diagnosis of prostate cancer is made with a trans-rectal ultrasound guided needle biopsy. Sextant pattern sampling is the minimum recommended procedure. We consider 12-17 cores to be routine.

Patients diagnosed following transurethral resection of prostate (TURP) should also undergo a trans-rectal ultrasound guided biopsy to establish the pattern and extent of intra-prostatic disease. Multiparametric MRI should be considered to rule out anterior or far lateral tumours for patients with a high suspicion of disease and negative ultrasound guided biopsies.

At the initial assessment, patients (particularly those with potentially curable cancers requiring multimodality input and/or treatment) should be assessed in a multidisciplinary environment.

Clinical Evaluation:

- Complete history in all patients
- Record of lower urinary symptomatology and erectile function
- Co-morbid conditions (previous cancers, heart disease, cerebrovascular disease, diabetes, renal dysfunction)
- Prior treatment of cancer, if any
- Complete physical examination in all patients, including DRE
- Voiding studies for patients under consideration for prostate brachytherapy

Oncologic Imaging and Laboratory Evaluations:
Evaluation of local extent of disease:

- All patients should undergo a diagnostic trans-rectal ultrasound and DRE to establish prostate volume and local extent of disease.
- Prostate MRI may provide complementary information concerning local disease extent in patients with suspected T3a or T3b disease.

Metastatic Workup:
Imaging is undertaken to determine the presence of nodal or skeletal metastases in high-risk individuals, or in those with signs or symptoms suggestive of metastatic disease.

- A contrast-enhanced CT of the abdomen and pelvis to detect metastases in pelvic or abdominal lymph-nodes is limited to patients with Gleason score 8-10 disease or a PSA $\geq$ 20 or neuroendocrine dedifferentiation. Metastases may be detected in the imaged skeleton, and these should be confirmed with a nuclear medicine bone scan.
- A nuclear medicine bone scan to detect metastases in the skeleton is limited to patients with T3 disease, Gleason score 8-10 disease or a PSA $\geq$ 20 or neuroendocrine dedifferentiation.
- 11(C)Choline-Positron emission tomography (PET)–CT may complement CT and nuclear medicine scan for determining the presence of nodal or skeletal metastases in patients with adenocarcinoma. This procedure is not recommended for routine use.

Laboratory Tests:

- Baseline PSA for all patients
- CBC, serum testosterone, electrolytes, calcium, creatinine, liver function studies, serum cholesterol and fasting glucose levels for selected individuals.

Other Investigations:

- CT or ultrasound guided aspiration biopsy to confirm malignancy in seminal vesicle, nodal or skeletal lesions suspicious on imaging.
- Baseline bone density assessment for those about to undergo androgen ablation therapy.

5. **PATHOLOGY**

All patients should have documentation of the tumor histology and its subtype (See WHO Classification for prostate cancer in Appendix I). On rare occasions where urgent palliation is required and the biopsy is not feasible or will delay care, the clinical and PSA diagnosis of prostate cancer is sufficient to proceed with management.

Pathology reports in prostate cancer should specify histological subtype and grade, including the Gleason score for adenocarcinoma. Needle biopsy specimens should report geographic location of disease, number of cores involved, and percent core involvement. In resection specimens, reports on type of specimen, tumor extensions, percent involvement of gland, lymph node status and resection margins status must also be provided so that an accurate pathological staging of the tumor can be rendered.

Expert uropathology review for patients whose tumor diagnoses were made at outside institutions is conducted at the request of treating oncologists. There is a multi-disciplinary agreement that expert uropathology review for external diagnoses of prostate cancer frequently changes the assigned Gleason score and should be obtained.

The 2002 WHO classification is the official classification system used for diagnosis, and is provided in Appendix I.

Staging is according to the Joint UICC & AJCC Staging Seventh Edition, 2010. The following is a brief summary of the clinically relevant stages of prostate cancer:

Stage I = disease confined to gland, involving no more than one half of one lobe.
Stage II = disease confined to gland, involving more than one half of one lobe.
Stage III = Extracapsular extension to periprostatic fat or seminal vesicle(s).
Stage IV = Extracapsular extension to other adjacent structures or metastases to lymph nodes or other organs.

More detailed description of these stages is provided in Appendix II.

The risk stratification of localized adenocarcinoma of the prostate is according to the Canadian Consensus Guidelines and is outlined in Appendix II.

6. MANAGEMENT

6.1 Adenocarcinoma of prostate

Management strategies for newly diagnosed patients with low risk of metastatic disease (unstaged) or no clinical evidence of metastatic disease (staged) are based on assigned risk classification (See appendix II) and patient factors such as serious co-morbidities, anticipated life-span and patient choice.
Options include active surveillance, radical radiotherapy (external beam or bracytherapy), radical prostatectomy, and watchful waiting.

6.2 Low risk

Management options include active surveillance, radical radiotherapy (external beam or bracytherapy), radical prostatectomy, and watchful waiting.

Active Surveillance (AS)
AS is a management strategy designed to provide selective treatment based upon the tumor behavior determined through a period of observation. The goal is to minimize the side effects of treatment by deferring therapy, or potentially avoiding therapy without adversely affecting oncologic outcomes.
Patients should be motivated, and compliance is optimal if benchmarks for abandoning AS are initially established and discussed with the patient.
Baseline (12+ sector) US guided biopsy and expert uropathology review.

PSA 3-6 monthly in the first year
PSA 6-monthly in years 2-5
PSA annually after year 5
DRE 6-monthly
A confirmatory biopsy should take place 6 – 12 months after the diagnostic biopsy. Repeat biopsy is then recommended every 24 months depending on doubling time, and only continued to a point when active intervention would be worthwhile. (Reference CCO guideline on Active Surveillance)

Clinical benchmarks to abandon AS
These will be modified by patient factors such as age and co-morbities.
Confirmed PSA doubling time $\leq$ 6 months
Gleason score upgrading to $\geq$ 7
Disease involving cores in multiple sites (> 3 or > 50% of core involvement)
PSA $\geq$ 15 ng/ml (must be taken in the context of prostate size)
Elderly patients with no evidence of progression on AS may be converted to a watchful waiting program.
Patients who progress on AS will be encouraged undergo definitive treatment with surgery or radiotherapy.

Watchful Waiting
This is a policy of minimal intervention for patients judged to have serious co-morbidities or an anticipated lifespan incompatible with definitive treatment.
Patients are followed clinically, and management is directed at treating disease-related symptoms.

Surgery
Selection factors for surgery include patient preference, acceptable anesthetic risk and estimated life expectancy > 10 years. Surgical technique is open or robot assisted laparoscopic radical prostatectomy with unilateral or bilateral nerve-sparing procedure whenever feasible**.**

Radiotherapy
Options are low dose rate (LDR) brachytherapy or external beam radiotherapy (EBRT)

Selection factors for LDR brachytherapy
Patient preference
Suitable for general or spinal anaesthetic
Prostate volume suitable for implant (generally < 60cc)
No history of transurethral resection of prostate
Adequate voiding studies
No pubic arch interference

Treatment technique for LDR brachytherapy
US guided transperineal I^{125} permanent seed implant
D100: 145 Gy to prostate +3 mm periprostatic margin

Selection factors for EBRT
Patient preference
No contraindication to pelvic radiotherapy
Anticipated life-span $\geq$ 5 years

Treatment technique for EBRT
Daily image-guided volumetric modulated arc therapy (VMAT)
CTV: prostate gland alone
PTV reflects guidance technique employed
10 mm/7 mm posteriorly with cone-beam image guidance on soft tissue
78 Gy in 39 fractions over 8 weeks prescribed to CTV minimum.

Androgen deprivation therapy
Androgen deprivation therapy is employed very selectively for low risk patients. It is used exclusively as cytoreductive agent to reduce the risk of acute radiation side effects for patients with BPH and poor pretreatment voiding function.

6.3 Intermediate risk

Active Surveillance (AS)
See section 6.1.1 for description. AS is not recommended for patients with intermediate risk disease. It may be considered selectively for older patients with one intermediate risk factor.

Watchful Waiting
See section 6.1.1 for description. Selected patients may be considered for watchful waiting.

Surgery
Selection factors for surgery include patient preference, acceptable anesthetic risk and estimated life expectancy >10 years. Older fit individuals will be selectively considered. Surgical technique is open or robot assisted laparoscopic radical prostatectomy with unilateral or bilateral nerve-sparing procedure whenever feasible. Depending on the risk of lymph node involvement a pelvic lymphadenectomy is also performed.

Radiotherapy
Options include EBRT, LDR brachytherapy or a combination of EBRT and brachytherapy. *Selection factors for EBRT*
Patient preference
No contraindication to pelvic radiotherapy
Anticipated life-span $\geq$ 5 years.

Treatment technique for EBRT
Daily image-guided volumetric modulated arc therapy (VMAT)

CTV: prostate gland alone.
Base of seminal vesicle (1 cm above prostate) is included in CTV for patients with a Parton risk of involvement $\geq$ 15%
PTV reflects guidance technique employed
10 mm/7 mm posteriorly with cone-beam image guidance on soft tissue
78 Gy in 39 fractions over 8 weeks prescribed to CTV minimum.

Selection factors for LDR brachytherapy
Patient's with one intermediate risk factor may be considered for LDR brachytherapy.
Selection factors are otherwise the same as for LDR btrachytherapy

Selection factors for combined EBRT/brachytherapy
Patients with 2 or 3 intermediate risk factors can be considered for a combination of EBRT and brachytherapy using either LDR or HDR brachytherapy techniques.
HDR brachytherapy is the preferred technique for combined therapy at PMCC.
Other selection factors are
Patient preference
Anatomic considerations suitable for brachytherapy.
Voiding function suitable for brachytherapy

Androgen deprivation therapy
Androgen deprivation therapy is employed very selectively for intermediate risk patients. It is used exclusively as cytoreductive agent to reduce the risk of acute radiation side effects for patients with BPH and poor pretreatment voiding function.

6.4 High risk

Active Surveillance (AS)
See section 6.1.1. for description, is not recommended for patients with high risk disease.

Watchful Waiting
See section 6.1.1. for description. Watchful waiting is unlikely to be a successful strategy for patients with high risk disease. Patients not fit for definitive treatment should be considered for androgen deprivation therapy.

Surgery
Radical prostatectomy should be considered selectively for high risk individuals. Preferred candidates should not have overt evidence of unresectable T3 disease. Selection factors for surgery include patient preference, acceptable anesthetic risk and estimated life expectancy > 10 years. Older fit individuals will be selectively considered. Surgical technique is open or robot assisted laparoscopic radical prostatectomy. Unilateral or bilateral nerve-sparing procedure can be considered for patients with a low risk of T3b disease. A pelvic lymphadenectomy is also performed.

Radiotherapy
Selection factors are patient preference and anticipated life-span $\geq$ 5 years.
Option is EBRT or EBRT and brachytherapy.

Selection factors for EBRT
No contraindication to pelvic radiotherapy

Treatment technique for EBRT
Daily image-guided volumetric modulated arc therapy (VMAT)
CTV prostate gland and seminal vesicles
PTV reflects guidance technique employed
10 mm/7 mm posteriorly with cone-beam image guidance on soft tissue
Dose is 78 Gy in 39 fractions over 8 weeks prescribed to CTV minimum.
Pelvic lymph node radiotherapy is at the treating oncologist discretion
Volume includes bilateral common iliac nodes, external iliac nodes to level of upper femoral head, internal iliac nodes to level of levator muscles
These are defined by a 7 mm expansion around contoured vessels
PTV nodes is 5 mm
Dose is 54Gy in 27 fractions given concomitantly with first phase of prostate and SV irradiation using daily image-guided volumetric modulated arc therapy (VMAT)
Dose nodes may be compromised to respect small bowel, rectal and bladder dose constraints.

Selection factors for combined EBRT/brachytherapy
Patients with high risk factors can be considered for a combination of EBRT and brachytherapy using either LDR or HDR brachytherapy techniques.
HDR brachytherapy is the preferred technique for combined therapy at PMCC.
Other selection factors are
Patient preference
Anatomic considerations suitable for brachytherapy.
Voiding function suitable for brachytherapy

Androgen deprivation therapy
Adjuvant ADT is recommended for a minimum of 2 years and is commenced with radiotherapy.

Patients are advised to take daily supplements of calcium (1000mg) and vitamin D (800-1200 IU).

Bone density is evaluated at baseline and annually while testosterone is suppressed.

6.5 Presentation with N1 or M1 disease

Patients presenting with clinical evidence of metastatic disease should be considered for chemo-hormonal therapy with docetaxel (75mg/m2 without prednisone) in combination with LHRH agent treatment. The strength of the recommendation will depend on the location and number of the metastases, the patients medical condition and patient acceptance. Usual initial treatment is with continuous LHRH agonist monotherapy. An antiandrogen is employed for 2 prior and thereafter 2 weeks after the first injection.

An LHRH antagonist may be employed in specific circumstances where rapid response is desirable, such as with extreme pain or impending spinal cord compression. Surgical castration also remains an option.

Radiotherapy is not routinely employed for horomone sensitive metastatic disease, except to treat impending or actual spinal cord compression in conjunction with the initiation of hormone therapy.

Patients are advised to take daily supplements of calcium (1000mg) and vitamin D (800-1200 IU).

Bone density is evaluated at baseline and annually while testosterone is suppressed.

6.6 Management of progression after initial therapy

Post-operative radiotherapy

Post-operative radiotherapy to the prostate bed is recommended ***in*** individuals with adverse prostatectomy pathological findings such as one or more positive surgical margins and/or T3a or T3b disease. Patients with biochemical evidence of disease based upon persistently elevated post-operative PSA or a rising PSA in the post-operative period may also be candidates for post-operative radiotherapy to the prostate bed.

The optimal timing of post-operative radiotherapy has not been established. Patients with adverse prostatectomy pathology should be referred soon after surgery to a radiation oncologist for a discussion about the risks and benefits of post-operative radiotherapy.
For those electing to defer radiotherapy, results are optimal if radiotherapy is commenced when the PSA is < 0.2.

Treatment technique for EBRT
Daily image-guided volumetric modulated arc therapy (VMAT)
CTV is prostate bed, defined according to ASTRO consensus guidelines.
PTV reflects guidance technique employed
10 mm/15 mm superiorly with cone-beam image guidance on soft tissue
Dose is 66 Gy in 33 fractions over 6.5 weeks prescribed to ICRU point
Pelvic lymph node radiotherapy is at the treating oncologist discretion
Volume includes bilateral common iliac nodes, external iliac nodes to level of upper femoral head, internal iliac nodes to level of levator muscles
These are defined by a 7 mm expansion around contoured vessels

PTV nodes is 5 mm
Dose is 50Gy in 25 fractions given concomitantly with first phase of prostate bed irradiation using daily image-guided volumetric modulated arc therapy (VMAT)
Dose to nodes may be compromised to respect small bowel, rectal and bladder dose constraints.

Androgen deprivation therapy
Adjuvant ADT is not routinely recommended with post-operative radiotherapy.

Biochemical progression after primary radiotherapy

Biochemical failure after primary radiotherapy is defined using the definition of nadir PSA+2. Recommended management of biochemical failure is deferred intermittent ADT. Selected individuals may be considered for local salvage therapy and referral to a uro-oncologist should be made sooner than later.

Selection factors include patient preference, good performance status, initial diagnosis of low or intermediate risk disease, PSA doubling time > 6 months, positive post-treatment prostate biopsy, negative bone scan and negative CT abdomen and pelvis.

Post-treatment biopsy should not be performed sooner than 2.5 years post-treatment. Pathology should be interpreted by an expert uropathologist to reduce the risk of false-positive interpretation.

Management options
Radical prostatectomy
LDR or HDR brachytherapy
Thermal or cryoablation of prostate.

Castrate resistant prostate cancer (CRPC)
Castrate resistance is defined as biochemical progression with castrate levels of testosterone following total androgen blockade.

Imaging and blood indices in this setting are carried out as clinically indicated but as a general rule imaging is appropriate every 6 months to detect disease progression that may occur in the absence of a rise in PSA, while PSA testing is appropriate at 3-month intervals.

Anti-androgen withdrawal response may be evident after up to 6 weeks following the discontinuation of drugs such as flutamide, bicalutamide and nilutamide; withdrawal responses only occur if there was a prior PSA response to these agents.

For men with slowly progressive disease and prior response to other hormonal maneuvers other hormonal manipulations such as DES, glucocorticoids, ketoconazole + hydrocortisone are appropriate. Sipuleucel-T (Provenge) is currently available in the United States in this setting, it is not used in Canada due to a combination of lack of access and concern about efficacy. More recent options for men with asymptomatic or minimally symptomatic disease include abiraterone (and steroid) or enzalutamide. Both

of these agents have a significant benefit in this setting include an increase OS and decreased in SREs Following the failure of initial or subsequent hormonal therapies, clinical trials may be appropriate before the institution of chemotherapy.

Chemotherapy for prostate cancer

For patients with symptomatic metastatic CRPC, docetaxel 75mg/m2 + prednisone 5mg bid remains the regimen of choice.

It is reasonable to offer docetaxel to men with asymptomatic metastatic disease with the following adverse features; visceral metastases, PSA doubling time < 3m or rapidly progressive symptoms related to tumour bulk.

Patients undergoing chemotherapy for prostate cancer undergo imaging every 3^{rd} -4^{th} cycle with PSA, testosterone, CBC, electrolytes, liver function tests, calcium, magnesium, phosphate every 3-6 weeks.

Second line agents that have a demonstrated survival benefit after docetaxel include abiraterone.acetate, cabazitaxel, radium-223 and enzalutamide.

Mitoxantrone is an option in men who would not tolerate docetaxel and has demonstrated palliative benefits in 3 randomised trials. Mitoxantrone may also be used for palliation.

Sequencing

There is no data to asssit with deciding how to sequence the available agents in prostate cancer. Our practice has been to offer 1 novel agent (eg abiraterone, enzaltumide) bfefore chemthera and a further agents (pending availability) afterwards.

Bone health for men with CRPC and bone metastases.

Men with CRPC and bone metastases are offered treatment with zoledronic acid or denosumab to reduce the risk of adverse skeletal events at a clinically appropriate time.

The approved schedule for zoledronic acid 4mg every 3 weeks. We recommend the less intense schedule of zoledronate 4mg every 3 months given the lack of evidence that such a frequent schedule is necessary. The approved schedule for denosumab is 120mg monthly. On both drugs, men should take regular calcium and vitamin D to prevent hypocalcemia. Monitoring for osteonecrosis of the jaw should be carried out and dental health optimized prior to the initiation of these agents.

Other management options for symptomatic CRPC

Patients with local progression following primary hormone therapy should be considered for definitive prostate radiation therapy.

Palliative external beam radiotherapy should be considered for treatment of localized pain, bleeding, lymphedema secondary to lymph node metastases.

Urethral, ureteral, or bowel obstruction should be managed surgically or with stents as appropriate. Palliative radiotherapy may be considered following these interventions to delay progression.

Spinal cord compression is usually managed with palliative radiotherapy although surgical decompression followed by radiotherapy may be considered for fit individuals with limited volume disease.

Bone targeted radioisotopes like radium-223, Strontium -89 and Samarium-153 are acceptable treatment modalities in men with bone symptoms, limited volume disease adequate marrow reserve. These may cause myelosuppression and make it more difficult to give subsequent chemotherapy.

Prostate Cancer with low PSA production

Some men with aggressive metastatic prostate cancer have low serum PSA values. These patients are more likely to have a poor response to ADT, visceral disease and osteolytic bone lesions. Serum PSA cannot be used as a marker of treatment benefit.

There are no randomized trials to guide management of patients with CRPC and low serum PSA. Treatment of these patients will depend upon the histology and is more dependent upon imaging for assessment of response.

Men with tumors that contain neuroendocrine features are relatively sensitive to chemotherapy regimens used for small cell cancer of the lung such as platinum/etoposide, and this represents a reasonable treatment option.

6.7 Oncology Nursing Practice

Refer to general oncology nursing practices

7. SUPPORTIVE CARE

7.1 Patient Education

Patient education is an integral aspect of cancer management in the GU site group. In addition to one-on-one education specific to the patient situation, written educational materials are provided to patients. The specific educational content is provided depending on the patient's diagnosis and management options. In addition, there is a library with resources available to the patient. Patients are encouraged to participate in prostate cancer support groups. These groups provide important peer support and education to recently diagnosed men and their families.

7.2 Psychosocial Care

Refer to general psychosocial oncology care guidelines

7.3 Symptom Management

Men with prostate cancer may have a multitude of physical and emotional symptoms related to their disease, treatment and co-morbid condition. DART and ESAS (Distress Assessment and Response Tool and Edmonton Symptom Assessment System) are the screening tools used to identify the symptoms of most concern to the patient. They add to the clinical assessment of the patient made by the clinician at an individual attendance, but are also recorded serially at each attendance, to observe outcomes of interventions used. Patients answers are reviewed by the nurse and oncologists, symptom management guides are used in response to this screening and patients with significant burden of symptoms can be referred to appropriate services (eg palliative care, social work etc).
Referral for expert management of treatment related complications such as urinary incontinence, erectile dysfunction, rectal bleeding or hematuria should be considered if conservative measures fail.

7.4 Clinical Nutrition

Written materials on nutrition and prostate health and access to a dietician are made available to men with prostate cancer. Proper nutrition is especially important to maintain bone health and limit the effects of metabolic syndrome in men on long-term ADT.

7.5 Palliative Care

Refer to general oncology palliative care guidelines

8. FOLLOW-UP

Patients treated with curative radiotherapy or surgery
Follow-up is individualized during the acute period following radiotherapy or surgery.
Once acute treatment related symptoms have resolved and biochemical response (radiotherapy) or remission (surgery) is established patients are followed 6-monthy to year 5 and annually to year 10. Follow-up beyond year 10 is at the discretion of the treating oncologist.

Patients receiving adjuvant ADT will be seen according to their LHRH protocol, or 6 monthly if the LHRH is administered outside the institution.
Follow-up investigations (no ADT)
Serum PSA
Assessment of bowel (radiotherapy), bladder and sexual function
Follow-up investigations (ADT)
Serum PSA

Serum testosterone
Assessment of bowel (radiotherapy), bladder and sexual function
Annual bone density assessment

Patients treated with non-curative intent
Follow-up interval and investigations are individualized to the type of treatment employed, symptoms present and pace of disease.

APPENDIX I PATHOLOGICAL CLASSIFICATION OF PROSTATE CANCER

2002 WHO Classification for prostate cancer:

Epithelial tumours
Glandular neoplasms
Adenocarcinoma (acinar)
Atrophic
Pseudohyperplastic
Foamy
Colloid
Signet ring
Oncocytic
Lymphoepithelioma-like
Carcinoma with spindle cell differentiation (carcinosarcoma, sarcomatoid carcinoma)
Prostatic intraepithelial neoplasia (PIN)
Prostatic intraepithelial neoplasia, grade III (PIN III)

Ductal adenocarcinoma
Cribriform
Papililary
Solid

Urothelial tumours
Urothelial carcinoma

Squamous tumours
Adenosquamous carcinoma
Squamous cell carcinoma

Basal cell tumours
Basal cell adenoma
Basal cell carcinoma

Neuroendocrine tumours
Endocrine differentiation within adenocarcinoma
Carcinoid tumour
Small cell carcinoma
Paraganglioma
Neuroblastoma

Prostatic stromal tumours

Stromal tumour of uncertain malignant potential
Stromal sarcoma

Mesenchymal tumours
Leiomyosarcoma
Rhabdomyosarcoma
Chondrosarcoma
Angiosarcoma
Malignant fibrous histiocytoma
Malignant peripheral nerve sheath tumour
Haemangioma
Chondroma
Leiomyoma
Granular cell tumour
Haemangiopericytoma .
Solitary fibrous tumour

Hematolymphoid tumours
Lymphoma
Leukaemia

Miscellaneous tumours
Cystadenoma
Nephroblastoma (Wilms tumour)
Rhabdoid tumour
Germ cell tumours
- Yolk sac tumour
- Seminoma
- Embryonal carcinoma & teratoma
- Choriocarcinoma

Clear cell adenocarcinoma
Melanoma

Metastatic tumours

Tumours of the seminal vesicles

Epithelial tumours
Adenocarcinoma
Cystadenoma

Mixed epithelial and stromal tumours
- Malignant
- Benign

Mesenchymal tumours Leiomyosarcoma
Angiosarcoma
Liposarcoma
Malignant fibrous histiocytoma
Solitary fibrous tumour
Haemangiopericytoma
Leiomyoma

Miscellaneous tumours
Choriocarcinoma
Male adnexal tumour of probable Wolffian origin

Metastatic tumours

APPENDIX II – **PROSTATE CANCER STAGING** (Joint UICC & AJCC Staging Seventh Edition, 2010):

Primary Tumor (T)
TX Primary tumor cannot be assessed,
T0 No evidence of primary tumor
T1 Clinically inapparent tumor, neither palpable or visible by imaging
T1a: Tumor incidental histologic finding in 5% or less of tissue resected
T1b: Tumor incidental histologic finding in more than 5% of tissue resected
T1c: Tumor identified by needle biopsy (eg. because of elevated PSA)
T2: Tumor confined within prostate
T2a: Tumor involves one-half of one lobe or less
T2b: Tumor involves more than one-half of one lobe but not both lobes
T2c: Tumor involves both lobes
T3: Tumor extends through the prostatic capsule
T3a: Extracapsular extension (unilateral or bilateral), including microscopic bladder neck involvement.
T3b: Tumor invades seminal vesicle(s)
T4: Tumor is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum levator muscles and/or pelvic wall.

Regional Lymph Nodes (N)
NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastases
N1: Regional lymph node metastasis

Distant Metastasis (M)
M0 No distant metastasis
M1: Distant metastasis
M1a: Non-regional lymph node(s)
M1b: Bone(s)
M1c: Other site(s)

Stage Groupings

Stage I	T1, T2a	N0	M0	
Stage II	T2b,T2c	N0	M0	
Stage III	T3	N0	M0	
Stage IV	T4	N0	M0	
	Any T	N1	M0	
	Any T	Any N	M1	

RISK CLASSIFICATION FOR CLINICALLY LOCALIZED DISEASE
(Canandian Consensus Guidelines Classification)

Low risk: All of Gleason score 6 or less; PSA 10 or less; T classification T1 or T2a.

Intermediate risk: Any of PSA greater than 10 and less than 20; Gleason score 7; T classification T2b or T2c

High risk: Any of PSA greater than 20; Gleason score greater than 7; T classification T3 or T4.