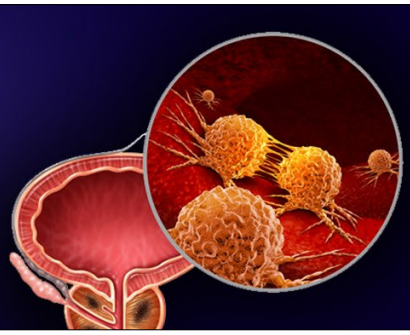
Prostate Cancer Practice Review™



Making Education Easy

Issue 11 - 2023

In this issue:

Abbreviations used in this issue:

EAU = European Association of Urology
IGRT = image-guided radiation therapy
IMRT = intensity-modulated radiation therapy
ISUP = International Society of Urological Pathology
LND = lymph node dissection
mCSPC = metastatic castration-sensitive prostate cancer
RARP = robot-assisted radical prostatectomy
TGA = Therapeutic Goods Administration
VMAT = volumetric modulated arc therapy

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Welcome to the 11th issue of Prostate Cancer Practice Review.

This Review covers news and issues relevant to clinical practice in prostate cancer. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find our COVID-19 resources, and a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne
Editor
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Clinical Practice

Prostate-specific antigen testing for prostate cancer: Time to reconsider the approach to screening

Prostate cancer is the most common cancer in men in Australia, often remaining asymptomatic until advanced. This paper stresses that Australian guidelines for primary care PSA testing should be updated to reflect long-term data showing survival advantages from PSA testing. Indeed, recent studies show improved metastasis-free survival rates with early intervention compared with observation/delayed treatment. The use of MRI and PSMA PET has lowered risk, increased accuracy and improved staging. Biopsy techniques have improved to reduce the risk of infection. Studies show that the increased use of active surveillance in patients with low to intermediate risk of prostate cancer can lessen the risk of treatment-related harms in men with low risk of progression. There have also been improvements in medical therapies for advanced disease.

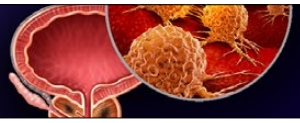
Aust J Gen Pract. 2023;52(3):91-95

Prostate-specific antigen screening in transgender patients

Approximately 0.4–1.3% of the worldwide population is transgender. While many transgender women may undergo gender-affirming hormone therapy or surgery, they retain their prostate. This article reviews PSA screening strategies in this population.

Little is known about the incidence and appropriate screening for prostate cancer in transgender women. There are no PSA screening guidelines available from any of the major urologic guideline societies in this setting. It remains unclear whether prostate cancer is underdiagnosed in this population or whether it is a rare occurrence. Although it is thought that prostate cancer occurs at a lower rate among transgender women, case reports show that transgender women who develop prostate cancer may have more aggressive disease, suggesting that these cancers may have been present before gender-affirming hormone therapy or may be castrate-resistant. The authors recommend age-based screening according to the appropriate regional guidelines as well as obtaining baseline PSA levels for age-appropriate patients prior to the initiation of gender-affirming therapy. The authors could not make recommendations for PSA screening cut-offs given the lack of data; however, they note that a PSA level of >1 ng/mL may be abnormal based on data from patients with hypogonadism or those on gender-affirming hormone therapy. Further development of PSA screening guidelines for transgender women is warranted.

Eur Urol. 2023;83(1):48-54



EAU prostate cancer guidelines

For the 2023 EAU guidelines on prostate cancer, all chapters have been updated based on a review of the literature. Key changes to recommendations are as follows:

Screening and individual early detection

- In asymptomatic men with a PSA 3–10 ng/mL and a normal digital rectal examination (DRE), repeat PSA before further investigations (weak recommendation).
- In asymptomatic men with a PSA 3–10 ng/mL and a normal DRE, use one of the following to determine whether biopsy is indicated:
  - risk-calculator (strong recommendation)
  - MRI of the prostate (strong recommendation)
  - an additional serum, urine biomarker test (weak recommendation).

Staging

- For patients being staged in any risk group, treatment should not be changed based on PSMA PET/CT results (strong recommendation).

General guidelines for treatment

- Offer watchful waiting to asymptomatic patients with localised disease and with a life expectancy <10 years (strong recommendation).
- Radical prostatectomy (RP) can be delayed for 3 months from diagnosis in any risk category (weak recommendation).
- When a lymph node dissection (LND) is necessary, perform an extended LND template for optimal staging (strong recommendation).
- Offer moderate hypofractionation with IMRT/VMAT plus IGRT to patients with localised disease (strong recommendation).
- Offer low-dose brachytherapy monotherapy to patients with good urinary function and low-risk or favourable intermediate-risk disease (strong recommendation).
- Offer low- or high-dose brachytherapy boost combined with IMRT/VMAT plus IGRT to patients with good urinary function and unfavourable intermediate-risk or high-risk disease and/or locally-advanced disease (weak recommendation).
- Only offer focal therapy with high-intensity focused ultrasound or cryotherapy within a clinical trial or prospective registry (strong recommendation).

Follow-up during active surveillance

- Follow-up during AS should include DRE at least yearly, PSA at least 6-monthly and repeat biopsy every 2-3 years (strong recommendation).
- Perform MRI and repeat biopsy if PSA is rising (doubling time <3 years; strong recommendation).
- Re-classify patients with low-volume ISUP grade group 2 disease undergoing AS, if repeat non-MRI-based biopsies performed during monitoring show >3 positive cores or maximum CI >50%/core of ISUP 2 disease (weak recommendation).
- Change in treatment should be based on biopsy progression not MRI/PSA progression (weak recommendation).
- Patients with a PI-RADS 1-2 findings on MRI and a low PSA density (<0.15) may be excepted from repeat biopsy (weak recommendation).

Management of low-risk disease

- Manage patients with a life expectancy <10 years and low-risk disease by watchful waiting (strong recommendation).
- Manage patients with a life expectancy >10 years and low-risk disease by AS (strong recommendation).

Treatment of intermediate-risk disease

- Offer watchful waiting in asymptomatic patients with life expectancy <10 years (strong recommendation).
- Offer RP to patients with a life expectancy of >10 years (strong recommendation), which can be delayed for at least 3 months (weak recommendation).
- Patients with a low risk of extra-capsular disease on that side should be offered nerve sparing surgery (weak recommendation).
- Offer low-dose brachytherapy boost combined with IMRT/VMAT plus IGRT to patients with good urinary function and unfavourable intermediate-risk disease, in combination with short-term ADT (weak recommendation).
- Offer high-dose brachytherapy boost combined with IMRT/VMAT plus IGRT to patients with good urinary function and unfavourable intermediate-risk disease, in combination with short-term ADT (weak recommendation).
- Only offer whole-gland ablative therapy or focal ablative therapy within clinical trials or registries (strong recommendation).

Treatment of high-risk localised disease

- Offer watchful waiting to asymptomatic patients with life expectancy <10 years (strong recommendation).
- RP can be delayed for at least 3 months (weak recommendation).

Treatment of locally-advanced disease

- Patients with cN0 disease should be offered RP as part of their treatment regimen (weak recommendation).
- Offer IMRT/VMAT plus IGRT to the prostate in combination with long-term ADT and abiraterone to cN0M0 patients with ≥2 high-risk factors (strong recommendation).
- Offer IMRT/VMAT plus IGRT to the prostate plus pelvis in combination with long-term ADT and abiraterone to cN1M0 patients (strong recommendation).
- Patients with cN1 disease should be offered either RP or IMRT/VMAT plus IGRT plus long-term ADT (strong recommendation).

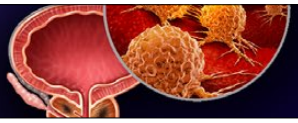
Adjuvant treatment for pN0 and pN1 disease after radical prostatectomy

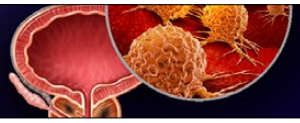
- In pN0 patients with ISUP grade group 4-5 and pT3 ± positive margins, offer adjuvant IMRT/ VMAT plus IGRT (strong recommendation).
- In pN1 patients, after an extended LND, management should be based on nodal involvement characteristics (weak recommendation):
  1. Offer adjuvant ADT;
  2. Offer adjuvant ADT with additional IMRT/VMAT plus IGRT;
  3. Offer observation to a patient after extended LND and ≤2 nodes and a PSA <0.1 ng/mL.

First-line treatment of hormone-sensitive metastatic disease

- At the start of ADT offer LHRH antagonists or orchiectomy to patients with impending complications such as spinal cord compression or bladder obstruction (strong recommendation).
- Offer docetaxel in combination with ADT plus abiraterone or darolutamide to fit patients with M1 disease (strong recommendation).
- Offer ADT combined with non-curative prostate radiotherapy to patients whose first presentation is M1 disease and who have low volume of disease (strong recommendation).

Download the guidelines here





Time trends and variation in the use of active surveillance for management of low-risk prostate cancer in the US

In this analysis, researchers found that the use of active surveillance (AS) for low-risk prostate cancer in US patients has more than doubled in recent years but remains suboptimal and has wide variations at the urology practice and individual practitioner levels.

The investigators stated, "AS is endorsed by clinical guidelines as the preferred management strategy for low-risk prostate cancer, but its use in contemporary clinical practice remains incompletely defined."

The retrospective analysis involved data from the American Urological Association Quality Registry, comprising more than 8.5 million patients. The analysis cohort included 20,809 patients with low-risk disease (PSA <10 ng/mL, Gleason grade group 1, and clinical stage T1c or T2a) newly diagnosed between January 2014 and June 2021.

The median age of patients was 65 years. The rates of AS increased from 26.5% in 2014 to 59.6% in 2021. During the study period, use of AS varied from 4.0% to 78.0% at the urology practice level and from 0% to 100% at the practitioner level. AS rates were similar among Black patients (39.4%) and White patients (39.8%) and higher among patients with other or missing race/ethnicity (46.4%).

Multivariable analysis showed that year of diagnosis was the variable most strongly associated with use of AS, with an odds ratio (OR) per year between 2014 and 2021 of 1.25. Compared with 2014, the OR for 2021 was 4.48. ORs were significant for some age decades of diagnosis, with 0.71 for patients aged in their 40s, 1.12 for those in their 60s, and 1.24 for those in their 70s. Higher PSA level at diagnosis was associated with reduced likelihood of AS (OR = 0.98).

The authors concluded that "National and community-based rates of AS have increased but remain suboptimal, and wide variation persists across practices and practitioners. Continued progress on this critical quality indicator is essential to minimize overtreatment of low-risk prostate cancer and by extension to improve the benefit-to-harm ratio of national prostate cancer early detection efforts."

JAMA Netw Open. 2023;6(3):e231439

Same day discharge for robot-assisted radical prostatectomy: An Australian approach

After robot-assisted radical prostatectomy, patients are usually discharged the next day. However, during the ongoing COVID-19 pandemic, The Royal Melbourne Hospital facilitated a cohort of same-day discharges with initial success. Twenty-eight patients undergoing PARP between January and April 2021 were included. Patients were carefully selected and pre-counselled. Twenty patients (71%) fulfilled pre-operative criteria for day zero (i.e., same day) discharge. Eleven patients (55%) agreed pre-operatively to day zero discharge and all were successfully discharged on the same day as their procedure. For those who did not agree, common reasons for opting to stay overnight included apprehension for the possibility of poor pain control and placing extra demand on carers at home. All patients were satisfied with their care and all believed that their post-operative length of stay was appropriate. Median time from completion of surgery to discharge was 7.1 hours in the day zero discharge cohort.

ANZ J Surg. 2023 Jan 13.

First-line systemic treatment options for metastatic castration-sensitive prostate cancer

In a systematic review and meta-analysis researchers found that first-line triplet therapy in metastatic castration-sensitive prostate cancer (mCSPC) did not appear to offer an overall survival advantage versus androgen pathway inhibitor doublet therapy.

The network meta-analysis included 10 phase III randomised trials assessing first-line treatment options for mCSPC, with a total of 11,043 patients in nine different treatment groups. Evidence in the overall population indicated that the triplet of darolutamide, docetaxel, and androgen-deprivation therapy (ADT; HR 0.68; 95% CI 0.57–0.81) and the triplet of abiraterone, docetaxel, and ADT (HR 0.75; 95% CI 0.59–0.95) were associated with improved overall survival versus the docetaxel plus ADT doublet, but not compared with androgen pathway inhibitor doublets of abiraterone plus ADT, enzalutamide plus ADT, or apalutamide plus ADT.

Data were not available by volume of disease for darolutamide, docetaxel, and ADT. Among patients with high-volume disease, abiraterone, docetaxel, and ADT improved overall survival versus docetaxel plus ADT (HR 0.72; 95% CI 0.55–0.95) but not compared with abiraterone plus ADT, enzalutamide plus ADT, or apalutamide plus ADT. Among patients with low-volume disease, abiraterone, docetaxel, and ADT did not improve overall survival versus apalutamide plus ADT (HR 1.45; 95% CI 0.73–2.89), abiraterone plus ADT (HR 1.27; 95% CI 0.68–2.33), enzalutamide plus ADT (HR 1.14; 95% CI 0.56–2.32), or docetaxel plus ADT (HR 0.83; 95% CI 0.50–1.38).

According to the authors, "The potential benefit observed with triplet therapy must be interpreted with careful accounting for the volume of disease and the choice of doublet comparisons used in the clinical trials. These findings suggest an equipoise to how triplet regimens compare with androgen pathway inhibitor doublet combinations and provide direction for future clinical trials."

JAMA Oncol. 2023 Mar 2:e227762

Regulatory News

TGA – new indications

The indication for **darolutamide** (Nubeqa), has been extended to include the treatment of metastatic hormone-sensitive prostate cancer in combination with the existing standard of care chemotherapy (docetaxel).

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COSA – Events
MOGA – Events
USANZ – Events
COMS – Conferences and Meetings on Urology

Research Review Publications

Prostate Cancer Research Review with Associate Professor Niall Corcoran and Professor Nathan Lawrentschuk

Urology Research Review with Professor Eric Chung