# EAU - EANM - ESTRO -ESUR - ISUP - SIOG Guidelines on Prostate Cancer

## Epidemiology, aetiology, classification and diagnosis I

## EPIDEMIOLOGY AND AETIOLOGY:

**Prostate cancer (PCa) was estimated as the 4th most common cancer in Europe in 2020, and is by far the most frequent cancer and the third predicted cause of all cancer deaths among males.**

Incidence and disease stage distribution patterns follow biological, genetic, and/or lifestyle factors, but are also influenced by (inter)national organisations' recommendations on the use of PSA testing.

| Summary of evidence | LE |
|---|---|
| Prostate cancer is a major health concern in men, with incidence mainly dependent on age. | 3 |
| Genetic factors are associated with risk of (aggressive) PCa. | 3 |
| A variety of dietary/exogenous/environmental factors have been associated with PCa incidence and prognosis. | 3 |
| Selenium or vitamin-E supplements have no beneficial effect in preventing PCa. | 2a |
| In hypogonadal men, testosterone supplements do not increase the risk of PCa. | 2 |
| No conclusive data exit which could support specific preventive or dietary measures aimed at reducing the risk of developing PCa. | 1a |

## CLASSIFICATION AND STAGING SYSTEMS:

### Clinical Tumour Node Metastasis (TNM) classification of PCa:

| | |
|---|---|
| **T - Primary Tumour (stage based on digital rectal examination [DRE] only)** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| T1 | Clinically inapparent tumour that is not palpable |
| T1a | Tumour incidental histological finding in 5% or less of tissue resected |
| T1b | Tumour incidental histological finding in more than 5% of tissue resected |
| T1c | Tumour identified by needle biopsy (e.g. because of elevated prostate-specific antigen [PSA]) |
| T2 | Tumour that is palpable and confined within the prostate |
| T2a | Tumour involves one half of one lobe or less |
| T2b | Tumour involves more than half of one lobe, but not both lobes |
| T2c | Tumour involves both lobes |
| T3 | Tumour extends through the prostatic capsule |
| T3a | Extracapsular extension (unilateral or bilateral) |
| T3b | Tumour invades seminal vesicle(s) |
| T4 | Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall |
| **N - Regional (pelvic) Lymph Nodes[1]** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Regional lymph node metastasis |
| **M - Distant Metastasis[2]** | |
| M0 | No distant metastasis |
| M1 | Distant metastasis |
| M1a | Non-regional lymph node(s) |
| M1b | Bone(s) |
| M1c | Other site(s) |

[1] *Metastasis no larger than 0.2 cm can be designated pNmi.*
[2] *When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.*

### Gleason score (GS) and International Society of Urological Pathology (ISUP) 2014

**The most extensive (primary) pattern, plus the second most common (secondary) pattern.**
**In the original Gleason grading system, 5 Gleason grades (1–5), but in the 2005 and subsequent 2014 ISUP Gleason score Modifications, Gleason grades 1 and 2 were eliminated.**

### ISUP 2014 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 |

### EAU risk groups for biochemical recurrence of localised and locally advanced PCa:

| 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** |

| Recommendations | Strength rating |
|---|---|
| Use the Tumour, Node, Metastasis (TNM) classification for staging of PCa. | Strong |
| Use the International Society of Urological Pathology (ISUP) 2014 system for grading of PCa. | Strong |

## DIAGNOSTIC EVALUATION I: SCREENING OR EARLY DETECTION:

**Screening (population or mass): systematic examination of asymptomatic men to identify individuals at risk ( Not recommended by any country / society )**

**Early detection: an individualised risk-adapted strategy to well informed man ( Recommended )**

| Recommendations | Strength rating |
|---|---|
| Do not subject men to prostate-specific antigen (PSA) testing without counselling them on the potential risks and benefits. | Strong |
| Offer an individualised risk-adapted strategy for early detection to a well-informed man and a life-expectancy of at least 10 to 15 years. | Weak |
| Offer early PSA testing to well-informed men at elevated risk of having PCa:<br>• men from 50 years of age;<br>• men from 45 years of age and a family history of PCa;<br>• men of African descent from 45 years of age;<br>• men carrying *BRCA2* mutations from 40 years of age. | Strong |
| Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of 2 years for those initially at risk:<br>• men with a PSA level of > 1 ng/mL at 40 years of age;<br>• men with a PSA level of > 2 ng/mL at 60 years of age;<br>Postpone follow-up to 8 years in those not at risk. | Weak |
| Stop early diagnosis of PCa based on life expectancy and performance status; men who have a life-expectancy of < 15 years are unlikely to benefit. | Strong |

### GUIDELINES FOR GERMLINE TESTING:

**Increasing evidence supports the implementation of genetic counselling and germline testing in early detection and PCa management.**

| Recommendations | Strength rating |
|---|---|
| Consider germline testing in men with metastatic PCa. | Weak |
| Consider germline testing in men with high-risk PCa who have a family member diagnosed with PCa at age < 60 years. | Weak |
| Consider germline testing in men with multiple family members diagnosed with PCa at age < 60 years or a family member who died from PCa. | Weak |
| Consider germline testing in men with a family history of high-risk germline mutations or a family history of multiple cancers on the same side of the family. | Weak |

**CLINICAL DIAGNOSIS: Prostate cancer is usually suspected on the basis of digital rectal examination (DRE) and/or PSA levels.**

**DIGITAL RECTAL EXAMINATION: An abnormal DRE is associated with an increased risk of a higher ISUP grade. and is an indication for MRI and biopsy.**

**PROSTATE-SPECIFIC ANTIGEN (PSA): PSA is organ but not cancer specific. It is a continuous parameter, with higher levels indicating greater likelihood of PCa.**

| Recommendations | Strength rating |
|---|---|
| In asymptomatic men with a prostate-specific antigen (PSA) level between 3–10 ng/mL and a normal digital rectal examination (DRE), repeat the PSA test prior to further investigations. | Weak |

**RISK CALCULATORS: by combining clinical data (age, DRE findings, PSA level, etc.) may help determine the potential risk of cancer on an individual basis, thereby reducing the number of unnecessary biopsies.**

**MAGNETIC RESONANCE IMAGING (MRI): Do not use MRI as an initial screening tool, but in patients with clinical suspicion of prostate cancer perform it before prostate biopsy (Strong).**

BIOMARKERS:
- Blood based biomarkers
- Urine biomarkers

| | |
|---|---|
| In asymptomatic men with a PSA level between 2–10 ng/mL and a normal DRE, use one of the following tools for biopsy indication:<br>• risk-calculator;<br>• Magnetic resonance imaging of the prostate | Strong |
| • an additional serum, urine or tissue-based biomarker test. | Weak |

**NEXT EAU-UROLOGY CHEAT SHEET: Diagnosis II (magnetic resonance imaging , prostate biopsy and staging)**