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PROSTATE CANCER: BASICS ON DIAGNOSIS

EPIDEMIOLOGY

15% of all cancer
The **second most commonly** diagnosed cancer in men
Mortality generally higher in men of African descent

AETIOLOGY

-FAMILY HISTORY/GENETICS: Genetic factors are associated with risk of (aggressive) PCa
-A variety of **exogenous/environmental factors** may have an impact on PCa incidence and the risk of progression
-No specific preventive or dietary measures are recommended to reduce the risk of developing prostate cancer (PCPT, REDUCE and Select trials)

GRADING AND STAGING

GLEASON SCORE (GS): is a sum of **the most predominant grade (primary) and the second most predominant grade (secondary)**

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

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

-Low risk: PSA < 10 ng/mL and GS < 7 and cT1-2a
-Intermediate -risk: PSA 10-20 ng/mL or GS 7 or cT2b
-High-risk: PSA > 20 ng/mL or GS > 7 or cT2c
Any PSA, any GS, cT3-4 or cN+ *

TNM 2017	
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	**T1a** incidental histological finding in 5% or less of tissue resected **T1b** incidental histological finding in more than 5% of tissue resected **T1c** Tumour identified by needle biopsy
T2	**T2a** Tumour involves one half of one lobe or less **T2b** Tumour involves more than half of one lobe **T2c** Tumour involves both lobes
T3	**T3a** Extracapsular extension **T3b** Tumour invades seminal vesicle(s)
T4	Tumour invades adjacent structures: external sphincter, rectum, muscles, and/or pelvic wall
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M0	No distant metastasis
M1	**M1a** Non-regional lymph node(s) **M1b** Bone(s) **M1c** Other site(s)

DIAGNOSIS

- **PSA (Prostate-specific antigen):** organ but not cancer specific

SURROGATES OF PSA [EAU Guidelines 2021]	
PSA density (PSAD) **Total PSA (ng/mL) divided by prostate volume (cc)**	**Higher → Greater the likelihood of csPCa** **PSAD < 0.15** → < 10% of csPCa at biopsy if PIRDAS 1-2 **PSAD < 0.15** Important criteria to select patients for AS
PSA velocity (PSAV) **Absolute annual increase in PSA (ng/mL/year)** **PSA doubling time (PSA-DT)** **Length of time (months) needed for the PSA level to double**	**Prognostic and predictive value** **Concerns regarding their usefulness compared to PSA alone** **Variable cut-offs**
Free/total PSA ratio (f/t PSA) **Free PSA (ng/mL) divided by total PSA (ng/mL)**	**If PSA 4-10 ng/mL: f/t PSA < 0.10** → 56% of PCa at biopsy **f/t PSA > 0.25** → 8% of PCa at biopsy **Limited clinical value**

Limited PSA elevation alone should not prompt immediate biopsy: should be verified after a few weeks! And should certainly not be treated with antibiotics unless infection is proven by Urine culture.

PSA SCREENING: Offer PSA testing to men at elevated risk of PCa, with a life-expectancy of at least 10-15 years:
- 50 years without other risk factors
- 45 years + family history of PCa
- 45 years + African descent
- 40 years + BRCA2 mutations

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

- **URINE TESTS:** PCA3 marker/ SelectMDX/ Mi Prostate score (MiPS)/ ExoDX

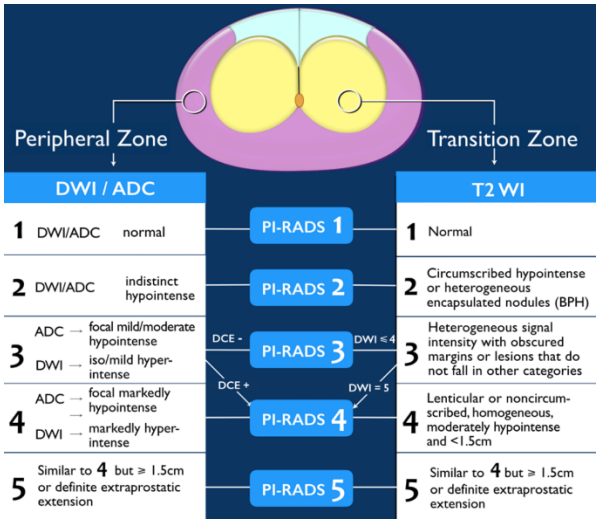
- **BLOOD Tests :** 4K score, PHI

- **PROSTATE BIOPSY:** Ultrasound (US)-guided biopsy: **standard of care, transrectal or transperineal.**
***A meta-analysis of seven studies including 1,330 patients showed significantly reduced infectious complications in patients undergoing transperineal biopsy as compared to transrectal biopsy**

Perform prostate biopsy using the transperineal approach due to the lower risk of infectious complications.	Strong

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING (mpMRI):

-Magnetic resonance imaging-targeted biopsies substantially **improve the detection of ISUP grade > 2 PCa, most notable in the repeat-biopsy setting.**
-It is less marked in biopsy-naïve patients in whom systematic biopsy retain a higher added value.
-mpMRI decrease the number of biopsy procedures and the detection of low-grade PCa improving the detection of csPCa compared to systematic biopsy.



PI-RADS SYSTEM

Source: https://radiologyassistant.nl/

1 Most probably benign
2 Probably benign
3 Equivocal
4 Probably malignant
5 Most probably malignant

PRECISION trial: 500 biopsy-naïve patients. The detection rate of ISUP grade>2 cancers was significantly higher in men assigned to MRI-TBx (38%) than in those assigned to systematic biopsy (26%) (p = 0.005, detection ratio 1.46)

MRI-FIRST trial: 251 biopsy-naïve patients. MRI-TBx detected significantly more ISUP grade>3 cancers than systematic biopsy (19.9% vs. 15.1% p = 0.0095; detection ratio: 1.32).

Met Prostaat MRI Meer Mans (4M) study: 626 biopsy-naïve patients. A detection ratio for ISUP grade>2 cancers of 1.09 (detection rate: 25% for MRI-TBx vs. 23% for systematic biopsy). MRI-TBx and systematic biopsy detected an equal number of ISUP grade > 3 cancers s (11% vs. 12%; detection ratio: 0.92)

Recommendations in biopsy naïve patients
Perform mpMRI before prostate biopsy.
When mpMRI is positive (i.e. PI-RADS ≥ 3), combine targeted and systematic biopsy.
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient.

Recommendations in patients with prior negative biopsy
Perform mpMRI before prostate biopsy.
When mpMRI is positive (i.e. PI-RADS ≥ 3), perform targeted biopsy only.
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is high, perform systematic biopsy based on shared decision making with the patient.

REPEAT BIOPSY [EAU Guidelines 2021]

- **Rising and/or persistently elevated PSA**
- **Suspicious DRE**
- **Positive multiparametric MR (PIRADS =>3)**
- **Intraductal carcinoma as a solitary finding:** > 90% risk of associated high-grade PCa

**The recommendation to repeat biopsy after a diagnosis of atypical small acinar proliferation and extensive high-grade PIN is based on earlier studies on systematic biopsies. In a contemporary series the likelihood of finding a csPCa after a diagnosis of atypical small acinar proliferation was only 6%