PSA: Prostate-Specific Antigen

Serine protease (kallikrein 3 - KLK3)
T ½ 2-3 days
Organ-specific (produced by the epithelial cells of the prostate) but not tumor-specific marker (increases with BPH, prostate cancer, prostatitis, other non-malignant conditions)
Fragmentation of semenogelins → Liquefaction of semen coagulum → Promotion of spermatozoa motility

MAIN CLINICAL SETTINGS OF USE	
PCA	Diagnostic process; risk stratification and nomograms; response to treatment; follow-up
BPH	Differential diagnosis with PCa; predictor of prostate volume and growth; predictor of clinical progression, AUR, and BPH surgery
PROSTATITIS	No practical diagnostic information

GOLDEN RULES

- **PSA is a continuous parameter,** higher PSA → greater the likelihood of PCa
- **May be a PCa with low PSA levels** (undifferentiated tumors)
- **Necessary to verify the PSA rising in several measurements**

EARLY DETECTION OF PCA [EAU Guidelines 2020]

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

Age- and Ethnicity- Specific Reference Ranges for PSA				
Age (years)	**PSA** (ng/mL) in **Caucasian** [Oesterling et al. JAMA 1993]	**PSA** (ng/ mL) in **African Americans** [Morgan et al. NEJM 1996]	**PSA** (ng/mL) in **Asians** [Liu et al. AJA 2009]	**PSA** (ng/mL) in **Latinos** [De Antoni et al. Urology 1996]
40-49	0 to 2.5	0 to 2.0	0 to 2.15	0 to 2.1
50-59	0 to 3.5	0 to 4.0	0 to 3.20	0 to 4.3
60-69	0 to 4.5	0 to 4.5	0 to 4.10	0 to 6.0
70-79	0 to 6.5	0 to 5.5	0 to 5.37	0 to 6.6

CUT-OFF TO REMEMBER [EAU Guidelines 2020]

- Low PSA levels (in naïve patients): < 4 ng/mL
- Use of imaging, risk calculator, or urine/blood-based tests to avoid biopsies: 2-10 ng/mL (with normal DRE)
- Persistent PSA after RP: > 0.1 ng/mL (within 4-8 weeks of surgery)
- BCR post-RP: > 0.4 ng/mL and rising
- BCR post-RT: > 2 ng/mL higher than the PSA nadir
- PSMA PET/CT post-RP: > 0.2 ng/mL
- Choline PET/CT post-RP (if PSMA PET/CT is not available): > 1 ng/mL

Risk of PCa in relation to low PSA levels [Thompson et al. NEJM 2004]		
PSA (ng/mL)	Risk of PCa (%)	Risk of ISUP grade > 2 PCa (%)
0.0-0.5	6.6	0.8
0.6-1.0	10.1	1.0
1.1-2.0	17.0	2.0
2.1-3.0	23.9	4.6
3.1-4.0	26.9	6.7

EAU RISK GROUPS FOR BCR OF LOCALIZED AND LOCALLY ADVANCED PCA FOCUS ON PSA LEVELS [EAU Guidelines 2020]

Low-risk	Intermediate-risk	High-risk	
< 10 ng/mL	10-20 ng/mL	> 20 ng/mL	any PSA
Localized			Locally advanced

SURROGATES OF PSA [EAU Guidelines 2020]

Surrogate	Definition	Clinical use
PSA density (PSAD)	Total PSA (ng/mL) divided by prostate volume (cc)	Higher the PSAD → Greater the likelihood of csPCa PSAD < 0.15 → < 10% of csPCa at biopsy if PIRDAS 1-2 PSAD < 0.15 is among the most used criteria to select patients for AS
PSA velocity (PSAV)	Absolute annual increase in PSA (ng/mL/year)	Prognostic and predictive value Concerns regarding their usefulness compared to PSA alone Variable cut-offs
PSA doubling time (PSA-DT)	Length of time (months) needed for the PSA level to double	
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

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