PSA basiertes ProstataScreening

Leitliniensuche

Für den Inhalt verantwortlich:

Hauptverband der österreichischen Sozialversicherungsträger

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Kurzbericht

Hintergrund

Aufgrund der aktuellen Empfehlungen der U.S. Preventive Services Task Force (2012) hinsichtlich PSA-Bestimmung im Rahmen eines Prostata Screenings wurde die Abteilung EbM/HTA ersucht die derzeitigen aktuellen Empfehlungen hinsichtlich Prostata Screening mittels PSA-Bestimmung, die relevant sein können, kurz zusammenzufassen.

Methodik

Es wurde eine Leitliniensuche über den Zeitraum 2010-2012 durchgeführt. Die Aussagen wurden extrahiert und tabellarisch dargestellt.

Ergebnisse

Insgesamt wurden 8 Leitlinien zum Thema Prostata Screening gefunden, die Aussagen zur PSA-Bestimmung enthielten.

4 Leitlinien raten von PSA-basiertem Screening ab.

3 Leitlinien empfehlen PSA-Bestimmungen bei (kaukasischen) Männern ab dem 50. Lebensjahr (UpToDate: alle 2-4 Jahre bis zum 75. Lebensjahr bzw. Beendigung, wenn aufgrund von Komorbidität die Lebenserwartung < 10 Jahre ist oder bis zum 65. Lebensjahr, wenn PSA < 1,0 ng/mL ist). PSA-Bestimmung ab dem 40. Lebensjahr wird empfohlen bei Afroamerikanern und Männern mit familiärem Risiko (ProstataCa bei Verwandten ersten Grades) (3 Leitlinien), bei Einnahme von 5-alpha-Reduktasehemmer (1 Leitlinie), bei bekannter oder Verdacht auf BRCA1-Mutation (1 Leitlinie). 3 Leitlinien geben Empfehlungen zu Untersuchungsintervallen in Abhängigkeit vom PSA-Wert.

1 Leitlinie empfiehlt PSA-Screening nur bei Vorhandensein von qualitätsgesicherten Screening-Programmen.

Verfasserin: Mag. Bettina Maringer

LEITLINIEN

PSA-basiertes Prostatakarzinom- Screening (Zusammenfassung)

	Generelles PSA Screening empfohlen?		Screening	
	Nein	Ja	Population/ Alter/ Intervall	Individuell/ Intervall
U.S. Preventive Services Task Force, 2012	X			
NCCN, 2012		X	Kaukasier ab 50 Intervall: k.A.	PSA+DRE mit 40→ PSA ≥ 1,0 ng/mL: jährlich in Folge PSA < 1,0 ng/mL: Wiederholung mit 45 Afroamerikaner + Männer mit familiärem Risiko (ProstataCa bei Verwandtem ersten Grades): PSA ab 40, öfter (?) testen. Bei Einnahme von 5-alpha-Reduktasehemmer: jährlich Ältere (?) Männer: seltener PSA-Test, abhängig von Gesundheitszustand und familiärer Disposition
UpToDate, 2012		50-75 (bzw. wenn aufgrund von Komorbidität die Lebenserwartung < 10 Jahre) Bis 65, wenn PSA < 1,0 ng/mL	Kaukasier ab 50: alle 2-4 Jahre PSA (kein DRE)	ab 40-45 Schwarze, Männer mit positiver Familienanamnese, bei bekannter oder Verdacht auf BRCA1-Mutation

Deutsche Gesellschaft für Urologie, 2011	X			
Canadian Guidelines Prostate cancer screening, 2011		X	Jährlich ab 50 bei Männern mit einer Lebenserwartung von mind. 10 Jahren Intervall: k.A.	ab 40 sollte Screening bei familiärem Risiko oder afrikanischer Abstammung angeboten werden. Baseline-PSA (PSA, PSA free/total ratio)+ DRE für Männer zwischen 40-49.
European Association of Urology, 2010	X			Baseline PSA mit 40: wenn PSA<1 ng/mL: Intervall 8 Jahre kein PSA-Test bei Männern > 75 Jahren und einem Baseline PSA < 3 ng/mL.
American Cancer Society, 2010		Nur bei Vorhandensein von qualitätsgesicherten Screening-Programmen		Jährlich bei Männern mit PSA ≥ 2,5 ng/mL alle 2 Jahre bei Männern mit PSA < 2,5 ng/mL
ESMO, 2010	X			

DRE Digitale rektale Untersuchung, k.A. keine Angabe, PSA Prostataspezifisches Antigen

Version	Fachgesellschaft	Kernaussage
2012	U.S. Preventive Services Task Force: Screening for Prostate Cancer http://www.uspreventiveservicestaskforce.org/prostatecancerscreening.htm	**Do not use prostate-specific antigen (PSA)-based screening for prostate cancer.** Contemporary recommendations for prostate cancer screening all incorporate the measurement of serum PSA levels; other methods of detection, such as digital rectal examination or ultrasonography, may be included. There is convincing evidence that PSA-based screening programs result in the detection of many cases of asymptomatic prostate cancer, and that a substantial percentage of men who have asymptomatic cancer detected by PSA screening have a tumour that either will not progress or will progress so slowly that it would have remained asymptomatic for the man's lifetime (i.e., PSA-based screening results in considerable overdiagnosis). The **reduction in prostate cancer mortality 10 to 14 years after PSA-based screening is, at most, very small**, even for men in the optimal age range of 55 to 69 years. The harms of screening include pain, fever, bleeding, infection, and transient urinary difficulties associated with prostate biopsy, psychological harm of false-positive test results, and overdiagnosis. Harms of treatment include erectile dysfunction, urinary incontinence, bowel dysfunction, and a small risk for premature death. Because of the **current inability to reliably distinguish tumours that will remain indolent from those destined to be lethal**, many men are being subjected to the harms of treatment for prostate cancer that will never become symptomatic. The **benefits of PSA-based screening for prostate cancer do not outweigh the harms**.

2012	NCCN (National Comprehensive Cancer Network): Early Detection of Prostate Cancer http://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf	Studies have shown that among the general population of men in their 40s, baseline PSA level is predictive of diagnosis of prostate cancer many years later. Hence for men opting to participate in an early detection program, baseline DRE and PSA testing at age 40 is useful. The median PSA level is approximately 0,7 ng/mL for age 40-49. Annual follow-up is recommended for men who have a PSA value ≥ 1,0 ng/ml. This is above the 75th percentile for younger men. Men with PSA below 1,0 ng/ml should test again at age 45. **Regular testing should be offered to all participants starting at age 50.** Men of African-American descent and men with a first-degree relative diagnosed with prostate cancer (especially at a young age) have a significantly higher risk. For these men, panelists agreed that earlier (start in the 40s) and more frequent testing is appropriate. Annual testing is also recommended for men receiving 5-alpha-reductase-inhibitors as these agents have been associated with increased ability of PSA to detect high-grade prostate cancer. Panelists also agree that testing and biopsy decisions should be individualized for men over 75; less frequent PSA/DRE may be reasonable for older patients. This is supported by a recent longitudinal study of 849 men that found no prostate cancer deaths among age 75-80 men with PSA levels below 3,0 ng/mL. **In tailoring testing for older men, the general health as well as family history of life expectancy should be taken into account.** **These guidelines are not designed to provide an argument for the use of population screening programs for prostate cancer.**

2012	UpToDate: Screening for prostate cancer: http://www.uptodate.com/contents/screening-for-prostate-cancer?source=search_result&search=PSA+screening+guidelines&selectedTitle=2~100	However, prostate cancer screening has been a controversial issue because decisions were made about adopting PSA testing in the absence of efficacy data from randomized trials [12]. Subsequently, the European Randomized Study of Screening for Prostate Cancer (ERSPC) reported a small absolute survival benefit with PSA screening after nine years of follow-up [13]; however, 48 additional patients would need to be diagnosed with prostate cancer to prevent one prostate cancer death. Although the report did not address quality of life outcomes, considerable data show the potential harms from aggressive treatments, including erectile dysfunction, urinary incontinence, and bowel problems [14]. Further sustaining the uncertainty surrounding screening, a report from the large United States trial, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, published concurrently with the European trial, found no benefit for annual PSA and digital rectal examination (DRE) screening after 7 to 10 years of follow-up [15]. Although screening for prostate cancer with PSA can reduce mortality from **prostate cancer, the absolute risk reduction is very small**. Given limitations in the design and reporting of the randomized trials, there remain important concerns about whether the benefits of screening outweigh the potential harms to quality of life, including the substantial risks for overdiagnosis and treatment complications. • Health care providers should periodically discuss prostate cancer screening with men who are expected to live at least 10 years and are old enough to be at significant risk for prostate cancer. We suggest that discussions begin at age 50 in average risk white men and at age 40 to 45 in black men, men with a positive family history, and men who are known or likely to have the BRCA1 mutation (Grade 2B). **Men who are at increased risk of prostate cancer because of race or family history may be more likely to benefit from screening.** (See 'Age to begin screening' above.) • **When a decision is made to screen, we suggest that screening be performed with prostate specific antigen (PSA) tests at intervals ranging from every two to four years** (Grade 2B). **We suggest not performing digital rectal examination as part of screening** (Grade 2C). (See 'Frequency and method of screening' above.) • When a decision is made to screen, **we suggest that screening be performed until comorbidities or age (75 years) limit life expectancy to less than 10 years or the**

		patient decides against further screening (Grade 2B). **Stopping screening at age 65 may be appropriate if the PSA level is less than 1.0 ng/mL.** (See 'Stopping screening' above.)
2011	Deutsche Gesellschaft für Urologie: Interdisziplinäre Leitlinie der Qualität S3 zur Früherkennung, Diagnose und Therapie der verschiedenen Stadien des Prostatakarzinoms: http://www.awmf.org/uploads/tx_szleitlinien/043-022OLl_S3_Prostatakarzinom_2011.pdf	Der Anteil von nachgewiesenen Prostatakarzinomen ist signifikant höher in Screeninggruppen verglichen mit Beobachtungsgruppen. Durch das Screening werden auch zahlreiche Karzinome entdeckt, die keiner Behandlung bedürfen. Die prostatakarzinomspezifische Mortalität wird durch das **Screening** entweder gesenkt oder nicht signifikant beeinflusst. **Ein Einfluss auf die Gesamtüberlebenszeit ist nicht nachgewiesen.** **Nutzen des Prostatakarzinom-Screenings:** Die Ergebnisse der randomisierten kontrollierten Studien ergeben ein heterogenes Bild bezüglich des Nutzens eines populationsbezogenen Screenings. In zwei Studien (n = 19.904 bzw. 162.243) wurde eine signifikante Senkung der prostatakrebsspezifischen Mortalität nach einer Nachbeobachtungszeit von 14 bzw. neun Jahren in einer Größenordnung von relativ 20-40 % aufgezeigt. In absoluten Zahlen starben in den Screening-Gruppen 35 und 102 Männer weniger an Prostatakrebs als in den Kontrollgruppen (43 vs. 78 und 261 vs. 363 Todesfälle). Beide Studien hatten keine ausreichende Fallzahl zum Nachweis einer Veränderung der Gesamtsterblichkeit, da der Anteil der prostatakrebsspezifischen Sterblichkeit sehr gering ist. Die prostatakrebsspezifische Sterblichkeit wurde in der schwedischen Studie nach 14 Jahren von 0,9 % in der Kontrollgruppe auf 0,5 % in der Screeninggruppe gesenkt. Die in der europäischen Studie (ERSPC-Studie) beobachtete Senkung der prostatakrebsspezifischen Mortalität um 20 % nach neun Jahren für die PSA-Screeninggruppe entspricht rechnerisch einer Senkung des durchschnittlichen Risikos für einen Mann am Prostatakarzinom zu versterben von derzeit etwa 3 % (ohne PSA-Screening) auf 2,4 % (mit PSA-Screening) nach einer Nachbeobachtungszeit von neun Jahren. Die Ergebnisse der europäischen Studie beruhen wesentlich auf dem Beitrag der schwedischen Screeninggruppe. Die schwedische Arbeit zeigt die weitaus höchste Inzidenz an Prostatakarzinom im Vergleich der europäischen Länder. In den anderen drei RCTs (n = 46.486, 9.026 bzw. 76.693) ergaben sich bei Nachbeobachtungszeiten von sechs bis elf Jahren keine signifikanten Effekte auf die prostatakrebsspezifische Mortalität. In der Metaanalyse aller Ergebnisse aus den RCTs zeigte sich ebenfalls keine signifikante Senkung der prostatakrebsspezifischen Mortalität oder des Gesamtüberlebens. Die zusammenfassende Interpretation der bisherigen Studienergebnisse wird erschwert durch die Unterschiedlichkeit der Screeningprogramme (z. B. bzgl. des Intervalls oder PSA-

		Grenzwertes), der untersuchten Populationen (Beteiligung an der Intervention und Kontamination in der Kontrollgruppe, allgemeines Erkrankungsrisiko) und der Nachbeobachtungszeiträume. **Schaden des Prostatakarzinom-Screenings:** In dem mit neun Jahren noch kurzen medianen Beobachtungszeitraum der europäischen Studie wurden in der Screeninggruppe 1.638 Fälle an Prostatakarzinom mehr diagnostiziert als in der Kontrollgruppe (5.990 vs. 4.397), das entspricht einer relativen Inzidenzerhöhung von 28 %. Die „Number needed to Screen“ nach neun Jahren wird mit 1.410 angegeben. In der Folge mussten 48 Prostatakarzinompatienten zusätzlich in der Screeninggruppe behandelt werden, damit statistisch ein Todesfall an Prostatakarzinom verhindert werden konnte. Diese Zahl gilt, wenn man alle der Diagnose folgenden Behandlungsmethoden (neben radikaler Prostatektomie und Strahlentherapie auch hormonablative Therapie und Watchful Waiting) einbezieht. Wertet man nur Therapien mit Operation und/oder Bestrahlung, dann kommen auf einen verhinderten Todesfall 40 Überbehandlungen. Die Ergebnisse nach neun Jahren, pro 10.000 Männern ausgedrückt: ➢ pro 10.000 Männer werden in der Screeninggruppe 822 Prostatakarzinome diagnostiziert und behandelt. 29 Männer versterben an einem PCa. ➢ Pro 10.000 Männer werden in der Kontrollgruppe 482 Prostatakarzinome diagnostiziert und behandelt. 36 Männer versterben an einem PCa. ➢ Auf sieben verhinderte PCa-Todesfälle kommen 340 Überbehandlungen1, bzw. auf einen verhinderten Todesfall kommen 48 Überbehandlungen. In der schwedischen Studie wurden im Zeitraum von 14 Jahren in der Screeninggruppe 420 Karzinome mehr als in der Kontrollgruppe diagnostiziert (1.138 vs. 718) [54]. Das entspricht einer absoluten Inzidenzerhöhung um 4,5 % von 8,2 % auf 12,7 % (relativ mehr als 50 % im Vergleich zur Kontrollgruppe). Die „Number needed to Screen“ nach 14 Jahren wird mit 293 angegeben, die Anzahl zusätzlicher Diagnosen um einen Todesfall an Prostatakarzinom zu verhindern mit 12. Demgegenüber stehen 120 mehr impotente Männer pro 10.000 Gescreenten aufgrund der zusätzlich durchgeführten, meist radikalen operativen Therapien

		sowie 25 mehr von Inkontinenz Betroffene pro 10.000. Die Ergebnisse aus der schwedischen Studie sind nicht bedenkenlos übertragbar, da nicht nur die Inzidenz des Prostatakarzinoms in Schweden höher ist als in Deutschland, sondern auch die prostatakrebsspezifische Mortalität. Diese liegt in Schweden – in relativen Zahlen ausgedrückt – um 72 % höher als in Deutschland. Die Existenz von Überbehandlungen in der Screeninggruppe ist aufgrund der Größe dieses Effektes wesentlich besser belegt als die Reduktion der PCa-Mortalität.
2011	Canadian Guidelines Prostate cancer screening: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3147035/pdf/cuaj-4-235.pdf	Prostate cancer screening allows the detection of potentially lethal cancer at a point in time when it is more likely to be curable. This comes at the expense of many patients being treated when their cancer poses no threat to their life. Therefore, the harms and benefits of PCa screening must be explained to each patient so they understand all the factors to be considered in the shared decision-making about screening. **Prostate cancer screening should be offered to all men 50 years of age with at least a 10-year life expectancy. Annual screening has been the standard; however, two screening studies demonstrate that screening is beneficial every 2 to 4 years. If there is a higher risk of PCa, such as family history of PCa or if the patient is of African descent, screening should be offered at age 40 years.** Furthermore, there may be benefit in offering a baseline PSA for men 40 to 49 years of age to establish future PCa risk. Initial screening should include DRE and PSA. **Prostate-specific antigen and PSA free/total ratio are currently the most reliable serum markers.** Both markers offer a continuum of PCa risk. No strict cut point should be used for all patients. The lowest cut point used in phase III trials (which demonstrates a benefit to screening) was 2.5 ng/mL. Many other factors may be used beyond the initial screening tests. If a biopsy is indicated, a 10- to 12-core TRUS-guided peripheral zone prostate biopsy incorporating the anterior horn area should be performed. For men diagnosed with screen-detected PCa, tumour volume, grade, DRE and PSA results direct management. Selectively treating patients with favorable risk PCa may significantly improve screening outcomes.
2010	European Association of Urology : Guidelines on Prostate Cancer http://www.uroweb.org/gls/pdf/Prostat	Based on the results of these two large, randomised trials, most if not all of the major urological societies conclude that **at present widespread mass screening for PCa is not appropriate**. Rather, early detection (opportunistic screening) should be offered to the well-

	e%20Cancer%202010.pdf	informed man (*see also* Section 6, Diagnosis). Two key items remain open and empirical: ○ at what age should early detection start? ○ what is the interval for PSA and DRE? A **baseline PSA determination at age 40 years** has been suggested upon which the subsequent screening interval may then be based (grade of recommendation: B). **A screening interval of 8 years might be enough in men with initial PSA levels < 1 ng/mL. Further PSA testing is not necessary in men older than 75 years and a baseline PSA < 3 ng/mL** because of their very low risk of dying from PCa.
2010	American Cancer Society Guideline for the Early Detection of Prostate Cancer: http://www.guideline.gov/content.aspx?id=24814	The screening decision is made best in partnership with a trusted source of regular care. Men who have no access to regular care should be tested only if high-quality, informed decision making can be assured through community-based screening programs. Such programs also must assure that participants with abnormal screening results receive appropriate counselling and follow-up care if needed. Availability of follow-up care must not be an afterthought. **Unless these program elements are in place, community-based screening should not be initiated.** For men who choose to be screened for prostate cancer after considering the possible benefits and risks: • Screening is recommended with PSA with or without DRE. • Screening should be conducted yearly for men whose PSA level is 2.5 ng/mL or greater. • For men whose PSA is less than 2.5 ng/mL, screening intervals can be extended to every 2 years. • A PSA level of 4.0 ng/mL or greater historically has been used to recommend referral for further evaluation or biopsy, which remains a reasonable approach for men at average risk for prostate cancer. • For PSA levels between 2.5 ng/mL and 4.0 ng/mL, health care providers should consider an individualized risk assessment that incorporates other risk factors for prostate cancer, particularly for high-grade cancer, that may be used to recommend a biopsy.

		Factors that increase the risk of prostate cancer include African American race, family history of prostate cancer, increasing age, and abnormal DRE. A previous negative biopsy lowers the risk. Methods are available that merge this information to achieve an estimate of a man's overall risk of prostate cancer and, more specifically, of his risk of high-grade prostate cancer There are implicit obstacles to IDM/SDM (informed and/or shared decision making) in community-based screening programs. First, men who attend screening programs may be inherently self selected to desire screening and may not be amenable to efforts at informed decision making. Second, there may not be an opportunity for shared decision making in community-based screening, because there is often no opportunity for interaction with a health care provider who has an adequate understanding of the participants' overall health status. This makes the accurate selection of men who have at least a 10-year life expectancy—the target population for informed decision making for prostate cancer screening—virtually impossible. On the basis of these concerns, the ACS discourages participation in community-based prostate cancer screening programs unless they can provide adequately for an informed decision-making process and appropriate follow-up care. These programs have a special obligation to provide high-quality, objective, informed decision making either through interaction with trained personnel or through the use of validated, high-quality decision aids appropriate to the target population. Moreover, it is incumbent on such programs to assure that participants with abnormal screening results receive appropriate counseling and follow-up care. Because virtually all men age 65 years and older have health insurance through Medicare, they should be discouraged from participating in community-based screening programs and should be referred to a primary care provider. **In summary, because of the uncertainties, risks, and potential benefits of prostate cancer screening, there is an ethical mandate to provide men who are considering screening with the opportunity to engage in an informed decision-making process**. Because of the complexity of the decision and the importance of individual values, men should have the opportunity to be assisted by a health professional in reaching this decision. Because there is now an established body of evidence supporting the value and effectiveness of decision aids in facilitating informed decision making, the availability and

		use of such aids should be promoted.
2010	Prostate Cancer: ESMO (European Society for Medical Oncology) Clinical Practice Guidelines for diagnosis, treatment and follow-up http://annonc.oxfordjournals.org/content/21/suppl_5/v129.full.pdf	Population-based screening of healthy men between 55 and 69 years old reduces prostate cancer mortality by an estimated 20 % using prostate-specific antigen (PSA) testing. Screening increases the prostate cancer incidence and leads to diagnosis of asymptomatic cancers that will not emerge during life. The European screening trial suggests an absolute reduction in prostate cancer mortality of 0.71 deaths per 1000 men after a median follow-up of 9 years, but at the cost of 48 additional radical treatments per life saved. There was no reduction in overall mortality. **Decisions on population screening await longer follow-up and the results of analyses of cost-effectiveness and quality of life [I,B]**