Screening and Diagnosis
Prostate Cancer

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Outline

• Screening
  – Evidence
  – Recommendations

• Diagnosis
MEASUREMENT OF PROSTATE-SPECIFIC ANTIGEN IN SERUM AS A SCREENING TEST FOR PROSTATE CANCER

William J. Catalona, M.D., Deborah S. Smith, Ph.D., Timothy L. Ratliff, Ph.D., Kathy M. Dodds, R.N., Douglas E. Coplen, M.D., Jerry J.J. Yuan, M.D., John A. Petros, M.D., and Gerald L. Andriole, M.D.

Abstract Background. Prostate-specific antigen (PSA) is secreted exclusively by prostatic epithelial cells, and its serum concentration is increased in men with prostatic disease, including cancer. We evaluated its usefulness in the detection and staging of prostate cancer.

Methods. We measured serum PSA concentrations in 1653 healthy men 50 or more years old. Those with PSA values $\geq$4.0 $\mu$g per liter then underwent rectal examination and prostatic ultrasonography. Ultrasound-directed prostatic needle biopsies were performed in the men with abnormal findings on rectal examination, ultrasonography, or both. The results were compared with those in 300 consecutively studied men 50 or more years old who underwent ultrasound-directed biopsy because of symptoms or abnormal findings on rectal examination.

Results. Serum PSA levels ranged from 4.0 to 9.9 $\mu$g per liter in 6.5 percent of the 1653 men (107). Nineteen of the 85 men in this group (22 percent) who had prostatic biopsies had prostate cancer. Serum PSA levels were 10.0 $\mu$g per liter or higher in 1.8 percent of the 1653 men (30). Eighteen of the 27 men in this group (67 percent) who had prostatic biopsies had cancer. If rectal examination alone had been used to screen the men who had biopsies, 12 of the 37 cancers (32 percent) would have been missed. If ultrasonography alone had been used to screen these men, 16 of the 37 cancers (43 percent) would have been missed. Serum PSA measurement had the lowest error rate of the tests, and PSA measurement plus rectal examination had the lowest error rate of the two-test combinations.

Conclusions. The combination of measurement of the serum PSA concentration and rectal examination, with ultrasonography performed in patients with abnormal findings, provides a better method of detecting prostate cancer than rectal examination alone. (N Engl J Med 1991; 324:1156-61.)
Screening 1000 men with PSA
- Age 55-69
- Over 13 year period
- PSA threshold 3 ng/ml

720: negative PSA

178: false positive PSA
  → 4 with bx complications

102: prostate cancer diagnosed
  → 33 no cancer-related illness/death
  → 5 still die regardless of screening
  → 1 life saved due to screening

Statistics for benefits and harms were calculated from the European Randomized Study of Screening for Prostate Cancer (ERSPC).
RESULTS OF SCREENING 1,000 MEN WITH THE PSA TEST
(age 55–69 years, screened over a 13-year period, and with a PSA screening threshold of 3.0 ng/ml)

What are my risks if I don’t get screened?

- Among men who are screened with the PSA test, the risk of dying from prostate cancer is 5 in 1,000
- Among men who are not screened with the PSA test, the risk of dying from prostate cancer is 6 in 1,000

720 men will have a negative PSA test
178 men with a positive PSA in whom follow-up testing does not identify prostate cancer

4 of those 178 will experience biopsy complications such as infection and bleeding severe enough to require hospitalization

102 men will be diagnosed with prostate cancer
33 of those 102 prostate cancers would not have caused illness or death
Because of uncertainty about whether their cancer will progress, most men will choose treatment and may experience complications of treatment

5 men will die from prostate cancer despite undergoing PSA screening
1 man will escape death from prostate cancer because he underwent PSA screening

Statistics for benefits and harms were calculated from the European Randomized Study of Screening for Prostate Cancer (ERSPC).
Does not apply to patients with symptoms

NO POPULATION-BASED SCREENING
PLCO PSA Screening Trial

76,693 patients screening vs not; 38+% contamination rate

Prostate Cancers Detected

Prostate Cancer Deaths

Andriole et al. NEJM 2009
<table>
<thead>
<tr>
<th>Organization</th>
<th>Age at initiation of PSA screening</th>
<th>Screening interval</th>
<th>Age at discontinuation of PSA screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Task Force on Preventive Health Care (current)</td>
<td>Routine PSA screening not recommended</td>
<td></td>
<td></td>
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<tr>
<td>Canadian Task Force on the Periodic Health Examination (1994)</td>
<td>Routine PSA screening not recommended as part of periodic health examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US Preventive Services Task Force (2012)</td>
<td>PSA screening not recommended; applies to men of all ages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian Urological Association (2011)</td>
<td>• Average risk: offer at age 50 yr to men with life expectancy ≥ 10 yr</td>
<td>Not specified</td>
<td>75 yr</td>
</tr>
<tr>
<td></td>
<td>• Increased risk (e.g., family history of prostate cancer, African descent): offer at 40 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Offer baseline PSA test at age 40-49 yr to establish future risk of prostate cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian Cancer Society (2014)</td>
<td>Men aged &gt; 50 yr should talk with their doctor about whether they should be tested for prostate cancer</td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td>American Cancer Society (2012)</td>
<td>Average risk; discussion at age 50 yr Increased risk; discussion at age 40 or 45 yr, depending on extent of risk</td>
<td>PSA &lt; 2.5 ng/mL: 2 yr life expectancy &lt; 10 yr</td>
<td></td>
</tr>
<tr>
<td>National Cancer Institute (2012)</td>
<td>Insufficient evidence to determine whether screening with PSA or digital rectal examination reduces prostate cancer mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Health Service (2013)</td>
<td>No organized screening program; informed-choice program = men concerned about the risk of prostate cancer receive clear and balanced information about the advantages and disadvantages of PSA testing and cancer treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate Cancer Canada (2013)</td>
<td>• Offer baseline PSA test at age 40-49 yr</td>
<td></td>
<td>≥ 70 yr; decision should be based on individual factors (not specified)</td>
</tr>
<tr>
<td></td>
<td>• Men aged &gt; 40 yr should talk with their doctor about early detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Men at high risk should talk with their primary care provider before age 40 yr about prostate cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>American Urological Association (2013)</td>
<td>• Routine screening not recommended for men aged 40–54 yr at average risk</td>
<td>≥ 2 yr</td>
<td>≥ 70 yr or life expectancy ≤ 10–15 yr</td>
</tr>
<tr>
<td></td>
<td>• Shared decision-making recommended for men aged 55–69 yr; decision to proceed based on patient’s values and preferences</td>
<td></td>
<td></td>
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<tr>
<td>American College of Physicians (2013)</td>
<td>Men aged 50–69 yr; clinicians should discuss the limited benefits and substantial harms of screening for prostate cancer; they should not screen for prostate cancer with the PSA test in patients who do not express a clear preference for screening</td>
<td>Not specified</td>
<td>≥ 70 yr or life expectancy &lt; 10–15 yr</td>
</tr>
<tr>
<td>Cancer Council Australia, Australian Health Ministers’ Advisory Council (2010)</td>
<td>PSA test not suitable for population screening</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ESMO recommendations 2015

• Population-based PSA screening for prostate cancer reduces prostate cancer mortality at the expense of over diagnosis and overtreatment and is not recommended [I, C].

• Testing for prostate cancer in asymptomatic men should not be done in men over the age of 70 years [I, B].
AUA Screening Recommendations

1. The Panel recommends against PSA screening in men under age 40 years. (Recommendation; Evidence Strength Grade C)

2. The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk. (Recommendation; Evidence Strength Grade C)
   – For men younger than age 55 years at higher risk (e.g. positive family history or African American race), decisions regarding prostate cancer screening should be individualized.

3. For men ages 55 to 69 years the Panel recognizes that the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in 1 man for every 1,000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, the Panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening, and proceeding based on a man’s values and preferences. (Standard; Evidence Strength Grade B)
AUA Screening Recommendations

- To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce overdiagnosis and false positives. (Option; Evidence Strength Grade C)
  - Additionally, intervals for rescreening can be individualized by a baseline PSA level.

- The Panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15 year life expectancy. (Recommendation; Evidence Strength Grade C)
  - Some men age 70+ years who are in excellent health may benefit from prostate cancer screening.
EUA Guidelines 2015

• From a public health point of view, mass screening of PCa is not indicated. However, early diagnosis on an individual basis is possible based on DRE and PSA testing.

• An individualised risk-adapted strategy for early detection might be offered to a well-informed man with a good performance status and at least 10-15 years of life expectancy.

• Early PSA testing should be offered to men at elevated risk for PCa. Risk groups are:
  – men over 50 years of age
  – men over 45 years of age and a family history of PCa
  – African-Americans
  – men with a PSA level of > 1 ng/mL at 40 years of age
  – men with a PSA level of > 2 ng/mL at 60 years of age

• A risk-adapted strategy might be considered (based on initial PSA level), which may be every 2 years for those initially at risk, or postponed up to 8 years in those not at risk.

• The age at which early diagnosis of PCa should be stopped is influenced by life expectancy and performance status; men who have < 15-year life expectancy are unlikely to benefit based on the PIVOT and the ERSPC trials.
Prostate Cancer

DIAGNOSIS
General Principles

• Abnormal DRE or PSA \(\rightarrow\) refer to urologist and biopsy
  – If based on abnormal PSA make sure you repeat it
• TRUS guided biopsy
  – TRUS may image prostate cancer as a hypoechoic area, but the test is used to direct prostate biopsy rather than as a diagnostic modality.
• MRI images and MRI-guided biopsy may also have a role when patients are being considered for salvage prostatectomy or for those with repeat biopsies.
• A negative biopsy does not exclude the diagnosis of prostate cancer. Biopsy is a sampling technique with a substantial potential for misdiagnosis. Repeat biopsy may be indicated if the PSA level increases further.
ESMO Recommendations 2015
Diagnosis

• A single elevated PSA level should not prompt a prostate biopsy, and should be verified by a second value [IV, B].

• The decision whether or not to have a prostate biopsy should be made in the light of DRE findings, ethnicity, age, co-morbidities, PSA values, free/total (f/t) PSA, history of previous biopsy and patient values [II, B].

• Transrectal ultrasound-guided prostate biopsy should be carried out under antibiotic cover and local anaesthesia, and a minimum of 10–12 cores obtained [II, B].

• Before repeat biopsy, multi-parametric MRI is recommended with a view to MRI-guided or MRI-transrectal ultrasound (TRUS) fusion biopsy [5] [III, B].
ESMO Recommendations 2015
Diagnosis

• The most dominant Gleason pattern and the pattern with the highest Gleason grade determine the biopsy Gleason score [6]. Biopsy pathology should be reported using the International Society of Urologic Pathology recommendations.

• The extent of involvement of each biopsy core, and the commonest and the worst Gleason grades should be reported [II, A].
Information Sessions for Patients

- Most patients in Calgary who have a positive prostate biopsy attend information session
  - What is prostate cancer?
  - How to read your pathology report
  - What risk group am I?
  - What are my options?
  - Information about prostatectomy, radiation, brachytherapy, cryotherapy, active surveillance, clinical trials, sexual health, counseling resources
Prostate Cancer Centre
Information Session
Tumor Staging

T1

T2

T3

T4
Robotic Prostatectomy
External Beam Radiation

What to expect

• Daily x-rays on treatment machine for targeting

• Daily outpatient treatments
  ➢ Monday – Friday, 5 treatments/week
  ➢ 30 minutes at the cancer clinic daily
  ➢ 12 minutes on treatment machine daily
  ➢ 37-40 treatments (8 weeks)
<table>
<thead>
<tr>
<th>Risk Groups</th>
<th>LOW</th>
<th>INTERMEDIATE</th>
<th>HIGH</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>&lt;10</td>
<td>10 - 20</td>
<td>&gt; 20</td>
</tr>
<tr>
<td>Gleason score</td>
<td>&lt;=6</td>
<td>7</td>
<td>8-10</td>
</tr>
<tr>
<td>T- Stage</td>
<td>T1-T2b</td>
<td>T2c</td>
<td>T3,T4</td>
</tr>
</tbody>
</table>
| Treatment Options | - Surveillance  
- Prostatectomy  
- Brachytherapy  
- EBRT  
- Cryotherapy | - Prostatectomy  
- EBRT (External Beam Radiation Therapy)  
- Cryotherapy  
- Brachytherapy(a subset of pts.)  
- Surveillance | - EBRT & hormones  
- Prostatectomy  
- Cryotherapy  
- Hormones only |
Couples’ Intimacy Workshop

- Afternoon workshop
- Offered regularly throughout the year
- Presented by

  - Clinical psychologists - Dr. John Robinson, Dr. Andrea Beck and Dr. Lauren Walker
  - Urologist/sexual medicine expert: Dr. Jay Lee

Register (403) 943-8958
Decision Making

- Computer decision aid
- Helps you decide which treatment is the best fit for you based on your values

Offered by: Queens University Cancer Care and Epidemiology

http://prostatecancer.qcancercare.com/DecisionAid_beta/
Decision aids:
http://decisionhelp.qcancercare.com
Your prostate cancer

Your PSA is between 10 and 20.

Your Gleason score is 7.

You are considering the following treatment option(s):

- No treatment for now
- Surgery
- External beam radiation
- Brachytherapy

Is the above information correct?  

[YES]  [NO]
Summary

• Prostate cancer screening controversial
  – But no generalized population based screening
• Diagnosis
  – Ultimately by biopsy
  – Once patient has results, they need to be adequately informed about the options