The PSA, Prostate Cancer Screening, and other Prostate Treatment Secrets

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Dilemmas in the screening for prostate cancer, the treatments for Cap, and other prostate problems

✓ What is the PSA?
✓ Problems with it and how to manage the PSA.
✓ How to identify and treat other common prostate problems such as BPH, prostatitis, and chronic pelvic pain.
Screening for prostate cancer

Meet the prostate

✓ Sex organ.

✓ Starts small, gets bigger.

✓ Cancers live in the periphery.

✓ Screening; PSA and DRE
Prostate exam

Male Urinary Bladder—Posterior View

- Serous coat
- Ureter
- Vas deferens
- Seminal vesicle
- Prostate gland
- Urethra
Prostate Specific Antigen, or Gamma-seminoprotein, or Kallikrein-related peptidase 3

✓ Made only in the prostate
✓ Liquefies the semen for sperm transport

“Normal” screening groups and parameters:

✓ Age 40 if 1st degree family history or African American
✓ Age 50 and over otherwise.
✓ “Normal” values 0.0 to 4.0 ng/ml
NEJM October 1987, Thomas Stamey

- PSA elevated in 122 of 127 pts. with CaP; 7/12 had unsuspected disease - no nodule.
- PSA advanced with clinical stage, and was proportional to amount of tumor.
- PSA dropped to zero after radical prostatectomy.
- PSA was increased in 86% of those with only BPH.
- “PSA…useful in detection of [CaP] and monitoring after treatment… but lacks specificity.”

Sensitivity vs. Specificity

- Sensitivity = “true positive”
- Specificity = “true negative”

If the test goes up when the disease is present, it has good “sensitivity” for the presence of the disease.
If the test is low when that specific disease not present, it’s said to have good “specificity.”

PSA has fair sensitivity in screening for prostate cancer.
PSA specificity is a real problem....
PSA is organ-specific, but not prostate-disease-specific:

- Prostatitis or inflammation
- Ejaculation
- Urinary retention
- Bladder infection
- Trauma
- Benign enlargement.
- Atrophy

Strategies developed to improve the specificity:

- PSA density...serum level vs. size of the gland
- PSA velocity...changes over time
- Age-adjusted PSA screening...relates to size of gland
- Nomograms and addition of PAP, PCA-3, free PSA%

The best additional test to improve sensitivity: DRE
- Presence of CaP is “50-50” if a nodule is present.
- The most aggressive prostate cancers may not elevate the PSA at all
Consider what has happened in 25 years since 1987:

- PSA becomes a standard of measurement for those recommended referral for biopsy.
- Almost every man over 50 knows his PSA
- Only about 15-20% of men undergoing biopsies for elevated PSA actually have prostate cancer; 80-85% do not.
- Still…if there is an elevated PSA and one elects not to pursue it aggressively…and cancer turns out to be present…who is to blame?
- For those who are diagnosed with CaP--then what?

Remember: **35,000 Americans die of prostate cancer annually.**

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Thomas Stamey, *Journal of Urology*, 2004, from Stanford:

“*The prostate specific antigen era in the US is over for prostate cancer: what happened in the last 20 years?*” (1317 cases)

- A single elevated PSA 4-10 has PPV of 2% for the actual presence of prostate cancer
- Of 260 post RRP cancers in 5 years to 6/03, none had PSA statistically specific to CaP, only to BPH
- “20 years ago, PSA was related to cancer…in the last 5, it relates *only to BPH.*”
- Higher PPV: DOB
US Preventative Services Task Force, 2011

Routine PSA screening:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
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<tbody>
<tr>
<td>A</td>
<td>The USPST recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer the service.</td>
</tr>
<tr>
<td>B</td>
<td>The USPST recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer the service.</td>
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<td>C</td>
<td>Notes: The following statement is undergoing revision. Clinicians may provide the service to selected patients depending on individual circumstances. However, for most individuals without signs or symptoms there is likely to be only a small benefit from this service.</td>
<td>Offer the service only if other considerations support offering or providing the service in an individual patient.</td>
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<td>D</td>
<td>The USPSTF recommends against the service. There is moderate to high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
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<td>Statement</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, inconsistent, unclear, and the balance of benefits and harms cannot be determined.</td>
<td>Read &quot;Clinical Considerations&quot; section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
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USPSTF, however, seems to neglect important epidemiologic data:

Highlighted 3 clinical trials, but gave little weight to the 2 trials that showed marked decrease in CaP mortality.

These showed 75% rate reduction in advanced cancers at diagnosis, and 40% reduction in CaP mortality in USA since beginning of PSA testing in US.

ERSPC in March 2012: Overall survival increase of 21% and for those followed over ten years, 38%.

"USPSTF denies men the chance to learn of, and make a choice about, the presence and treatment of CaP."
Detroit trauma victims….incidence of CaP

![Bar chart showing incidence of CaP by age and race]

One urologist’s view…

- We are probably finding more CaP because of the PSA, but mostly because it allows reason to biopsy.
- Many CaPs are survivable without treatment, but some aren’t.
- Upward change PSA/time of greatest value.
- Nodules of considerable importance.
- The patient should have the right to this inexpensive screen, the option to biopsy, and option to treat.
- You only occasionally can make a definitive decision for patient based on PSA.
- Choices by patients and caregivers must be carefully explained and documented; lawyers know you cannot make a correct decision.
- There will one day be a better test, and I will be able to go home about two hours earlier every day.
Prostate and PSA Screening take home:

- The DRE is important…more so than the PSA, and together they are best…but imperfect.
- Consider the other entities that make PSA go up.
- AUA recommends counseling and doing what the patient wants to do after he has the facts.
- Document! If he doesn’t want to screen and prostate cancer is found for whatever reason…documentation is all you have.
- If he does pursue screening, has CaP, and treatment goes awry, it is still all you have.
- When unsure, GU consult.
Non-surgical treatment of symptomatic hyperplasia of the prostate

Tamsulosin, prazosin, terazosin, doxazosin, alfuzosin….the “alpha-blockers.” These block sympathetic nerve activity in the bladder neck and prostate.

The area of (sympathetic n.s.) alpha adrenergic receptor activity in the bladder and prostate:
The alpha adrenergic blockers help about 70% of men with BPH symptoms void about 40% better.

- Well tolerated; SE include postural syncope, stuffy nose, “floppy iris syndrome.”
- If tolerated well, can be increased incrementally, usually with HS dosing.

Symptoms of BPH:
- Slowing stream, spraying, split stream.
- Hesitancy, “double voiding.”
- Nocturia, urgency.
- Typically, NOT burning and pain.

The 5 alpha reductase inhibitors; finasteride and dutasteride.

These medications block the formation of 5-hydroxy-testosterone in the body; which contributes to prostate growth. 5-OH testosterone = most potent form of T.
The 5 alpha reductase inhibitors; finasteride and dutasteride benefits and side effects:

**Benefits:**
- Decrease the size of the prostate slowly over 6-18 months.
- Can decrease vascularity and episodes of benign bleeding.
- Shown to decrease episodes of acute retention in large glands.
- Can decrease episodes of inflammation in chronic prostatitis.
- Will commonly *artificially* reduce the PSA by 50%
- Hair growth

**Side effects:**
- Decreased libido and sexual function; breast tenderness; fatigue; weight gain.
- Decreases PSA by 50%.

REDUCE trial 2008 showed dutasteride *decreased risk of CaP* in 6700 patients.

- 23% reduction in moderately aggressive tumors

*But:*
- High grade tumors found to be 50% more commonly diagnosed.
- Same findings were discovered in an older, finasteride trial.
- Clinical significance of these findings would take a 15-20 year trial to fully elucidate.
- Recent malpractice attorney TV spots have increased interest in “bad medicine” of this “cancer-causing” drug.
This leaves us with two viable options for BPH treatment:

Alpha-blockade and surgery; SPP, TURP, PVP

Cheat sheet;
The painful prostate and pelvic pain.
Several entities to deal with:

- Acute prostatitis
- Chronic prostatitis
- Chronic pelvic pain

Acute prostatitis

Rapid onset, with marked irritative voiding symptoms….
- Urgency and dysuria
- Void small amounts
- Back pain
- Perineal pain
- Occasionally fever and chills.
- Can have elevated WBC and RBC on UA—though otherwise unremarkable UA, and usually negative cultures.
Acute prostatitis - treatment:

- E. coli vs. GC/chlamydia
- Just about anything treats it…fluoroquinolones, sulfa, cephalosporins, doxycycline - due to high blood flow
- Fairly quick defervescence… but, can evolve to abscess.
- No DREs…..No PSAs!

Chronic prostatitis and CP flares.

More enigmatic with many presentations:
- More insidious onset and longer term aches
- Suprapubic pressure, low back pain.
- Urgency and near accidents without other symptoms except occasional dysuria.
- Thigh pain, testicular referred pain, uni-or-bilateral.
- Trace to 1+ microhematuria, negative cultures and bloodwork.
Chronic prostatitis treatment

- Start with a month of quinolones and see back. If not better, a 2nd month.
- Not improving? Consider Biaxin, doxy, or Keflex.
- Anti-inflammatories. Tramadol or other painkiller.
- Decrease sexual activity causes accumulation of ejaculatory proteinaceous debris = ejaculate more.
- Long term suppression. Prostate massages.

Chronic pelvic floor pain.

- Becomes a diagnosis of exclusion - when all the pills fail, but can be considered earlier.
- Males and females.
- Comes from musculo-skeletal tenderness/inflammation.
- Ache in pelvis and inguinal/groin pain, can radiate into testes; many if not all of the same chronic prostatitis symptoms mimicked.
- Sexual pain and dysfunction
Chronic pelvic floor pain…

- “Pelvic guarding”; history infections, abuse, or just unconscious habit of storing tension in the pelvis. Type “A” personality.
- All tests normal and “doctors can’t find out what’s wrong.”
- A focused exam of the pelvic floor muscles can help lead to the diagnosis.
- Myofascial trigger points

Treatments for pelvic floor pain

- Recognition of it and patient interest and cooperation.
- David Wise PhD and Rodney Anderson MD: A Headache in the Pelvis
- Pelvic floor physical therapy.
- Diet, exercise, relaxation techniques.
Pelvic pain summary:

2. Chronic prostatitis: Long term aching pelvis with myriad symptoms. Long term antibiotics, heat, massage *might* fix it.
3. Chronic pelvic pain: No traditional treatments work; no one can seem to find the reason for the pain. Patient cooperation and physical therapy with behavior modification slowly relieve it.