

PSA, Prostate Cancer and BPH Diagnosis

Norcal Urology

2014

PSA Background

- PSA - most widely used oncological biomarker today
- Serine protease involved in seminal liquefaction
- Found mainly in prostate tissue and seminal fluid
- Trace amounts in salivary, pancreatic and breast tissue
- PCA release 10x more PSA than benign tissue

PSA Background

- Prior to PSA, DRE was primary method for detection of Prostate CA (PCa)
- Detection rates for PCa w/ DRE 1-2%
- 48-85% of DRE detected PCa had non-organ confined disease at diagnosis
- PSA able to detect PCa during window of curability
- PCa specific mortality declining in countries using PSA screening

PSA Background

- Stamey in 1987 (NEJM) found
 - PSA was most sensitive marker for PCa
 - PSA levels increased directly with stage and were tightly correlated to cancer vol
 - PSA often decreased to undetectable levels after radical prostatectomy
 - PSA was useful for detecting residual disease

However b/c PSA also elevated in BPH or inflammation it was non-specific

PSA Background

- Cooner in 1990 (J Urol) examined 1,807 men who underwent PNBx for abnormal DRE or suspicious lesion on TRUS.
 - PSA has increasing predictive value for cancer as PSA increased in men with both normal and abnormal DRE
- Catalona in 1991 (NEJM) found DRE and TRUS used alone without PSA would have missed 37-43% PCa
- Therefore PSA could add to DRE for PCa detection

False Positive for PCA

Benign Prostatic Hypertrophy

Inflammation – PSA up to 30 can take 6-8 wks to return to normal

Urinary Retention – microinfarct can increase PSA to 200. Usually decrease 50% 2 days after catheterization

Ejaculation – PSA can rise 0.8-2.0 w/ peak 1 hour after ejaculation

PSA Clinical Use

- Major limitation of PSA is specificity (false +)
- Methods to improve specificity
 - Age Specific
 - Free PSA
 - PSA Density
 - PSA Velocity
- Concern for using these methods was that biologically important cancers would be missed if the prompt for PNBx was not based on absolute PSA levels

Age Specific

PSA at levels lower than 4.0 were more sensitive and specific for younger men

<u>Age</u>	<u>PSA</u>
40-49	2.5
50-59	3.5
60-69	4.5
70-79	6.5

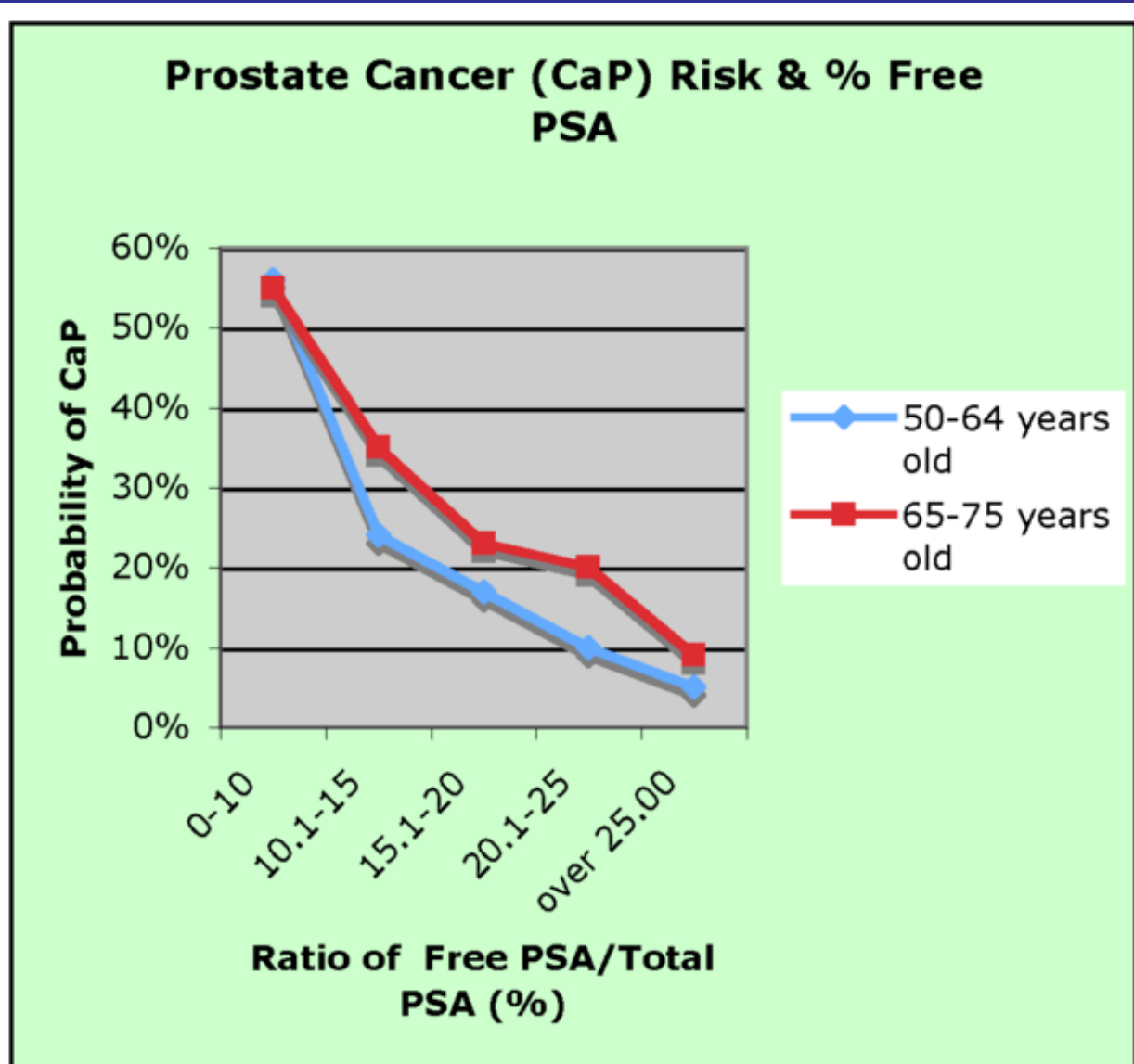
Percent Free PSA

- PSA occurs in 2 major forms, free and protein bound

$$\text{Free PSA} / \text{Total PSA} = \% \text{ Free PSA}$$

- Most useful for PSA 4-10 ng/ml
- Has been shown that if <25% used as cutoff
 - 20% unnecessary bx avoided
 - 95% PCA detected

Percent Free PSA



PSA Density

PSA Density = PSA (ng/ml) / Prostate Vol (cc)

- Popularized by Benson 1992
- Requires TRUS
- Higher density assoc w/ PCA especially for PSA 4-10
- PSA density > 0.15 – 0.28
- PSA density < 0.10 – 0.18 predictive of insignificant cancer

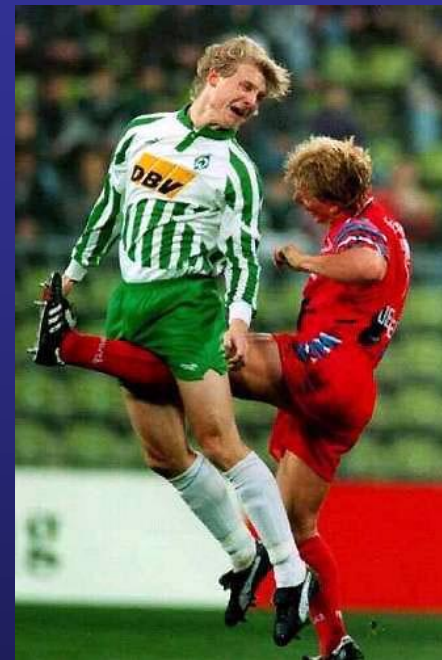
PSA Velocity

Carter (Jama 92') introduced PSA Velocity

- Cut point was created $> 0.75\text{ng/ml}$ rise per year up to 90% specific
- Many Urologists advocate watching velocity for 18mo.
- Some data suggest lower cut point for younger men $> 0.4\text{ng/ml/year}$ for age 50-59
 - Less likelihood for BPH / inflammation
- D'amico (NEJM 94') found velocity >2.0 pre-op predicts mortality with 10 years of surgery
- Doubling time another version of velocity used more to evaluate post-treatment prognosis

Factors that do compromise clinical use of PCA

- DRE
- Routine catheterization
- TRUS
- Cystoscopy
- Prostate Massage
- Saw Palmetto – controversial as no clear data on reduction of PSA but recommend getting pre-tx PSA.



False Negative for PCA

- 5 alpha reductase inhibitors – rapid decrease in PSA to half pre-treatment levels then stabilization at 6mo.
- Herbal Preparations “for prostate health” – could mask a high PSA level
- Post TURP – follow PSA baseline and velocity
- High Grade poorly differentiating cancers

PSA Benefits

1. PSA provides the opportunity to detect PCa during the window of curability
2. PSA improves assessment of disease extent after diagnosis
3. PSA provides a method for monitoring the success of prostate cancer tx.

PSA Diagnosis vs Screening

1. PSA Diagnostic Testing – used for men w/ LUTS or other underlying pathology
2. PSA Screening – use of PSA in asx men to find pre-clinical cancer

To Screen or Not to Screen

1. Burden of Disease is substantial
2. Test must be sensitive for pre-clinical phase
3. Treatments that lead to decrease in disease specific and overall mortality
4. Adverse events from screening and Treatment should not be significant

To Screen or Not to Screen

1. Burden of Disease is substantial
 - i. PCA 30,000 deaths annually
2. Test must be sensitive for pre-clinical phase
 - i. Prospective studies reveal good receiver operating characteristics for PSA age <70

To Screen or Not to Screen

3. Treatments that lead to decrease in disease specific and overall mortality

- i. Scand PCA grp: 15yr f/u – PCA specific survival and overall mortality 38%, 25% lower for RRP vs WW

4. Adverse events from screening and Treatment should not be significant

- i. Both carry risks but improved research and technology has improved both

Amer Ca Soc. recommendation

- recommends that men make an informed decision with their doctor about whether to be tested for prostate cancer.
- Starting at age 50, men should talk to a doctor about the pros and cons of testing so they can decide if testing is the right choice for them. If they are African American or have a father or brother who had prostate cancer before age 65, men should have this talk with a doctor starting at age 45. If men decide to be tested, they should have the PSA blood test with or without a rectal exam. How often they are tested will depend on their PSA level.

AUA Guideline 1 + 2

- The Panel recommends against PSA screening in men under age 40 years.
- The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk.

AUA Guideline 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.

AUA Guideline 4

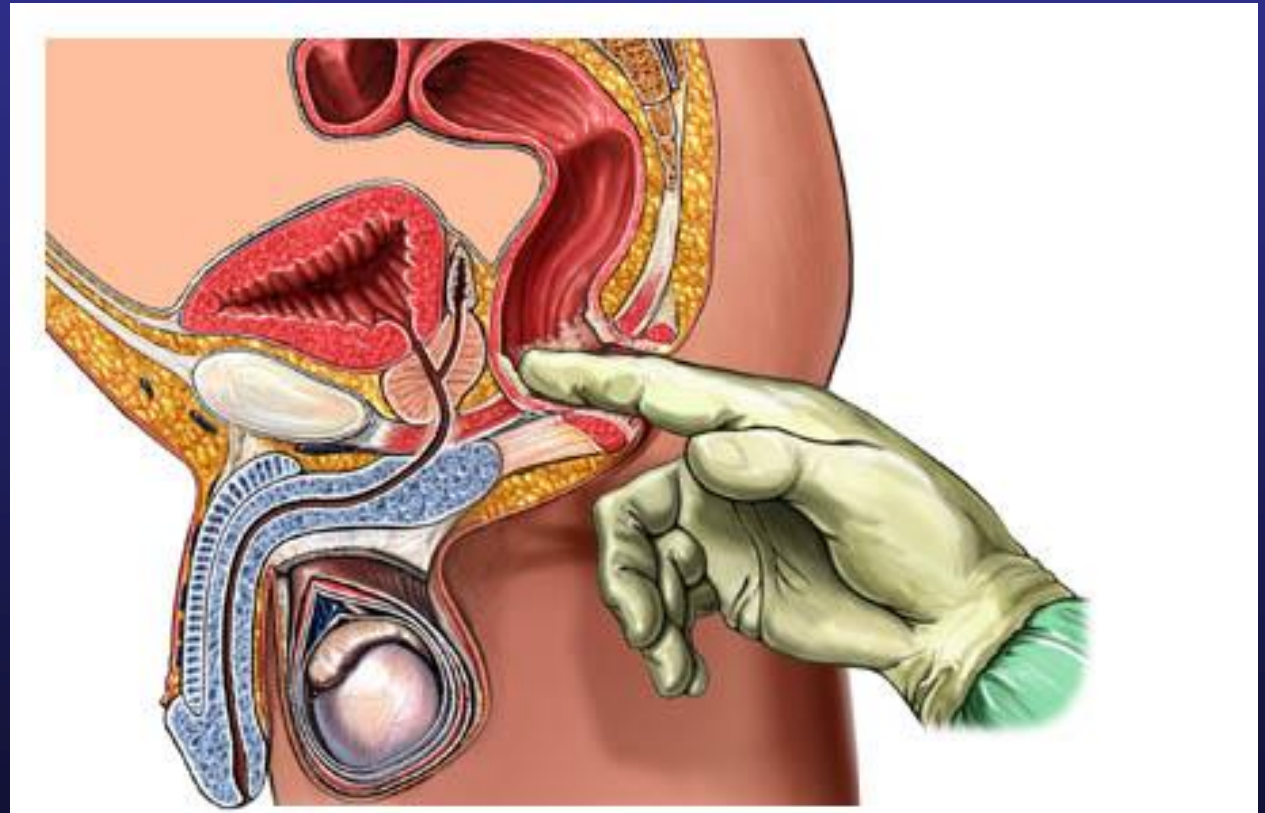
- To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve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

AUA Guideline 5

- 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.
- Some men age 70+ years who are in excellent health may benefit from prostate cancer screening.

Digital Rectal Exam

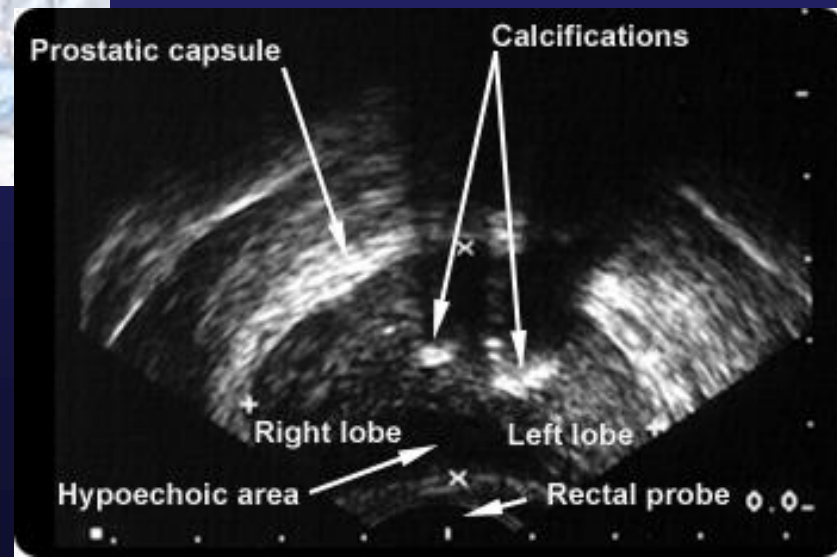
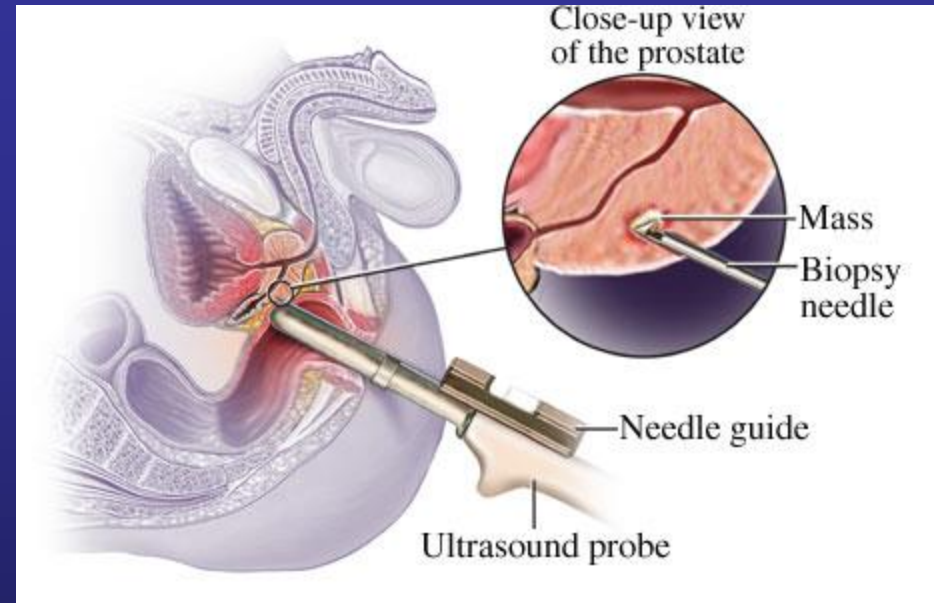
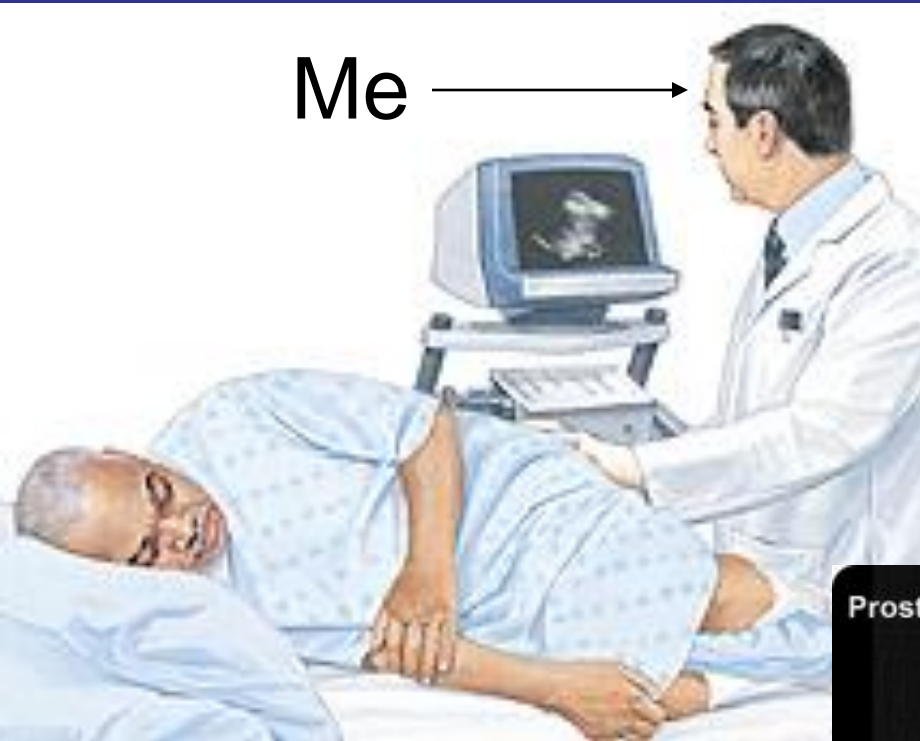
- **Size**
- **Symmetry**
- **Consistency**
- **Nodularity**



TRUS w/ Biopsy

- Hold anticoagulants x1wk prior to bx
- Flouroquinolone antibiotic x3-4 days starting before biopsy
- Fleets enema prior to bx
- TRUS
- Injection of local anesthetic
- Prostate Volume
- Standard 12 core biopsy
- Major Risks: Bleeding, infection 3%

TRUS w/ Biopsy



Diagnosis of BPH

- DRE
- PSA
- AUA symptom score
- Uroflow
- Post-void residual
- Urodynamic testing

Highlight or bold or change font color of the response correct for you and type in your score in the far right box for all SEVEN questions.

1. **Incomplete emptying:** Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

2. **Frequency:** Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

3. **Intermittency:** Over the past month, how often have you found that you stopped and started again several times when you urinated?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

4. **Urgency:** Over the past month, how often have you found it difficult to postpone urination?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

5. **Weak-stream:** Over the past month, how often have you had a weak stream?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

6. **Straining:** Over the past month, how often have you had to push or strain to begin urination?

Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
0	1	2	3	4	5	

7. **Nocturia:** Over the past month or so, how many times did you get up to urinate from the time you went to bed until the time you got up in the morning?

None	1 time	2 times	3 times	4 times	5 or more times	Your Score
0	1	2	3	4	5	

Add up your scores for total AUA score = _____

Quality of Life Due to Urinary Symptoms: If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that? (Bold, Highlight or Underline)

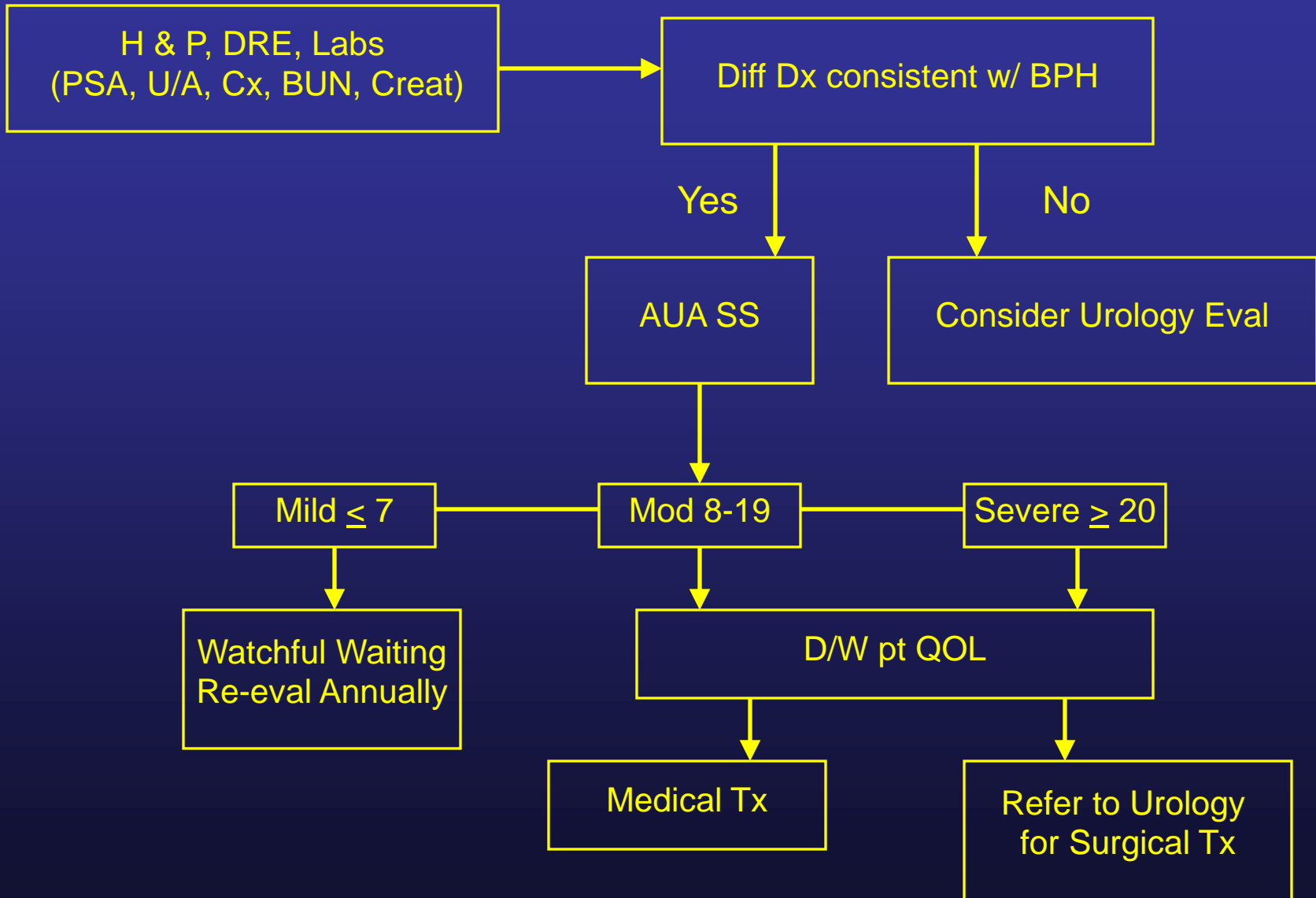
Delighted Pleased Mostly satisfied Mixed Mostly dissatisfied Unhappy Terrible

AUA SS

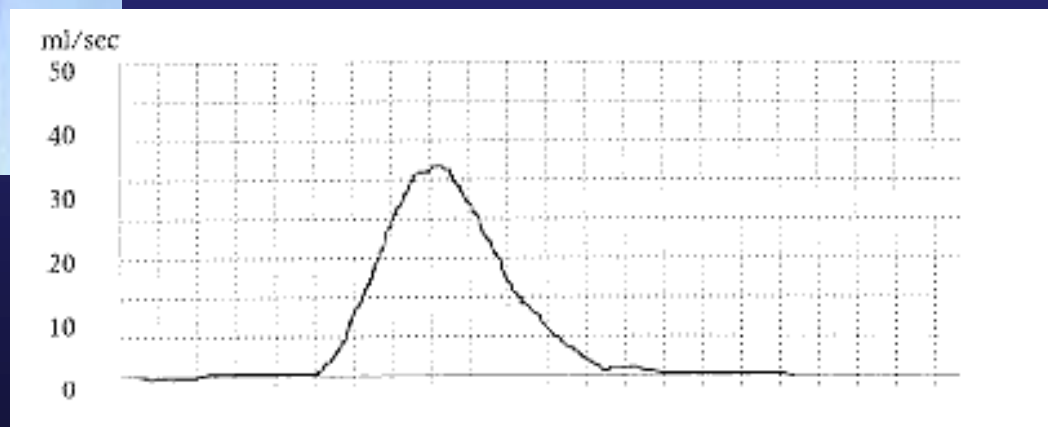
- Mild BPH Sx's ≤ 7
- Moderate 8-19
- Sever Sx's ≥ 20

- ROC in validation was 0.87
- Not all components are obstructive

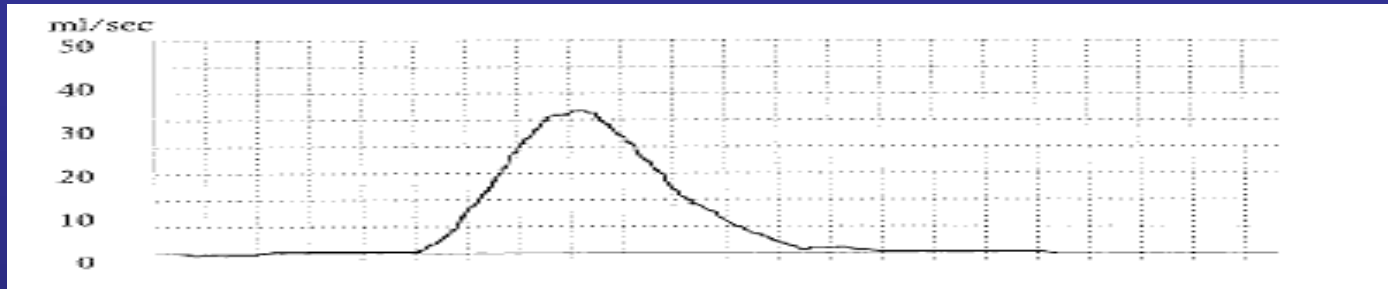
Diagnosis BPH Algorithm



Uroflow



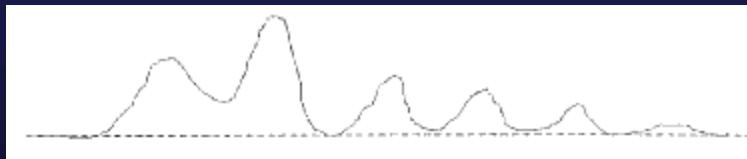
Uroflow



- Overactive



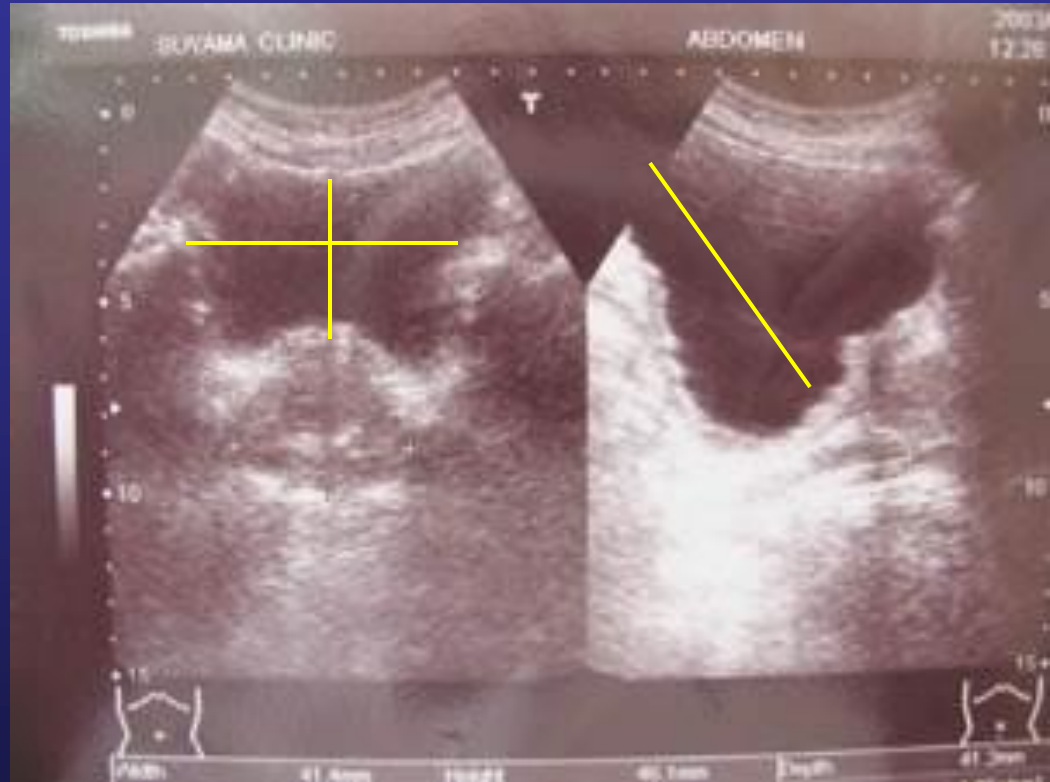
- Obstructed



- Intermittent

Post Void Residual

- Bladder US



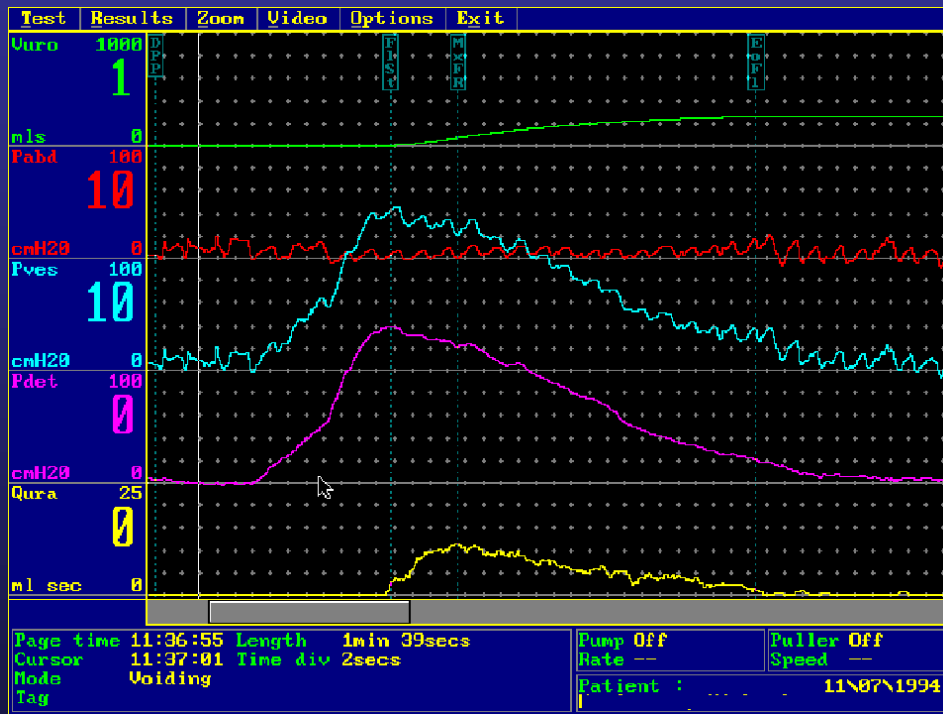
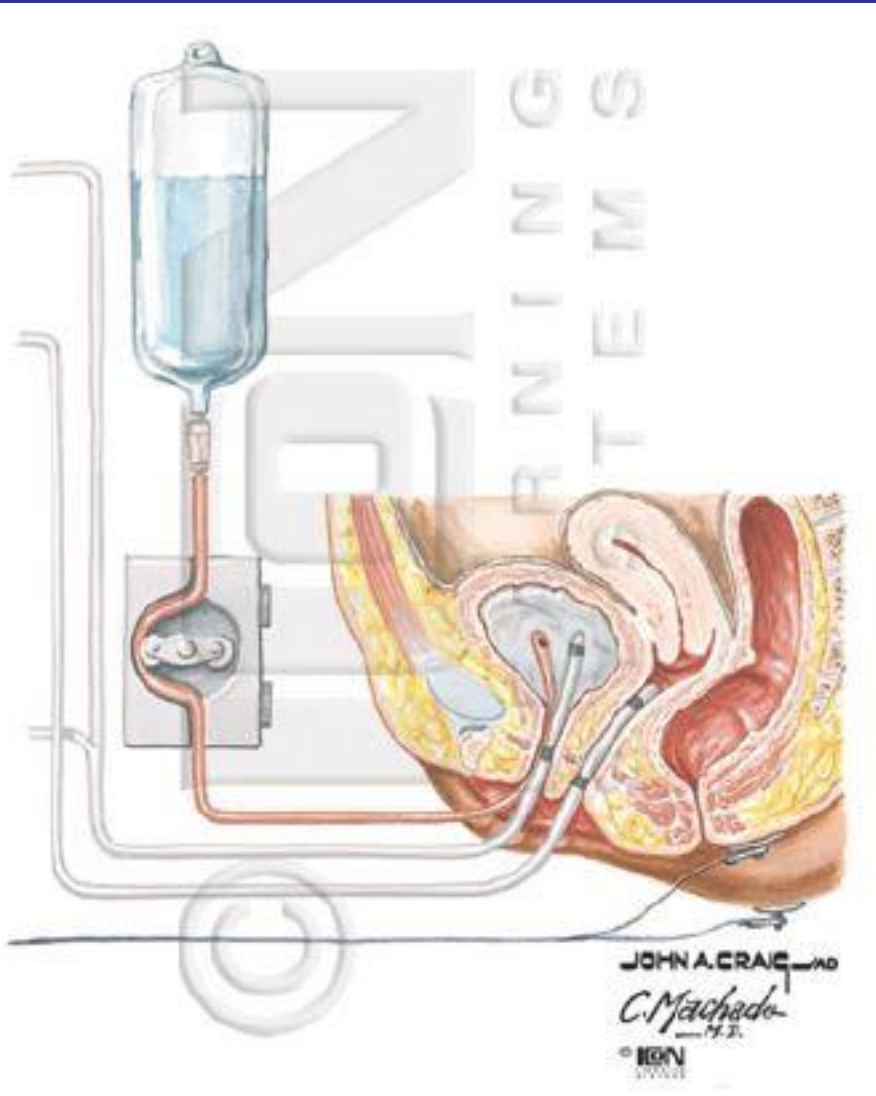
- Catheterized is more accurate

Urodynamic Testing

Recommended for:

- Patients with urinary retention
- Very High PVR (>250)
- Neurologic disease (Parkinson's)
- Young men, small prostate (sx's do not fit findings)

Urodynamics



Abrams Griffith Nomogram

