Geriatric Considerations in Prostate Cancer Diagnosis

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Prostate Cancer Definitions

- Histology = adenocarcinoma
  - Variants:
    - neuroendocrine, urothelial, lymphoma

- Incidence:
  - Up to 220,000 cases/year
  - 25,000-30,000 deaths/year

- Prevalence:
  - Most common non-skin cancer in men
Gleason Grading

Patterns based on degree of glandular differentiation and invasion, not cytologic changes.
Adenocarcinoma
Diagnosis - History

- Index of suspicion:
  - Age >50
  - Family History – prostate (m), breast (f)
  - Race: B>W>H>O ...

- Soft indicators:
  - Smoking
  - Obesity, dietary fat
  - Low selenium
Diagnosis - Exam

- **DRE** ... Subjective
  - **Sensitivity** depends on experience, training ...  
    - **Low** for low stage, low volume disease  
    - **High(er)** for locally advanced disease  
  - **Specificity** ... even experience fails us!  
    - **Very low** for low stage, low volume disease  
    - **Better to very good** for high stage disease  
  - Confounding variables:  
    - prostatitis, BPH, stones, scarring, etc
Prostate Cancer
Traditional Detection

- DRE
- Signs/Symptoms
  60-70% cT1-2
  30-40% cT3-4, N+/M+

But
50% of cT1-2 = pT3-4,N+

So
~75% advanced at detection!!!
Prostate Cancer Screening and Early Detection

Positive Predictive Value for Cancer by Diagnostic Modality

# Diagnosis - Lab

- **PSA - Current best tool for diagnosis:**

<table>
<thead>
<tr>
<th>Range</th>
<th>% Diagnosed</th>
<th>% Localized</th>
<th>% &gt; pT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0-2.5</td>
<td>&lt;10%</td>
<td>99% cT1-2</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>2.6-4.0</td>
<td>~20%</td>
<td>98% cT1-2</td>
<td>&lt;17%</td>
</tr>
<tr>
<td>4.1-10</td>
<td>~38%</td>
<td>95-98% cT1-2</td>
<td>18-32%</td>
</tr>
<tr>
<td>10-20</td>
<td>~65%</td>
<td>70-85% cT1-2</td>
<td>23-50%</td>
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<tr>
<td>&gt;20.1-50</td>
<td>&gt;75%</td>
<td>50-65% cT1-2</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>&gt;50</td>
<td>diagnostic</td>
<td>&lt;5% cT1-2</td>
<td>&gt;95%</td>
</tr>
</tbody>
</table>

- **Confounding variables:**
  - Prostatitis, BPH, obstruction, UTI, instrumentation ...

- **Most VA patients PSA 5-15 range**
Why is this important?

- **pT2 cancer can be effectively ‘cured’**
  - Surgery > IMRT = Brachytherapy
  - Younger, healthier patients

- **pT3 and above still incurable**
  - Becomes a ‘management’ issue
  - Survival can be increased but disease inevitably recurs
  - Significant source of morbidity
Treatment Issues

- Is there value in knowing if a patient has prostate cancer?
  - Slow growing tumors in general
  - Many options effective in early stages
  - Balance treatment goals with potential side-effects.

- Guidelines (NCCN, AUA, ACS, etc)
  - 10 year life-expectancy, grade, PSA
Treatment Issues

- Older patient - need to know:
  - His average/estimated life-expectancy
    - Modified by co-morbid variables
    - Family Hx longevity
  - The natural history of untreated disease
Male Average Life Expectancy vs Age

Ten year life expectancies

<table>
<thead>
<tr>
<th>Age</th>
<th>White</th>
<th>Black</th>
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<tbody>
<tr>
<td>32.5</td>
<td>44.9</td>
<td>38.3</td>
</tr>
<tr>
<td>37.5</td>
<td>40.4</td>
<td>34.2</td>
</tr>
<tr>
<td>42.5</td>
<td>35.9</td>
<td>30.2</td>
</tr>
<tr>
<td>47.5</td>
<td>31.4</td>
<td>26.4</td>
</tr>
<tr>
<td>52.5</td>
<td>27</td>
<td>22.8</td>
</tr>
<tr>
<td>57.5</td>
<td>22.8</td>
<td>19.3</td>
</tr>
<tr>
<td>62.5</td>
<td>19.3</td>
<td>16.2</td>
</tr>
<tr>
<td>67.5</td>
<td>16.2</td>
<td>13.4</td>
</tr>
<tr>
<td>72.5</td>
<td>13.4</td>
<td>10.8</td>
</tr>
<tr>
<td>77.5</td>
<td>10.8</td>
<td>8.7</td>
</tr>
<tr>
<td>82.5</td>
<td>8.7</td>
<td>6.7</td>
</tr>
<tr>
<td>87.5</td>
<td>6.7</td>
<td>5</td>
</tr>
</tbody>
</table>

75 years Black
76 years White

Vital Statistics of the US. V2, sec 6. Life Tables
Life Expectancy Considerations

Untreated Stage A1 (T1a), well differentiated
...irrelevant to the elderly ...
only 10-15% of ‘screened’ CAP
...<<10% of ‘traditional’ CAP
Life Expectancy Considerations

Untreated Stage A2-B2 (cT1b-c, T2b)

Low volume, low grade

Higher volume, higher grade

...relevant to the elderly

...80-95% of ‘screened’ CAP

...30-35% of ‘traditional’ CAP
Life Expectancy Considerations

...unusual in ‘screened’ population

...>30% ‘traditional’ CAP

...40% - 62% are N+ at diagnosis.

...50% progress to M+ within 5 years.
Life Expectancy Considerations

Untreated Stage D1 (Tx, N+, M0)

< 1% in ‘screened’ population
Common with >cT3 disease
> 50% Progression to M(+) in 3-5 yr
Untreated Stage D2 (Tx, Nx, M+)

<1% of screened population
Death from CA Prostate likely
20-year outcomes following conservative management of clinically localized prostate cancer.

Pre-PSA Era Patients

Albertsen PC, Hanley JA, Fine J.
Practical approach to Dx

- Be aware of the implications of PSA
- More sophisticated reasoning and planning
  - Do we want to know Dx?
  - Do we need to know Dx?
  - Will Dx make a difference in management?
Delayed the inevitable and made miserable?
Gained quality time?

“T'd have been here sooner if it hadn't been for early detection.”
Delayed the inevitable, but gained quality time!

“I’d have been here sooner if it hadn’t been for early detection.”
Issues that make Dx important

- GU symptoms:
  - Obstruction, irritative voiding
  - Uremia, upper tract obstruction

- Generalized signs, symptoms:
  - Weakness, weight loss, etc
  - Bone pain

- Family History

- Patient preference
  - Most in favor of more knowledge!
Geriatric Considerations in Prostate Cancer Management by Stage

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**Treatment – cT1,2**

- **Surgery**
  - RRPx
    - Laparoscopic RPx
    - Robotic/Lap RPx
  - RPPx

- **Radiotherapy**
  - Brachytherapy
    - +/- HT, XRT
  - IMRT
    - +/- HT, BrachyTx

- ‘Minimally Invasive Tx’
  - Cryoablation
  - HIFU
  - TURP (European)

- **Watchful Waiting**

- **Active surveillance**
  - PSA, DRE, biopsies

- **Hormone manipulation**

* Not recommended as initial or monotherapy
Prostate Cancer
Clinical T1/T2

- **Life Expectancy**
  - >10-15 years
  - <10 years
- **Co-morbid variables**
  - Minimal/Controlled
  - <20
- **PSA at detection**
  - <20
- **Tumor grade**
  - Higher
- **Patient preference**
  - Surgery
- **Local symptoms**
  - Any

- **Observation (Obs)**
- **Hormone Therapy (HT)**
  - Lower
  - No > Yes
- **Radiotherapy**
  - External Beam
  - Brachytherapy
- **Lymphadenectomy**
  - Open/Laparoscopic
- **Radical Prostatectomy**
  - Retropubic
  - Perineal

- **PSA/DRE**
  - Every 6 months
  - (Obs.)
  - (+/- HT)
  - pT3a, N0
  - pT3b, N0
  - pT2/3, N1
  - pT2a,b, N0
  - Gleason <7
  - PSA/DRE* Every 12 months

*(may add alkaline Phosphatase, Creatinine)*
Prostate Cancer
Clinical T1/T2 (Follow-up to Initial Observation Protocol)

PSA/DRE*: Every 6 months

PSA → Rising
DRE → Progression

Restage+/- ReBx (DRE, CT, Bone scan)

T1,2, N0, M0

Operative Candidate?
Yes → RPP
No → RT

Failure

HT + /- XRT

HT

T3,4/N0/M0

T3,4/N1/M0

Active Surveillance

Good life expectancy
(see advanced disease protocols)

RT

PSA/DRE*: Every 6 months

RPP

RRP

Failure
Prostate Cancer
Clinical T1/T2, (Follow-up to Initial Radiotherapy)

PSA/DRE* Every 6 months

PSA → >0.5ng/ml or Rising → Restage +/- ReBx (DRE, CT, Bone scan) → T3,4/N1/M1

DRE → Progression → T1,2, N0, M0

Operative Candidate?
Yes → Salvage RRP
No → Salvage RT**

(see advanced disease protocols)

HT Failure

PSA/DRE* Every 6 months

** Some advocate Adjuvant Brachytherapy for primary XRT and visa versa
Prostate Cancer
Clinical T1/T2: **Pathologic T2, R0, N0**
(Follow-up to Initial Radical Prostatectomy)

- **PSA/DRE***
  - Every 6 months

- **PSA**
  - $>0.2\text{ng/ml}$
  - or Rising

- **DRE**
  - Palpable Nodule

- **Restage** (DRE, CT, Mab scan, Bone scan)
  - N1/M1

- **N0, M0**
  - PSA $>2.0\text{ng/ml}$
  - **HT +/- XRT**

- **PSA < 2.0\text{ng/ml} (<0.2)**

- **Salvage RT**

- **HT**
  - Failure

- **PSA/DRE***
  - Every 6 months

(see advanced disease protocols)
Prostate Cancer
Clinical T1/T2: Pathologic T2, R1, N0
(Follow-up to Initial Radical Prostatectomy)

- **PSA/DRE**: Every 6 months
- **Rising after Nadir**
- **DRE**: Palpable Nodule
- **Adjuvant XRT**
- **Salvage XRT**
- **HT +/- XRT**
- **PSA < 2.0ng/ml**
- **N0, M0**: PSA > 2.0ng/ml
- **N1/M1**: Restage (DRE, CT, Mab scan, Bone scan)
- **Non-Zero Nadir**: HT +/- XRT

(see advanced disease protocols)
Prostate Cancer
Clinical T1/T2, (Follow-up to Initial Hormone Therapy*)

- **PSA/DRE*** Every 6 months

**PSA** → Rising → Restage (DRE, CT, Bone scan) → T3,4/N0/M0 → Modify HT

**DRE** → Progression → T1,2, N0, M0 → Operative Candidate?
- Yes: Consider RPP
- No: Modify HT

- RPP
- RRP
- RT

**Failure** → PSA/DRE*** Every 6 months

* Not recommended

(see hormone refractory protocols)
Prostate Cancer

Clinical T1/T2: **Pathologic T3, N0**
*(Follow-up to Initial Radical Prostatectomy)*

- **pT3a** Margin(s) → **CSP#553** → Obs.
  - **Adjuvant XRT**
  - **PSA/DRE* Every 6 months**
    - PSA >0.2ng/ml or Rising Palpable Nodule → Restage, (DRE, CT, Mab scan, Bone scan)
      - N0, M0 → **Salvage RT**
      - **Prev. HT only**
    - **N1/M1** → **Previous XRT only** → **HT**
      - **(see advanced disease protocols)**
  - **Failure**

- **pT3b** Seminal vesicle(s) → Obs.
  - **Adjuvant HT +/-XRT**
  - **PSA/DRE* Every 6 months**
    - **Previous XRT only** → **HT**
      - **(see advanced disease protocols)**
Prostate Cancer
Clinical T3/T4, N0-1, M0-1

**Obstructive Symptoms Requiring Local Control**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Control</td>
<td>General Control</td>
</tr>
</tbody>
</table>

**Surgery:**
- RRP, RPP +/- HT
- TURP + HT

**Radiotherapy:**
- XRT +/- HT

**HT**

**PSA/DRE* Every 4-6 months**
- PSA >0.2ng/ml
- Rising creatinine
- Progression on DRE

**Hydronephrosis**
*(see ureteral obstruction protocol)*

**Bony Lesions:**
- Weight-bearing area
- Painful

**Hydronephrosis**
*(see ureteral obstruction protocol)*

**(add alkaline Phosphatase, Creatinine, periodic upper tract imaging)**
Hormone Ablation Strategies**

* Typical Androgen Ablation Strategies

- Orchiectomy or LHRH agonist + Antiandrogen (3-4 weeks only)
- LHRH antagonist
- Orchiectomy

# Testicular Ablation
- LHRH antagonist
- Orchiectomy or LHRH agonist + Antiandrogen (3-4 weeks only)
- Orchiectomy or LHRH agonist + Antiandrogen (continuous)

- Intermittent Ablation*

+ Total Androgen Ablation

* at least 3-4 weeks to counter flare phenomenon
** small cell neuroendocrine and transitional cell carcinoma will not respond
# after orchiectomy, possible with androgen supplementation.
Due to the long term risk of osteoporosis, **bone density measurements** should be obtained prior to initiation of androgen ablation and periodically throughout treatment. Supplementation with bisphosphonates may be appropriate.

*( add alkaline Phosphatase, Creatinine, periodic upper tract imaging)
Due to the long term risk of osteoporosis, bone density measurements should be obtained prior to initiation of androgen ablation and periodically throughout treatment. Supplementation with bisphosphonates may be appropriate. Intermittent therapy may abate these changes.
Table 5. Outcomes of the Scandinavian Prostate Cancer Group Study No. 4: median follow-up of 8.2 years\textsuperscript{10}

<table>
<thead>
<tr>
<th></th>
<th>RP % (n)</th>
<th>WW % (n)</th>
<th>Relative risk (95% CI)</th>
<th>p value</th>
<th>Numbers needed to treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease-specific mortality</td>
<td>9.6% (30)</td>
<td>14.9% (50)</td>
<td>0.56 (0.36 to 0.88)</td>
<td>0.01</td>
<td>20</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>27% (83)</td>
<td>32% (106)</td>
<td>0.74 (0.56 to 0.99)</td>
<td>0.04</td>
<td>20</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>15.2% (50)</td>
<td>25.4% (79)</td>
<td>0.60 (0.42 to 0.86)</td>
<td>0.004</td>
<td>10</td>
</tr>
<tr>
<td>Local progression</td>
<td>19.2% (64)</td>
<td>44.3% (149)</td>
<td>0.33 (0.25 to 0.44)</td>
<td>&lt;0.001</td>
<td>4</td>
</tr>
</tbody>
</table>

CI, confidence interval; RP, radical prostatectomy; WW, watchful waiting.
WW patient LTF x 2 yr
Active Surveillance

- **Identify low risk cancer**
  - Gleason <7, low volume
  - +/- repeat biopsy – best if (-)
  - Periodic DRE, PSA
    - PSA dt > 15mo
    - PSA v <2.0ng/ml/yr

- **Caveats**
  - If you wait until the PSA dt <3mo – poor outcomes
Active Surveillance Failure

- **Failure**
  - Patient nervous, ave. 2yr on AS
  - Exam – palpability, fixed
  - PSA rising (rate, doubling time)
  - Repeat Bx
    - higher grade
    - increased volume

- Restage, Local treatment options
Total androgen ablation:
- Orchiectomy + AA
- LHRH agonist + AA
- LHRH antagonist + AA

**PSA/DRE**
- Every 6 months

**Failure:**
- PSA > 0.2ng/ml
- Alk. Phos. Elevated
- Creatinine rising
- Progression on DRE

**Rising PSA**
- (eg. > 0.2ng/ml)

**Consider:**
- Trial of alternate AA

**PSA/DRE**
- Every 2-3 months

**Cont’d Rising PSA**
- (eg. > 0.2ng/ml)

**Improved Or Stable**

**Monitor for:**
- Bony lesions,
- Ureteral, bladder obstruction

**Follow-up Protocol D**

**Declining/ Stable PSA**
- (eg. < 0.2ng/ml)

**Stop AA**

**PSA/DRE**
- Every month

*( add alkaline Phosphatase, Creatinine, periodic upper tract imaging)*
Hormone Ablation Strategies
Follow-up Protocol D – Hormone Refractory Disease

Stop Antiandrogens → PSA/DRE* Every 1-2 months

Consider:
Chemotherapy Trials

Monitor for:
Bony lesions, Ureteral, bladder obstruction

Goal:
Predict & prevent fractures
Recognize and prevent cord compression

Cancer Center Referral:
Combination Chemotherapy
Immune therapy
Antisense RNA therapy
Others

Ureter and Bladder Protocols

Palliative Care Hospice Referral

* (add alkaline Phosphatase, Creatinine, periodic upper tract imaging)
Prostate Cancer
Clinical T3/T4, N0-1, M0-1

Bladder Obstruction Protocol

Surgery:
- RRP,
- RPP +/- HT
- TURP + HT

Radiotherapy:
- XRT
- +/- HT

HT

PSA/DRE* Every 4-6 months
- PSA >0.2ng/ml
- Rising creatinine
- Progression on DRE

Bony Lesions:
- Weight-bearing area
- Painful

Hydronephrosis
(see ureteral obstruction protocol)

HT

Normal/Unchanged

Repeat Imaging

*(add alkaline Phosphatase, Creatinine, periodic upper tract imaging)
cT3 – Special Circumstances

**Bladder Obstruction Algorithm**

- High PSA
- Elevated creatinine, Decrease urine output
- Edema, congestive heart failure
- Irritative/obstructive symptoms
- Hematuria

**Cystoscopy**

- Non-obstructive
- Consider: Vesicle Dysfunction

**Urodynamics:**

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Residual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

- Renal Ultrasound
- IVP
- Hydronephrosis

**See Ureteral Obstruction Algorithm**

1. Transurethral Resection, GLL
2. Urethral stent
3. Radiotherapy
4. Hormone therapy

**Not improved**

**Improved**

**Continued to Monitor:**

- PSA
- IPSS
- Upper Tracts

**Urinary Analgesics**

- Follow
- Timed voiding, β-blockade
- CIC*, Foley catheter, stent
- Suprapubic cystostomy
- Supravesicle diversion
- Stent

* CIC, Clean Intermittent Catheterization
cT3 – RRPx Outcomes

- Pos. Margins .... >70%
- Pos. Nodes ... depends on PSA, Gl
  - non-curative but may decrease local Sx
  - ? Could XRT have done the same?
  - HT is the usual adjuvant Tx
  - XRT rarely needed for local control of recurrence
- Potency ... approaches normal +/- Viagra, other interventions
- Continence ... >90% with urethral sparing
Bladder outlet obstruction

Stenting
Prostate Cancer cT3, cT4

Ureteral Obstruction Algorithm

Newly diagnosed cancer

High PSA
Elevated creatinine, Decrease urine output
Edema, congestive heart failure
Irritative/obstructive symptoms

Known Cancer

Renal Ultrasound

Hormone Naïve

Unilateral

Bilateral

HT** and high dose
Dexamethasone x 4wk

HT** and high dose
Dexamethasone x 4wk

Hormone Naïve

Aggressive Management

Previous HT

Diversion$
PCN, Stent#
Ureteroneocystostomy

Hospice
Pain Control
Supportive care

Patient and Family Counseling

Expected Management

Deteriorating function

Impaired kidney function

Dialysis

Deteriorating function

PSA/DRE##

Every 3 months

Improved function

HT** and high dose
Dexamethasone x 4wk

Close Monitoring

Urgent Diversion$
PCN, Stent#

$ May be only minimally elevated.
## Add alkaline Phosphatase, Creatinine, periodic upper tract imaging
## Antegrade; retrograde cannulation is usually very difficult
** Total androgen blockade at least initially (see HT algorithm)

# Bilateral for aggressive management but may be necessary for palliation as well.

Bilateral for best kidney for palliation
Ureteral Obstruction
PCN & Resection

Stenting ... very difficult from below
Ureteral Obstruction
Outcomes...

- Bladder outlet
  - Re-TURP <10%
  - HT, XRT helpful

- Ureteral obstruction
  - Most success in un-irradiated
  - May require continued stenting or PCN, nephrostent

- Q 3 month follow-up
- Periodic imaging
  - US
  - Bone scan

- QOL measures
  - IVSS, Pain scores
  - Continually reassess
Summary

- Be aware of the implications of PSA and prostate cancer progression in the elderly
- Locally advanced disease
  - ‘management’ challenge
  - close follow-up needed
  - high index of suspicion to deal with progression
  - Multimodal treatment is the rule
- Advanced disease
  - Same issues + fractures and HT & its side-effects