Active Surveillance for Management of Low Grade Prostate Cancer

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General Surgery Grand Rounds
Resident Debate
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Purpose of Debate

• Discuss current clinical practice and epidemiology of prostate cancer
• Introduce active surveillance
• Review the literature
• Define who is a candidate
Since introduction of PSA, lifetime risk of being diagnosed with prostate cancer almost doubled.
- 10% to 17%
  - 232,000 new cases of prostate cancer in 2005
  - 50% are low grade
Prostate Cancer

• Lifetime risk of dying of prostate cancer = 3%
• Incidence to mortality ratio of 7:1
Current Treatment Practices

Scandinavia study

- 5% absolute survival benefit at 10 years and a 50% reduction in cancer mortality with surgery.
- Only 5% were diagnosed with PSA, few were low risk disease. No benefit in men > 65.

Current Treatment Practices

- 90% of men with low risk prostate cancer undergo radical treatment.
- 80-100 RRPs would be required for each prostate cancer death averted in cases of favorable risk disease.
Whitmoreism #1

• The current state of prostate cancer may not be good medicine but it sure is good business.
Whitmoreism #2

• The patient may not be dead but he wishes he was.
Goals

1) To provide definitive treatment for men with localized cancers that are likely to progress.

2) To reduce the risk of treatment-related complications for men with cancers that are not likely to progress.

What is watchful waiting?

- Pre-PSA era
- Conservative management until metastatic disease develops at which time patients are treated conservatively.
What is Active Surveillance?

- Using selected delayed definitive treatment in a subset of patients based on biological markers before the development of clinical disease progression.

What is Active Surveillance?

• Favorable Risk
  – Gleason sum of 6 or less
  – PSA 10ng/ml or less
  – T1c-T2a disease
• This group is 50% of all new diagnoses
• Cancer mortality of Gleason 6 cancer may be as low as 10% at 30 years.

Review of the Literature

- Watchful waiting 20 year data
- Considered worse case scenario as detected before PSA
- Patients died WITH disease, not BECAUSE of disease
Review of the Literature

• Choo et al
  – First prospective active surveillance protocol
  • Selective delayed intervention for pts with
    – Rapid PSA progression
    – Grade progression on repeat biopsy

Stage T1b–T2b N0M0, PSA ≤ 15, Gleason Score ≤ 7

Observation alone

Predefined Criteria for Disease Progression

No Progression

Progression

Follow

Appropriate Treatment (surgery, radiotherapy or hormone)
Choo et al

- Reasons for discontinuing ‘watchful surveillance’ in a population of 206.

<table>
<thead>
<tr>
<th>Reasons</th>
<th>No. Pts.</th>
</tr>
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<tbody>
<tr>
<td>Clinical progression:</td>
<td>15</td>
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<tr>
<td>Transurethral prostate resection</td>
<td>5</td>
</tr>
<tr>
<td>Increased nodule size on digital rectal examination</td>
<td>10</td>
</tr>
<tr>
<td>PSA progression</td>
<td>16</td>
</tr>
<tr>
<td>Histological progression</td>
<td>5</td>
</tr>
<tr>
<td>Death from other causes</td>
<td>4</td>
</tr>
<tr>
<td>Patient request</td>
<td>20</td>
</tr>
<tr>
<td>Protocol violations</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
</tr>
</tbody>
</table>
Choo et al

• 137 remain on surveillance protocol with no disease progression.
• Probability of remaining progression-free was 81% and 67% at 2,4 years.
• 88 pts with T1-2, N0,M0 avg. PSA 5.8
• Negative bx on repeat in 60%
• Progression in 22 over mean 48 months
• One biochemical recurrence
• 5 and 10 year progression free probabilities – 67% and 55%

**AN ANALYSIS OF MEN WITH CLINICALLY LOCALIZED PROSTATE CANCER WHO DEFERRED DEFINITIVE THERAPY**

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[Graph showing progression-free survival with rebiopsy results]
Is Waiting Safe?

• Warlick et al:
  – Compared 38 expectant management with 150 immediate RRP pts
  – No increased risk of incurable cancer at time of surgery

Who is a Candidate?

• The longer the life expectancy, the more stringent the criteria.
• Epstein criteria
  - < 1/3 of all cores positive, no more than 1/2 of any one core involved, PSA density <0.15
  - non-palpable on DRE, no Gleason 4 or 5

Epstein JI, Walsh PC, Carmichael M, and Brendler CB. Pathologic and clinical finding to predict tumor extent of non-palpable (Stage T1C) Prostate Cancer. JAMA 1994. 271:365.
Current Research

• 8 prospective phase 2 clinical trials of active surveillance
  – START (Surveillance Therapy Against Radical Treatment)
    • Opened in 2007
    • Endpoint is prostate cancer survival.
Conclusion

• Screen aggressively to detect intermediate and high grade cancers earlier when treatment is of benefit, but manage the low risk disease conservatively.
Whitmore’s conundrum

• Is a cure possible for those in whom it is necessary?
  Is a cure necessary for those in whom it is possible?
References

- Epstein JI, Walsh PC, Carmichael M, and Brendler CB. *Pathologic and clinical finding to predict tumor extent of non-palpable (Stage T1C) Prostate Cancer*. JAMA 1994. 271:365.