A Practical Guide to Active Surveillance for Prostate Cancer

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Objectives:
• Describe current, evidence-based criteria for selecting appropriate patients for active surveillance
• Describe current, evidence-based criteria for following appropriate patients in active surveillance
• Describe current, evidence-based criteria for defining progression in patients on active surveillance
• Discuss recent developments in active surveillance, including the use of MRI to select and follow patients
Active Surveillance for Prostate Cancer

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Declarations

• Myriad.
  • Consultant.
Goals

- Patient selection
- Evolving evidence-based follow-up protocols
- Role of 5-alpha reductase inhibitors
- Role of MRI
- Role of novel tissue tests
- Diet and exercise
Active Surveillance

• **Active surveillance:**
  • Identifies men with non-progressive cancers that, left untreated, will not shorten lifespan.

• **It uncouples diagnosis from treatment.**
  • Prostate cancer becomes a chronic disease, like DM or HTN.
Active Surveillance vs. Observation

• Active surveillance is not “observation.”

• Observation
  • Determine the proper time for instituting *palliative* treatment.
  • Does not aim to cure.
Observation

- Appropriate Patient
- Follow-up
- Symptoms Metastases Increasing PSA
- Initiate Palliation (Androgen Deprivation)
Active Surveillance

Selection
- Appropriate Patient

Follow-up
- Progression
- No Progression

Outcome
- Treatment with intent to cure
- Continue follow-up
Goals

• Reduce incidence of unnecessary treatment

• “Buy time”—increase quality of life for a finite period prior to treatment.
  • Usually applied to younger men.
Patient Selection: Clinical Criteria

- There is no consensus

- General principles
  - Clinical T1c or T2a
  - Age 50 to 80 years
  - PSA < 10 ng/mL
  - PSA density < 0.15
Patient Selection: Biopsy Criteria

- Gleason 6
  - Consider Gleason 3 + 4 = 7 in men > 70 years
- < 25% of cores positive
- < 50% of any one core
Follow-up: well defined

- General trend has been toward less.
  - Especially after the first 2 years.
- PSA every 3 to 6 months
- Clinic visit every 3 to 6 months
- Repeat prostate biopsy at 12 to 24 months
- Consider intermittent ultrasound for PSA density
Follow-up: not well-defined

- MRI

- New tissue prognostic markers

_unclear how these tests inform decision making_
Follow-up: when to treat

- No consensus
- Patient request
  - Anxiety
- PSA $\geq 10$ ng/mL
- PSA doubling time $< 3$ years
- PSA density $\geq 0.15$
Follow-up: when to treat

- Gleason pattern $\geq 4$
  - or Gleason 4 + 3 if followed for 3 + 4
- $> 50\%$ of any one core
- $\geq 25\%$ of cores
Prostate Cancer-Specific Survival on AS

Klotz et al. Journal of Clinical Oncology 2010
Long Term Follow-up: Probability of Being Alive and on AS

Klotz et al. *Journal of Clinical Oncology* 2010
Overall Survival on AS

Klotz et al. *Journal of Clinical Oncology* 2010
5-alpha reductase inhibitors
The REDEEM Study

- 302 patients randomized to dutasteride or placebo
  - T2a, Gleason 6 in < 4 cores with <50% any core +

- Followed for 3 years

- Primary outcome: pathologic progression or treatment (surgery, radiation, etc.)

- Patients not blinded to PSA
REDEEM

38% (dutasteride) vs. 48% (placebo) progression
p = 0.009

REDEEM—additional findings

• Dutasteride patients had greater declines in prostate cancer-related anxiety (p = 0.017).

• Adverse event rates similar.

• Stratified analyses by pathologic (biopsy) and therapeutic (treatment) progression non-significant.
Dutasteride: Bottom Line

- A safe treatment for BPH in AS patients.
- Decreases patient anxiety (from decreased PSA).
- Unclear if it truly prevents biologic progression.
  - But if the goal is to prevent overly-aggressive treatment, does the distinction matter?

  *Probably not.*
Active surveillance and MRI

• No consensus—*use is evolving*

• Two basic roles
  • Targeted biopsy for initial staging
  • Follow-up for “progression”
    • Changes in MRI appearance
    • Pathologic progression based on targeted biopsy
Targeted Biopsy: Predicting Eligibility for Active Surveillance

- NCI study
- 85 patients who met Hopkins AS criteria
  - Targeted biopsy
  - n=25 (29%) upstaged
  - 18% upgrading, 11% increased core volume

Stamatakis L et al. *Cancer* 2013 Sep 15;119(18):3359-66
MRI: Bottom Line

- Potentially may be useful for initial staging.

But requires:
- A 3T MR scanner.
- A radiologist experienced in prostate imaging.
- An ultrasound/MRI imaging fusion system for directing biopsies into the dominant lesions.
Novel tissue tests

• Through novel tissue signatures, these assays seek to:
  • Select appropriate candidates for AS
  • Identify progression

• Many companies currently competing in this space
Proposed Clinical Algorithm

Novel tissue tests: Bottom Line

- The jury is still out.
- Unclear how these tests inform clinical decisions.
- Sampling error of biopsies.
  - What if the “bad” area of tumor was missed?
- Not definitively proven superior to current (and much cheaper) prognostic algorithms.
Today’s Random Medical News

According to a report released today...

Jim Borgman
The Cincinnati Enquirer
King Features Syndicate

UC San Diego
Moores Cancer Center
**Diet and Prostate Cancer**

*Level 2 evidence: incidence, progression, and mortality*

<table>
<thead>
<tr>
<th>Increased Risk</th>
<th>Decreased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dairy/milk/calcium</td>
<td>Tomato sauce (lycopene)</td>
</tr>
<tr>
<td>Red/processed meats</td>
<td>Vegetables with carotenoids (i.e. carrots)</td>
</tr>
<tr>
<td>Eggs, poultry with skin</td>
<td>Cruciferous vegetables</td>
</tr>
<tr>
<td>Obesity</td>
<td>Fish and omega-3 fatty acids</td>
</tr>
<tr>
<td></td>
<td>Vegetable fat</td>
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Walking and prostate cancer progression

Richman et al. Cancer Res 2011
Diet and Exercise: Practical Approaches

• Streamline the message.
  • Heart healthy is prostate healthy.
  • No supplements.
  • Ignore press coverage.
• Educate through practice extenders.
• Keep PCF handouts in the office.