Surgery for the treatment of localized prostate cancer

Joseph Dall’Era
Division of Urology

November 24, 2008
General Surgery Grand Rounds
University of Colorado
Prostate Cancer Statistics

234,460 cases diagnosed annually

213,358 with localized disease (91%)

Stage
Gleason grade
PSA
Health status (age)
Patient preferences (QOL)

Informed Decision

Surgery 37%
EBRT 20%
Brachy Tx 24%
cryotherapy
Hormonal Tx
active surveillance

Randomized Controlled Trials (RCTs) provide the best evidence for therapeutic decision making.

RCTs comparing primary treatment modalities for prostate cancer are EXTREMELY LIMITED.

Most RCTs compare various interventions within a specific treatment modality (i.e., surgery with and without hormone therapy).
Signs of the coming Armageddon...
Surgery Vs. Radiation

• Effectiveness in cancer treatment (can’t look to RCTs)
  – Staging
  – Local control
  – Overall survival

• Quality of life

• Complications from treatment
  – Early
  – Delayed
  – Risk of secondary malignancies

• Cost
Staging

• Lymph nodes status
• Accuracy of gleason grading
IMMEDIATE HORMONAL THERAPY COMPARED WITH OBSERVATION AFTER RADICAL PROSTATECTOMY AND PELVIC LYMPHADENECTOMY IN MEN WITH NODE-POSITIVE PROSTATE CANCER

Edward M. Messing, M.D., Judith Manola, M.S., Michael Sarosdy, M.D., George Wilding, M.D., E. David Crawford, M.D., and Donald Trump, M.D.

- 98 men s/p RRP with + LNs
- Randomized to immediate ADT (LHRH agonist or orchiectomy) or observation
- median of 7 years follow up
## Prostate cancer specific mortality

### Treatment Arm

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Total</th>
<th>Died (disease specific)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone</td>
<td>47</td>
<td>3</td>
</tr>
<tr>
<td>Observation</td>
<td>51</td>
<td>16</td>
</tr>
</tbody>
</table>

*37 pts in obs group received ADT for disease recurrence

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2006 update: 12 years median follow up
Staging
Concordance of PNBX and RP grade

- 1363 pts underwent PNBx and RP from 1992-2006
- Pts receiving ADT excluded

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>265 (19.4)</td>
<td>428 (31.3)</td>
<td>670 (49.1)</td>
</tr>
<tr>
<td>Age at surgery</td>
<td>62.5 (±7.2)</td>
<td>59.6 (±7.4)</td>
<td>59.8 (±7.4)</td>
</tr>
<tr>
<td>Age range</td>
<td>40–75</td>
<td>39–75</td>
<td>35–79</td>
</tr>
<tr>
<td>Prebiopsy PSA (ng/mL)</td>
<td>8.3 (±6.3)</td>
<td>7.0 (±3.8)</td>
<td>7.3 (±6.5)</td>
</tr>
<tr>
<td>Clinical TNM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1C</td>
<td>164 (61.9)</td>
<td>273 (63.7)</td>
<td>427 (63.7)</td>
</tr>
<tr>
<td>T2</td>
<td>68 (35.1)</td>
<td>145 (33.9)</td>
<td>223 (33.2)</td>
</tr>
<tr>
<td>T3</td>
<td>8 (3)</td>
<td>10 (2.3)</td>
<td>20 (2.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individual GS concordance (2–10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exact agreement</td>
</tr>
<tr>
<td>Biopsy GS–undergraded</td>
</tr>
<tr>
<td>Biopsy GS–overgraded</td>
</tr>
</tbody>
</table>

Undergraded: 53% 37% 20%

Surgery versus radiation
In HIGH RISK DISEASE
prostate cancer specific mortality

Long-Term Survival in Men With High Grade Prostate Cancer: A Comparison Between Conservative Treatment, Radiation Therapy and Radical Prostatectomy—A Propensity Scoring Approach

Ashutosh Tewari,* † George Divine, Peter Chang, M. Mendel Shemtov, Matthew Milowsky, David Nanus and Mani Menon
From the Brady Urologic Health Center, New York Presbyterian Hospital and Robotic Prostatectomy and Urologic Oncology Outcomes, Weill Medical College of Cornell University, New York, New York

• 453 men with localized prostate cancer (Gleason ≥ 8) treated with,
  • 26% RP                   30% radiation                   44% conservative (early hormonal tx or WW)
  • retrospective cohort study
  • Median follow up = 68 months for RP, 53 months for conservative and radiation

Urology, 2006.
Results

Overall Risk of Death: 32% lower for RP compared to conservative tx

42% lower for RP compared to radiation

Median overall survival: 5.2 yrs for conservative tx

6.7 yrs for radiation

9.7 yrs for prostatectomy
Long-Term Survival in Men With High Grade Prostate Cancer: A Comparison Between Conservative Treatment, Radiation Therapy and Radical Prostatectomy—A Propensity Scoring Approach

Results

Cancer specific death: 68% lower for RP compared to conservative tx
49% lower for RP compared to radiation
Surgery versus radiation
prostate cancer specific mortality


- retrospective study, mean followup 4.5 yrs
- 550 pts tx with XRT + ADT (6 months LHRH agonist + antiandrogen)
- 2690 pts tx with RP
- Risk factors: PSA > 10 ng/ml, Gleason 7-10, T2b or T2c

<table>
<thead>
<tr>
<th>Covariate</th>
<th>All patients (n = 3240)</th>
<th>RP (n = 2690)</th>
<th>RT+AST (n = 550)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted HR (95% CI)</td>
<td>P&lt;sub&gt;Gray&lt;/sub&gt;</td>
<td>Adjusted HR (95% CI)</td>
</tr>
<tr>
<td>Risk factors present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any 1</td>
<td>Baseline</td>
<td>.15</td>
<td>Baseline</td>
</tr>
<tr>
<td>Any 2</td>
<td>1.6 (0.84–3.02)</td>
<td></td>
<td>1.7 (0.8–3.3)</td>
</tr>
<tr>
<td>All 3</td>
<td>7.1 (3.9–12.9)</td>
<td>&lt;.001</td>
<td>6.3 (3.2–12.2)</td>
</tr>
<tr>
<td>Age, continuous*</td>
<td>1.02 (0.98–1.06)</td>
<td>.27</td>
<td>1.02 (0.97–1.06)</td>
</tr>
</tbody>
</table>
Surgery versus radiation prostate cancer specific mortality


[Graphs showing prostate cancer specific mortality over time for XRT + HT and RP treatment options]
Surgery vs. Watchful Waiting

Bill-Axelson A et al. Radical prostatectomy versus watchful waiting in early prostate cancer. NEJM. 2005

- prospective, RCT
- 695 men with prostate cancer randomly assigned to RP (347) or WW (348).
- median 8.2 years followup
Surgery vs. Watchful Waiting

Bill-Axelson A et al. Radical prostatectomy versus watchful waiting in early prostate cancer. NEJM. 2005

• prospective, RCT
• 695 men with prostate cancer randomly assigned to RP (347) or WW (348).
• median 8.2 years followup
Colorectal complications of EBRT

- 183 pts EBRT
- Mean f/u 39 months

<table>
<thead>
<tr>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute GI toxicity</td>
<td>Diarrhea requiring parenteral support, severe mucous or bloody discharge requiring pads, abdominal distension, bleeding requiring multiple cauteries or surgery</td>
<td>Obstruction, fistula, or perforation; abdominal pain or tenesmus requiring decompression or diversion</td>
</tr>
<tr>
<td>Diarrhea requiring medications, rectal pain requiring analgesics, rectal bleeding requiring topical medications</td>
<td></td>
<td></td>
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43%

<table>
<thead>
<tr>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late GI toxicity (&lt;12 wk)</td>
<td>Watery diarrhea, obstruction requiring surgery, bleeding requiring surgery or ≥2 cauteries and/or transfusions</td>
<td>Necrosis, perforation, abdominal pain, or tenesmus requiring decompression or diversion</td>
</tr>
<tr>
<td>Moderate diarrhea; intermittent, severe cramping; bowel movements &gt;5 per day; frequent bleeding requiring single cautery treatment and/or transfusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

19%

- 3 pts with rectal bleeding requiring colonoscopy and cauterization
- 1 pt with anal stricture requiring dilation under anesthesia

Risk of secondary malignancies

Radiation Therapy for Prostate Cancer Increases Subsequent Risk of Bladder and Rectal Cancer: A Population Based Cohort Study

Alan M. Nieder,* Michael P. Porter and Mark S. Soloway

From the Department of Urology, University of Miami Miller School of Medicine, Miami, Florida (AMN, MSS), and the Departments of Urology & Epidemiology, University of Washington and the VA Puget Sound Health Care System, Seattle, Washington (MPP)

- 243,082 men undergoing RP or radiation therapy 1988-2003 (SEER)
- Increased risk of bladder and rectal cancers for EBRT and BT compared to RP
**Radiation Therapy for Prostate Cancer Increases Subsequent Risk of Bladder and Rectal Cancer: A Population Based Cohort Study**

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<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Radiation Therapy</th>
<th>Risk Factor</th>
<th>Time Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder CA</td>
<td>EBRT</td>
<td>2.3 x</td>
<td>5-10 years</td>
</tr>
<tr>
<td></td>
<td>BT</td>
<td>1.6 x</td>
<td>&gt;10 years</td>
</tr>
<tr>
<td>Rectal CA</td>
<td>EBRT</td>
<td>1.8 x</td>
<td>5-10 years</td>
</tr>
<tr>
<td></td>
<td>EBRT + BT</td>
<td>3.3 x</td>
<td>&gt;10 years</td>
</tr>
</tbody>
</table>
Cancer after radiation is WORSE !!!


- 34 pts underwent cystectomy for bladder CA after receiving RT for prostate CA
- 86% EBRT

53% locally advanced in radiation group
36% locally advanced in control group
Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

Martin G. Sanda, M.D., Rodney L. Dunn, M.S., Jeff Michalski, M.D., Howard M. Sandler, M.D., Laurel Northouse, R.N., Ph.D., Larry Hembroff, Ph.D., Xihong Lin, Ph.D., Thomas K. Greenfield, Ph.D., Mark S. Litwin, M.D., M.P.H., Christopher S. Saigal, M.D., M.P.H., Arul Mahadevan, M.D., Eric Klein, M.D., Adam Kibel, M.D., Louis L. Pisters, M.D., Deborah Kuban, M.D., Irving Kaplan, M.D., David Wood, M.D., Jay Ciezki, M.D., Nikhil Shah, D.O., and John T. Wei, M.D.

- prospectively measured patient reported outcomes of 1201 patients and 625 spouses after RP (603), EBRT (292), or BT (306)

- 2003 to 2006 with 24 mo follow-up
Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

<table>
<thead>
<tr>
<th>percent reporting at 24 months</th>
<th>Prostatectomy</th>
<th>EBRT</th>
<th>BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall urinary problem</td>
<td>7 %</td>
<td>11 %</td>
<td>16 %</td>
</tr>
<tr>
<td>Overall bowel problem</td>
<td>1 %</td>
<td>11 %</td>
<td>8 %</td>
</tr>
<tr>
<td>Poor erections</td>
<td>58 %</td>
<td>60 %</td>
<td>51 %</td>
</tr>
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</table>
Cost of Therapy

<table>
<thead>
<tr>
<th></th>
<th>Cost 1st 6 months</th>
<th>Cumulative Costs</th>
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</thead>
<tbody>
<tr>
<td>RP</td>
<td>$12,184</td>
<td>$36,888</td>
</tr>
<tr>
<td>EBRT</td>
<td>$24,204</td>
<td>$59,455</td>
</tr>
</tbody>
</table>

- Costs of outpatient visits, medications, and hospitalizations calculated.

Conclusions

• Surgery offers the best staging, QOL, fewer complications, decreased risk of secondary malignancies
• Radiation is a viable option for patients unfit for surgery
• Robotic assisted surgery has decreased recovery time and blood loss
• Overall, must be a patient involved decision making process