Management of Localized Prostate Cancer

Surgery

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Treatment Options

1. Active surveillance/Watchful waiting
2. Focal therapy
3. Radical prostatectomy
4. Brachytherapy
5. HDR monotherapy
6. External beam radiation
7. Brachytherapy plus external beam
8. Cryotherapy
9. Hyperthermia (HIFU)
Treatment Options

1. Active surveillance/Watchful waiting
2. Focal therapy
3. Radical prostatectomy
4. Brachytherapy
5. HDR monotherapy
6. External beam radiation
7. Brachytherapy plus external beam
8. Cryotherapy
9. Hyperthermia (HIFU)

Long term results of Radical Prostatectomy by pathological stage (MSK series)

<table>
<thead>
<tr>
<th>Pathological Stage</th>
<th>PSA Progression-Free Probability</th>
<th>Cancer Specific Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT2N0</td>
<td>1.0</td>
<td>100%</td>
</tr>
<tr>
<td>pT3aN0</td>
<td>0.8</td>
<td>99%</td>
</tr>
<tr>
<td>pT3bN0</td>
<td>0.6</td>
<td>96%</td>
</tr>
<tr>
<td>pT1-3 N+</td>
<td>0.4</td>
<td>94%</td>
</tr>
</tbody>
</table>

Time from RP (years)

- ADT
Survival after surgery for prostate cancer

Since 1998, 4% had a probability of PCSM >5% and 0.5% had a predicted risk >30%.

Stephenson et al (J Clin Onc 2009; 27:4300)

Risk of death from prostate cancer by AUA Risk Group*

Majority of deaths were among high risk group, but the risk of death from PCa (19%) was still less than from other causes (31%).

*AUA Prostate Cancer Guidelines, 2008
Outcomes After Radical Prostatectomy

• Early post-op complications
• Bladder neck contracture
• Urinary incontinence
• Erectile dysfunction
• Rate of positive surgical margins
• Biochemical recurrence

• Have all been associated with surgical technique

Does a patient’s chance of cure depend on the surgeon?

• MSKCC, Baylor, Cleveland Clinic, Wayne State
• 9376 patients undergoing RP from 1987 - 2003:
  – 210: missing data; 1316: neoadjuvant therapy
  – 7850 patients in sample
• 73 surgeons
  – 38 only conducted RP at a study institution
  – 23 conducted < 20 RP’s before treating 1st study patient
Radical Prostatectomy

- Robotic-assisted laparoscopic RP (RALP)
- Laparoscopic RP
- Open retropubic RP
- Perineal RP

Open versus Minimally Invasive Radical Prostatectomy

**Open**
- Advantages
  - Familiarity/Experience
  - Well defined results
  - Excellent cancer control
- Disadvantages
  - Incisional pain
  - Higher blood loss
  - Difficult to visualize nerves without loupes

**Minimally Invasive**
- Advantages
  - Shorter recovery
  - Rapid return to work
  - Less blood loss
  - Early catheter removal
  - Magnified image
- Disadvantages
  - Technically challenging
  - Loss of sense of touch
  - Immature outcome data
  - ? long-term CA control
Robotic Radical Prostatectomy: da Vinci Si
Outcomes after RP

- Continence
- Potency
- Cancer control
  - Surgical margins
Continence* After RALP and Open RP

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. patients</th>
<th>Continence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kleinhans (1999)</td>
<td>44</td>
<td>98%</td>
</tr>
<tr>
<td>Steiner (2000)</td>
<td>593</td>
<td>95%</td>
</tr>
<tr>
<td>Walsh (2000)</td>
<td>64</td>
<td>93%</td>
</tr>
<tr>
<td>Bianco (2006)</td>
<td>1472</td>
<td>91%</td>
</tr>
<tr>
<td>Tewari (2003)</td>
<td>200</td>
<td>91%</td>
</tr>
<tr>
<td>Patel (2005)</td>
<td>200</td>
<td>98%</td>
</tr>
<tr>
<td>Esposito (2006)</td>
<td>625</td>
<td>86%</td>
</tr>
<tr>
<td>Zorn (2007)</td>
<td>300</td>
<td>90%</td>
</tr>
</tbody>
</table>

*Defined as “no pads” at 12 months

Functional Outcomes: Continence

- RALP versus Open: single surgeon
- 320 RALP versus 120 Open
  - Continence defined as “total control or occasional dribbling”
  - At 12 months: 90% versus 88%

Schachter, et al. AUA 2007
Outcomes after RP

- Continence
- Potency
- Cancer control
  - Surgical margins

Potency After RALP and Open RP

<table>
<thead>
<tr>
<th>Reference</th>
<th>No.</th>
<th>% BNS</th>
<th>Time after OR</th>
<th>Potent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catalona (1999)</td>
<td>798</td>
<td>86</td>
<td>18 months</td>
<td>68%</td>
</tr>
<tr>
<td>Walsh (2000)</td>
<td>64</td>
<td>100</td>
<td>18 months</td>
<td>86%</td>
</tr>
<tr>
<td>Graefen (2006)</td>
<td>542</td>
<td>NA</td>
<td>12 months</td>
<td>90%</td>
</tr>
<tr>
<td>Eastham (2007)</td>
<td>97</td>
<td>60</td>
<td>6 months</td>
<td>72%</td>
</tr>
<tr>
<td>Tewari (2003)</td>
<td>200</td>
<td>100</td>
<td>12 months</td>
<td>84%</td>
</tr>
<tr>
<td>Joseph (2006)</td>
<td>150</td>
<td>86</td>
<td>6 months</td>
<td>68%</td>
</tr>
<tr>
<td>Esposito (2006)</td>
<td>160</td>
<td>NA</td>
<td>24 months</td>
<td>70%</td>
</tr>
<tr>
<td>Zorn (2007)</td>
<td>161</td>
<td>62</td>
<td>12 months</td>
<td>80%</td>
</tr>
</tbody>
</table>
Outcomes after RP

- Convalescence
- Continence
- Potency
- Cancer control
  - Surgical margins

Positive Surgical Margins

<table>
<thead>
<tr>
<th>Reference</th>
<th>No.</th>
<th>pT2</th>
<th>pT3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hull (2002)</td>
<td>1000</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Harris (2003)</td>
<td>508</td>
<td>2%</td>
<td>48%</td>
</tr>
<tr>
<td>Touijer (2006)</td>
<td>692</td>
<td>5%</td>
<td>22%</td>
</tr>
<tr>
<td>Menon (2003)</td>
<td>100</td>
<td>11%</td>
<td>40%</td>
</tr>
<tr>
<td>Menon (2004)</td>
<td>565</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>Ahlering (2003)</td>
<td>1-50</td>
<td>27%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>51-140</td>
<td>5%</td>
<td>44%</td>
</tr>
</tbody>
</table>
Economic Considerations

• Cost advantage of open RP
  – $487 over laparoscopic RP
  – $1726 over RALP

Conclusions: Radical Prostatectomy

• Most patients are candidates for either RALP or open RP
• Either approach is technically demanding with functional and cancer control outcomes dependent on the skill/experience of the surgeon
• Studies to date have shown that RALP:
  • Results in shorter hospital stay, lower transfusion rates, fewer BNC
  • No advantage in continence and potency (? Inferior results)
• Costs are higher for RALP
  • Initial costs of procedure
  • ? Secondary treatment costs (continence and potency)
Focal Therapy in Low-risk Prostate Cancer
Focal Cryotherapy Outcomes

- Focal cryoablation is 48 men: mean follow-up: 4.5 yrs
- 45 of 48 patients (94%) have stable PSA levels (ASTRO)
- Of 24 patients who were biopsied all were negative
- Potency was maintained to the satisfaction of the patient in 36 of 40 patients
- All were continent

HIFU

• HIFU, or high intensity focused ultrasound, is a therapy that destroys unhealthy tissue with rapid heat elevation

• Ultrasound energy is focused at a specific location in the body. At that location, or focal point, the temperature rapidly rises to almost 90 degrees Celsius (195 degrees Fahrenheit). Any tissue at the focal point is destroyed.
Minimally invasive laser ablation system for destruction of tumors and other soft tissue

MRI-guided Focal LASER Therapy

- Minimally invasive laser ablation system for destruction of tumors and other soft tissue
- 100% MR Compatible
- Most controllable, most precise, fastest ablation technology ever introduced
- First and only technology that allows real time thermal monitoring of ablation and modeling of kill zone
- Focus on cancer markets virtually untouched by previous thermal ablative therapies: brain, spine, prostate
- Platform technology with applications in liver, kidney, thyroid, bone, as well as non-cancer applications
• 66 year old male
• Low-grade prostate cancer found in single core
• No prior treatment

Guide catheter transperineal placement under U/S

Axial view with needle visible

Pre-treatment MRI Shows Applicator placed into Right Lobe of Prostate
Focal Therapy in Prostate Cancer
Conclusions

- Feasible and safe
- Issues
  - Which patient is best suited for focal therapy?
  - What is the best energy source?
  - How should patients be monitored?
Conclusions

• Screening with PSA identifies prostate cancer when it is more likely confined to the prostate
• Radical Prostatectomy has a high likelihood of cure but is technically challenging with results dependent on the surgeon
• New technologies for focal treatment are being developed