Management of Localized Prostate Cancer

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Associate Professor of Clinical Urology
Case

- 68 y/o male with hx of lower urinary tract symptoms-on flomax
- Hx of elevated PSA (4.5-10.1)
- SHIM score 18, IPSS 7

- TRUS biopsy
  - Prostatic adenocarcinoma (acinar), Gleason score 7 (3+4), Grade Group 2, involving three cores in left base and apex, 3-8 mm length and 30-70% of biopsy tissue
  - Clinical T1c
  - Imaging: None

- Plan?
Prostate ca; Epidemiology

Age-adjusted cancer incidence rates for men, United States, 1975-2010

Estimated New Cases in 2019: 174,650
% of All New Cancer Cases: 9.9%
Estimated Deaths in 2019: 31,620
% of All Cancer Deaths: 5.2%

Percent Surviving 5 Years: 98.0%
2009-2015

Year

0
50
100
150
200
250


New Cases - SEER 13
Deaths - U.S.

NATIONAL CANCER INSTITUTE
Surveillance, Epidemiology, and End Results Program

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PSA screening

- < 40: not recommended (ES Grade C)
- 40-54: routine screening in not recommended in men at average risk (ES Grade C)
- 55-69: shared decision-making is recommended for men that are considering PSA screening, and proceeding based on a man’s values and preferences (ES Grade B)
- > 70: routine PSA screening is not recommended in men > 70 or any man with less than a 10 to 15 year life expectancy (ES Grade C)

Localized PC is defined as clinical stage T1-T2, N0 or NX, M0 or MX
# Risk stratification

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Very low risk</strong></td>
<td>PSA &lt;10 ng/ml AND Grade Group 1 (3+3) AND clinical stage T1-T2a AND &lt;34% of biopsy cores positive AND no core with &gt;50% involved, AND PSA density &lt;0.15 ng/ml/cc</td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td>PSA &lt;10 ng/ml AND Grade Group 1 (3+3) AND clinical stage T1-T2a</td>
</tr>
</tbody>
</table>
| **Intermediate risk** | PSA 10-20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c  
➢ Favorable: Grade Group 1 (3+3) (PSA 10-20) OR Grade Group 2 (3+4) (PSA<10)  
➢ Unfavorable: Grade Group 3 (4+3) (PSA 10-20 or clinical stage T2b-c) OR Grade Group 3 (4+3) (PSA < 20) |
| **High risk**    | PSA >20 ng/ml OR Grade Group 4-5 (4+4 or more)OR clinical stage >T3                                  |
### Recommended approaches for localized PC

<table>
<thead>
<tr>
<th>Evidence Level/Recommendation Strength</th>
<th>Prostate Cancer Severity/Aggressiveness</th>
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<tbody>
<tr>
<td></td>
<td>Low Risk</td>
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<tr>
<td></td>
<td>Very Low Risk</td>
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<tr>
<td>A / Strong</td>
<td>Active Surveillance</td>
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<td>B / Moderate</td>
<td>NA</td>
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<tr>
<td>B / Conditional</td>
<td>NA</td>
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<tr>
<td>C / Conditional</td>
<td>NA</td>
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<tr>
<td>No evidence / clinical principle or expert opinion</td>
<td>NA</td>
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Radical Prostatectomy vs. Watchful Waiting

Scandinavian SPCG-4 trial
- **men <65 years:** higher survival from RP in comparison to WW
- **men >65 years:** trend for RP towards longer life and decrease in metastases

American PIVOT
- RP was associated with higher survival over WW among men with PSA > 10 ng/ml and those with intermediate or worse risk by clinical criteria


At a median of 10 years, surgery and radiotherapy were associated with lower incidences of disease progression and metastases than active monitoring.

Comparative Effectiveness of Radical Prostatectomy Versus External Beam Radiation Therapy Plus Brachytherapy in Patients with High-risk Localized Prostate Cancer

Sebastian Berg\textsuperscript{a,b}, Alexander P. Cole\textsuperscript{a}, Marieke J. Krimphove\textsuperscript{a,c}, Junaid Nabi\textsuperscript{a}, Maya Marchese\textsuperscript{a}, Stuart R. Lipsitz\textsuperscript{d}, Joachim Noldus\textsuperscript{b}, Toni K. Choueiri\textsuperscript{b}, Adam S. Kibel\textsuperscript{e}, Quoc-Dien Trinh\textsuperscript{a,*}

In an analysis restricted to young and healthy men presenting with high-risk localized prostate cancer, initial radical prostatectomy is associated with an overall survival benefit compared with external beam radiation therapy plus brachytherapy.
Brachytherapy-Based Radiotherapy and Radical Prostatectomy Are Associated With Similar Survival in High-Risk Localized Prostate Cancer

Ronald D. Ennis, Liangyuan Hu, Shannon N. Ryerson, Joyce Lin, and Madhu Mazumdar

(A) Unweighted versus (B) inverse probability of treatment weighting–adjusted Kaplan-Meier curves stratified by the three treatments.

Trends of surgical approaches for RP in US

68 y/o male
cT1c, GG2, opted for Rob RRP, unilateral NS with PLND-2014
Prostatic Adenocarcinoma, acinar type (pT3a N0)
Gleason Score: 3(60%)+4(40%)=7 (GG 2)
EPE: Focal
Surgical margins: neg
Bilateral seminal vesicles: Uninvolved

5 years out: NED
Continence: 0-1 pad for safety
Sexually active with PDE-inh
RARP: nerve sparing
Open versus Robotic: blood loss, transfusion

mean blood loss: 166 ml (range: 69–534 ml)

mean transfusion rate: 2% (range: 0.5–5%)

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Open versus Robotic: operative time

mean operative time: 152 min (range: 90–291 min)
Open versus Robotic: positive surgical margin

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic vs open, OR (95% CI)</th>
<th>p value</th>
<th>Robotic vs open, OR (95% CI)</th>
<th>p value</th>
<th>Robotic vs laparoscopic, OR (95% CI)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Unadjusted logistic regression</td>
<td>0.66 (0.60–0.72)</td>
<td>&lt;0.001</td>
<td>0.54 (0.50–0.59)</td>
<td>&lt;0.001</td>
<td>0.82 (0.71–0.91)</td>
<td>&lt;0.001</td>
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<tr>
<td>Logistic regression classic</td>
<td>0.76 (0.69–0.84)</td>
<td>&lt;0.001</td>
<td>0.76 (0.69–0.83)</td>
<td>&lt;0.001</td>
<td>0.99 (0.89–1.11)</td>
<td>0.88</td>
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<td>adjustment (with covariates age,</td>
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<td>preoperative PSA, ln [PSA + 1],</td>
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<td>postoperative Gleason score,</td>
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<td>pathologic stage, and year of</td>
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<tr>
<td>Logistic regression with propensity</td>
<td>0.73 (0.66–0.88)</td>
<td>&lt;0.001</td>
<td>0.75 (0.68–0.82)</td>
<td>&lt;0.001</td>
<td>1.03 (0.93–1.15)</td>
<td>0.58</td>
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<td>scores for adjustment and</td>
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<td>year of surgery</td>
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<tr>
<td>Cox regression with propensity</td>
<td>0.76 (0.69–0.84)</td>
<td>&lt;0.001</td>
<td>0.76 (0.69–0.83)</td>
<td>&lt;0.001</td>
<td>0.99 (0.89–1.11)</td>
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<td>covariates age, preoperative PSA,</td>
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<td>ln [PSA + 1], postoperative</td>
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<td>Gleason score, pathologic stage,</td>
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<td>and year of surgery) (double</td>
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CI = confidence interval; OR = odds ratio; PSA = prostate-specific antigen.

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Open versus Robotic: Urinary continence

Open versus Robotic: Erectile function

<table>
<thead>
<tr>
<th>Study or subcategory</th>
<th>RRP</th>
<th>RARP</th>
<th>OR (random) 95% CI</th>
<th>Weight %</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krambeck, 2008</td>
<td>155/417</td>
<td>61/203</td>
<td>22.40</td>
<td>1.38</td>
<td>[0.96, 1.97]</td>
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<tr>
<td>Ficarra, 2009</td>
<td>21/41</td>
<td>12/64</td>
<td>16.71</td>
<td>4.55</td>
<td>[1.89, 10.94]</td>
</tr>
<tr>
<td>Ou, 2009</td>
<td>1/2</td>
<td>10/15</td>
<td>4.03</td>
<td>0.60</td>
<td>[0.03, 11.47]</td>
</tr>
<tr>
<td>Rocco, 2009</td>
<td>126/214</td>
<td>30/78</td>
<td>20.71</td>
<td>2.29</td>
<td>[1.35, 3.90]</td>
</tr>
<tr>
<td>Di Pierro, 2011</td>
<td>35/47</td>
<td>10/22</td>
<td>14.60</td>
<td>3.50</td>
<td>[1.21, 10.15]</td>
</tr>
<tr>
<td>Kim, 2011</td>
<td>65/122</td>
<td>60/373</td>
<td>21.56</td>
<td>5.95</td>
<td>[3.79, 9.33]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>843</td>
<td>756</td>
<td>1.00</td>
<td>2.84</td>
<td>[1.48, 5.43]</td>
</tr>
</tbody>
</table>

Total events: 403 (RRP), 183 (RARP)
Test for heterogeneity: \( \chi^2 = 28.01, df = 5 (p < 0.0001), I^2 = 62.1\% \)
Test for overall effect: \( z = 3.15 (p = 0.002) \)

**potency range:**
- 12-mo: 54% to 90%  
- 24-mo: 63% to 94%
Summary of evidence for localized PC

**Very low risk**
- active surveillance is the best available care option
  - Recommendation/Evidence grade: Strong/A

**Low risk**
- active surveillance is the preferable care option for most patients.
- offer definitive treatment to selected patients with a high probability of progression on active surveillance.
  - Recommendation/Evidence grade: Moderate/A Conditional/B

**Intermediate risk**
- radical prostatectomy or radiotherapy plus ADT are standard treatment options (Strong Recommendation; EL: Grade A)
  - Recommendation/Evidence grade: Strong/A

**High risk**
- radical prostatectomy or radiotherapy plus ADT are standard treatment options.
  - Recommendation/Evidence grade: Strong/A

Conclusion