Surgical Management of Prostate Cancer

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DISCLOSURE

- Nothing to disclose
Agenda

• History of Prostatectomy
• Evolution of Robotic Prostatectomy
• City of Hope Techniques
• Functional Outcomes
• Oncological Outcomes
• Future Technology and Advances
• Questions
History of Prostatectomy

• 1\textsuperscript{st} radical perineal prostatectomy – Kuchler – 1886
• Technique of radical perineal prostatectomy improved by Hugh Hampton Young – 1904
  – Father of modern urology
  – Technique remained largely unchanged for 40+ years
  – Remained the standard treatment for prostate cancer until 1945
• Radical retropubic prostatectomy
  – 1\textsuperscript{st} performed by Terence Millin – 1940s
  – Revolutionized by Patrick Walsh

History of Prostate Cancer Treatment. Thompson et al. Surgical Oncology (2009) 18. 185-191
History of Prostatectomy

- Patrick Walsh – Professor of Urology at John’s Hopkins
  - Revolutionized understanding of prostatic / pelvic anatomy
  - Identified cavernosal nerves – responsible for potency
  - 1\textsuperscript{st} nerve sparing radical prostatectomy – 1982
  - Prostatectomy remained largely unchanged until the advent of minimally invasive surgery

History of Prostate Cancer Treatment. Thompson et al. Surgical Oncology (2009) 18. 185-191
History of Prostatectomy

- Laparoscopy
  - Early 1900s – Georg Kelling
    - Insufflated peritoneal cavity of a dog and inserted cystoscope
  - Urologists used laparoscopy in 1970s to look for undescended testes
  - Ralph Clayman – 1st laparoscopic nephrectomy in 1991
- Laparoscopic Radical Prostatectomy
  - 1st laparoscopic pelvic lymphadenectomy – 1997
  - Shuessler et al – 1997 - 9 laparoscopic radical prostatectomies
    - Averaged over 9 hours per surgery
Evolution of Robotic Prostatectomy

• Robot assisted laparoscopic surgery
  – Grew out of a defense initiative in the 1980s to develop remote surgical systems for warzone use
  – DaVinci system launched in 1999
  – FDA approved for laparoscopic surgery in 2000
Evolution of Robotic Prostatectomy

• 1\textsuperscript{st} robot assisted laparoscopic radical prostatectomy
  – Frankfurt in 2000
• 1\textsuperscript{st} large robotic series
  – Menon et al – Henry Ford Vattikuti Urology Institute
• Advances
  – Athermal dissection of neurovascular bundles
  – High release of lateral prostatic fascia
  – Rocco posterior reconstruction
  – Van Velt Hoven continuous urethro-vesical anastomosis
  – Extended pelvic lymph node dissection


City of Hope Techniques

- Extended Pelvic Lymph Node dissection
  - Offered to most patients with D’Amico intermediate or high risk disease
  - NCCN guidelines – patients with >2% risk of lymph node metastases on nomogram
  - Limits of dissection:
    - Proximal – where the ureter crosses the common iliac artery
    - Distal – Crossing of circumflex iliac vein on external iliac artery
    - Lateral – Lateral aspect of external iliac artery
    - Medial – Perivesical fat
    - Posterior – Posterior aspect of obturator fossa
City of Hope Techniques

• Bladder neck preservation
  – Preservation of circular bladder neck fibers (internal urethra sphincter)
  – 360 degree dissection
City of Hope Techniques

• Cavernosal nerve sparing
  – Can be modified according to extent of disease and baseline erectile dysfunction
  – Non nerve sparing
    • Wide excision for higher risk disease / extra-prostatic extension
    • Excise lateral prostatic fascia
  – Partial nerve sparing
    • Used for moderate risk of extra-prostatic extension
    • Excise lateral prostatic fascia
  – Total nerve sparing
    • Used for lower risk of extra-prostatic extension with desire to preserve potency
    • May also improve continence
    • Preserve lateral prostatic fascia
Functional and Oncological Outcomes

• “Trifecta”
  – Potent
  – Continent
  – Negative surgical margins
• Partially surgeon / technique dependent
• Patient dependent
  – Extent of disease affects nerve and bladder neck sparing
  – Strong erections pre-op → better potency post-op
• Technique dependent??
  – Conflicting data between open and robot assisted approaches
# Functional and Oncological Outcomes

A Prospective Comparison of RRP and Robot-Assisted Prostatectomy

<table>
<thead>
<tr>
<th></th>
<th>RRP</th>
<th>DVP</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>100</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Op time (min)</td>
<td>163</td>
<td>160</td>
<td>ns</td>
</tr>
<tr>
<td>EBL (cc)</td>
<td>910</td>
<td>150</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transfusions</td>
<td>67%</td>
<td>0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complications</td>
<td>20%</td>
<td>5%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hgb g/dl (post op)</td>
<td>10</td>
<td>13</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>3.5</td>
<td>1.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Catheter time (days)</td>
<td>15.8</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Margins positive</td>
<td>23%</td>
<td>9%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Time to continence (days)</td>
<td>160</td>
<td>40</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Time to erections (days)</td>
<td>440</td>
<td>180</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Time to intercourse (days)</td>
<td>&gt;700</td>
<td>340</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

## Functional and Oncologic Outcomes

### Table 4: Erectile function and pad use at 6 months, 12 months, and 24 months by surgery type

<table>
<thead>
<tr>
<th>Erections firm enough for intercourse*</th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No sexual activity or almost never</td>
<td>Radical retropubic prostatectomy group (n=134)</td>
<td>76 (57%)</td>
<td>69 (51%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=144)</td>
<td>85 (59%)</td>
<td>69 (47%)</td>
</tr>
<tr>
<td>Less than half the time or about half the time</td>
<td>Radical retropubic prostatectomy group (n=135)</td>
<td>28 (21%)</td>
<td>25 (19%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=146)</td>
<td>24 (17%)</td>
<td>23 (16%)</td>
</tr>
<tr>
<td>More than half the time or almost always</td>
<td>Radical retropubic prostatectomy group (n=131)</td>
<td>29 (22%)</td>
<td>40 (30%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=138)</td>
<td>32 (22%)</td>
<td>51 (35%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pad for incontinence†</th>
<th>None</th>
<th>One pad per day</th>
<th>Two pads per day</th>
<th>Three or more pads per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>Radical retropubic prostatectomy group (n=134)</td>
<td>114 (85%)</td>
<td>17 (13%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=144)</td>
<td>121 (84%)</td>
<td>18 (13%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>12 months</td>
<td>Radical retropubic prostatectomy group (n=135)</td>
<td>123 (91%)</td>
<td>10 (7%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=146)</td>
<td>131 (90%)</td>
<td>14 (10%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>24 months</td>
<td>Radical retropubic prostatectomy group (n=131)</td>
<td>124 (95%)</td>
<td>7 (5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>Robot-assisted laparoscopic prostatectomy group (n=138)</td>
<td>126 (91%)</td>
<td>9 (7%)</td>
<td>3 (2%)</td>
</tr>
</tbody>
</table>

Data are n (%). Percentages might not sum to 100 because of rounding and missing data. *Erection quality generated from single International Index of Erectile Function item. †Use of pads generated from single Expanded Prostate Cancer Index Composite item.
# Functional and Oncological Outcomes

<table>
<thead>
<tr>
<th>Progression</th>
<th>Radical retropubic prostatectomy group (n=151)</th>
<th>Robot-assisted laparoscopic prostatectomy group (n=157)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging evidence of progression</td>
<td>3 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Biochemical recurrence</td>
<td>13 (9%)</td>
<td>4 (3%)</td>
</tr>
</tbody>
</table>

**Additional treatment**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Radical retropubic prostatectomy group (n=151)</th>
<th>Robot-assisted laparoscopic prostatectomy group (n=157)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy</td>
<td>10 (7%)</td>
<td>15 (10%)</td>
</tr>
<tr>
<td>Androgen deprivation therapy</td>
<td>4 (3%)</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>At least one treatment</td>
<td>13 (9%)</td>
<td>16 (10%)</td>
</tr>
</tbody>
</table>

Data are n (%). Imaging evidence of progression test of equivalence $p=0.2956$; biochemical recurrence test of equivalence $p=0.0199$; at least one treatment $\chi^2$ $p=0.635$. *Numbers of men who had additional treatments are not additive because some patients received more than one type.

*Table 2: Oncological outcomes within 24 months by surgery type*

Gardiner et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: 24 month outcomes from a randomised controlled study. Lancet Oncology 2018: 19 1051-1060
Cytoreductive Prostatectomy

- Radical prostatectomy in the setting of known or suspected metastatic disease
- Previously considered a contraindication to surgery
  - Standard of care 1st line therapy
    - Previously androgen deprivation therapy
    - Abiraterone, enzalutamide, chemotherapy
- Newer studies show a possible benefit to surgical management
- Phase 1 multi-center trial completed
- Phase 2/3 study pending
Cytoreductive Prostatectomy

Figure 2. Kaplan-Meier survival curve of ACM (A) and PCSM (B) in patients with MPCA treated with RP, IMRT, CRT or NLT adjusted for treatment group, age, diagnosis year, marital status, PSA, Gleason score, AJCC staging (TNM), CCI, ADT, bone radiation within 6 months of diagnosis and registry.

Cytoreductive Prostatectomy

- Reduction in locoregional complications
  - 7.0 vs 35%, p <0.01

Mandel et al. Does cytoreductive prostatectomy really have an impact on prostate cancer patients with low-volume bone metastasis? Results from a prospective case-control study. European Urology Focus 3 (2017) 646-649
Salvage Lymphadenectomy

- Patients with biochemical recurrence
- Retroperitoneal or pelvic lymphadenopathy seen on cross sectional imaging or PET/CT
- Improved ability to visualize oligometastatic disease in early biochemical recurrence on imaging
  - F-18 PET
  - Anti-PSMA PET
  - C-11 PET
- Will this lead to a survival benefit?
Salvage lymphadenectomy

- 59 patients with biochemical recurrence and C-11 PET detected lymph node mets
- Underwent pelvic and/or retroperitoneal salvage lymphadenectomy
- Median follow up – 81 months
- 59% had biochemical response
- 8 yr complete BCR rate – 23%
- 8 yr CSM-free survival – 81%

Salvage Lymphadenectomy

Salvage Lymphadenectomy

Intra-operative Optical Imaging

- Improve identification of prostate cancer tissue in vivo
- Fluorescent tagged anti-PSMA (prostate specific membrane antigen) antibody
- Given intravenously 2-5 days pre-operatively
- Benign prostate tissue should glow lightly
- Prostate cancer tissue should glow vividly
Intra-operative Optical Imaging

LNCaP 100ugs MDX-1201-A488 48 hours iv
Robotic autonomy / Remote surgery

- Complete autonomy unlikely in the near future
- Automation of simple steps may be feasible
- Remote surgery likely in the near future
  - Higher volume surgeons
  - Improved outcomes???
Piss like a Stallion!
Donate your prostate to science.
Questions?