Quality of life issues after treatment for prostate cancer

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Definition of Health

not merely the absence of disease or infirmity, but a concept that incorporates well-being or wellness in all areas of life (physical, mental, emotional, social, spiritual)

World Health Organization
Domains most commonly affected

- Sexual function quality of life
- Urinary function quality of life
- Bowel function quality of life
- Anxiety
- Marital intimacy/effect on spouses
Health Related Quality of Life

- How do we measure it?
- Who should assess it?
- Are there major differences among treatments?
Longitudinal tracking of QOL

- QOL measured at baseline
- Then followed over time to determine the long-term impact of treatment
Health Related Quality of Life Measurement in CaPSURE

Patients complete questionnaires every 6 months

• RAND 36-item health survey (8 domains covering physical and emotional function) and 2 summary scores
• UCLA prostate cancer index
  – Urinary function and bother
  – Bowel function and bother
  – Sexual function and bother
Quality of life improves with increasing vertical score (on a 100-point scale)
Sexual Function CaPSURE

Male Sexual Health

• Male sexual functioning is comprised of desire, ejaculatory function, orgasmic ability, and erectile dysfunction.

• Erectile Dysfunction (ED) is defined as “the inability to achieve or maintain an erection sufficient for satisfactory sexual performance” (1992 NIH Consensus Statement).
<table>
<thead>
<tr>
<th>Age Group</th>
<th>Always or almost always able To achieve erection</th>
<th>Usually Able To achieve erection</th>
<th>Sometimes Able To achieve erection</th>
<th>Never Able To achieve erection</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>65% (62-68)</td>
<td>17% (15-18)</td>
<td>12% (11-14)</td>
<td>6% (5-8)</td>
</tr>
<tr>
<td>20-29 years</td>
<td>81% (78-84)</td>
<td>12% (9-16)</td>
<td>5% (3-7)</td>
<td>2% (1-3)</td>
</tr>
<tr>
<td>30-39 years</td>
<td>88% (84-92)</td>
<td>8% (5-11)</td>
<td>3% (1-5)</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>40-49 years</td>
<td>72% (67-76)</td>
<td>20% (15-25)</td>
<td>7% (4-10)</td>
<td>1% (0-3)</td>
</tr>
<tr>
<td>50-59 years</td>
<td>56% (50-63)</td>
<td>20% (14-26)</td>
<td>20% (15-25)</td>
<td>4% (1-7)</td>
</tr>
<tr>
<td>60-69 years</td>
<td>29% (22-35)</td>
<td>28% (22-33)</td>
<td>27% (23-31)</td>
<td>17% (11-22)</td>
</tr>
<tr>
<td>70-74 years</td>
<td>19% (11-27)</td>
<td>21% (14-29)</td>
<td>39% (29-48)</td>
<td>22% (14-29)</td>
</tr>
<tr>
<td>75+ years</td>
<td>6% (1-10)</td>
<td>17% (12-21)</td>
<td>30% (24-36)</td>
<td>47% (40-55)</td>
</tr>
</tbody>
</table>
Prevalence of ED among men with comorbid diagnosis.

<table>
<thead>
<tr>
<th>Comorbid Diagnosis</th>
<th>ED Absent</th>
<th>ED Present</th>
<th>Prevalence of ED among men with comorbid diagnosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>3,675,146</td>
<td>3,572,607</td>
<td>49%</td>
</tr>
<tr>
<td>Obesity</td>
<td>16,206,023</td>
<td>4,990,098</td>
<td>23%</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>3,055,592</td>
<td>3,344,306</td>
<td>52%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13,124,111</td>
<td>7,184,282</td>
<td>35%</td>
</tr>
<tr>
<td>Smoking</td>
<td>20,088,443</td>
<td>3,543,914</td>
<td>15%</td>
</tr>
</tbody>
</table>
ED: Physiology
Physiology of Erection

- NO production by nNOS
- NO diffuses to the smooth muscle cells (SMCs)
- NO causes relaxation of SMCs, leading to erection
Physiology of Erection
ED treatment: oral agents

Introduced in 1998

Inhibitors of phosphodiesterase-5

Introduction was associated with 50% increase in physician visits for ED by 2000.
Mechanism of Smooth Muscle Cell Relaxation in the Penis
ED treatment: oral agents

- Must be taken on an empty stomach
- Require stimulation, intact cavernous nerves
- Cardiac risks: contraindicated with nitrates
  AHA guidelines suggest caution in men with:
  Positive exercise stress test, CHF and low BP,
  Men with complicated anti HTN regimens
ED treatment: oral agents

PDE-5 inhibitors: 70% ‘beneficial’ treatment effect vs 30% placebo
Benefit is dose dependant
70% in hypertensive patients
56% in diabetics
80% spinal cord injury patients
43% in men s/p radical prostatectomy
ED treatment: oral agents

- Yohimbine
  Associated with anxiety, GI distress
  May be helpful in men with psychogenic ED
- L-arginine
  Small studies showed benefit of 3 g/day in younger men, other studies showed no benefit
  ? Valuable in men with low urinary NO?
ED treatment: urethral suppository

Medicated Urethral System for Erection (MUSE)

Intraurethral alprostadil (PGE1)

Penile pain in one third of men

Response rates less than with intracorporeal injection
ED treatment: Intercavernous Injection

Alprostadil alone

Papaverine, Phentolamine, Alprostadil (trimix)
As effective as alprostadil alone, less priapism

Risks: priapism (1%-20%), penile fibrosis (1%-15%)
ED treatment: non-pharmacologic
Vacuum Erection Device
ED Treatment: penile prosthesis

- Inflatable
- Semi rigid
Urinary Incontinence
urinary incontinence

• Rates at 12 months 7-35% wearing pads
• Rates depend on definition (total control vs ‘no pads)
• Of those reporting ‘no pads’ 47% reported ‘total control’
• By 2 years, further improvement unlikely
Urinary Function
CaPSURE

Urinary Bother
CaPSURE

UI management

• Medications: anti-cholinergics
• Kegel exercises
• Artificial urinary sphincters
• Urethral slings
• Collagen injection
Anxiety
• 1 in 3 men with prostate cancer in a GU clinic met criteria for anxiety disorder

Roth Cancer 1998
Prostate Cancer Follow Up

PSA
Prostate Cancer Follow Up

After radical prostatectomy

Any detectable level

Single value > 0.4 ng/mL

Two values ≥ 0.2 ng/mL

Ultrasensitive PSA identifies recurrence 1-2 years earlier
Prostate Cancer Follow Up

After Radiation (XRT)

ASTRO Consensus Panel in 1997
- PSA recurrence *per se* does not justify additional treatment
- 3 consecutive rising PSA levels
- Nadir PSA strong prognosticicator, best if <1.0

After Radiation (Brachy)
- Nadir PSA strong prognosticicator, but no absolute level has been defined
Prostate Cancer Follow Up

Pound et al, JAMA 1999

2,000 men post RP

PSA q 3 mo x 1 yr, q 6 mo x 1 yr, then q 12 mo

PSA recurrence if any PSA $\geq 0.2$ ng/mL

Distant mets diagnosed with annual bone scan, CXR in men with PSA recurrence
Prostate Cancer Follow Up

At 15 years 15% had PSA recurrence

33% of these developed clinical mets
Timing of PSA recurrence after radical prostatectomy

PSA never falls to undetectable post-op or falls but rises rapidly

→ **Systemic disease**

PSA becomes undetectable then slowly rises 1-4 years post-op

→ **Local recurrence**
Secondary Treatment

- Rate of second cancer treatment
- Longitudinal disease registry
- RP 1,254, radiation 499, and cryotherapy 141
- Compare types of second treatment

## Secondary Treatment

<table>
<thead>
<tr>
<th></th>
<th>RP</th>
<th>RT</th>
<th>Cryotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second treatment (%)</td>
<td>14</td>
<td>27.2</td>
<td>22.4</td>
</tr>
<tr>
<td>Mean years at risk</td>
<td>2.52</td>
<td>2.92</td>
<td>2.12</td>
</tr>
</tbody>
</table>

Many survivors have secondary treatments

- These continue to impact quality of life
- Decision regret
- Partner impact
Complementary Therapy
Prostate Cancer: Ornish Study

- 93 men with prostate cancer randomized to diet and exercise vs usual care
- 1 daily serving of tofu plus 58 gm of a fortified soy protein powdered beverage
- fish oil (3 gm daily)
- vitamin E (400 IU daily)
- selenium (200 mcg daily)
- vitamin C (2 gm daily)
- 10% calories from fat
Ornish Study

- moderate aerobic exercise (walking 30 minutes 6 days weekly),
- stress management techniques (gentle yoga based stretching, breathing, meditation, imagery and progressive relaxation for a total of 60 minutes daily)
Ornish Study: results

- 6 patients in the control group chose treatment vs none in the experimental group.
- PSA decreased (4%) in the experimental group, increased (6%) in the control group.
- Serum from experimental group decreased prostate cancer cell line growth by 70%.
Prostate Cancer and Herbal Medicine

• Buyer beware
• The case of PC-SPES
• Saw Palmetto and Pygeum not indicated for prostate cancer treatment
• Integrated approach may be most beneficial to patient
## Prostate cancer prevention during 7-year finasteride study


<table>
<thead>
<tr>
<th>Variable</th>
<th>Finasteride Group</th>
<th>Placebo Group</th>
<th>Relative Risk of Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. at Randomization</td>
<td>No. Included in Analysis</td>
<td>No. Positive for Prostate Cancer (%)</td>
</tr>
<tr>
<td>All men</td>
<td>9423</td>
<td>4368</td>
<td>803 (18.4)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;55 Yr</td>
<td>1</td>
<td>0</td>
<td>0 (14.9)</td>
</tr>
<tr>
<td>55–59 Yr</td>
<td>2954</td>
<td>1380</td>
<td>205 (17.6)</td>
</tr>
<tr>
<td>60–64 Yr</td>
<td>2970</td>
<td>1442</td>
<td>254 (17.6)</td>
</tr>
<tr>
<td>≥65 Yr</td>
<td>3498</td>
<td>1546</td>
<td>344 (22.3)</td>
</tr>
<tr>
<td>Race or ethnic group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>8667</td>
<td>4056</td>
<td>739 (18.2)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>356</td>
<td>152</td>
<td>41 (27.0)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>262</td>
<td>117</td>
<td>19 (16.2)</td>
</tr>
<tr>
<td>Other</td>
<td>138</td>
<td>43</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Prostate cancer in a first-degree relative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1458</td>
<td>719</td>
<td>176 (24.5)</td>
</tr>
<tr>
<td>No</td>
<td>7965</td>
<td>3649</td>
<td>627 (17.2)</td>
</tr>
</tbody>
</table>
Testis Cancer
TREATMENT RISKS - XRT

• Short term:
  – Constitutional
  – GI symptoms - nausea, diarrhea
  – Skin changes
  – Bone marrow suppression
  – Infertility

• Long term:
  – Irritative GI / bladder symptoms: ~5-10%
  – Bowel obstruction: ~5-10%
  – Secondary malignancy: RR ~1.5-2
TREATMENT RISKS - RPLND

• Short term:
  – Invasive / Structural injury
  – Post-op pain / disability
  – Ileus
  – Atelectasis/pneumonitis
• Long term:
  – Retrograde ejaculation: 2-30%
  – Bowel obstruction: ~5%
TREATMENT RISKS - CHEMO

• Short term:
  – Constitutional
  – Mucositis
  – Rash
  – Alopecia
  – GI Distress
  – Neutropenia
  – Infertility

• Long term:
  – Pulmonary fibrosis: ~2%
  – Raynaud’s phenomena: 10-50%
  – Nephrotoxicity
  – Hypercholesterolemia
  – Neuropathy: 15-45%
  – Secondary malignancy: RR ~1.8
  – ? Chemo Brain?
RISKS - SURVEILLANCE

- Noncompliance → Undetected recurrence
- Anxiety ?
- Impairment in mental health measures ?