Sexual Dysfunction and Recovery After Treatment for Prostate Cancer

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Disclosures

• **Endo Pharmaceuticals** – speaker, advisor, research / fellowship support

• **Bayer AG** – speaker

• **Antares Pharmaceuticals** – advisor

• **Woven Health** – leadership position
Objectives

• To present rates of sexual problems after prostate cancer treatment and how these affect the individual and his relationships

• To present changes in sexual function after prostate cancer treatment

• To examine evaluation and management of erectile dysfunction after prostate cancer treatment

• To discuss evaluation and treatment of Peyronie’s disease after prostate cancer treatment
Prostate Cancer in Kenya and in the U.S.

Kenya
- Leading male cancer
- 1/6 likely to be diagnosed
- Likely to be diagnosed late and therefore more advanced disease

United States
- Leading male cancer
- 1/7 likely to be diagnosed
- African American men likely to be diagnosed late and therefore have more advanced disease
- 3,306,760 men live in prostate cancer survivorship

Siegel et al., Cancer Statistics, 2017
Miller et al., Survivorship Statistics, 2017

United States 5-year Survival by Stage and Race

Prostate

- All Races
- White
- African American

Survival rates by stage and race for Prostate cancer, showing higher survival rates for localized and regional stages compared to distant stages and all stages.
## Patients Pay a Price for Prostate Cancer Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Long-Term Effect</th>
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<tbody>
<tr>
<td>Surgery (radical prostatectomy)</td>
<td>• Urinary dysfunction (incontinence or irritability, urethral stricture)</td>
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<tr>
<td></td>
<td>• Sexual problems (ED, lack of ejaculation, <strong>changed orgasm</strong>, penile shortening, <strong>Peyronie’s Disease</strong>), infertility</td>
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<tr>
<td>Radiation (external beam or brachytherapy)</td>
<td>• Urinary dysfunction (incontinence, irritability, hematuria, urethral stricture)</td>
</tr>
<tr>
<td></td>
<td>• Sexual problems (<strong>progressive ED</strong>, decrease in semen volume), infertility</td>
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<td></td>
<td>• Bowel dysfunction (urgency, frequency, fecal incontinence, irritability and pain)</td>
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<tr>
<td>Hormone (androgen deprivation)</td>
<td>• Sexual problems (loss of libido, <strong>ED</strong>), infertility</td>
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<tr>
<td></td>
<td>• Other symptoms (hot flashes, bone density loss, emotional volatility, hair loss, gynecomastia, metabolic syndrome)</td>
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</tbody>
</table>
Post-Prostatectomy Erectile Dysfunction
15-year Follow Up of Prostate Cancer Survivors’ Erectile Function After Treatment with RP or RT

**ED at 2 years**
- 79% prostatectomy patients
- 61% radiation patients

**ED after 15 years**
- 87% surgically treated
- 93% treated with radiation

**ED in general population**
- 50% general population, mean age 73
Erectile Dysfunction After Radical Prostatectomy

• 72% of men are unable to achieve a natural erection sufficient for penetration 5 years after a RP

• Approximately 75,000 new patients each year in the U.S. suffer from ED following RP

• Erectile function PRIOR TO SURGERY → important determinant of erectile function recovery

Nerve Damage (Neuropraxia) Following Radical Prostatectomy

• Neuropraxia → temporary damage of the cavernous nerves
• May take up to 5 years for nerve function to recover
• Neuropraxia can be caused by
  • Mechanically induced nerve stretching during prostate retraction
  • Thermal damage to nerves caused by electrocautery
  • Ischemia of the nerves
  • Local inflammatory effects associated with surgical trauma

“Erectile Preservation” Protocol

• 1 WEEK PRIOR TO SURGERY:
  • Sildenafil 25mg or tadalafil 5mg every night.
  • Blood hormone evaluation.
  • Sex therapy evaluation if indicated.

• AFTER SURGERY:
  • Resume sildenafil 25mg every night or daily tadalafil 5mg starting 3 days after surgery.

• 1 MONTH AFTER SURGERY:
  • Sildenafil 25mg every night or tadalafil 5mg + sildenafil 100mg prior to intercourse.
  • Start vacuum erection device use 5-10 min/day.

• 3 MONTHS AFTER SURGERY:
  • Check PSA; if undetectable, replace testosterone if low.
  • Consider penile injection therapy 2x/week if above regimen not effective.
  • Blood hormone evaluation.

• FOLLOW-UP AT 6, 9, AND 12 MONTHS
Current Treatment Options

• Oral Therapy: PDE5 Inhibitors
• (Intraurethral therapy: MUSE)
• Vacuum Erection Device (VED)
• Penile injection therapies
• Penile prosthesis
• Hormone therapy: Androgens
Yes or No?

Daily PDE5i Dosing for Treatment of ED Post RP
Montorsi et al.

Screening period
36 wks treatment
6 wks washout
12 wks open-label

Primary outcome IIEF≥22 after washout
Specifically targeted UNASSISTED erections

Daily vs. On-Demand Tadalafil After Nerve Sparing Radical Prostatectomy (REACTT)

N=315
Post-NS RP

Tad 5 mg Daily
Tad 20 mg prn
Placebo

Tad 5 mg Daily

Eur Urol. 2014; 65:587
Vacuum Erection Device
VED: When Should it be Used?

• Therapeutic exercise after prostatectomy
  • 5-10 minutes daily
    • Engorgement → improved O$_2$ delivery
    • Stretch → length preservation

• Can achieve functional erections soon after RP!!
Intracavernosal Injection Therapy (ICI)

Alprostadil (PGE1)

Trimix
(PGE1, Phentolamine, Papaverine)
Trimix Injections

- Papaverine, PGE-1, phentolamine

**Advantages**
- Minimal pain
- ↑ efficacy with 3 drugs
- Inexpensive: ~ $3 per injection
- Numerous formulations

Can achieve functional erections soon after RP!!
Combination Therapies
Montorsi et al.

- 15 patients started on ICI within 1 month after radical prostatectomy → started on sildenafil 4 months after surgery

- 12 patients were started on sildenafil alone after 4 months without prior ICI use

**Results:**

- **Combination**: 82% responded to sildenafil at 6 months
- **Sildenafil-Only**: 52% responded to sildenafil at 6 months
Current Treatment Options

• Oral therapy: PDE5 Inhibitors
• (Intraurethral therapy: MUSE)
• Vacuum Erection Device (VED)
• ICI therapy: Aprostadil, Trimix
• Penile prosthesis
• Hormonal treatment: Androgens
Inflatable Penile Prostheses

Boston Scientific

Coloplast
Penile Implants Have High Satisfaction Rates

Overall Patient Satisfaction with ED Treatments

- Penile Injection: 40%
- Oral Medications: 51%
- Penile Implant: 93%

(J Urol, 2003. 170: 159.)
Penile Implants: High Patient and Partner Satisfaction

• 96% → would undergo the procedure again
• 92% → would recommend the device to others
• 96% partner satisfaction
• 90% of partners → would recommend a penile implant to other couples
Current Treatment Options

• Oral therapy: PDE5 Inhibitors
• (Intraurethral therapy: MUSE)
• Vacuum Erection Device (VED)
• ICI therapy: Edex, Caverject, Trimix
• Penile prosthesis
• Hormone therapy: Androgens
Testosterone is Needed for Normal Erectile Function

- Androgen deficiency results in
  - Increased penile tissue shrinkage
  - Increased fat deposits
  - Decreased penile blood flow
  - Decreased nitric oxide

- Venous leak may be reversed with testosterone
- Hypogonadal men with ED can restore erectile function with testosterone alone
- Testosterone improves response to PDE5i’s

Current Treatment Options

• Oral therapy: PDE5 Inhibitors
• (Intraurethral therapy: MUSE)
• Vacuum Erection Device (VED)
• ICI therapy: Edex, Caverject, Trimix
• Penile prosthesis
• Hormonal treatment: Androgens
Impact of the Female Partner

- Pre-operative FSFI scores → predicted which men would proceed with ICI use at 3 months (p=0.026)
- Pre-operative FSFI scores → predicted which men were able to obtain erections at 3 months (p=0.025)

Wittmann et al. 2015:
- 20 couples interviewed
- Couples’ engagement in sex was in part driven by partner interest

Female partner sexual function and interest predict post-operative male partner erectile function
Peyronie’s Disease
Prevalence of PD

- Overall, 0.5-20.3% of men have PD (≈9%)

Subgroups With Higher Incidence:
- Type 2 DM → 8%
- Radical Prostatectomy → 20%
- Erectile Dysfunction and DM → 20%

https://www.auanet.org/education/guidelines/peyronies-disease.cfm
Natural History of PD

- 80-90% will have improvement in pain

Change in curvature

- Improved: 12%
- Unchanged: 40%
- Worsened: 48%
PD Diagnosis

1. The minimum requirements are a careful history and a genital exam

2. A penile injection test +/- penile duplex Doppler ultrasound prior to intralesional injections

3. Hormone testing
   • Men with ED
   • Men with symptoms of low testosterone

https://www.auanet.org/education/guidelines/peyronies-disease.cfm
Treatment Options for PD

• Oral medications
• Intralosional injection therapy
• Surgery
• Penile traction therapy
• (Shockwave therapy)
Intralesional Injection Therapy

- Corticosteroids
- Interferon α2b
- Verapamil
- Collagenase Clostridium Histolyticum (Xiaflex®)

INDICATIONS FOR SURGERY

• PD for at least 6-12 months
• Stable phase disease for at least 6 months
• Stable penile curvature
• Penile curvature with inability to have sexual intercourse
• No penile pain

Photos courtesy of Dr. Wayne Hellstrom

https://www.auanet.org/education/guidelines/peyronies-disease.cfm
Penile Plication


Incision/Partial Excision and Grafting

- Dorsal penile curvature during preop erection
- Elevated neurovascular bundle
- Excision of fibrous plaque
- Tunica albuginea
- Erectile tissue
- Stay sutures

- Preop measurement of penile curvature using goniometer
- Intraoperative elevation of neurovascular bundle
- Excised fibrous plaque

- Determination of Tutoplast® graft size
- Elevated neurovascular bundle
- Stay sutures

- Fashioning of appropriately-sized Tutoplast® graft material
- Suturing of Tutoplast® processed human pericardial graft over defect created by removal of fibrous plaque using running 4-0 polydioxanone suture
- Stay sutures

- Measurement of graft size
- Labeling of graft size (4 x 6 cm)
Penile Traction Therapy

Can Help With:

• Penile straightening

• Penile length preservation / increase

Shockwave Therapy

Proposed Mechanisms:

• Plaque destruction $\rightarrow$ inflammatory response $\rightarrow$ changes in vascularity / plaque resorption

• Direct trauma $\rightarrow$ scar formation on the contralateral side of the penile shaft

• Degradation of the plaque $\rightarrow$ increase of the surface area in contact with the drugs introduced either locally or systemically

• No proven efficacy to date – EXPERIMENTAL
• Currently supported ONLY for penile pain in PD
Summary – Peyronie’s Disease

• Peyronie’s disease is an abnormal penile curvature / deformity resulting from fibrous plaque formation in the tunica albuginea

• Peyronie’s disease is more prevalent than previously thought

• PD is *highly treatable* through a number of options, including injections, traction therapy, and surgery
Conclusions

• ED affects most men after prostate cancer treatment, regardless of treatment modality

• Erectile function can be facilitated using medical therapies and can be surgically restored

• Recovery of erectile function is not hastened by medical therapy

• Peyronie’s disease affects many men after prostate cancer therapy

• Numerous effective treatment options exist for Peyronie’s disease
Thank You!!

Questions?

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