Penile Rehabilitation after Radical Prostatectomy

The PRO Position

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FACTS

• EFR not routine after RP: 55% (14-97%)
• Back to baseline EFR uncommon: 22% (4% >60y)
• Technology has not changed these figures
• ED independent predictor of bother and depression
• Greatest barrier to rehabilitation is surgeon apathy
• Greatest patient barrier is cost of medication
Dr. Trost will say ....

• It's costly!
• There are side effects
• There is no level 1 EBM
• The animal model is not representative of humans
ED Pathophysiology

- Vascular Damage
- Neural Injury
- Smooth Muscle Damage
CCSM Alterations After RP

Elastic and collagen fibers in 19 patients before, and 2 and 12 months after radical prostatectomy

<table>
<thead>
<tr>
<th></th>
<th>Mean Fibers ± SD</th>
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<tr>
<td></td>
<td>Elastic/High Power Field</td>
<td>Collagen/% Biopsy Area</td>
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<tr>
<td>Before</td>
<td>129.32 ± 13.13</td>
<td>44.80 ± 5.73</td>
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<tr>
<td>After 2 mos</td>
<td>80.80 ± 23.26</td>
<td>55.05 ± 5.29</td>
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<tr>
<td>After 12 mos</td>
<td>44.20 ± 11.58</td>
<td>73.10 ± 7.85</td>
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Before vs after 2 and 12 months, and after 2 vs 12 months p <0.0003.

Iacono F et al. J Urol, 163:1673-76, 2005
ERECTION DYSFUNCTION AFTER RADICAL PROSTATECTOMY: HEMODYNAMIC PROFILES AND THEIR CORRELATION WITH THE RECOVERY OF ERECTILE FUNCTION

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% Patients

CAI

CVOD

Time interval since radical prostatectomy (Months)
Penile Rehabilitation

- **Definition**: Penile rehabilitation is defined as the use of any drug or device to maximize erectile function recovery.

- **Purpose**: The prevention of smooth muscle and endothelial structural alterations to maximize chances of a man returning to his preoperative erectile function level.

- **Candidates**:
  - Radical pelvic surgery
  - Pelvic radiation
  - Diabetes
  - Pelvic fracture
Penile Rehabilitation Survey
ISSM Members

Do you perform Penile Rehabilitation?

- Yes: 87%
- No: 13%
Given the strong animal and basic science evidence and understanding the strengths and weaknesses of the existing human studies and the negative consequences of long-term ED after RP, the committee suggests that penile rehabilitation has significant potential benefits for the patient/partner and should be considered after RP.
Animal Data

• Muller A et al. The functional and structural consequences of cavernous nerve injury are ameliorated by sildenafil citrate. J Sex Med, 2008; Epub ahead of print

• Kovanecz I et al. Long-term continuous sildenafil treatment ameliorates CVOD induced by cavernosal nerve resection in the rats. IJIR, 2008; 20:202

• Ferrini M et al. Vardenafil prevents fibrosis and loss of smooth muscle after bilateral cavernosal nerve resection in the rat. Urology, 2006; 68:429

• Vignozzi L et al. Effect of chronic tadalafil administration on penile hypoxia induced by cavernous neurotomy in the rat. J Sex Med; 2006; 3:419

• Kovanecz I et al. Chronic daily tadalafil prevents the corporal fibrosis and venoocclusive dysfunction that occurs after cavernosal nerve resection. BJUI; 2008; 101:203

• Lysiak JJ et al. Tadalafil increases AKT and extracellular signal-related kinase 1/2 activation and prevents apoptotic cell death in the penis following denervation. J Urol, 2008; 179:779
RCT in Post-RP Rehabilitation

• Sildenafil¹
  - n=76, BNS, P v S50 v S100, 1-9m
  - Natural erections assessed at 11m
  - 27% responders in V v 4% in P arm

• Vardenafil² (REINVENT)
  - n=483, BNS, P v L10 QD v L20 OD, 1-9m
  - Assessments: 9m (EOT), 11m (P), 13m (V)
  - L20 OD > L10 QD at 9m, no Δ at 11 or 13m

• Tadalafil³ (REACCT)
  - n=423, BNS, P v C5 QD v C20 OD, 1-9m
  - Similar assessment and outcomes to REINVENT
  - Penile length preservation

Current Rehabilitation Strategies

• **PDE5i**
  - Prevention of endothelial structural alterations\(^1,2\)
  - Prevention of smooth muscle structural alterations\(^3\)
  - Preservation of smooth muscle relaxation profile\(^4\)
  - Neuroregeneration\(^5,6\)
  - Erection-independent cavernosal oxygenation?\(^7\)

• **ICI**
  - Oxygenation +++
  - CCS< stretch

• **VED**
  - Stretch

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Given the potentially devastating consequences of **acute** onset, **long-term** ED after RP, should we not be discussing rehabilitation with these men while we await **definitive** evidence confirming or refuting its benefit and thus facilitate the patient to making the final decision.
Principal Arguments Against

- Unproven strategy - Lack of level I EBM
- Translating animal data to human model
- Cost
Principal Arguments in Favor

- ED associated with depression and reduced QOL
- Apathy leads to time-dependent changes in CCSM
- Signals from studies are clear & robust
- Sexual medicine experts are routinely doing rehabilitation post-RP
Is Dr. Trost?