Sexual Concerns in Men after Transplantation

Celebrating a Second Chance at Life Survivorship Symposium

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Sexual Concerns in Men after Transplant

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Disclosures (COI)

Grants
- National Institutes of Health (NCI)
- Sexual Medicine Society of North America
- Department of Defense

Academic Leadership Positions
- Editor-in-Chief, The Journal of Sexual Medicine
- Editorial Board, AUA Updates
- Board of Directors, Sexual Medicine Society of North America
- Member, Practice Guidelines Committee, AUA

Male Sexual Dysfunctions
- Erectile dysfunction
- Low libido
- Failure to ejaculate
- Premature ejaculation
- Low testosterone
- Absence of orgasm
- Painful orgasm
- Orgasm associated urine leak
- Penile length alterations
- Penile curvature
Low Sex Drive

- Low testosterone level
- High prolactin level
- Hypothyroidism level
- Antidepressant medications
- Psychological causes

Delayed Orgasm (Anorgasmia)

- SSRI antidepressants
- Low testosterone level
- Penile sensation loss
- Psychological causes
**Infertility**

- Bank sperm prior to transplant
- Avoid risk of pregnancy for at least 12 months after transplant
- Check semen analysis (2-5 years after transplant)

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**How Cancer Causes Sexual Problems**

- Psychological Factors
- Surgery
- Radiation
- Chemo/Hormone therapy
Sexual dysfunction in young adult survivors of childhood cancer

- 2,546 men and women survivors of childhood cancer (aged 19-40 years) in Sweden
- Sexual function compared to general population sample (n = 819)
- Sexual dysfunction was reported by 57% of female and 35% of male survivors
- Among males, most common dysfunctions were satisfaction with sex life (20%), sexual interest (14%) and erectile function (9%)
- Compared with the general population, male survivors had an increased likelihood of difficulty with orgasm (two-fold risk) and erectile problems (two-fold risk)
- A more intensive cancer treatment, emotional distress and body image disturbance were associated with sexual dysfunction in survivors.

Impact of Allogeneic Stem Cell Transplantation on Testicular and Sexual Function

- This observational, single-center study consecutively enrolled 105 subjects
- Testicular function and sexuality were evaluated through hormonal testing and a sex questionnaire.
- A higher occurrence of low testosterone (21%), impaired sperm production (87%), and erectile dysfunction (72%) compared with the general population
- Chronic graft-versus-host disease was associated with an increased risk of developing ED (6 times more likely).
Sexuality and quality of life in patients with hematologic malignancy and hematopoietic stem cell transplantation

• Fourteen studies were included in the review
• They present heterogeneity regarding measurement tools, time of measurement and type of HSCT
• The common theme that emerged from most studies is that sexual dysfunction negatively impacts QoL
• The most common sexual problems reported were erectile dysfunction for men and lack of desire for women
• In the majority of studies, improvement in physical, psychological symptoms and sexual function lead to improvement in QoL over time.

Erectile Dysfunction
Has Your Doctor Asked Whether You Have Sexual Difficulties?

Barriers to Discussing ED

**Patient**
- Embarrassment
- Shame
- Ignorance about normal function
- Cultural beliefs
- Religious beliefs
- Discomfort

**Physician**
- Discomfort
- Lack of Knowledge
- Personal bias
- Time

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Organic Causes of ED

- 40% Vascular
- 30% Diabetes
- 15% Medication
- 5% Neurological causes
- 3% Endocrine problems
- 6% Pelvic surgery, radiation, or trauma
- 2% Other

ED & Medical Conditions

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>4.1</td>
</tr>
<tr>
<td>Benign Prostate disease</td>
<td>2.9</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>2.6</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>2.5</td>
</tr>
<tr>
<td>Cardiac problems</td>
<td>1.8</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.6</td>
</tr>
</tbody>
</table>
### Process of Care Model

<table>
<thead>
<tr>
<th>Level</th>
<th>Treatment Options</th>
</tr>
</thead>
</table>
| **First-line therapy** | • Lifestyle modification  
                      | • Medication adjustment  
                      | • Psychology input  
                      | • Oral agents  
                      | • Vacuum devices |
| **Second-line therapy** | • Intracavernosal injections  
                      | • Intraurethral alprostadil |
| **Third-line therapy** | • Penile implants  
                      | • Vascular reconstruction |

PDE5 Inhibitors (Viagra etc)

- **Candidacy:** no nitroglycerin, ‘2 flight of stairs’
- **Maximum dose** is a good starting dose
- **Reduce dose** for side effects or for excellent response
- **Patient instructions**
  - Empty stomach (Viagra, Levitra, Stendra)
  - Sexual stimulation required
  - Wait 1h prior to commencement (V, L)
  - Wait 4h prior to initiation with Cialis
- **Duration of action**
- **Follow-up** with patient
PDE5 Inhibitors: Side Effects

- Headache
- Facial flushing
- GI side effects
- Nasal congestion
- Visual disturbances
- Myalgia
- Auditory disturbances

PDE5 Inhibitors: High Risk Groups

- Inadequate exercise reserve
- Retinal diseases
- Certain HIV medications
- Certain pulmonary hypertension medications
Urethral Suppository (MUSE)
Penile Injection Therapy

Precautions

• Contraindications:
  - MAO inhibitor therapy

• Precautions
  - Large abdomen
  - Manual dexterity concerns
  - Visual impairment
  - Blood thinners
  - Peyronie’s disease
Penile Injections

- Advantages
  - Highly effective
  - Mimics natural physiology of erection
  - No effect on sensation, ejaculation, fertility
  - High level of discretion, thus spontaneity

- Disadvantages
  - Poor long-term tolerability (dropout rate >60%)
  - Requires training, follow-up
  - Insurance issues

Sexual Over the Counter Supplements

- Multi-billion-dollar industry
- No current regulatory agency control
- 30% placebo response rate in ED drug studies
- Some products contain testosterone
- Some products contain PDE5 inhibitors
- Not a “victimless” crime
Low Testosterone

Causes of Low Testosterone

- Unexplained anemia
- Bone density loss
- Diabetes
- Exposure to chemotherapy
- Exposure to testicular radiation
- HIV/AIDS
- Chronic narcotic use
- Male infertility
- Pituitary dysfunction
- Chronic corticosteroid use
Signs and Symptoms of Low Testosterone

- Decreased sexual desire (libido)
- Loss of energy
- Afternoon Fatigue
- Depression
- Irritability
- Loss of muscle mass
- Weight gain
- Bone density loss
- Decreased productivity


Variation in T Levels during the Day

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Total Testosterone (ng/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0800</td>
<td>400-800</td>
</tr>
<tr>
<td>1200</td>
<td>500-700</td>
</tr>
<tr>
<td>1600</td>
<td>600-700</td>
</tr>
<tr>
<td>2000</td>
<td>500-600</td>
</tr>
<tr>
<td>2400</td>
<td>400-500</td>
</tr>
<tr>
<td>0400</td>
<td>300-400</td>
</tr>
<tr>
<td>0800</td>
<td>400-500</td>
</tr>
</tbody>
</table>

Young Men: 500-800 ng/dL
Old Men: 300-600 ng/dL

### Risks & Benefit of Low Testosterone

<table>
<thead>
<tr>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CV events (MACE)*</td>
<td>• None</td>
</tr>
<tr>
<td>• Glycemic control issues*</td>
<td></td>
</tr>
<tr>
<td>• Bone density loss*</td>
<td></td>
</tr>
<tr>
<td>• Impaired nerve recovery#</td>
<td></td>
</tr>
<tr>
<td>• Impaired PSA production*</td>
<td></td>
</tr>
<tr>
<td>• Higher stage/grade prostate cancer*</td>
<td></td>
</tr>
</tbody>
</table>

*Human data

### Risks & Benefits of Testosterone Therapy

<table>
<thead>
<tr>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High hemoglobin (2-14%)</td>
<td>• Improved physical symptoms</td>
</tr>
<tr>
<td>• Breast enlargement (rare)</td>
<td>• Improved cognitive symptoms</td>
</tr>
<tr>
<td>• Prostate cancer?</td>
<td>• Reduced heart attacks risk?</td>
</tr>
<tr>
<td></td>
<td>• Improved sugar control?</td>
</tr>
<tr>
<td></td>
<td>• Bone density preservation?</td>
</tr>
</tbody>
</table>
Testosterone Deficiency and Treatment

• Low testosterone is a risk factor for heart attacks/strokes
  Strong Recommendation; Evidence Level Grade B

• It cannot be stated whether T therapy increases or decreases the risk of MACE
  Moderate Recommendation; Evidence Level Grade B

• Testosterone therapy should not be commenced for 3-6 months in patients with a history of a MACE
  Expert Opinion
Testosterone Therapy and Heart Attacks

• Large observational studies and meta-analyses evaluating T therapy and risk of MACE have reported conflicting data

  Increase in MACE
  (Vigen, Finkle, Layton, Xu)

  Decrease in MACE
  (Shores, Jones, Sharma, Muraleedharan, Cheetham)

  Neutral effect on MACE
  (Nair, Borst, Amory, Snyder, Fernandez, Balsells, Calof, Haddad, Corona, Baillargeon)

Testosterone Therapies

• Gels/creams
• Patch
• Pills
• Nasal spray
• IM injections
• Subcutaneous injections
• Subcutaneous pellets
**Testosterone & Fertility**

TD patients interested in fertility should have a reproductive health evaluation pre-T therapy and should avoid testosterone therapy.

**Moderate Recommendation; Evidence Level Grade B**

- TTH turns off fertility hormones
- Clomiphene, HCG, aromatase inhibitors

<table>
<thead>
<tr>
<th>Item</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient preference</td>
<td>Identify the patient’s preference for TTH modality</td>
</tr>
<tr>
<td>Cost</td>
<td>Which (if any) agents are covered?</td>
</tr>
<tr>
<td>Baseline Hematocrit Level</td>
<td>Hematocrit level ≥50% (Yes/No)</td>
</tr>
<tr>
<td>Baseline PSA Level</td>
<td>Baseline PSA (yes/no and level)</td>
</tr>
<tr>
<td></td>
<td>Digital rectal exam (normal/abnormal)</td>
</tr>
<tr>
<td></td>
<td>Personal diagnosis of prostate cancer (yes/no)</td>
</tr>
<tr>
<td></td>
<td>Family history of prostate cancer (yes/no)</td>
</tr>
<tr>
<td>Transference Risk</td>
<td>Potential transference risk (low/moderate/high)</td>
</tr>
<tr>
<td>Fertility interest</td>
<td>Fertility interest (yes/no)</td>
</tr>
<tr>
<td>Baseline LH level</td>
<td>Low/low-normal LH levels (yes/no)</td>
</tr>
<tr>
<td>Prolactin level</td>
<td>Elevated level (yes/no)</td>
</tr>
<tr>
<td>Anticoagulant Medication Use</td>
<td>Anticoagulant medication use (yes/no)</td>
</tr>
<tr>
<td>Risk of VTE</td>
<td>History of VTE (yes/no)</td>
</tr>
<tr>
<td>History of Cardiovascular Events</td>
<td>Myocardial infarction (yes/no)</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular accident (yes/no)</td>
</tr>
<tr>
<td></td>
<td>Congestive heart failure (yes/no, date of diagnosis)</td>
</tr>
<tr>
<td>Breast Symptoms</td>
<td>Breast symptoms (yes/no)</td>
</tr>
<tr>
<td></td>
<td>Gynecomastia (yes/no)</td>
</tr>
<tr>
<td></td>
<td>History of breast cancer (yes/no)</td>
</tr>
</tbody>
</table>
Take Home Messages

• Transplant patients are at high for sexual dysfunction for a variety of reasons

• Dysfunctions and QOL improve over time

• Very little research in this specific population

• ED and low T are the commonest problems

• Both conditions are treatable

• See a clinician with expertise

Questions?

Celebrating a Second Chance at Life Survivorship Symposium 2022

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