Sexual Concerns in Men after Transplant

Celebrating a Second Chance at Life Survivorship Symposium
April 29 – May 5, 2023

Robert Kovell MD
University of Pennsylvania, Perelman School of Medicine

Sexual Dysfunction & Transplant

Background Information

- Sexual dysfunction is common after transplant
- Nearly 50% of patients experience impaired function post-transplant
  - Onset can be early or delayed
  - Symptoms may resolve or persist for many years
- Can have a substantial effect on overall quality of life
Sexual Dysfunction
More Than Just Erectile Dysfunction

- Ejaculatory dysfunction
  - Delayed ejaculation
  - Retrograde ejaculation
  - Premature ejaculation

- Orgasmic dysfunction
  - Anorgasmia
  - Pain with orgasm

- Climacturia (leakage with orgasm)

- Decreased libido
- Decreased testosterone
- Loss of penile length/girth
- Decreased fertility
- Decreased genital sensation
- Decreased lubrication
- Peyronie’s disease
  - Penile curvature
  - Penile wasting

Sexual Dysfunction
Potential Causes

- **Psychogenic factors**
- Radiation
- **Chemotherapy**
- Medical conditions
- Medications
- Surgery
- Endocrinologic issues
- Hormonal therapies

*Most common in the transplant population*
Sexual Dysfunction
Long Term Evaluation Childhood Cancer Survivors

- Swedish registry (2,546 survivors of childhood cancer, age 19-40)
- Survivors of childhood cancers: high degree of sexual dysfunction
- Reported in
  - 35% of male
  - 57% of female survivors
- Increased erectile dysfunction (2x) and orgasmic dysfunction (2x) in men compared to general population

Sexual Function
Survivorship after Transplant

- 50% reported no discussion with health care provider
- Depression significantly correlated with function 3 years after
- Men: decreased libido/lack of interest
  - Year 1 – concerns about attractiveness, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction
  - Year 3 – increased concern about attractiveness, others improved
- Women: Self perceived issues with attractiveness
  - Year 3 – increased sexual interest but concerns about vaginal lubrication, appearance, painful intercourse, orgasmic function
Sexual Dysfunction after Transplant
Changes in Function & Hormone Levels

- Sexual dysfunction decreased one month after BMT
- T levels actually up at one month, but erectile function, desire, orgasmic function down


Sexual Dysfunction after Transplant
Changes in Function & Hormone Levels

- Sexual dysfunction rebounds in many by 1 year
- Total T and dihydrotestosterone at 1 month associated at month 1 recovery
- Pre-SHBG, estradiol and change in estrogen predictive of year 1 recovery

Sexual Dysfunction After Transplant

**Trends & Quality of Life**

- Meta-analysis of 14 studies
- Heterogenous studies, multiple different tools and time periods
- Sexual dysfunction negatively impacts quality of life
- Most common:
  - Men – erectile dysfunction
  - Women – lack of sexual desire
- Improvement in physical, psychologic, and sexual function \(\rightarrow\) improved quality of life over time

J BUON. 2020, 25(4): 1693-1706

---

Sexual Function after Transplant

**Potential Impacts**

- Observation, single centered study – 105 consecutive subjects
- Compared to general population, increased rates of:
  - Erectile dysfunction (72%)
  - Low testosterone (21%)
  - Decreased sperm production (87%)
- If developed chronic GVHD \(\rightarrow\) 6x rate of developing ED

Transplant Cell Ther. 2021 Feb. 27(2): 182
Normal Erections
A Brief Review of Physiology

- Nerve stimulation
- Smooth muscle relaxation
- Cavernosal artery brings in blood
- Blood trapped inside by compressing veins

Erectile Dysfunction
Medical Risk Factors

<table>
<thead>
<tr>
<th>Medical Issue</th>
<th>Relative Risk over Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>4.1</td>
</tr>
<tr>
<td>Benign prostate issues</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>
Erectile Dysfunction
Treatment Options

Many options available – treatment individualized

1st Line Therapies
• Sex therapy/counseling
• Oral medications
• Vacuum erectile devise/constrictive devices

2nd Line Therapies
• Intraurethral suppositories
• Intracavernosal injection therapy
• Low intensity shockwave therapy?
• Penile prosthesis

Erectile Dysfunction
Barriers to Care

• Embarrassment
• Lack of knowledge about normal function
• Lack of familiarity with treatment options
• Cultural or religious beliefs
• Provider – lack of comfort with/knowledge about sexual health care
• Insurance coverage for therapies
Oral Medications for Erectile Dysfunction

*Phosphodiesterase 5 Inhibitors (PDE5is)*

*Sildenafil (Viagra), Vardenafil (Levitra), Tadalafil (Cialis), Stendra (Avalafil)*

- Relatively safe
- Can titrate dose up or down (preferred)
- Similar efficacies
- Different times to onset of action and duration of action
- Difference in absorption with food
- As needed versus daily dosing
- More cost effective now with generic dosing

**Phosphodiesterase 5 Inhibitors**

*High Risk Groups*

- Significant cardiovascular disease
- Recent heart attack, chest pain with exertion, stroke, heart failure, significant valve disease
- Poor exercise tolerance
- Retinal disease
- Certain classes of HIV medications
- Select pulmonary hypertension medications
Phosphodiesterase 5 Inhibitors

Side Effects

• Headaches
• Flushing
• GI Upset
• Hypotension
• Muscle aches/cramps
• Vision changes
• ?Priapism (sustained, painful erection)

• Decreased blood pressure: No nitrates (nitroglycerin), care with alpha blockers

Vacuum Erectile Devices

• Creates a negative pressure – draws blood in
• Primarily venous blood
• Coupled with a constrictive band around the penile base

• Advantages
  • Spontaneous, rapid onset
  • Benefit for most men

• Disadvantages
  • Have to wear band
  • Can cause bruising
Intraurethral Suppositories - MUSE

- Comes in applicator
- Place small suppository within the urethra
- PGE1 (alprostadil)
- Can titrate dose

**Advantages**
- Relatively rapid onset
- Works ~50%

**Disadvantages**
- Burning, urethral irritation
- Blood in urine

Intracavernosal Injection Therapies (ICI)

- Injection of medications into the penis
- Small needle, rapid onset
- Arterial inflow – natural erection

**Advantages**
- Quick onset
- Effective, titrate

**Disadvantages**
- Needles
- Cold storage
- Risk of priapism
- Risk of scarring
- High drop out rates
Intracavernosal Injection Therapies

Precautions

• **Contraindications:**
  • MAO inhibitors
  • Severe blood pressure issues

• **Potential Challenges**
  • Obese abdomen
  • Issues with dexterity
  • Vision problems
  • Blood thinners
  • Penile curvature/Peyronie’s

Penile Prosthesis

• Cylinders placed within corpora to recreate erections
• “Erection Replacement” – does not usually affect:
  • Sensation
  • Orgasm
  • Ejaculation
• First developed in 1972

• Highly effective
• High rates of satisfaction → > 90%
• Both for individuals and their partners
Penile Prosthesis

Types of Implants

Different models available
- Malleable prosthesis
- Inflatable penile prosthesis
  - Two-piece prosthesis
  - Three-piece prosthesis
    - Cylinders (penis)
    - Control (scrotum)
    - Reservoir (pelvis)

Penile Prosthesis

Risks

- Infection
  - <1% for most men
  - Increased with immunosuppression, diabetes
- Malfunction/need for replacement over time
- Post-procedure discomfort, recovery time
Erectile Dysfunction – Nutraceutical Options

- Multi-billion dollar a year industry
- No regulation of ingredients, dosages or reporting
  - Some contain testosterone
  - Some contain phosphodiesterase 5 inhibitor medications
- 30% placebo response for Erectile Dysfunction medications

![Table 2: Top 20 most commonly identified ingredients based on product nutrition labels](image)

J Sex Med. 2015 Nov; 12(11):2105-17

Low Intensity Shockwave Therapy

*Wave of the Future?*

Proposed mechanisms for improved erectile function:

- New blood vessel formation
- Stimulate Schwann cells
- Nerve regeneration
- Decreased fibrosis
- Cavernosal remodeling
- Reduction in sympathetic tone
**Low Intensity Shockwave Therapy**

*Where Do We Stand?*

- 70 patients with moderate ED randomized
- 12 sessions over six weeks: LiSWT v sham
- 5,000 impulses, 5Hz, 0.096mJ/mm²
- 79% showed minimal clinically important differences compared to 0% in sham
- IIEF score differed by 4.4 (3.4-5.4)
- No data for post-BMT
- *Is this truly significant?*

---

**Hypogonadism (Low T)**

*Causes/Risk Factors*

- Chemotherapy exposure
- Radiation exposure to the testicles
- Chronic opioid/narcotic use
- Chronic steroid use
- Pituitary dysfunction
- Diabetes
- HIV/AIDS
Hypogonadism (Low T)
Not All Decreased Libido is from Low T

- Endocrinologic/hormonal contributions
  - Decreased testosterone levels
  - Increased prolactin levels
  - Decreased thyroid hormone levels

- Medications
  - Antidepressant usage – SSRIs, SNRIs
  - Buspirone/Wellbutrin tends to be more “friendly”

- Psychogenic causes

Hypogonadism (Low T)
Signs and Symptoms

- Decreased libido (sexual desire)
- Decreased energy
- Decreased muscle mass
- Loss of bone density
- Weight gain, increased fat
- Depression
- Irritability
- Decreased productivity!

A lot of overlap with other conditions – not all from testosterone
Hypogonadism (Low T)

Work-Up

- T levels decrease naturally over time from about the age 30 on
- T levels highly variable throughout the day
- No reference range for the individual

- Generally check first thing in the morning – 8AM-10AM
- Often will repeat with more extensive hormonal testing if low

Risks of Having Low Serum Testosterone Levels

- Increased rate of cardiovascular events (including major events)
- Loss of bone mineral density
- Cognitive issues
- Difficulty with glucose control
- Impaired nerve recovery

- PSA production decreased → difficult with screening for prostate cancer leading to later detection
Hypogonadism (Low T)

T Levels and Mortality

• Low T levels associated with increased mortality in male veterans
• Held true for low T after adjusting for:
  • Age
  • Medical co-morbidities
  • Multiple clinical co-variates


Testosterone Replacement Therapy

Risks and Benefits

Risks
• Increased hemoglobin
• Breast enlargement
• Mood changes
• Changes in prostate cancer risk
• Smaller/softer testicles
• Decreased sperm counts

Benefits
• Better libido
• Better energy
• Improved cognition
• Improved glucose control
• Possible improved bone density
• Possible decrease MI risk?
• Possible decreased mortality?
Testosterone Replacement Therapy
Routes of Administration

**Shorter acting**
- Topical gels/creams
- Patches
- Intramuscular injections
- Nasal sprays
- Oral pills

**Longer acting**
- Subcutaneous injections/oils
- Subcutaneous pellets

All require close monitoring:
- Symptom checks
- Lab work (PSA, hemoglobin, liver function, lipids, etc.)

Orgasmic Dysfunction
*Delayed Orgasm or Anorgasmia*

- SSRI medications
- Hypogonadism
- Decreased genital sensation
  - Diabetes mellitus
  - Chemotherapy
  - Spinal cord pathology
- Psychogenic contributions
  - Decreased stimulation
  - Increased threshold to reach orgasm
**Post-Transplant Survivorship**  
*Fertility Concerns*

- Treatments may affect sperm counts
  - Maybe temporary or more permanent
  - Chemotherapy, radiation, immunosuppressants
  - Consider sperm preservation therapy/banking BEFORE transplant
- Avoid pregnancy for at least 1 year post-transplant
- Optimal sperm recovery at 2-5 years post-transplant
- Semen may appear normal (but diminished or damaged sperm)

---

**Potential Causes of Sexual Dysfunction**  
*Emotional Health / Psychogenic Causes*

- Re-engaging in sexual relationships following transplant: one model
  - Identifying the importance of sexual relationships
  - Taking responsibility
  - Seeking resources
  - Navigating the partnered relationship
- Gender specific and non-linear progression
- Sex therapy/relational counseling important part of treatment for many!

Eur J Oncol Nurs. 2020 Apr 7;46:101756
Take Home Messages

• Patients undergoing transplant are at risk for sexual dysfunction both early and late
• Erectile dysfunction and decreased testosterone common
• Often improves over time but not for all
• Treatment options are available
• Providers are available to help – seek care if needed and when ready!

QUESTIONS?

Robert Kovell MD
University of Pennsylvania, Perelman School of Medicine
LET US KNOW HOW WE CAN HELP YOU

Visit our website: bmtinfonet.org
Email us: help@bmtinfonet.org
Phone: 888-597-7674 or 847-433-3313

Find us on:
Facebook, facebook.com/bmtinfonet
Twitter, twitter.com/BMTInfoNet