

Sexual Concerns in Men after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

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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***
- Most common in the transplant population*
- Medical conditions
 - Medications
 - Surgery
 - Endocrinologic issues
 - Hormonal therapies

Sexual Dysfunction

Long Term Evaluation Childhood Cancer Survivors

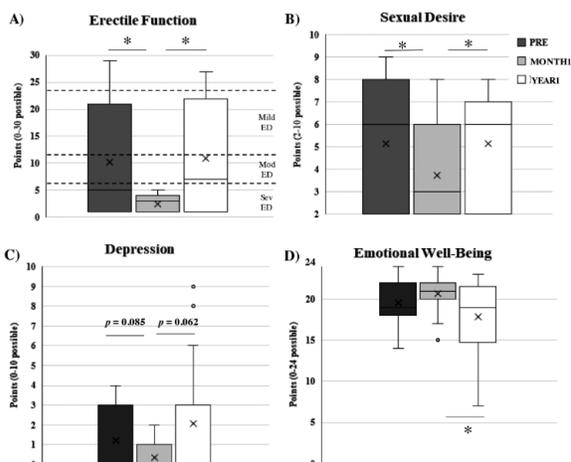
- Swedish registry (2,546 survivors of childhood cancer, age 19-40)
- Survivors of childhood cancers: high degree of sexual dysfunction
- Reported in
 - 35% of male
 - 57% of female survivors
- Increased erectile dysfunction (2x) and orgasmic dysfunction (2x) in men compared to general population

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



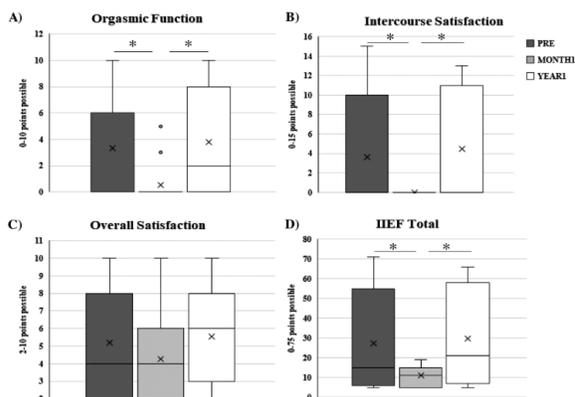
- Sexual dysfunction decreased one month after BMT
- T levels actually up at one month, but erectile function, desire, orgasmic function down

Andrology. 2022 Feb;10(2):291-302.

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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

FIGURE 3 Box and whisker plots for (A) Orgasmic function from International Index of Erectile Function (IIEF), (B) Intercourse satisfaction from IIEF, (C) Overall satisfaction from IIEF, and (D) IIEF total. PRE, baseline visit; MONTH1, follow-up 1; YEAR1, follow-up 2; x = mean; mid-line = median. *p < 0.05

Andrology. 2022 Feb;10(2):291-302.

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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, psychological, and sexual function → improved quality of life over time

Sexual Function after Transplant

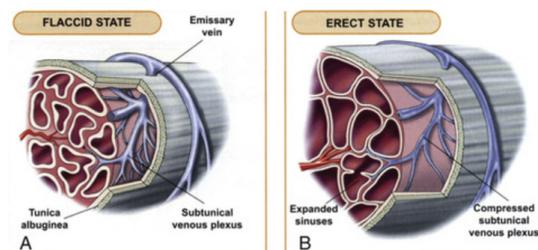
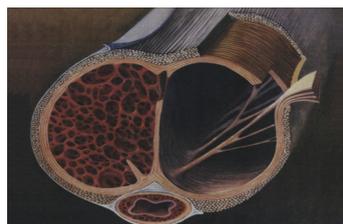
Potential Impacts

- 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 → 6x rate of developing ED

Normal Erections

A Brief Review of Physiology

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



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Erectile Dysfunction

Medical Risk Factors

<u>Medical Issue</u>	<u>Relative Risk over Baseline</u>
• Diabetes	4.1
• Benign prostate issues	2.9
• Peripheral vascular disease	2.6
• Metabolic syndrome	2.5
• Cardiac problems	1.8
• Hyperlipidemia	1.7
• Hypertension	1.6

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), Avanafil (Stendra)

- 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

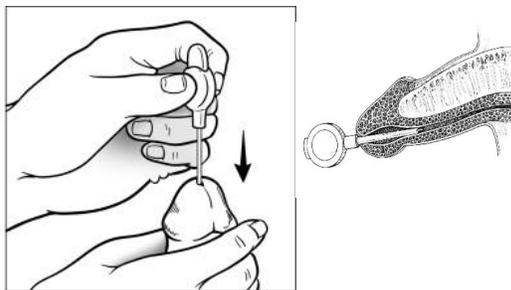
Vacuum Erectile Devices

- 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

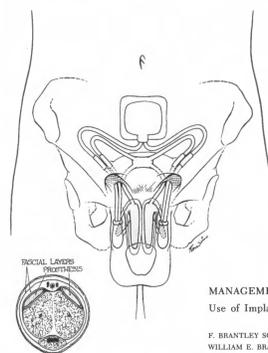


FIGURE 1. Implantable inflatable prosthesis for erectile impotence.

MANAGEMENT OF ERECTILE IMPOTENCE*
Use of Implantable Inflatable Prosthesis

F. BRANTLEY SCOTT, M.D.
WILLIAM E. BRADLEY, M.D.
GERALD W. TIMM, M.D.

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)



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Penile Prosthesis

Risks

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



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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

Ingredient name	Number of products containing ingredient
Ginseng	13
Tribulus spp.	13
Zinc	13
Epimedium spp. (Horny goat weed)	11
Vitamin B6	10
Fenugreek	10
L-Arginine	10
Vitamin B12	9
Maca	9
Vitamin B3 (also as Niacin)	6
Saw Palmetto	6
Vitamin B9 (also as Folate)	5
Dehydroepiandrosterone (DHEA)	5
Vitamin E	5
Ginkgo Biloba	5
Magnesium	5
Yohimbine	5
Vitamin B1 (also as Thiamin)	4
Vitamin B2 (also as Riboflavin)	4
Selenium	4

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

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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?*

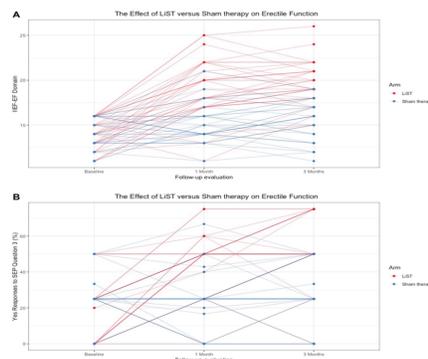


Figure 3. Parallel coordinate plots of patient level data about the effect of LiSWT versus sham therapy on IIEF-5 (A) and "Yes" responses to IIEF question 3 (B).

J Urol. 2022 Aug;208(2):388-395.

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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
 - Bupropion/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

Hypogonadism (Low T)

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

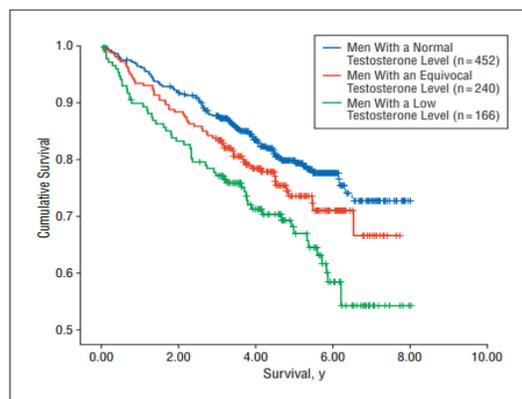


Figure. Unadjusted Kaplan-Meier survival curves for the 3 testosterone level groups. Men with low and equivocal testosterone levels had a significantly shorter survival than men with normal testosterone levels (log-rank test; $\chi^2=14.4$, $P=.001$).

Arch Intern Med. 2006 Aug;166(15):1660-5.

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Testosterone Replacement Therapy Risks and Benefits

Risks

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

Not all issues related to Testosterone!

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

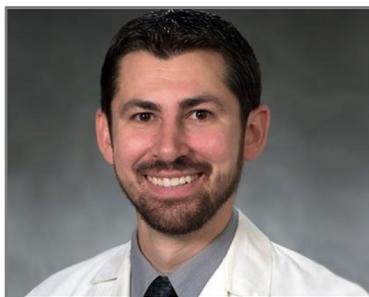
- Re-engaging in sexual relationships following transplant: one model
 - Identifying the importance of sexual relationships
 - Taking responsibility
 - Seeking resources
 - Navigating the partnered relationship
- Gender specific and non-linear progression
- Sex therapy/relational counseling important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

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?



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