Iatrogenic Sexual Dysfunction in Prostate Cancer

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Iatrogenic Sexual Dysfunction in Prostate Cancer

• Sexual dysfunction in cancer patients
  • Biological (anatomical alterations, physiological changes, secondary effect os medical intervention)
  • Psychological (negative emotional states: anxiety, depression and anger)
  • Social

Dobkin PL. J Psy Oncology 1991
Iatrogenic Sexual Dysfunction in Prostate Cancer and Quality of Life

- Unsure of remission state
- Cancer control > continence > Sexual dysfunction
- Threat to patient masculine identity

- Unmet sexuality-related needs > younger men

- Post-Radical Prostatectomy – sexual dysfunction – moderate to large problem (6,12,24 months- 61%, 52%, 42%)
- Detriments in sexual function - long-term QoL (10-15 years) for RP, EBRT and BT
Sexual Dysfunction in Active Surveillance Patients

- Limited data Vs no Prostate Cancer
- Psychological distress diagnosis associated - psychosexual counseling

**RESULTS:** A total of 65-68% of men on AS, 35-36% of those who underwent RP, 36-37% of those who underwent RT and 36% of men in the RP and RT groups combined (combined Tx) were sexually active. • A total of 20-30% of men in the AS group, 86-91% of men in the RP group, 56-60% of men in the RT group and 71-76% of men in the combined Tx group were sexually inactive as a result of erectile dysfunction. • A total of 44-51% of men in the AS group, 96% of men in the RP group, 73-76% of men in the RT group and 84-85% of men in the combined Tx group who were sexually active had problems getting or keeping an erection. • In multivariable analysis these differences were significant, except for AS vs RT.

**CONCLUSIONS:** Men with localized PCa on AS were more often sexually active than similar men who received radical therapy, especially RP. If not sexually active, this was less often attributable to erectile dysfunction for those on AS. If sexually active, this was less often associated with problems getting or keeping an erection for those on AS. • The study was non-randomized; the latest advances in RP and RT might impact results.
CONCLUSIONS: Men on AS experienced a gradual decline in sexual function during the first 24 months of enrollment. Older age, PSA × time, and diabetes were all independent predictors of diminished sexual function over time. Anxiety, AUA-SI, the number of cores and the number of biopsies were not predictors of reduced sexual function in men in AS.
Sexual Dysfunction after Radical Prostatectomy

• **Erectile dysfunction**
  
  • self-reported-60% (18 months), Kendirci 2006
  • 70% (60 months), Penson 2005
  • 80%, Scandinavian study, 2002

  • Age – erection for intercourse
    • 39-54 years -61%
    • 60-64 years – 44%
  
  • Pre-treatment erectile function
  • Post- treatment erectile function effectiveness

• Surgical technique
  
  • Nerve sparing (NS)
    • 35% (1 ano) – 25% (>2 anos)
    • Non-nerve-sparing (NNS)
  
  • cautery to accessory pudendal arteries

• Surgical approaches
  
  • Open/Laparoscopic/Robotic

• Blood flow changes:
  
  • At surgery/Early after RP

• Blood flow anormalities in the penis – predictor of long term ED

• Ohebshalom – n=111
  
  • 29% normal
  • 71% abnormal penile blood flow
  • 15% **venous leak** – predictor of failure of functioning erections after RP with/without PDE5 inhibit

• trauma to neurovascular bundles – loss of normal nerve tissue connections to penile bodies

• Blood flow anormalities in the penis – predictor of long term ED

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  • 29% normal
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Sexual Dysfunction after radical prostatectomy

- **Climacturia** – 20-93%
  - Orgasm-associated incontinence
- Damage of the bladder neck – Sympatic fibers responsible for bladder neck contraction/external sphincter relaxation – in expulsion phase
  - Video-urodynamic – lower functional urethral length
    - Manassero, 2012
- **Subjective loss of penile length** - 47%
- **Penile curvature** - 30%

- **Impaired sensation/intensity of orgasm** - 60%-80%
- **Anorgasmia** – 5%
- **Orgasm-associated pain** – 10-19%
  - Penis or other sites (testes, rectum, lower abdomen)
  - Muscular spasm/dystonia – bladder neck/pelvic floor
  - ≈ pelvic pain syndrome

- Mongorovich, 2013, J Sex Med
  - RP with preservation of seminal vesicles
  - Contraction of seminal vesicles
Neglected side effects after radical prostatectomy: a systematic review.

Frey AU¹, Sønsken J, Fode M.

INTRODUCTION: A series of previously neglected sexually related side effects to radical prostatectomy (RP) has been identified over the recent years. These include orgasm-associated incontinence (OAI), urinary incontinence in relation to sexual stimulation (UISS), altered perception of orgasm, orgasm-associated pain (OAP), penile shortening (PS), and penile deformity.

RESULTS: A total of 43 articles were included. OAI and UISS are experienced by 20-93% of RP patients at least a few times after surgery. Although these issues are associated to postoperative daytime incontinence, previous transurethral resection of the prostate (TURP) is the only known predicting factor. Alterations of orgasmic function are experienced by approximately 80% after RP. Erectile dysfunction seems to play an important role in waning orgasmic function. OAP is only experienced by a subset of the patients with reported rates varying between 3% and 19%. Sparing of the tips of the seminal vesicles has been shown to double the risk of OAP. PS occurs in 15-68% of RP patients. Nerve sparing and preservation of erectile function may help preserve penile length. With regard to all side effects, studies indicate that they are reduced over time.

CONCLUSIONS: The sexually related side effects summarized in this review are common after RP. Meanwhile, it is difficult to predict which patients are at risk. Daytime incontinence, previous TURP, a lack of nerve sparing, and erectile dysfunction are all associated with the above-mentioned sexually related side effects.
Changes in penile length after radical prostatectomy: investigation of the underlying anatomical mechanism.


PATIENTS AND METHODS: The stretched PL (SPL) of 102 patients was measured before, 10 days after, and at 1, 3, 6, 9, 12, 18, and 24 months after RP. The perpendicular distance from the distal end of the membranous urethra to the midline of the pelvic outlet was measured on mid-sagittal magnetic resonance imaging (MRI) slice at three time points: preoperatively, 10 days after RP, and 12 months after RP. Pre- and postoperative SPLs were compared using paired Student's t-test. Predictors of PL shortening at 10 days and at 12 months after RP were evaluated on univariate and multivariate analyses.

RESULTS: The SPL was shortest 10 days after RP (mean PL shortening from preoperative level: 19.9 mm), and gradually recovered thereafter. SPL at 12 months after RP was not significantly different from preoperative SPL. On MRI examination, the distal end of membranous urethra was found to have moved proximally (mean proximal displacement: 3.9 mm) at 10 days after RP, and to have returned to the preoperative position at 12 months after RP. On univariate analysis, only the volume of the removed prostate was a predictor of SPL change at 10 days after surgery; on multivariate analysis, the association was not statistically significant. No predictor of SPL change was found at 12 months after RP.

Changes in Penile Morphometrics in Men with Erectile Dysfunction after Nerve-Sparing Radical Retropubic Prostatectomy.

Fraiman MC¹, Lepor H, McCullough AR.

better libido but more severe ED than men presenting with ED of other causes. There was a decrease in all penile dimensions after NSRRP. The flaccid and erect measurements of length and circumference decreased 8% and 9%, respectively after surgery (p > 0.05). The most substantial change occurred between the first 4 and 8 months postoperatively. The average change in volume between the first 4 and 8 months was 19% to 22% in the flaccid and erect state, respectively. There is a significant decrease in penile size in men with ED after NSRRP. The etiology may be denervation smooth muscle atrophy, apoptosis, or hypoxia-induced damage to the corpora. Further research is needed to elucidate the nature of these postoperative changes.
Patient-reported Functional Outcomes Following Open, Laparoscopic, and Robotic Assisted Radical Prostatectomy Performed by High-volume Surgeons at High-volume Hospitals.

Gershman B¹, Psutka SP¹, McGovern EJ², Dahl DM², Tabatabaei S², Gettman MT¹, Frank I¹, Carlson RE³, Rangel LJ³, Barry MJ⁴, Blute ML², Karnes RJ⁵.

OBJECTIVE: To examine contemporary patient-reported functional outcomes following open RP (ORP), laparoscopic RP (LRP), and robotic assisted RP (RARP) performed by high-volume surgeons at high-volume hospitals.

DESIGN, SETTINGS, AND PARTICIPANTS: This was a retrospective cohort study of 1686 men with cT1-cT2 prostate cancer treated with ORP (n=441), LRP (n=156), or RARP (n=1089) by high-volume surgeons (annual volume ≥25 cases) at two academic centers from 2009 to 2012. Surveys containing the Expanded Prostate Cancer Index Composite urinary and sexual domains were administered at a median of 30.5 mo postoperatively.

RESULTS AND LIMITATIONS: In total, 6.4% of men reported a moderate or big problem with overall urinary function (ORP 5.8%, LRP 5.1%, RARP 6.8%; p=0.62), whereas 37.3% reported a moderate or big problem with overall sexual function (ORP 37.2%, LRP 36.1%, RARP 37.5%; p=0.95). On multivariable analysis, older age at surgery (odds ratio [OR] 1.08; p<0.0001) was associated with overall urinary bother, whereas older age at surgery (OR: 1.03; p=0.005), preoperative erectile dysfunction treatment (OR: 2.22; p<0.0001), greater prostate volume (OR: 1.01; p=0.02), and RP Gleason score (7 vs 6: OR: 0.96; p=0.004; 8-10 vs 6: OR: 2.25; p=0.0006) were associated with overall sexual bother. Surgical technique was not associated with either functional outcome. Limitations included selection bias and a retrospective design.

CONCLUSIONS: In this study of high-volume surgeons at high-volume hospitals, patients reported excellent functional outcomes independent of surgical technique. These results have implications for patient counseling.
Sexual dysfunction after radiotherapy

- **Erectile dysfunction**
  - EBRT - >41%
  - 3DCRT – 7-72% (1990’s, less studies)
  - IMRT-2-5%?
  - Brachytherapy (0-61%)
  - Brachytherapy + EBRT – 89%

- Vascular damage / multifactorial etiology
  (age, comorbidity, previous prostate surgery, drugs, pre-treatment erectile function, hormonal manipulation)

- Doppler:
  - 63% arteriogenic dysfunction
  - 32% cavernosal
  - 3% neurogenic

- **Predominante etiology of ED in EBRT – arteriogenic**
  - Zelefsky, 1998

- **Ejaculatory disturbances (3-56%)**
  - Reduction/absence of ejaculate volume
  - Discomfort during ejaculation
  - Hemospermia

- **Decreased sexual desire (12-58%)**
- **Decreased intesity of orgasm**

- Dose (<70 Gy)
- Volume of the penile bulb that receives radiation (>70%)
- 18-24 months
In February 2015, men treated with EBRT at our center 3 months to 5 years previously (N = 519) purpose-built questions and validated tools including the Erection Hardness Scale radiation dose of 78 Gy Androgen deprivation therapy was administered according to disease characteristics One hundred nine patients were eligible (sexually active and had completed androgen deprivation therapy) for inclusion.

CONCLUSION:
Orgasmic dysfunction, changes in penile morphology, and sensory disturbances in the penis are common side effects of ERBT.

Results:
- 24% anorgasmia, 44% decreased intensity of their orgasms, 40% increased time to reach orgasm
- 11% anejaculation
- 15% orgasm-associated pain
- 4% climaturia
- 42% subjective penile length loss > 1 cm; 12% altered curvature of their penis
- 6% painful erections
- 27% decreased sensitivity in the penis
- 2% reported a cold sensation, and 2% reported paresthesia
- Increasing time since final treatment increased the risk of penile sensory disturbances (odds ratio = 1.05; P = .028).

Prevalence and Predicting Factors for Commonly Neglected Sexual Side Effects to External-Beam Radiation Therapy for Prostate Cancer.
Frey A¹, Pedersen C², Lindberg H³, Bisbjerg R⁴, Sønksen J⁴, Fode M⁶.
Ten-year outcomes of sexual function after radical prostatectomy: results of a prospective longitudinal study.

Sivarajan G¹, Prabhu V, Taksler GB, Laze J, Lepor H.

OBJECTIVE: To determine the long-term effect of RP on male SF and EF over 10 yr of follow-up.

RESULTS AND LIMITATIONS: After an expected initial decline, time-dependent improvements in SF and EF were observed through 2 yr postoperatively. Overall, SF and EF were both generally stable between 2 and 10 yr following RP. The subgroups of younger men and men with better preoperative function were more likely to maintain their EF and SF through 10 yr following RP. The primary limitation is the potential bias attributable to nonresponders.

CONCLUSIONS: The recovery of EF can extend well beyond 2 yr. There is a significant association between younger age and better preoperative function and the likelihood of experiencing improvements beyond 2 yr. Assessing the comparative effectiveness of treatment options for localized prostate cancer must examine SF beyond 2 yr to account for delayed treatment effects and the natural history of SF in the aging male population.
Sexual Dysfunction and Androgen Deprivation Therapy

• Erectile dysfunction
• Decreased sexual desire
• Ejaculatory and orgasmic disorders

• Decreased testis, penis size anf fibrosis of the corpus cavernosum
• Relational changes, cognitive, affective symptoms, fatigue, sleep disturbance, depression
Sexual bother in men with advanced prostate cancer undergoing androgen deprivation therapy.

Benedict C¹, Traeger L, Dahn JR, Antoni M, Zhou ES, Bustillo N, Penedo FJ.

RESULTS: Participants (N = 80) were 70 years old (standard deviation [SD] = 9.6) and reported 18.7 months (SD = 17.3) of ADT. Sexual dysfunction (mean = 10.1; SD = 18.0) was highly prevalent. Greater sexual bother (lower scores) was related to younger age (β = 0.25, P = 0.03) and fewer months of ADT (β = 0.22, P = 0.05). Controlling for age, months of ADT, current and precancer sexual function, sexual bother correlated with more depressive symptoms (β = -0.24, P = 0.06) and lower QOL (β = 0.25, P = 0.05). Contrary to hypotheses, greater sexual bother was related to greater dyadic satisfaction (β = -0.35, P = 0.03) and cohesion (β = -0.42, P = 0.01).

Effect of androgen deprivation therapy on sexual function and bother in men with prostate cancer: A controlled comparison.

Donovan KA¹, Gonzalez BD¹, Nelson AM², Fishman MN³, Zachariah B⁴, Jacobsen PB¹.

CONCLUSIONS: Most men on ADT for prostate cancer will never return to baseline levels of sexual function. Interventions focused on sexual bother over function and designed to help couples build and maintain satisfying relationship intimacy are likely to more positively affect men’s psychological well-being while on ADT than medical or sexual aids targeting sexual dysfunction.
Iatrogenic Sexual Dysfunction in Prostate cancer

- **Pre-treatment sexual function/ sexual dysfunction consultation**
  - ED pré-treatment? ED medication?
  - Apply questionnaire
    - IIEF - International Index of Erectile Function
      - 5 domains: erection, orgasm, desire, satisfaction and overall satisfaction
    - MSHQ – Male Sexual Health Questionnaire
      - Ejaculation, erection, satisfaction

- **Treat comorbidities**
- **The post-treatment**

- **Decision with the patient**
Take Home Messages

- Iatrogenic sexual dysfunction is very prevalent
- ED is the main complain
- Neglected sexual dysfunction (climatúria, orgasm dysfunction, penile morphometric changes and ejaculation/anejaculation changes) are important for patients and partners
- Discuss sexual dysfunction complications with patients before treatment decision
- Sexual evaluation must be done before treatment
- Erection is different from sexual satisfaction
- Maintaining of intimacy is essential for the recovering process