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Prevalence and treatment options for erectile dysfunction following retropubic prostatectomy for prostate cancer.

Abstract

Prostate cancer is the most common cancer affecting men in the UK. Treatment options for prostate cancer depend on the grade of tumour, the patient's co-existing diseases, and patient choice of treatment. One potentially curative option is surgery, specifically a radical retropubic prostatectomy or variation thereof. As a consequence of the surgery, men commonly experience two side effects, urinary incontinence and erectile dysfunction (ED). This paper outlines the clinical management of ED following surgery and aims to provide an overview of how to assess a man who has developed ED and discuss the various treatment options available, along with the efficacy in terms of recovery of erections.

Key words: erectile dysfunction; prostate cancer; radical retropubic prostatectomy; nursing; treatment; IIEF; Assessment; neuropraxia

Introduction

Prostate cancer is the most common cancer in men, accounting for approximately 23% of all new diagnoses and around 13% of deaths, or around 35,000 new diagnoses each year with 10,000 deaths in England and Wales (Bolland, 2008). Early stage prostate cancer is essentially a symptomless disease, particularly if the tumour is localised to the prostate, and tends to be found during digital rectal examination and/or via a blood sample (prostate

specific antigen or PSA). If the rectal examination is abnormal (i.e. a hard or woody feeling prostate is felt) and/or the PSA level is above the age-adjusted norm, the patient is referred to the Urology team for further investigation (usually biopsy and computerised tomography or bone scan to determine if the tumour has spread).

For organ-confined prostate cancer, treatment options include watchful waiting, active surveillance (where patients are not given active treatment but are reviewed every 6 months radical retropubic prostatectomy (RRP); robotic assisted, radical radiotherapy; brachytherapy; and hormone treatment. A radical prostatectomy has the potential to completely remove the tumour although the common side effects include erectile dysfunction (ED) (20-80%) and urinary incontinence (4-21%) (Bolland, 2008). The cause of these side effects is related to the damage to the neurovascular bundles that lie close to the prostate. Although surgeons attempt to preserve the neurovascular bundles with nerve-sparing surgery, ED is a common side effect, as is penile shortening and urinary incontinence. Even with nerve-sparing surgery, there is a temporary period of neuropraxia where the patient has no spontaneous erections and this can predispose him to penile hypoxia, resulting in permanent damage to the structures in the penis (Raina, 2007). It is difficult to predict the length of time that neuropraxia can last, with some researchers suggesting it is between 9 and 24 months (Zippe, et al. 2001). A goal of ED management is therefore to restore blood flow (and oxygenation) to the penis at an early stage and prevent neuropraxia. This paper examines how to assess a man who has developed ED and explains what treatment options are available to help a) prevent neuropraxia, b) recover erections, and c) limit penile shortening.

Erectile dysfunction

Erectile dysfunction (ED) is the inability to maintain an erection sufficient for adequate sexual intercourse (NIH Consensus, 1993). Following radical prostatectomy Korfage, et al. (2005) reported an 88% increase in the prevalence of ED, which can have a major effect on the individual's self-esteem, quality of life, confidence and life satisfaction resulting in depression and fear (Kubin, et al. 2003).

Assessment of ED

A critical question is *when* to introduce the discussion to patients, i.e. whether pre-surgery or post-surgery. Since ED is a known and common side effect of prostatectomy, patients ideally need to be seen by the ED team before surgery, after the multi-disciplinary panel and the patient have agreed on the most suitable treatment for the cancer.

Taking a comprehensive history (refer to Box 1) enables accurate treatment of ED to be offered. Although the cause of ED is most likely to be the radical prostatectomy, it is also necessary to determine if the patient is hypertensive, diabetic, has vascular disease, renal disease or hypogonadism (Steggall, 2011). Ideally the assessment should involve the patient's sexual partner although this is not always possible.

Assessment	Rationale	Implication for treatment
Surgical history	Nerve-sparing or non-nerve sparing surgery?	An earlier recovery of erectile function may be possible men who have had nerve-sparing surgery
Medical history	Co-existing disease, e.g. diabetes mellitus, cardiac disease? Continence difficulty following surgery?	Pre-existing ED will mean recovery of sexual function may be more difficult/take more time. Severe ED pre-surgery will make recovery of erections extremely difficult. If incontinent, treatment may be delayed until continence resolved
Current medication	Anti-hypertensive use can make management of ED more difficult	Check for contra-indications to pharmacological treatment for ED
Allergies	Interaction with treatment	Interaction with treatment
Tobacco	On-going tobacco use worsens vascular damage	Smoking cessation is strongly recommended
Alcohol (or illicit drugs);	Desensitises the individual to stimulation	Potential to effect success of treatment
Specific history		
Description of the problem	Erection failure/loss of desire? Duration of problem?	ED is an expected consequence of radical prostate surgery but patients need to remain intimate with their partner
Early morning tumescence (EMT)?	A small cohort of men will maintain EMT	Indicates that recovery of erections may be early
Libido	Assess desire for on-going sexual activity	Men may prefer to delay treatment (to recover from surgery) although penile rehabilitation should ideally begin around 6 weeks' after surgery (after removal of a urinary catheter)
Is penetration possible?	Assess strength of erection	Assesses blood flow; may indicate 'strength' of medication required. Is the erection better during masturbation? If yes, there may be a relationship issue to

		be explored
Is intimacy still present?	Need to know if there is some sexual activity	Absence of intimacy is important for both physical and mental health
Psychological factors. Social problems (particularly prior to onset of problem)	Anxieties inhibit function	Feelings of 'impotence' in other areas will be reflected in sexuality – need to resolve underlying problem.
Does the partner know of their visit?	Status of relationship	Address unresolved issues with both partners

Box 1 Assessment of ED in men following radical prostatectomy

International index of erectile function (IIEF)

One way of establishing the severity of ED is by using the International Index of Erectile Function or IIEF, which is either a 5- or 15-item that 'scores' erection difficulty (Rosen, et al. 1997). The 5-item inventory (also referred to as the Sexual Health Inventory Male or SHIM) has good reliability and validity, and has been used extensively in studies of ED (Mahmood et al, 2012). It classifies ED severity with the breakpoint scores of: 1–7 = severe ED; 8–11 = moderate ED; 12–16 = mild to moderate ED; and 17–21 = mild ED. Scores > 21 indicated 'normal' sexual function (Cappelleri and Rosen, 2005). Following surgery, SHIM scores tend to fall from a baseline of around 22 (no ED) to around 4 (Severe ED) (Raina, et al. 2006), irrespective of whether the surgery was nerve sparing or non-nerve sparing).

When is sexual activity advisable following radical retropubic prostatectomy?

Provided there are no surgical complications treatment for ED can begin around 6 weeks after surgery. If incontinent of urine, resumption of sexual activity may be delayed, but this should not prevent some form of treatment for ED as the goal is to prevent or limit neuropraxia. However, patients should refrain from attempting sexual activity if they have any unstable cardiac condition or have had any cardiac event within the last 3 months.

There is an energy requirement for sexual activity of 3.7 to 5 metabolic equivalents (METs) (Sainz, et al. 2004) which equates to climbing 2 flights of stairs without getting very short of breath/use a lawn mower to cut a small lawn. If the patient cannot undertake those activities they should not be considered fit enough to attempt sexual activity (Steggall and Butler, 2012).

Treatment options

The aim of treatment for erectile dysfunction is to restore sexual function, although it is not necessarily penetration/maintenance of an erection that is of critical importance, but the intimacy that sexual activity brings. A man who has undergone RRP will have to come to terms with the initial cancer diagnosis as well as the changes to his body that the surgery brings, and his partner will have also had to rationalise the journey that they have been through. Sexual activity is primarily concerned with communication as well as sexual intercourse; in a relationship where avoidance of intimacy has occurred, the first step should be a discussion with the sexual partner of what each person expects from the encounter and what will need to be done to aid return of erections.

There are a range of options for managing ED in men who have had RRP and these include tablets, phosphodiesterase type 5 inhibitors (PDE5Is), Medicated Urethral System for Erections (MUSE), intracavernosal injections, vacuum devices, counselling and penile prosthesis (Steggall, 2011). There is no formal 'first-line' therapy and the decision regarding which option to choose is based on patient preference, tolerability and likely efficacy (refer to table 2).

Name	Dosage	Administration guidance	Contraindications
Sildenafil Citrate	25, 50 or 100mg as required	Takes an hour to work; taken on an empty stomach;	Where sexual activity is inadvisable; concomitant use of nitrates; caution with alpha blockers (recommend reduced dose); use with Nicorandil;
Tadalafil	2.5 or 5mg once a day; 10-20mg as required	Daily dosing takes 5-7 days to reach steady-state plasma concentrations; PRN – takes between 30 minutes and 2 hours to work; can be taken with food and alcohol;	As above
Vardenafil	10-20mg as required	Takes around 30 minutes to work; can be taken with food and	As above

		alcohol	
Medicated Urethral System for Erections (MUSE)	125-1000µg as required	Need to pass urine beforehand; takes 15 minutes to be absorbed	Both MUSE and ICI can also lower blood pressure, and therefore baseline blood pressure levels are needed before administration. Test doses of MUSE and ICI should be given in secondary care in case of anaphylaxis or other adverse event
Intracavernosal injections (Viridal/Caverject)	2.5-40µg as required	Takes around 15 minutes to work;	As above, but additionally: bleeding from the injection site, needle phobia, scarring, increased risk of acquiring sexually transmitted infections and priapism (an erection that lasts for several hours) (Urciuoli <i>et al.</i> , 2004).
Vacuum (erection) devices	Used daily as a training aid; with a constriction band for sexual activity	Takes between 10-30 minutes to get an erection;	Should be avoided in men with a pre-disposition to bruising;

Table 2 Treatment options for managing erectile dysfunction following RRP

The role of the nurse

A key role for the nurse is to identify the risks for developing ED, and to have a strategy or pathway to begin discussions of ED treatment options, preferably before the patient has surgery. Once the patient is having treatment, the plan is then one of guidance and encouragement until the man has restored his sexual function.

Phosphodiesterase type 5 inhibitors (PDE5Is)

There are a number of studies that have used PDE5Is in men who have had RRP that utilised the IIEF to determine 'successes or 'failure' Zagaja, et al. (2000) contended that daily use Sildenafil resulted in improved quality erection, although the results were more marked in men who were younger and previously potent, and had nerve-sparing surgery. These results were echoed in Padma-Nathan, et al. (2008) although they used sildenafil citrate each night, and concluded that administration of 50 or 100mg for 36 weeks increased return of spontaneous erections. Although Gontero, et al. (2005) identified that up to 10% of men using sildenafil citrate improved the quality of their erection, 50% of men had ceased to use any form of intervention within 1 year of surgery. Furthermore, Chen, et al. (2001) using sildenafil citrate identified that 79% reported adverse reactions to the medication such as flushing, headache, dizziness and eye redness, which may contribute to discontinuation long term. From the literature available, it can be concluded that PDE5Is may improve erection recovery (Montorsi and McCullough, 2005) although it remains to be seen whether men remain on therapy long term.

Alprostadil

Intracavernosal injections (ICI) have been used in the clinical management of ED although the need for motivation is high as the man needs to give himself and injection into his penis on each occasion that sexual activity is desired. Yiou, et al. (2010) concluded that, whilst ICI improved tumescence post-surgery, the quality of the erection was not as firm as pre-operative levels, and there was a high drop out from treatment due to the side effect of painful erections. Raina, et al. (2007) used Medicated Urethral System for Erection (MUSE) three times per week for 6 months, and reported that this resulted in a shortened time to erectile recovery; half of their sample were able to have successful penetration after 6 months of treatment although all reported side effects of urethral burning/penile pain.

Non-pharmacological interventions

The studies that have used vacuum devices have found an overall improvement in IIEF and satisfaction with erections at various time points following surgery, as well as preventing penile atrophy (Yuan, et al. 2010). Raina, et al. (2006) who used daily use vacuum therapy 1-month post-surgery identified that IIEF increased in the treatment group and that those who regularly used the vacuum device had markedly less penile shortening. Kohler, et al. (2007) conducted a similar study although they used a longer time frame for active treatment (12-months) and also identified an increase in IIEF and reduction in penile shortening.

Combination approaches

Chen, et al. (2001) compared preference between vacuum therapy and sildenafil citrate and although preference was for oral medication, efficacy (in terms of improved IIEF) was greater in men using a vacuum device. Raina, et al. (2010) compared vacuum therapy with sildenafil citrate, identifying that both sexual satisfaction and penile rigidity was improved with a combination approach compared with single therapy alone. Mydlo, et al. (2005) examined Sildenafil Citrate or Vardenafil titrated to maximum doses followed by ICI, concluding that a combination approach facilitated improvements in sexual satisfaction and erection recovery.

From the corpus of literature available, it would seem that vacuum devices have a role in both recovery of erections, reducing neuropraxia *and* in preventing penile shortening (Dalkin, et al. 2007) provided they are used regularly (every day or two) over a 3- 6-month period, although could be longer, particularly in men who had erection trouble before surgery. However, not all men will benefit from (or want) combination approaches and may wish to consider a penile prosthesis.

Penile prosthesis

If pharmacological or vacuum therapy is unsuccessful, or if the patient prefers, he can opt for a penile prosthesis or implant. This requires surgery to replace the corpus cavernosa with malleable rods or fluid filled chambers that can be 'inflated/deflated' on demand. Success rates for penile prostheses have been reported as up to 90% (Cummings, 2006).

Irrespective of which treatment the man and his partner agree to, some men will benefit from relationship or psychosexual counselling.

Psychosexual counselling

ED can have a profound effect on the man's sense of self and this can affect his relationship with his sexual partner. Although the cause of ED in this group of patients is almost certainly associated with surgery, the man has also had to come to terms with a cancer diagnosis, which has the potential to alter the way he feels about himself. Some men may prefer to explore issues that may arise as a result of either the cancer diagnosis or the side effects of the treatment, and therefore psychosexual or relationship counselling may be required.

Conclusion

ED is common following a radical retropubic prostatectomy (whether nerve-sparing or not). Men who had erections that were firm enough for penetration and maintenance of sexual activity may find it 'easier' to regain erections post operatively compared with men who had ED prior to surgery, although it is difficult to predict how long that recovery will take (if ever).

Men should be encouraged to talk about the potential for erectile dysfunction pre-surgery to allow accurate assessment of whether ED is present or not, and to prepare the man for coping after surgery. Although options for treatment include PDE5Is, Alprostadil or Vacuum Devices alone, there is a growing body of literature that points to a combination approach

yielding earlier recovery of erections compared with monotherapy. Therapy selection should remain patient driven but based on the best available evidence to support any decision.

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