Erectile dysfunction (ED) remains a common cause of significant post-operative morbidity for men undergoing radical therapies for prostate cancers or other pelvic malignancies, as the cavernous nerves (CNs) are inadvertently transected, lacerated, or stretched (neuropraxia) at the time of surgery.

Refrainments in anatomic surgical technique, as evidenced by an improved understanding of penile autonomic innervation, first advocated by Walsh and Lue in the 1980s, and the implementation of innovative technological advances, such as laparoscopic and robot-assisted surgery, have led to significant improvements in post-operative erectile function. Most men, however, still demonstrate compromised erectile function (delayed, compromised or lack of post-surgical potency) as varying degrees of CN damage occur even with successful bilateral nerve-sparing procedures. Contemporary data indicate that the probability of ED following radical prostatectomy for clinically localised cancer of the prostate is 20-90% at 24 months, even in institutions with high surgical volumes.

With CN injury, definite pathological changes are observed in the penis: including apoptosis of smooth muscle and endothelium, reduction of nitric oxide synthase (NOS) nerve density, up-regulation of fibroproliferative cytokines, and smooth muscle fibrosis or loss of cavernosal cycling between flaccid and erect state, with the potential for further structural damage to the cavernosal smooth muscle. With transection or neuropraxia, there can be degeneration distal to the level of injury, compromising the transport of neurotrophins (neurotrophic factors).

It is imperative, therefore, that penile erectile function rehabilitation starts as soon as the early post-operative period after radical prostatectomy. There are three different approaches to rehabilitation: Neuromodulation, Electrical Stimulation and use of PDE-5 inhibitors.

Nerve Growth Factor, a neurotrophin, has received considerable interest because of its ability to regenerate peripheral nerves in experimental animals. The immunosuppressant drug FK506 (tacrolimus), as an immunophilin ligand, has neuroprotective and neuregenerative properties, which was first demonstrated at the in vivo level in animals. Use of stem cell/tissue engineering or gene therapy is still confined to the laboratory and will not be in clinical trials anytime soon.

Erectile stimulation, with or without the use of a surgural nerve graft, is used in cases where there is CN loss during prostatectomy. Riding on the success of using direct electrical stimulation of the cavernous nerves in animal studies and also during radical prostatectomy, direct electrical stimulation of the corpus cavernosum nerves is somewhat successful in restoring response to vasoactive medications in ED patients. The feasibility of implanting electrical stimulating devices near the CN at the time of surgery is being studied.

The use of other types of medications, like tacrolimus, as an immunophilin ligand, or large amounts of corticosteroids, have been tried with limited success only. The theory behind using steroids was to minimise the level of inflammation at the surgical site. Even at high doses, there was no discernible differences between the steroid group or the placebo group. In a phase II, multicentre, randomised, double blind, placebo-controlled trial using a non-immunosuppressant immunophilin ligand in preoperatively potent men undergoing nerve-sparing radical prostatectomy has been initiated to determine whether the treatment improves erectile function recovery. The study combines preoperative and postoperative dosing and allows for phosphodiesterase 5 (PDE-5) inhibitor use on an intermittent basis.

The most success in the treatment of erectile dysfunction after radical prostatectomy is with PDE-5 inhibitors. In a study published in the British Journal of Urology (February 2008), 43 men were divided into a sildenafil 25 mg nightly group and a placebo group. The medication was started the night after catheter removal, usually 5 to 8 days after the radical prostatectomy. It is interesting to note that, even on the first night after catheter removal, 95% of the men had one to five nocturnal erections, as measured by the nocturnal tumescence penile scans. At 52 weeks, a significant difference was demonstrated in the time to recovery, the International Index of Erectile Function, IIEF-5, scores and overall potency (86% vs 66%).

In another study published in the J Sexual Medicine, the group from New York University used higher doses of sildenafil at 50 and 100 mg. The study period was for 36 weeks of nightly medications after radical prostatectomy. Post-operative IIEF scores all decreased, as expected. There was a dose-related gradual increase in rigidity with time in the two
treatment groups compared with the placebo group, which showed little improvement. Eight weeks after termination of the medications, natural or native erections reported by the three groups were: 24% for the 50 mg group, 33% of those receiving 100mg of sildenafil, and only 5% in the placebo group. Sildenafil demonstrated a definite efficacy in improving nocturnal and native, pharmaceutically unassisted erectile function.

The group from Johns Hopkins University Brady Urological Institute, reviewed their experience and research in an article published in February 2008 issue of the International Journal of Impotence Research. They reviewed the basic physiology of penile erections. Novel means of delivering stem and endothelial cells and stem cell biology were discussed as potential cell-based therapy is showing promise in the treatment of erectile dysfunction.

References

4. Burnett AL. Erectile dysfunction following radical prostatectomy. JAMA 2005; 293; 2648.