

Management of post-prostatectomy erectile dysfunction

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The management of post-prostatectomy erectile function has been debated since the nerve sparing radical prostatectomy was first introduced. A number of penile rehabilitation protocols have been proposed with varying degrees of success and patient satisfaction. My management of post-prostatectomy erectile dysfunction has evolved based on an honest and critical appraisal of the literature and my own experience and research. A review of major studies published on the topic of post-prostatectomy penile rehabilitation is included here, in addition to a critical evaluation of my own clinical practice. After evaluating the efficacy of

these various approaches, it is clear to me that a nerve sparing procedure is only one of many factors involved in recovering erectile function. Moreover, in addition to assessing a patient's goals and their motivation for erectile function after prostatectomy, setting appropriate patient expectations is paramount to avoiding patient frustration. A frank evaluation and discussion with a patient and their partner is paramount to managing these expectations. A "one size fits all" approach is not appropriate. Herein, I discuss the evolution of my approach to managing post-prostatectomy erectile dysfunction.

Key Words: phosphodiesterase type-5 inhibitor, erectile dysfunction, radical prostatectomy, vacuum erection device, rehabilitation

Introduction

The optimal management of post-prostatectomy erectile function has been a point of both research and controversy since the nerve sparing radical prostatectomy was introduced as a mainstay treatment for organ confined prostate cancer. Reporting of the incidence of erectile function after this surgery has varied widely, with no true consensus regarding what a man can expect immediately after surgery and in the subsequent years. Potency rates have been reported anywhere between 14% and 84%.¹⁻⁴ Inconsistent reporting of this problematic consequence of surgery has historically led to an underestimation of the problem due to several factors.

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Defining post-prostatectomy impotence

There is no standard definition of acceptable potency after prostatectomy. The definition most often found in our literature, "an erection adequate for intercourse within one year of surgery," is entirely inadequate. It does not require a firm erection nor does it require an erection that lasts long enough to reach orgasm. It also does not specify whether the hand is used to stabilize or insert the erection during the act of intercourse. I have found that most men who would be considered potent by this definition consider themselves impotent and can be quite unhappy. It may be true that in younger, highly motivated patients undergoing a prostatectomy in experienced hands, this endpoint may be achieved in upwards of 90% of patients.⁵ I have found, however, that counseling patients that they will return to baseline performance with this level of certainty almost uniformly generates a level of expectation that will lead to disappointment.

I use the definition of potency that most impotence researchers use, which is “the ability to achieve successful intercourse, completed by orgasm, during over fifty percent of attempts.” Most of these patients will consider themselves potent, but not perfect or baseline. When using this measure of success, far fewer than 90% of men achieve potency. The International Index of Erectile Function (IIEF) questionnaire is our most useful validated survey to measure post-prostatectomy erectile function. Even in large series of high volume surgeons, an average of only 50%-60% of patients return to a degree of function approximating their baseline score at 1 year, regardless of technique.⁶ While these series may show continued improvement up to 5 years after prostatectomy, absolute baseline levels are rarely reached.⁷

Background on nerve sparing

Since the advent of the open nerve sparing radical retropubic prostatectomy, the idea has been fomented that success or failure in restoring preoperative erectile levels is solely dependent on the quality of the nerve sparing portion of the operation. Indeed, erectile rates have been tied to experience, an assessment I agree with.⁸ However, I feel, as do most other experienced robotic surgeons, that the ability to spare erectogenic nerve bundles is just one of the many factors that will dictate success. Rather, I believe that a man's return of erectile function has more to do with blood flow. As a result, at least part of the reason that function improves over time is the vascular collateralization that is presumably taking place in the years after suffering the initial insult of pelvic surgery. Moreover, robotic surgeons can usually see arterial flow within the dorsal venous complex or accessory pudendal arteries that can often be spared during the surgery, vessels that are not typically appreciated in the open setting.⁹

Patients will often see claims for high success rates without any stratification in a series allowing for important factors such as age, preoperative function, preoperative cardiovascular status that may be indicative of blood flow, or interest levels of both patient and partner. I feel that these factors are as important, if not more important, than the nerve sparing portion of the procedure, which is, in experienced hands, the only relative constant among these variables. I will explain to patients that unless they are in the highest stratification for all of these indicators of sexual performance, they cannot expect the high success rates they have seen on the internet or elsewhere. I will also point out that a man will generally need the next level up of medical help for achieving an erection after prostatectomy from the help they needed before

the procedure. If they are phosphodiesterase type-5 inhibitor (PDE-5i) dependent before the surgery, they will likely permanently need intraurethral medications, intracavernosal injections (ICI), or a vacuum erection device (VED) after the procedure. If they need no help before the procedure, they will generally at least need PDE-5 inhibitors permanently after the procedure, if only to feel confident in their abilities. Sometimes I think the worst thing a patient can hear is the success rate of a series of patients who are young, have perfect erections, maintain rigorous exercise regimens, and are not only highly motivated for sex themselves but who have partners that are perhaps even more motivated than they are. This will only lead to disappointment unless they themselves are in that stratification, and few patients are. I uniformly present an average outcome, from a group of patients within which the patient would find himself. I feel that management of expectations is perhaps the single most important thing in helping patients with their erections after prostatectomy.¹⁰

The evolution of post-prostatectomy penile rehabilitation techniques

My approach to helping patients get their erections back after prostatectomy has transformed over the last several years, in many ways shaped not only by personal experience but by reported data over time. Montorsi introduced the concept of penile rehabilitation in 1997 with a small series of patients who received intracavernous injection (ICI) on a regular basis after prostatectomy.¹¹ In the study, 30 patients with clinically localized prostate cancer were randomized to either alprostadil injections three times per week for 3 months or observation without the use of erectogenic treatments. At a 6 month follow up, patient erectile function was assessed and revealed 67% of patients in the treatment arm achieved spontaneous erections sufficient for sexual intercourse versus 20% in the control arm ($p < 0.01$). The study had several notable limitations including a small sample size, lack of assessment of patient satisfaction/questionnaire, and a short duration of follow up as erectile function continues to improve over time. However, it served as a proof of principle for several years of the notion that a regular drug regimen could aid in spontaneous recovery after prostatectomy. The general theory is that by forcing the penis to ask for blood flow on a regular basis, a quicker return of blood flow necessary to achieve erections would occur. Some small, poorly controlled studies using the VED have also been performed lending itself to this conclusion, although most believe the VED to only deliver poorly oxygenated blood to the penis, thus the etiology of success here is less clear.^{12,13}

Padma-Nathan, McCullough and authors solidified this idea by showing that daily use of sildenafil for 9 months following prostatectomy led to an almost 7 fold increase in spontaneous erections at 1 year.¹⁴ Patients enrolled in the study had to have normal preoperative erectile function (based on an IIEF Q3 and Q4 sum greater than 8), wish to return to sexual activity after surgery and be in a stable, heterosexual relationship. Patients were randomly assigned to start a 36 week course of placebo, sildenafil 50 mg, or sildenafil 100 mg, beginning 4 weeks after their surgery. After the 36 week treatment period, patients were left untreated for 8 weeks without being allowed to use any form of ED treatment. The authors found that 4% of placebo and 26% of sildenafil treated patients had spontaneous erections sufficient for intercourse without the use of any other ED therapies. They concluded that in this selected, highly motivated, good preoperative functioning group, nightly sildenafil resulted in the return of spontaneous erections. These findings were in line with the 1997 Montorsi findings that penile rehabilitation could result in spontaneous erections, but could now be performed with something far more feasible such as a pill instead of a penile injection. This approach became popularized using a PDE-5 inhibitor either daily or in other dosing regimens. For years, I used tadalafil three times a week for this purpose, and various regimens using PDE-5 inhibitors on a regular basis have become the standard in the community after prostatectomy.¹⁵

Building on this paradigm, McCullough, Engel and authors reported on a study using intraurethral alprostadil (IUA) in a sub-therapeutic daily dose versus sildenafil (50 mg)¹⁶ using the same study design as the previous sildenafil penile rehabilitation study.⁶ What was found was mild superiority of IUA early in the 1 year study period, and no difference at 1 year. There was no placebo arm, but both the IUA group and the sildenafil group resulted in IIEF curves typical of other experienced surgeons in the absence of a penile rehabilitation regimen, thus raising some concern that penile rehabilitation may have not been the determining factor of success in this study. This study also impressed upon me the need to offer patients some form of combination therapy, whereby a part of the regimen over the first year must include something with higher efficacy than a PDE-5 inhibitor so that the patient can reliably achieve a usable erection (in this case, IUA). When this occurred in this study, patients tended to be far more patient and willing to wait the year or two it typically takes the PDE-5 inhibitor to offer reliable efficacy. Patients seemed uniformly happier when they were able to achieve sexual intimacy while waiting for their own function to return.

The most definitive study on the efficacy of an oral penile rehabilitation protocol was a large, multi-site, placebo controlled trial performed in Europe reported by Montorsi and authors.¹⁷ The study authors felt that the nightly sildenafil study¹⁴ was limited due to the relatively small and highly selected patient cohort, and the lack of comparison with a third arm of patients who would take the PDE-5 inhibitor on an as needed (on-demand) basis. In this study, over six hundred patients at 87 centers were evaluated, providing a population where selection bias is eliminated, and where surgeon experience and patient and partner motivation are not the prime factors; where an "average" population is being studied. The patients were randomly assigned to one of three groups for 9 months after surgery, similar to the model of the sildenafil study. One third received daily vardenafil as a true penile rehabilitation regimen, one third were simply given vardenafil for on-demand use, and one third placebo. After the 9 month treatment period, all patients entered a 2 month single-blind placebo washout period such that none received a PDE-5 inhibitor. Finally, a 2 month open-label vardenafil on-demand period followed with dose adjustment. IIEF scores ≥ 22 were found in 24.8%, 32.0%, and 48.2% for the placebo, vardenafil nightly, and vardenafil on demand groups, respectively ($p < 0.01$ for both vardenafil on-demand versus placebo and vardenafil on-demand versus nightly). The study showed that the group that had the best result was the group using on-demand vardenafil only. This study, combined with my study of IUA, raised my concerns that penile rehabilitation with PDE-5 inhibitors may not be efficacious. Perhaps the original sildenafil study, which was not of the quality of this latter vardenafil study, could not be reproduced.

The other problem with the notion of implementing a daily or near daily PDE-5 inhibitor based program of penile rehabilitation is that the medication can be costly over time. PDE5 inhibitors and IUA are rarely covered by insurance in our area of the country, and each dose can cost over \$20USD. Over a 36 week penile rehabilitation course as suggested by the sildenafil study, the cost would be \$5040USD for sildenafil or \$2160USD for tadalafil, with no better, or even worse outcome than on-demand use. The cost for IUA used on a daily basis would be even higher. I had noticed poor compliance in my own practice, and decided to study it. Previous studies generally report on data achieved by supplying patients with free medicine. I designed a small, pilot study, where I combined my observation that the perfect post-prostatectomy program should include a combination of approaches where part of it could provide a means by which to allow for an erection early in the recovery phase while the other part would

be the use of PDE-5 inhibitors. I selected approximately 40 of my most motivated patients. All had undergone a nerve sparing robotic prostatectomy, and all were asked to take tadalafil 20 mg, three times per week. However, roughly one half were asked to use a VED, unbanded, for 5-10 minutes per day. All were asked to try to achieve intercourse either with tadalafil or with the VED. Study visits were every 3 months for 1 year following surgery. What was found in this study was that both groups had poor compliance to tadalafil (approximately 40%). However, the patients using the VED had success early in the study period which improved over the year such that their IIEF-5 was almost 90% of original values. Patients taking PDE-5 inhibitors alone, on the other hand, had an approximate 60% return of IIEF-5 score,

a pattern repeated in nearly every previous study using this validated questionnaire.¹⁸

Current post-prostatectomy penile rehabilitation technique

This small study has thus helped shape what I do today for these patients. I am always honest with them. I make sure to manage their expectations of outcome after I have stratified them based on all of their factors, not just whether I will spare their nerves or not. I have a frank discussion with both patient and partner about the time course of return of function, and I ask them to decide what their level of motivation is to work on their erections after surgery. I make sure they understand

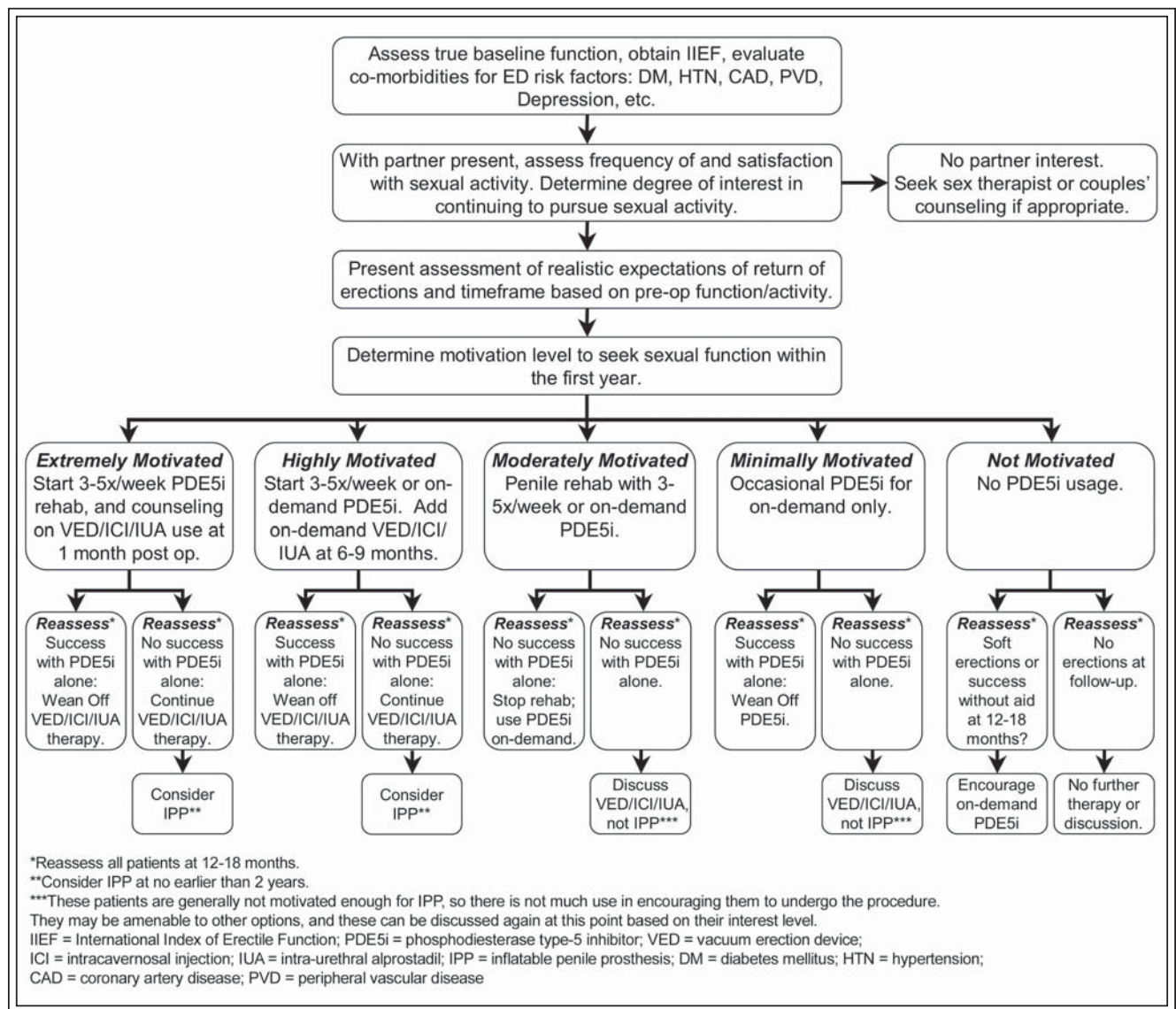


Figure 1. Algorithm on management strategies for post-prostatectomy erectile function.

that PDE-5 inhibitors alone will generally not provide a reliable solution within the first year after surgery. For those that are motivated, I teach them self injection therapy or provide a VED once continence is achieved, generally between 1 and 3 months after surgery. I do ask that they take a PDE-5 inhibitor as frequently as possible after surgery for the first year, recognizing that they will likely not comply fully. I point out early on that insurance will not provide the medication, and that at the very least I would like them to use the PDE-5 inhibitor for on-demand usage several times before seeing me each 3 month period so I can gauge their response, compare their results to others, and predict their eventual success. My use of IUA has focused primarily on those patients that are close to success with PDE-5 inhibitors but not quite there yet. A full algorithm on this approach is provided here in Figure 1. I recommend reassessing the patient at 12-18 months after surgery to determine their level of function, overall satisfaction, and how to best manage their erectile function in the future.

In this way, I feel I have happier patients with realistic expectations. The "one size fits all" approach is not appropriate here. In this way, I am able to apply the amount of help that the couple wants. Therefore, what is offered to the highly motivated patient will be very different in my practice than the more typical couple who is not particularly sexually active and would not be willing to undergo an aggressive postoperative penile rehabilitation program. By being honest with the patient about expectations and allowing the couple to play a major part in finding a regimen that would best match their needs and their relationship more individually, I feel I can increase overall patient satisfaction and achieve an acceptable outcome more readily.

Disclosures

Joseph E. Jamal, MD - None

Jason D. Engel, MD - Researcher for Vivus and Spectrum Pharmaceuticals

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