Erectile dysfunction in robotic radical prostatectomy: Outcomes and management

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ABSTRACT

Robot-assisted laparoscopic prostatectomy (RALP) has emerged as the most common treatment for localized prostate cancer. With improved surgical precision, RALP has produced hope of improved potency rates, especially with the advent of nerve-sparing and other modified techniques. However, erectile dysfunction (ED) remains a significant problem for many men regardless of surgical technique. To identify the functional outcomes of robotic versus open and laparoscopic techniques, new robotic surgical techniques and current treatment options of ED following RALP. A Medline search was performed in March 2014 to identify studies comparing RALP with open retropubic radical prostatectomy (RRP) and laparoscopic radical prostatectomy, modified RALP techniques and treatment options and management for ED following radical prostatectomy. RALP demonstrates adequate potency rates without compromising oncologic benefit, with observed benefit for potency rates compared with RRP. Additionally, specific surgical technical modifications appear to provide benefit over traditional RALP. Phosphodiesterase-5 inhibitors (PDE5I) demonstrate benefit for ED treatment compared with placebo. However, long-term benefit is often lost after use. Other therapies have been less extensively studied. Additionally, correct patient identification is important for greatest clinical benefit. RALP appears to provide beneficial potency rates compared with RRP; however, these effects are most pronounced at high-volume centers with experienced surgeons. No optimal rehabilitation program with PDE5Is has been identified based on current data. Additionally, vacuum erection devices, intracavernosal injections and other techniques have not been well validated for post RALP ED treatment.

Key words: Erectile dysfunction, robotic radical prostatectomy, penile rehabilitation

INTRODUCTION

Prostate cancer (CaP) remains the most common malignancy in men in the United States.[1] Retropubic radical prostatectomy (RRP) remains the gold standard for locally invasive disease;[2] however, robot-assisted laparoscopic prostatectomy (RALP) has emerged as the most common technique.[3] Although RALP has reduced complications and length of stay,[4] there is still unclear evidence whether RALP reduces erectile dysfunction (ED) post-operatively. Data show that 60% of men report ED 18 months post-operatively,[5] 20% report erections strong enough for intercourse at —5 years of follow-up[5] and only 20% of men return to pre-operative erectile function at —1 year post-operatively.[6] These findings have led to the development of penile rehabilitation programs to improve long-term erectile function. The functional outcomes of robotic versus open and laparoscopic techniques, new robotic surgical techniques and current treatment options and management of ED following RALP are examined in this paper.

MATERIALS AND METHODS

A systematic review using the Medline database was performed in March 2014. The search terms included "radical prostatectomy," "erectile dysfunction" and "robot" and "radical prostatectomy," "erectile dysfunction" and "robotic" with the following limits used: Humans, English and gender (male). Articles were screened using abstracts and those selected underwent full review. Two hundred and thirty-three articles were obtained. All articles' abstracts were reviewed. Those that compared RALP with RRP or laparoscopic radical prostatectomy (LRP) and articles comparing modified RALP techniques with traditional

RALP were included. All articles' abstracts were reviewed. To identify treatment options for ED post-RALP, a similar Medline database search was performed. The search terms included "radical prostatectomy," "erectile dysfunction" and "penile rehabilitation." One hundred and twenty articles were obtained. All abstracts were reviewed. Given the numerous articles available for such a broad subject matter, those that are included in this article were determined to be most critical to the subject matter.

RESULTS

Erectile function outcomes following RRP

After a thorough review of the articles obtained, 23 articles addressing ED following RALP were included in this review as outlined in Table 1. Improved surgical precision and reduced complication rates have provided hope that RALP provides greater potency rates with preservation of oncologic outcomes. A meta-analysis by Ficarra *et al*. identified 31 studies that assessed potency following RALP.[7] At 1 and —2 years, the potency rates were 70% (54-90%) and 79% (63-94%), respectively. When including only studies that fulfilled six or more of the Mulhall criteria, the 1- and 2-year potency rates were 76% (62-90%) and 82% (69-94%), respectively. The Mulhall criteria were developed to better assess the validity of reported ED rates following radical prostatectomy (RP).[8] Criteria from the analysis determined to be most important were study population factors, population demographics, means of data acquisition, variability in questionnaire use, duration post-operatively at evaluation, baseline erectile function status, the definition of adequate erectile function and the definition of quality and consistency of erection. When comparing multiple studies, it is easier to compare the results if a greater number of these criteria are met.

In the same study, seven studies compared RALP with RRP.[7] The 1-year potency rates were superior for RALP (OR 2.84, $P = 0.002$). A recent meta-analysis from Moran *et al*.[9] identified nine studies comparing potency following RALP and RRP. Men undergoing RALP were more likely to regain sexual function at —1 year post-operatively than RRP (RR 1.60, $P < 0.001$). One randomized control study produced 1-year potency rates of 77% and 32% ($P < 0.0001$) in 52 and 64 men who underwent RALP and LRP, respectively.[10] However, meta-analyses of RALP versus LRP have only shown a trend in favor of RALP in potency recovery (OR 1.89, $P = 0.21$;[7] RR 1.49, $P = 0.392$[9]).

Novara *et al*. analyzed the potency rates (International Index of Erectile Function-Erectile Function domain [IIEF-EF] >18) of 208 men who underwent bilateral nerve sparing (BNS) RALP.[11] Potency was 62% at 12 months post-operatively. Independent predictors of potency were age (HR 2.828, $P < 0.001$), Charlson comorbidity index (CCI) (HR 2.992, $P = 0.007$) and baseline IIEF-EF score (HR

0.843, $P < 0.001$). The potency rates were 81.9%, 56.7% and 28.6% ($P < 0.001$) for the low-, intermediate- and high-risk groups, respectively, as proposed by Briganti *et al*.[12] Further, substratification of the intermediate-risk group to pre-operative IIEF-EF scores of 18-21 and 11-17 produced potency rates of 68.8% and 27% ($P < 0.001$), respectively. A prospective comparative study of 609 patients treated with BNS RALP or RRP[13] stratified the patients similarly.[12] The 2-year potency rates (IIEF-EF > 22) were higher in the overall, low- and intermediate-risk populations for RALP versus RRP (67.8% vs. 52.1%, $P < 0.001$; 87.6% vs. 77.5%, $P < 0.001$; 67.2% vs. 55.7%, $P < 0.001$). Further studies have shown that age (OR 0.92, $P < 0.0001$;[14] OR 0.95, $P = 0.004$[15]), baseline Sexual Health Inventory of Men (SHIM) score (OR 1.1, $P < 0.0001$),[14] erection suitable for intercourse (ESI) at baseline (OR 0.95, $P = 0.019$)[15] and BNS (OR 2.92, $P < 0.001$)[14] were independently associated with recovering erectile function. However, this is in contrast to data reporting 87.5% and 89% of Medicare-aged men having "moderate or big problems with sexual function" for RALP and RRP, respectively, at an average of 14 months of follow-up.[16]

Several attempts at modified RALP techniques have been performed and the results are shown in Table 2.

Data comparing extraperitoneal versus transperitoneal BNS RALP did not identify a difference in the 12-month potency rates.[17] Comparing cautery and non-cautery techniques has produced conflicting results, with Ahlering *et al*. showing a benefit with the cautery-free technique[18] but Samadi *et al*. not demonstrating any benefit with the athermal technique in a larger study.[19] Traction-free techniques have also been conflicting. In a technique where O_2 tissue monitoring allowed intraoperative surgical modification for reduced traction, benefit was noted.[20] However, a study from Kowalczyk *et al*. did not demonstrate benefit in the traction-free technique at 12 months.[15] Thus far, only retrograde[21] and intraoperative cooling[22] dissection have proven beneficial in potency rates.

The Veil of Aphrodite technique was developed to provide the greatest nerve sparing (NS) possible. Now known as the Vattikuti Institute prostatectomy (VIP) technique, the technique has been further modified and now involves "superveiling," bladder drainage through a suprapubic tube and limited obturator and internal iliac node dissection with preference to the external iliac nodes for low- and intermediate-risk patients.[23] In 85 men with these modifications, 94% of men were able to complete successful intercourse at 6-18 months post-operatively with an average SHIM score = 18.[23] These modifications are in addition to previously described early transection of the bladder neck, preservation of the prostatic fascia and control of the dorsal vein complex after dissection of the prostatic apex.[24] Analysis of the original VIP technique of 1142 men

Table 1: Studies included in the analysis for ED outcomes following RALP

Source	Study type	Age (years)	Validated criteria	Comparison (no. of patients)	Outcomes
[7]	Meta-analysis	N/A	ESI, SHIM>21, SHIM>18	RALP (756) vs. RRP (843)	OR 2.84 with RALP for potency return
[9]	Meta-analysis	60.5 vs. 61.6	N/A	RALP (774) vs. RRP (1175)	RR 1.60 with RALP for potency return
[10]	Randomized, prospective	61.1 vs. 59.6, *P*=0.13	12-month capability for intercourse rate with or without PDE5Is	RALP (64) LRP (64)	77% 32%
[11]	Prospective observational	61.2	IIEF-6≥18	RALP (208) Low risk Intermediate risk High risk	 81.9% 56.7% 28.6%
[12]	Retrospective cohort	61.9	IIEF-EF≥22	BNS RALP Low risk (184) Intermediate risk (115) High risk (136)	 81.9% 56.7% 28.6%
[13]	Non-randomized, prospective observational	61.2 vs. 61.3, *P*=0.5	IIEF-EF≥22	RALP (315) vs. RRP (294) Low risk Intermediate risk High risk	 67.8% vs. 52.1% 87.6% vs. 77.5% 67.2% vs. 55.7%
[14]	Prospective observational	60	ESI	RALP (1436)	75%
[15]	Retrospective cohort	59.6 vs. 57.9, *P*=0.001	ESI	No traction (58) Traction (35)	50% 54%
[16]	Retrospective population based	>65	Non-validated "having moderate or big problem" with sexual function	RALP (406) RRP (220)	87.5% 89.0%
[7]	Prospective observational	66.3 vs. 65.8, *P*=0.612	SHIM≥22	Extraperitoneal (93) Transperitoneal (56)	55% 52%
[18]	Prospective observational	56.5 vs. 56.3	ESI	Cautery free (52) Cautery (38)	92% at 24 months 63% at 24 months
[19]	Prospective observational	60 vs. 58.5, *P*=0.02	ESI	Extrafascial (20) Interfascial (215)	40% 64%
[20]	Prospective observational	61.6 vs. 61.3	ESI	Cooling (112) Standard (157)	66% 83%
[21]	Prospective observational	59.4 vs. 59.0, *P*=0.55	SHIM≥16	Cautery (421) Athermal (590)	77% 79%
[22]	Prospective observational	57.8 vs. 57.8, *P*=0.942	ESI>50% attempts	Antegrade (172) Retrograde (172)	92.3% at 9 months 85.3% at 9 months
[23]	Prospective observational	58 vs. 59, *P*=0.343	SHIM≥22	O_2 tissue monitoring (64) No O_2 monitoring (192)	83.7% 68%
[24]	Prospective observational	59.0	ESI	VIP with superveil	94%
[25]	Prospective observational	60.2	ESI	VIP	93% in men without ED (SHIM≥22)
[26]	Prospective observational with historical control	59.9 vs. 63.1, *P*>0.05	Median length of time to ESI	VIP (200) RRP historical control (100)	340 days>700 days
[27]	Prospective observational	58	ESI	NS grade 1 (659) NS grade 2 (441) NS grade 3 (172) NS grade 4 (63)	92.4% 81.4% 66.3% 58.7%
[28]	Retrospective review	67.1 vs. 63.4, *P*>0.05	ESI	Prostate≥100 g Prostate≤50 g	61.9% 72.9%
[29]	Prospective observational		ESI	≥20 lymph nodes<20 lymph nodes	55.2% 70.0%

ESI=Erection suitable for intercourse, SHIM=Sexual Health Inventory of Men, IIEF-EF=International Index of Erectile Function-Erectile Function domain, BNS=Bilateral nerve sparing, RALP=Robot-assisted laparoscopic prostatectomy, RRP=Retropubic radical prostatectomy, OR=Odds ratio, ED=Erectile dysfunction, VIP=Vattikuti Institute prostatectomy, RR=Relative risk

Table 2: Potency rates observed during various modified RALP techniques

Source	Patient characteristics	Surgical technique	Potency definition	12-month potency rates
[17]	BNS RALP Pre-operatively potent	Extraperitoneal (93) Transperitoneal (56)	SHIM>21	55% 52%
[18]	NS RALP Pre-operatively potent<65 years	Cautery free (50) Cautery (38)	ESI	92% at 24 months 63% at 24 months
[19]	BNS RALP Pre-operatively potent	Extrafascial Interfascial	ESI	40% 64%
[20]	BNS RALP Pre-operatively potent	Cooling (112) Standard (157)	ESI	66% 83%
[21]	BNS RALP Pre-operatively potent	Cautery (421) Athermal (590)	SHIM>15	77% 79%
[15]	BNS RALP Pre-operatively potent	No traction (58) With traction (35)	ESI	50% 54%
[22]	NS RALP Pre-operatively potent	Antegrade (172) Retrograde (172)	SHIM>21	92.3% 85.3%
[23]	NS RALP Pre-operatively potent	O_2 tissue monitoring (64) No O_2 monitoring (192)	SHIM≥17	83.7% 68%

BNS=Bilateral nerve sparing, RALP=Robot-assisted laparoscopic prostatectomy, ESI=Erection suitable for intercourse, SHIM=Sexual Health Inventory of Men, NS=Nerve sparing

with a pre-operative SHIM score >21 showed that 93% of men reported ESI with or without phosphodiesterase-5 inhibitors (PDE5Is) at >1 year follow-up.[24] However, only 51% returned to baseline. A prospective, non-randomized analysis of pre-operatively potent (SHIM ≥ 18) men undergoing VIP (n = 200) compared with RRP (n = 100) showed that return to erection and intercourse were 180 versus 440 days (P < 0.05).[25]

Although most studies broadly classify patients who have undergone nerve sparing radical prostatectomy (NSRP), the NS technique is not an all-or-none technique. Correlation between degree of NS was shown, where potency rates for 1335 men undergoing RALP with >1 year follow-up and pre-operative SHIM score > 21 were 90.6, 76.2, 60.5 and 57.1% for NS grades 1, 2, 3 and 4, respectively (P < 0.001).[26] Additionally, comparison of interfascial and extrafascial NS technique produced 12-month potency rates of 64% and 40% (P = 0.02), respectively.[27] Additionally, men with larger prostates (>100 vs. <50 g) have decreased post-operative potency rates (61.9% vs. 72.9%, P < 0.05) at 12 months post-operatively.[28] When examining extended pelvic lymph node dissection (PLND) in a single-center study of 561 men (SHIM ≥ 17) who underwent RALP, men with a lymph node yield ≥20 and <20 reported potency rates of 55.2% and 70%, respectively (P = 0.020).[29]

Timing and patient selection

After a thorough review, 17 articles were determined to be most relevant for clinical application of treatment of ED post-RALP. Those addressing PDE5Is are shown in Table 3. All other forms of post-RALP ED treatment are shown in Table 4. The purpose of penile rehabilitation has been proposed to prevent alterations of the smooth muscle of the corpora cavernosa, limit venous leak development and

maximize the chances of returning to pre-operative erectile function.[30] Iacono *et al.* demonstrated increased evidence of fibrosis at increasing time points post-operatively.[31] In a study of bilateral NSRP patients, 84 subjects were divided into a penile rehabilitation program starting either less than 6 months or >6 months after surgery.[30] Two years post-operatively, the early rehabilitation group reported superior IIEF-EF scores (22 vs. 16, P < 0.001), higher Sildenafil-assisted erection rates (86% vs. 45%, P < 0.01), and higher Sildenafil-unassisted erection rates (58% vs. 30%, P < 0.01) than the delayed rehabilitation group.

Compliance with therapy is important as potency recovery may require 1 year or more. Seventy-seven men were prospectively followed after NS RALP and enrolled in a penile rehabilitation program with sildenafil or tadalafil three times weekly.[32] At <2 months after RALP, 32% of men stopped therapy and 39% or more stopped therapy by 6 months, with high cost (65%) being the primary reason. Pre-operative ED and long-term compliance were independent predictors of potency.

Active surveillance (AS) is frequently employed for the management of CaP. A group of 367 low-risk patients post-RALP, who were well matched and divided into single and multiple biopsy groups, reported 6-month potency rates of 80% and 57% (P = 0.03), respectively.[33]

PDE5Is

PDE5Is have emerged as the gold standard of treatment for ED. Several animal models have demonstrated histological and functional benefit with PDE5Is in animal studies.[34-37] Although the pathways behind these results are not clear, it has been theorized that PDE5Is can provide a protective role to preventing post-operative ED following RP.

Table 3: Study design and primary outcomes of long-term, randomized control trials evaluating PDE5Is for penile rehabilitation after RP

Reference	Patient population	Treatment 1	Treatment 2	Placebo	Treatment period, drug-free washout (DFW), open-label	Primary outcome
[38]	BNSRP w/combined Q3 and Q4 score≥8 on IIEF and desire to return to sexual activity	Sildenafil 50 mg nightly (*n*=23)	Sildenafil 100 mg nightly (*n*=28)	Placebo nightly (*n*=25)	36 weeks, 8 weeks, no therapy	26%* of sildenafil 50 mg, 29%** of sildenafil 100 mg, 4% of placebo were responders
[39]	BNSRP w/IIEF-EF≥26 and desire to return to sexual activity	Vardenafil 10 mg nightly and placebo on-demand (*n*=137)	Placebo nightly and vardenafil 10 mg on-demand (*n*=141)	Placebo nightly and on-demand (*n*=145)	9 months, 2 months placebo, 2 months vardenafil	No difference in % of men w/IIEF-EF≥22 after DFW
[40]	NSRP w/IIEF-EF>16 and preserved nocturnal erections	Sildenafil 25 mg nightly (*n*=23)	No treatment (*n*=18)	None	52 weeks, none, none	IIEF-EF scores 14.1 vs. 9.3*** for sildenafil vs. no treatment
[41]	BNSRP w/IIEF-EF≥22 and no self-reported history of ED	Tadalafil 5 mg nightly and placebo on-demand (*n*=139)	Placebo nightly and tadalafil 20 mg on-demand (*n*=143)	Placebo nightly and on-demand (*n*=141)	9 months, 6 weeks, 3 months tadalafil	No differences of % men w/IIEF-EF≥22 after DFW

*P=0.04, **P=0.03, ***P<0.001, IIEF-EF=International Index of Erectile Function-Erectile Function domain, BNSRP=Bilateral nerve sparing radical prostatectomy, ED=Erectile dysfunction, DFW=Drug-free washout, NSRP=Nerve sparing radical prostatectomy

Table 4: Studies included in analysis for ED management following RALP

Source	Study type	Age (years)	Validated criteria	Comparison (no. of patients)	Outcomes
[44]	Randomized prospective	<65	ESI	PDE5I w/VED (13) PDE5I w/o VED (7)	92% 57%
[45]	Randomized prospective	58.2 60.5 P=0.332	ESI	VED 1 month post-op (17) VED 6 months post-op (11)	0% 0%
[46]	Non-randomized prospective	58.2	ESI	VED (74) No treatment (35)	17% 29%
[47]	Randomized prospective	59 62	Needing ICI<50% of attempts at intercourse	ICI (15) No treatment (15)	67% 20%
[48]	Non-randomized prospective	58 58 P>0.05	ESI	PDE5I or ICI (58) No treatment (74)	52% 19%
[49]	Randomized prospective	56.8 55.6	IIEF-EF	Intraurethral alporstadil (97) Sildenafil (59)	15.28 17.65
[50]	Non-randomized prospective	59	ESI	MUSE (56) No treatment (35)	74% 37%
[54]	Randomized prospective	65	IIEF-EF	Counseling (50)	11.1
[55]	Randomized prospective	62.4 64.0 P=0.517	SHIM>20	Pelvic floor biofeedback (17) Verbal instructions (16)	47.1% 12.5%

ESI=Erection suitable for intercourse, SHIM=Sexual Health Inventory of Men, IIEF-EF=International Index of Erectile Function-Erectile Function domain, ICI=Intraurethral Injections/Intracavernosal Injections, RALP=Robot-assisted laparoscopic prostatectomy, ED=Erectile dysfunction, MUSE=Medicated urethral system for erections, RALP=Robot-assisted laparoscopic prostatectomy, VED=Vacuum erection device

Currently, three large, randomized, double-blind, placebo-controlled studies evaluating PDE5Is as penile rehabilitation following RP have been performed. Additionally, a randomized control trial without placebo evaluating sildenafil was also performed. Trial designs and primary outcomes are outlined in Table 3.

Padma-Nathan *et al.* were the first to demonstrate benefit from PDE5I use versus placebo.[38] Additionally, the IIEF-EF score was higher in the sildenafil group compared with placebo (13.1 vs. 8.8). However, the study was terminated prematurely after the interim review showed response rates less than expected compared with the rates of spontaneous recovery in the literature.

Mortosi *et al.* demonstrated that although on-demand vardenafil was associated with higher IIEF-EF scores after 9 months (P < 0.0001), benefit was lost after drug-free washout (DFW).[39] Similarly, although benefit was noted with SEP-3 success rates after 9 months with nightly and on-demand use (34.5% vs. 25.0%, P = 0.0344; 45.9% vs. 25.0%, P < 0.0001), benefit was lost after DFW. Vardenafil

on-demand was also superior to vardenafil nightly for SEP-3 success rates (45.9% vs. 34.5%, P = 0.0114).

Bannowsky demonstrated superior IIEF-EF scores with sildenafil compared with no treatment.[40] Additionally, spontaneous erection rates were 47% and 28% for men receiving sildenafil and no treatment, which improved to 86% and 66%, respectively, with the use of sildenafil on-demand.

Montorsi *et al.* demonstrated that although nightly tadalafil was associated with a greater percentage of men with IIEF-EF ≥22 after 9 months versus placebo (25.2% vs. 14.2%, P = 0.016), benefit was lost after DFW.[41] Similarly, although nightly tadalafil demonstrated superior SEP-1-5 response rates at 9 months, benefit was lost after DFW. However, superior SEP-1 and -2 success rates were observed after open-label therapy for both formulations of tadalafil. Further statistical analysis demonstrated positive response for tadalafil nightly versus placebo (P = 0.019) at 9 months and tadalafil nightly at 9 months (P = 0.007) and 13.5 months (P = 0.010), respectively. Significantly less penile shrinkage was noted in the tadalafil nightly group versus placebo at 9 months (2.2 mm vs. 6.3 mm, P = 0.003).

Briganti *et al.* proposed that the correct selection of patients is critical to those who will benefit from a penile rehabilitation program.[12] A retrospective study divided 435 men post-bilateral nerve sparing radical prostatectomy (BNSRP) into three groups based on risk of ED post-operatively: Low (age < 65 years or IIEF-EF = 26 or CCI < 1 [n = 184]), intermediate (age 66-69 years or IIEF-EF = 11-25 or CCI > 1 [n = 115]) and high (age > 70 years or IIEF-EF <10 or CCI > 2 [n = 136]). The population included 193 men untreated after surgery; 147 using on-demand PDE5Is and 95 using daily/every other day PDE5Is. Potency (IIEF-EF > 22) was greater in those receiving any PDE5Is compared with no treatment. Only in the intermediate-risk group was potency superior with daily versus on-demand PDE5I use (74% vs. 52%, P = 0.02).

Vacuum erection device
VED benefit was first demonstrated in several markers of inflammation, fibrosis and erectile function in animal models.[42,43] Recently, a study randomized 20 men post-BNSRP to tadalafil 20 mg three times weekly with or without VED.[44] The combination group had higher SHIM scores at 6, 9 and 12 months and higher penile hardness scores at 6 and 9 months. In the combination and tadalafil groups, 92% and 57% of patients, respectively, were able to achieve erection satisfactory for vaginal penetration.

Other results with VED use have been less conclusive. A study of 28 men post-unilateral nerve sparing or BNSRP randomized patients to receive penile rehabilitation with VED starting at 1 or 6 months post-operatively.[45] No spontaneous erections adequate for intercourse or difference of IIEF scores were observed at 12 months. Stretched penile length was greater in the early intervention group (P< 0.044); however, there was no difference in either group relative to their own pre-operative measurements.

A study randomized 109 men to daily VED for 9 months after RP or no treatment.[46] After 9 months, the SHIM score was higher in the treatment group (16 vs. 11.1, P < 0.05). However, there was no difference in the spontaneous erection rates or ESI rate. In those who quit and completed VED use, 85% versus 23% of patients reported decreased penile length and girth.

Intraurethral injections/intracavernosal injections
Prostaglandin E1 (PGE1) causes erection via vasodilation and smooth muscle relaxation to expand the corpora. Montorsi *et al.* first demonstrated penile rehabilitation benefit using ICI of PGE1 three times weekly or no treatment for 12 weeks in men post-NSRP.[47] The ICI and no treatment groups reported potency rates (needing ICI < 50% of attempts at intercourse) of 67% and 20% (P < 0.01), respectively.

A non-randomized study of 132 men post-RP examined 58 men receiving penile rehabilitation (23% used PDE5Is, 77% required ICI).[48] The non-rehab group was composed of 74 patients who did not desire rehabilitation. The rehab group and non-rehab group reported spontaneous ESI rates of 52% and 19% (P < 0.01), respectively, at 18 months post-operatively. Additionally, those who underwent rehab had improved responses to sildenafil (64% vs. 24%, P < 0.001) and ICI (95% vs. 76%, P < 0.01).

A study of medicated urethral system for erections (MUSE) therapy randomized 139 men following BNSRP to intraurethral alprostadil or nightly sildenafil 50 mg for 1 months, 1 month DFW and open-label sildenafil 100 mg for 1 month.[49] There were no differences in IIEF-EF scores after completion of therapy. A non-randomized study of 91 men following BNSRP investigated 56 men with MUSE therapy (three times per week for 6 months) and 35 men with no treatment.[50] ESI rates of 74% and 37% and SHIM scores of 18.9 and 15.8 were reported in each group.

Psychosocial and alternative interventions
Psychological factors play an important role for sexual function after RALP.[51,52] A randomized study of 101 men post-RP showed that cognitive-behavioral stress management for 10 weeks resulted in improved sexual function 2-3 weeks after the completion of counseling.[53] A study of 84 men who had undergone curative treatment for CaP with ED underwent four sessions of counseling.[54] Although short-term benefits were observed in several IIEF subscales, most were lost at —6 months of follow-up.

A study randomized 52 men to receive early post-operative pelvic-floor biofeedback weekly for 3 months or a control group with verbal instructions to contract the pelvic floor.[55] The 12-month potency rates (SHIM > 20) were 47.1% and 12.5% in the treatment and control groups, respectively.

Inflatable penile prosthesis
IPP remains the most definitive surgical treatment for ED refractory to oral or other therapies. However, it should only be used as a last resort, as, once installed, IPP is the only means by which erection can be achieved and natural erections are no longer attainable.

DISCUSSION

CaP will continue to remain a serious and prevalent disease that requires RP for treatment. Although current robotic techniques are improving, there is still clear evidence that ED will be encountered for men choosing to undergo RALP. All men should be counseled that potency return could take up to 1 year or more. The wide range of reported potency rates (54-94%)[7] is likely due to the different inclusions of pre-operative potency, definitions of potency, penile rehabilitation used and surgical technique. The risk stratification proposed by Briganti *et al.*[12] has been the best-validated predictor of recovery, which has now been externally validated by Novara *et al.*[11] and Gandaglia *et al.*[13] Other studies have confirmed that age and baseline erectile function are independent predictors of potency recovery.[14,15] This provides the greatest information for educating patients pre-operatively to potency recovery.

There is evidence that certain surgical techniques performed at high-volume centers lead to more promising results. Nerve sparing techniques have been confirmed to be superior to non-nerve sparing techniques. Unilateral nerve sparing should be considered when bilateral nerve sparing is not feasible for oncologic control. Additionally, although NS techniques are superior, it is evident that the degree of NS leads to different post-operative potency rates.[26] Various dissection techniques of fascial planes have been developed[27] in addition to the VIP.[23-25] More accurate description of the NS technique would allow for better comparison of operative techniques. Although retrograde[21] and intraoperative cooling[22] have demonstrated benefit in potency recovery, these are single-center studies. Although traction-free techniques have been proposed to reduce neuropraxia, results between studies have been conflicting.[15,26] Additionally, athermal dissection theoretically results in less damage to the cavernosal nerves. However, similar to traction-free techniques, athermal studies have produced conflicting results.[18,19] Nonetheless, there is early benefit from the athermal technique, and it is likely that any potential harm is minimized.

Two recent meta-analyses have demonstrated that RALP is superior to RRP for potency recovery without oncologic compromise.[7,9] This is in addition to the recent prospective control series from Gandaglia *et al.*, where RALP demonstrated superior potency rates versus RRP.[13] However, no randomized prospective control studies have been performed. Additionally, the use of validated questionnaires has been inconsistent. ESI or various cut-offs of SHIM or IIEF-EF scores have been used. A firmer definition of potency would allow for greater comparison in future studies. The retrospective population study from Barry[16] should be interpreted with caution as a non-validated questionnaire was used to assess potency. Patients were not matched for pre-operative erectile function, age, comorbidities or other factors. Additionally, 58% of men were >70 years old, a population which is not ideal population for radical prostatectomy, nerve sparing or with a strong interest in sexual activity.[56]

Recovery from this ED is very important to improving patients' quality of life. Although the evidence from animal models suggests that PDE5Is can help prevent and provide recovery from ED,[34-37] this has not always translated to humans. PDE5Is provide benefit compared with placebo during active treatment and are an effective treatment for post-RALP ED.[38-41] However, the long-term benefit of PDE5Is in preventing ED has not been demonstrated.[38-41] Given that potency can take over 1 year to return, it is possible that current studies and treatment duration were not long enough to demonstrate benefit in the current clinical studies. Additionally, the psychological effect of not receiving treatment during DFW might result in a regression of erectile function. Furthermore, there have been no studies comparing the effect of different PDE5Is with each other. Although, theoretically, they have the same mechanism of action, different half-lives may contribute to the different results observed in on-demand or daily PDE5I use. There is likely benefit to compare different PDE5Is in future trials. Additionally, there is a lack of consistency in use of placebo, DFW, trial length, inclusion criteria, degree of NS technique, use of robotic or open technique and, maybe most notably, potency definition.[38-41] To date, no trials have evaluated PDE5I penile rehabilitation specifically in patients undergoing RALP. Current evidence suggests that PDE5Is can play a role in penile rehabilitation, although the dosing, frequency and PDE5I used cannot be recommended based on current data.

VEDs have increasingly been used in penile rehabilitation programs.[44-46] Although there is evidence that VED can prevent shortening of penile length,[45] long-term potency benefits have not been demonstrated. ICI and MUSE appear to have some role in penile rehabilitation; however, long-term data are lacking.

When counseling a patient on RALP, it is necessary to explain that recovery of erectile function can take up to

1 year, if not greater. Therefore, it is important to identify the patients that will be willing to complete a rehabilitation program to provide the greatest clinical benefit.

CONCLUSION

RALP demonstrates beneficial potency rates without compromising oncologic benefit compared with RRP. However, these data lack prospective randomized control studies. Retrograde dissection, intraoperative cooling and VIP have demonstrated benefit for potency recovery compared with traditional RALP. Although benefit is demonstrated during use of PDE5Is compared with placebo, it is often lost after use. Subsequently, no optimal rehabilitation program with PDE5Is has been developed. Although VED, ICI and MUSE have shown promise in penile rehabilitation, long-term, randomized control studies have not been performed. It is important to identify patients who will most likely recover erectile function for patient education. Although the future is promising with improved robotic techniques, an optimal robotic technique has not been identified. Additionally, no definitive recommendations regarding a penile rehabilitation program can be made without further evidence.

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