SEXUAL MEDICINE ORIGINAL RESEARCH

ERECTILE DYSFUNCTION

Efficacy and Safety of Tadalafil 5 mg Once Daily for the Treatment of Erectile Dysfunction After Robot-Assisted Laparoscopic Radical Prostatectomy: A 2-Year Follow-Up

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ABSTRACT

Background: Although nerve-sparing robot-assisted radical prostatectomy (NS-RALP) is performed, a large number of patients still experience erectile dysfunction (ED) after surgery.

Aim: To evaluate the efficacy and safety of tadalafil 5 mg once daily (OaD) in ED treatment over 2 years and investigate the cause of vascular ED after NS-RARP.

Methods: We retrospectively evaluated 95 men who underwent NS-RARP and had a penile rehabilitation treatment with tadalafil 5 mg OaD. They were classified into 3 groups: tadalafil 5 mg OaD for 2 years (group I), tadalafil 5 mg OaD for 1 year (group II), and no tadalafil (group III). All patients in group I underwent penile color duplex ultrasound to evaluate the cause of vascular ED.

Outcomes: Patients were surveyed using the abridged 5-item International Index of Erectile Function (IIEF-5).

Results: Statistically significant improvements were observed in group I for all IIEF-5 domain scores ($P = .000$). There was no statistically significant difference in recovery of erectile function (EF) the 2-year follow-up between groups I and II. Sub-analysis based on NS status showed no difference in recovery of EF. However, group I showed better trends in EF improvement. Those with venogenic ED had poor responses compared with those with arteriogenic ED or unremarkable findings with tadalafil 5-mg OaD treatment (14.2% vs 55.0% vs 53.3%). The overall side effects included hot flushing in 9.5%, headache in 7.1%, and dizziness in 2.3% of patients.

Clinical Implications: Long-term usage of tadalafil 5 mg OaD after RARP can be an effective option for penile rehabilitation.

Strengths and Limitations: The present study is a retrospective study with a relatively small sample.

Conclusions: Although the responses of patients with venogenic ED were limited compared with those with arteriogenic ED, tadalafil 5-mg OaD treatment was well tolerated and significantly improved EF up to 2 years after NS-RARP. **Kim S, Sung GT. Efficacy and Safety of Tadalafil 5 mg Once Daily for the Treatment of Erectile Dysfunction After Robot-Assisted Laparoscopic Radical Prostatectomy: A 2-Year Follow-Up. Sex Med 2018;X:XXX–XXX.**

Key Words: Erectile Dysfunction; Penile Rehabilitation; Phosphodiesterase Type 5 Inhibitor; Robot-Assisted Radical Prostatectomy

INTRODUCTION

Radical prostatectomy (RP) has been the primary treatment modality for localized prostate cancer and is considered the best option for improving patient survival compared with conservative management.[1,2] However, RP is associated with a variable loss of urinary continence and erectile function (EF) postoperatively. With an increased rate of RP in young men, a greater emphasis must be placed on the appropriate management of urinary continence and erectile dysfunction (ED) to address

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patients' quality of life. Recent advances in surgical anatomy and improvements in surgical techniques have yielded satisfactory urinary continence outcomes after RP. Further, the advent of pioneering nerve-sparing (NS) robot-assisted laparoscopic radical prostatectomy (RALP) has significantly increased the potency rate after RP.[1–3] However, although NS-RALP is performed, a large number of patients still experience ED after surgery. After RP, the reported ED incidence rates vary from 30% to 87%.[4,5] Although anatomic NS-RARP promises a high likelihood of postoperative recovery from ED, many men require more than 2 years to satisfactorily return to their baseline function, which can result in absent or decreased EF.[6] Several penile rehabilitation (PR) programs have been introduced; however, most have achieved modest outcomes. After its advent in 1998, orally administered phosphodiesterase 5 inhibitors (PDE5-Is) have been increasingly used as the 1st-line management option for ED after RP. A recent literature review showed that PDE5-Is are safe and effective in treating patients with ED after RP. The administration of PDE5-Is once daily (OaD) has proved to have a protective role in ED, and early administration of PDE5-Is helps prevent cavernosal hypoxia, which leads to smooth muscle apoptosis and penile fibrosis.[7–11] Although PDE5-Is are the most frequently recommended treatment for ED after RP, a consensus has not been reached on their use, such as time of initiation, treatment duration, or treatment regimen. Some investigators have recommended starting oral PDE5-Is immediately after an NS procedure to achieve optimal recovery of erections after 2 years, whereas others have reported compliance issues with the regimen, which can pose a significant barrier to an effective treatment. However, patients undergoing NS-RARP could represent a unique cohort who might be more motivated with higher expectations for recovery of potency.

AIMS

This study analyzed the long-term clinical efficacy and safety of PR using tadalafil 5 mg OaD for more than 2 years in the treatment of patients with ED who underwent NS-RARP for clinically localized prostate cancer.

METHODS

We retrospectively evaluated the records of 95 patients who underwent NS-RARP by a single experienced surgeon for localized prostate cancer from March 2010 through December 2013. The standard NS-RALP techniques, including bladder neck preservation, interfascial NS, and posterior urethral reconstruction, were performed in all patients. Patients with localized prostate cancer with clinical stage no higher than T2, Gleason score lower than 8, serum prostate-specific antigen level lower than 20 ng/mL, and normal preoperative EF were included in the study. Preoperative EF was assessed by the 5-item International Index of Erectile Function (IIEF-5). We excluded patients who underwent non—NS-RALP and hormonal or radiation therapy and those who received any kind of preoperative ED treatment.

Of the 95 patients, 59 were prescribed with tadalafil and 36 patients were not. In the tadalafil group, all patients were prescribed with tadalafil at a dose of 5 mg OaD; tadalafil was taken 1 hour before bedtime. Oral tadalafil 5-mg OaD treatment was initiated soon after Foley catheter removal within 7 to 10 days after surgery.

The tadalafil group was further stratified based on duration of tadalafil intake: 2-year tadalafil group (group I) and 1-year tadalafil group (group II). Patients who were not prescribed tadalafil were designated as the non-tadalafil group (group III). In groups I and II, all patients were counseled on ED, tadalafil intake, and its side effects at each visit. All 3 groups were followed up for 2 years after surgery. Patient age, clinical stage, Gleason score, comorbidities, and drug side effects were retrospectively reviewed using medical records after receiving approval from the institutional review board. Postoperative EF was assessed through patients' responses to the IIEF-5. Then, each group was classified by NS status: bilateral NS and unilateral NS procedures. Positive responders were those patients whose combined score for question 2 ("When you had erections with sexual stimulation, how often were your erections hard enough for penetration?") and question 3 ("During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?") on the IIEF-5 was at least 8.

The IIEF-5 was administered before surgery and at 6 months, 1 year, and 2 years after surgery in all patient groups. Outcomes from the tadalafil group and the non-tadalafil group were compared and analyzed according to the NS status based on the patients' IIEF-5 score. In the subgroup analysis, we routinely performed penile color duplex ultrasound (PCDU) using vasoactive intracavernosal injections (ICIs) 1 year after surgery in group I to evaluate the therapeutic responses to tadalafil 5-mg OaD treatment. ED was categorized as arteriogenic, venogenic, or unremarkable depending on the PCDU findings. Arteriogenic ED was defined as the difference in peak systolic velocities greater than 10 cm/s or no greater than 30 cm/s between the 2 cavernosal arteries, and venogenic ED was defined as end-diastolic velocities of the cavernosal artery greater than 5 cm/s. Unremarkable findings were defined as peak systolic velocities and end-diastolic velocities of the 2 cavernosal arteries showing a normal range and spectral waveform.

Categorical variables were presented as frequency and percentage and continuous variables were presented as mean and SD. The Pearson χ^2 test or Fisher exact test was used for categorical variables and 1-way analysis of variance or the Kruskal-Wallis test was used for continuous numerical variables. 2-factor analysis of variance was used to test the difference between group and period, and then the Wilcoxon rank sum test or paired t-test was used to test the differences in IIEF-5 domains between time points. 1-way analysis of variance or the