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BRIEF COMMUNICATION

Sexual Rehabilitation After Nerve-Sparing Radical Prostatectomy: Free-of-Charge Phosphodiesterase Type 5 Inhibitor Administration Improves Compliance to Treatment

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ABSTRACT

Background: In December 2006, the region of Tuscany (Italy) authorized the free-of-charge provision of phosphodiesterase type 5 inhibitors (PDE5I) for all patients with Tuscan citizenship who undergo nerve-sparing radical prostatectomy (NSRP).

Objective: To compare sexual rehabilitation outcomes in patients with low risk of erectile dysfunction and minimal comorbidities who received PDE5Is free of charge (PDE5I-F) with those who paid for PDE5Is (PDE5I-P) after bilateral NSRP.

Methods: We reviewed prospectively recorded clinical data of 2,368 patients with Tuscan (PDE5I-F) and non-Tuscan (PDE5I-P) citizenship treated with NSRP at 3 different institutions in Tuscany from 2008 to 2013. Inclusion criteria for the final analysis were open or robot-assisted bilateral NSRP; low risk of postoperative erectile dysfunction according to the Briganti risk stratification tool; no smoking and no drug and alcohol abuse; no cardiovascular risk factors; no major surgery before and after NSRP; no neoadjuvant or adjuvant treatment; and no biochemical relapse. Dropout was defined as an interruption longer than 40 days of the treatment protocol indicated in the inclusion criteria. Treatment compliance was defined as more than 90% consumption of the prescribed PDE5I.

Outcomes: The Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) and the Italian version of the University of California—Los Angeles Prostate Cancer Index sexual function (UCLA-PCI-s) questionnaires were administered to assess patients' satisfaction with PDE5I treatment and sexual function.

Results: Overall, 648 patients in the PDE5I-F group and 182 in the PDE5I-P group met the inclusion criteria and were eligible for the study. Patients had comparable preoperative and surgical characteristics. The PDE5I-F group had a significantly higher early rehabilitation onset ($P < .001$), lower treatment dropout at 12, 24, and 36 months ($P < .001$ for all comparisons), and higher compliance to the treatment protocol at 6 and 12 months ($P = .01$ and $P < .001$, respectively). At multivariable analysis, the PDE5I-F protocol was an independent predictor of an EDITS score higher than 50 (hazard ratio = 1.54, $P = .03$) and a UCLA-PCI-s score higher than 50 (hazard ratio = 3.12, $P = .01$) after adjusting for the effects of several clinical features.

Clinical Implications: The free-of-charge protocol has a significant impact on patients' satisfaction with PDE5I treatment.

Strengths and Limitations: To our knowledge, this is the first study comparing free vs paid access to a sexual rehabilitation protocol. Major limitations are the observational nature of the study and the different population sizes of the 2 groups.

Conclusions: In a selected cohort of patients after NSRP, free-of-charge access to a sexual rehabilitation protocol was significantly associated with higher early rehabilitation onset, major compliance to the protocol, minor treatment dropout, and higher satisfaction rate of patients. **Siena G, Mari A, Canale A, et al. Sexual Rehabilitation After Nerve-Sparing Radical Prostatectomy: Free-of-Charge Phosphodiesterase Type 5 Inhibitor Administration Improves Compliance to Treatment. J Sex Med 2018;15:120—123.**

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INTRODUCTION

Phosphodiesterase type 5 inhibitors (PDE5Is) are generally well-tolerated and effective drugs for the sexual rehabilitation of patients treated with nerve-sparing radical prostatectomy (NSRP).[1] However, with the high cost of PDE5Is, continuous treatment is associated with decreased compliance, which undermines success.[2] In December 2006, for the first time worldwide, the region of Tuscany (Italy) authorized the provision of sildenafil, tadalafil, and vardenafil for patients with Tuscan citizenship who had undergone NSRP. We investigated whether a free-of-charge PDE5I administration protocol improved long-term erectile function (EF) outcomes and satisfaction of men treated with NSRP.

METHODS

From 2008 to 2012, 2,368 patients underwent RP by 6 experienced surgeons in 3 different institutions in Tuscany. For the final analysis, patients younger than 65 years with a low risk of postoperative erectile dysfunction,[3] with a Charlson Comorbidity Index score no higher than 1, with no cardiovascular risk factor or smoking and alcoholic habit, underwent bilateral intra- or interfascial NSRP, and were treated with different PDE5I schemes were included. Patients started the PDE5I treatment 1 month after surgery. Early rehabilitation onset was defined as starting PDE5I treatment less than 40 days after surgery.[4] Dropout was defined as an interruption longer than 40 days of the treatment protocol indicated in the inclusion criteria. Treatment compliance was defined as more than 90% consumption of the prescribed PDE5I. The 5-item International Index of Erectile Function (IIEF-5), the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS), and the University of California—Los Angeles Prostate Cancer Index sexual function (UCLA-PCI-s) questionnaires were self-administered to assess sexual function and patients' and their partners' satisfaction with PDE5I treatment.[5,6] Descriptive and comparison statistics were reported. Multivariable Cox regression analyses were used to assess satisfaction rate by an EDITS score higher than 50 and a UCLA-PCI-s score higher than 50.

RESULTS

The clinical data of 648 Tuscan citizens (PDE5I free of charge [PDE5I-F]) and 182 non-Tuscan citizens (PDE5I with payment [PDE5I-P]) were included. No statistical differences were observed between the 2 study groups for epidemiologic and clinical preoperative characteristics. Patients were treated with the open and robotic approach in 89.6% and 10.4% of the PDE5I-P group and in 87.7% and 12.3% of the PDE5I-F group ($P = .52$), respectively. The 2 groups had comparable intraoperative (2.2% vs 2.7%, respectively) and overall postoperative (7.7% vs 7.3%, respectively) complication rates. Median follow-up was 41.0 months (interquartile range = 36.5−53). The duration of treatment was significantly longer in the PDE5I-F than in the PDE5I-P group (26 months [interquartile range = 12.0−31.5] vs 15 months [interquartile range = 10.5−22.5]; $P = .001$). The number of patients who had undergone early rehabilitation was significantly larger in the PDE5I-F than in the PDE5I-P group (98% vs 80.8%; $P < .001$). Treatment dropout was significantly higher in the PDE5I-P group than in the PDE5I-F group at 12, 24, and 36 months ($P < .001$ for all comparisons). Compliance to the treatment protocol was 96.1% and 89.9% vs 78% and 60.9% for the PDEI5-F vs PDEI5-P groups at 6 and 12 months, respectively ($P = .01$ and $P < .001$). The IIEF-5 score was significantly higher in the PDE5I-F group than in the PDE5I-P group at 8 (13 vs 11; $P = 0.04$), 12 (15 vs 12; $P = .02$), 24 (15 vs 12; $P = .02$), and 36 (16 vs 12; $P = .01$) months.

Patients in the PDE5I-F group had a significantly higher EDITS score compared with patients in the PDE5I-P group at 8 ($P = .01$), 12 ($P = .01$), 16 ($P = .02$), and 20, 24, 30, and 36 ($P < .001$ for all comparisons) months and a significantly higher UCLA PCI-s score at 12 ($P = .002$), 16 ($P = .01$), 20 ($P = .04$), and 24, 30, and 36 ($P < .001$ for all comparisons) months (Figure 1).

At multivariable analysis, after adjusting for the effects of body mass index, Charlson Comorbidity Index score, preoperative prostate-specific antigen level, surgical approach, and secondary biopsy Gleason score, age (hazard ratio [HR] = 0.96, $P = .01$) and PDE5I-F (HR = 1.54, $P = .03$) were independent predictive factors of an EDITS score higher than 50, and age (HR = 0.94, $P = .001$), body mass index (HR = 0.97, $P = .01$), PDE5I-F (HR = 3.12, $P = .01$), and robotic approach (HR = 1.46, $P = .03$) were independent predictive factors of a UCLA-PCI-s score higher than 50.

DISCUSSION

A possible rationale for our results could be that free-of-charge availability allows an early rehabilitation onset, greater compliance, and minor treatment dropout. Evidence that an early onset of penile rehabilitation improves EF outcomes after RP has been widely investigated. Mulhall et al[7] reported a highly statistically significant difference in IIEF-EF domain score between early and delayed groups at 2 years after surgery (22 vs 16; $P < .001$). Although the initial results of the rehabilitation could be unsatisfactory, the continuity of treatment potentially improves EF