PHD CORNER

Efficiency of Early Penile Rehabilitation on Erectile Function Recovery after Open Radical Prostatectomy

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RESEARCH BACKGROUND

Prostate cancer (PC) is one of the most commonly diagnosed malignancies worldwide and the second leading cause of mortality among men (1). Nowadays, radical prostatectomy is considered the primary therapeutic modality for treating patients with localized PC (stage pT2), providing a five-year survival rate of nearly 100% (2). Sexual dysfunction in men associated with PC treatment encompasses three distinct entities: erectile dysfunction (ED) and penile shortening; ejaculatory and orgasmic dysfunction; and psychosexual dysfunction, which pertains to sexual desire, intimacy, and mental health (3). Penile rehabilitation (PR) is defined as the use of any intervention or combination of procedures aimed not only at achieving an erection sufficient for satisfactory sexual intercourse but also at restoring erectile function to its preoperative level (4).

Despite efforts to preserve the neurovascular bundle during radical prostatectomy, ED remains a common outcome. Although prevalence rates of ED after the procedure vary widely, recent studies report rates as high as 85% (5). This is primarily due to the lack of control over factors that significantly influence the erection recovery, such as the patient's age, preoperative erectile function, comorbidities, surgical approach (open, laparoscopic, or robot-assisted), surgical technique (non-, uni-, or bilateral nerve-sparing), and the surgeon's skills and experience. The pathophysiology of postoperative ED is multifactorial. The primary mechanisms are believed to be damage to the cavernous nerves, whether through dissection or neuropraxia, and vascular injury, which includes damage to the accessory pudendal arteries, hypoxia and fibrosis of the endothelium and smooth muscle, resulting in penile shortening (6-8).

Although there is no consensus on the optimal approach to PR, accepted modalities include the use of phosphodiesterase type 5 inhibitors (PDE-5i; such as sildenafil, vardenafil, tadalafil) and vacuum erection devices (VED) or vacuum constriction devices (VCD) as first-line therapies. Second-line treatments involve prostaglandin E1 preparations for intracavernous, or intraurethral (MUSE - "Medicated Urethral System for Erection") administration. The final therapeutic option is the implantation of penile prostheses (3-10).

HYPOTHESIS AND OBJECTIVES

Given the current knowledge, this research is based on the hypothesis that early PR methods are effective and safe in treating erectile dysfunction following open radical prostatectomy. The study aims to determine and compare the effectiveness of the most commonly used modalities, assess their safety profiles, and investigate whether perioperative variables can predict the PR outcomes. It also aims to determine if it is justifiable to persist with PR efforts if erectile function does not initially recover within the first 6 months following surgery.

Additionally, the objectives are to examine the role of preoperative penile ultrasonography in patient selection, establish the correlation between preoperative and postoperative hemodynamic profiles and the degree of erectile function recovery, evaluate the rationale for including patients who underwent a non-nerve-sparing procedure in PR programs, and assess the impact of PR on the quality of life (QoL) of patients following open prostatectomy.

MATERIALS AND METHODS

The study will be conducted in the form of a prospective, placebo-controlled randomized clinical trial, and will include 80 patients treated surgically by open retropubic prostatectomy. Patients are randomized into 4 groups according to the preferred PR modality: A: PDE5i (tadalafil 5 mg, daily), B: VED (daily, for 10 min), C: combination therapy (PDE5i + VED), D: placebo group. The follow-up will last 12 months and the erectile function analysis will be performed preoperatively, then after 3, 6 and 12 months, and after a wash-out period of 2 months, using the International Erectile Function Index - 5 (IIEF-5), Erection Hardness Score (EHS) and Penile Color Doppler ultrasonography. The answers to SEP2 and SEP3 (Sexual Encounter Profile) questions will be used as the main inclusion criteria, and the Global Assessment Question (GAQ) as the patient reported outcome.

The term "recovery of erectile function" is defined as a return to the base IIEF-5 score. A specialized FACT-P questionnaire (Functional Assessment of Cancer Therapy – Prostate) will be used to assess QoL. Penile color Doppler ultrasonography (CDUS) at rest and after intracavernosal administration of vasoactive drug (alprostadil, 20 μg) will register hemodynamic variables (PSV, EDV, RI), on the Mindray DC-70 device (Mindray Bio-Medical Electronics Co. Ltd., Shenzhen, China).

OUTCOMES AND EXPECTED RESULTS

Some patients may not complete the PR program due to decreased sexual desire, treatment complications, or ineffectiveness. Those who complete the program will be divided into the group of responders (those reporting recovery of spontaneous erection) and non-responders. The responders will be divided into complete responders (those achieving full recovery of spontaneous erection sufficient for sexual activity) and partial responders (those with partial recovery, experiencing inadequate erection in less than 50% of sexual attempts).

Significant differences between the two groups are expected concerning age, ASA status, smoking status, and CCI (Charlson Comorbidity Index). Younger non-smokers with a lower ASA score and fewer comorbidities, patients who had a nerve-sparing procedure, specially who underwent bilateral nerve-sparing surgery, are more likely to be in the responder group. No significant difference is expected regarding the status of resection margins. Univariate analysis is expected to show that age and PSA levels are associated with the outcome of erectile rehabilitation. Bivariate analysis may reveal that CCI, ASA status, and Gleason score are linked to poorer rehabilitation prognosis. Smoking, alcohol abuse, higher pT stage, preoperative PSA, and surgical technique are likely to be confirmed as significant predictors of rehabilitation outcomes. Multivariate analysis may demonstrate that age over 65, higher BMI, non-nerve-sparing

surgery, and higher ASA status are associated with worse outcomes.

Patients in group C (PDE-5i+VED) may have an advantage in rehabilitation outcomes and be predominant in the responder group. It is expected that the sexual aspect of QoL, as well as overall QoL, will improve across all groups during the follow-up period, though the placebo group may be slightly behind in this regard. Adverse effects of treatment are expected to be sporadic, mild to moderate in intensity, and are unlikely to lead to discontinuation of the rehabilitation program.

CONCLUSIONS

Following the hypothesis and the expected results, we conclude that early penile rehabilitation modalities are effective and safe in the treatment of erectile dysfunction after open radical prostatectomy. Combination therapy with PDE5i and VED may have an advantage over other modalities. Penile CDUS can play a significant role, both in preoperative patient selection and in monitoring rehabilitation efficacy.

ORIGINAL SCIENTIFIC CONTRIBUTION

Most current knowledge on PR following radical prostatectomy is derived from retrospective studies, which should be interpreted cautiously due to methodological limitations, small sample sizes, and short follow-ups. This study stands out by integrating the latest research methodologies and offering a novel approach. It is the first of its kind in the region, aiming to enhance understanding of post-PC surgery conditions and improve monitoring. A key aspect is analyzing self-reported outcomes alongside objective ultrasonographic assessments, which is unique in this context.

The study will identify factors that differentiate patients likely to benefit from PR from those who might not recover erectile function despite intensive treatment. This is vital due to the high cost of rehabilitation programs and helps in setting realistic expectations and exploring more effective alternatives. In a society where sexual health is often taboo, this research will contribute to better understanding and treatment of ED, and propose a culturally adapted PR protocol for our urological centers.

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