



A Pilot Randomized Trial of Preoperative Pelvic Floor Muscle Exercise versus Usual Care to Treat Urinary Incontinence after Robotic-Assisted Radical Prostatectomy (RARP): A Study Protocol

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Abstract

Background: Radical prostatectomy represents the most common and effective treatment for localised prostate cancer. Recently, robot-assisted radical prostatectomy (RARP) has become increasingly used worldwide. Although a recent systematic review and meta-analysis found that RARP had higher postoperative continence rates than retropubic or laparoscopic radical prostatectomy, urinary incontinence (UI) and sexual dysfunction remain the most bothersome postoperative complications even after RARP. Pelvic floor muscle training (PFMT) may represent a valid treatment to improve postoperative urinary continence as well as sexual function. The aim of this study will be to carry out a randomised controlled trial in order to determine a causal relationship between preoperative PFMT and postoperative functional outcomes in patients undergoing RARP.

Methods/Design: This is a double-arm, single-centre, pilot randomized control trial conducted at an academic teaching hospital; at least 100 men undergoing RARP for prostate cancer with no contraindications to PFMT will be recruited and randomized to a pre-and post-operative PFMT program or usual care. PFMT participants will engage in a PFMT program. The PFMT prescription will begin with instructions on how to engage the pelvic floor delivered by the research coordinator trained in PFMT. Usual care participants will not receive any formal training in PFMT neither preoperatively nor after surgery. Estimates of intervention efficacy will be captured through measurements at baseline (4–8 weeks preoperatively), within 1 week prior to surgery, and postoperatively at 4, 12, and 26 weeks. UI will be assessed using the 24-h pad test, a 3-day, bladder diary. The ICIQ-Urinary Incontinence (ICIQ-UI) will be administered as an additional self-reported measure of Post-RARP UI. Quality of life (QoL) will be measured using the following widely used and psychometrically valid and reliable measures, validated in Italian language: The UCLA-PCI and the Short-Form 36 (SF-36). Additional urological symptoms will be assessed using the valid and reliable, 7-item International Prostate Symptom Score (IPSS) with its further item on QoL. Erectile function will be assessed using the 5-item International Index of Erectile Function (IIEF) scale.

Discussion: The primary outcome of this study will be to examine a structured pre-, peri-, and post-surgical exercise program of PFMT for men undergoing RARP for prostate cancer. This trial will advance our understanding of strategies aiming at an early recovery of continence and sexual activity after RARP, and to efficiently and effectively use the pre-and peri-operative period to optimize post-operative continence and sexual recovery, improving patients' QoL.

Keywords: Prostate cancer; RARP; PFMT; Randomized controlled trial; Rehabilitation

Introduction

Radical prostatectomy represents the most common and effective treatment for localised prostate cancer [1]. Most of these patients have favourable cancer control outcomes after surgery [2]. Unfortunately, a considerable proportion of them may suffer from long-term surgical sequelae, including postoperative urinary incontinence (UI) and sexual dysfunction [3], which can significantly affect patient's quality of life (QoL) and result in both physical and psychosocial burdens [4].

Recently, robot-assisted radical prostatectomy (RARP) has become increasingly used worldwide.

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Although a recent systematic review and meta-analysis found that RARP had higher postoperative continence rates than retropubic or laparoscopic radical prostatectomy [5], UI remains one of the most bothersome postoperative complications even after RARP.

Normally, the pelvic floor muscles (comprised of the internal sphincter, levatorani, coccygeus, striated urogenital sphincter, external anal sphincter, ischiocavernosus, and bulbospongiosus) work in a coordinated fashion to promote urinary control [6,7]. Consequently, pelvic floor muscle training (PFMT), intended to improve urinary control by increasing the strength, endurance, and coordination of the pelvic floor muscles and functional activation of the external sphincter, represents a traditional fist-line intervention, limited to the post-operative period, to improve continence recovery after radical prostatectomy. A recent systematic review and meta-analysis on the role of PFMT on the management of post-prostatectomy incontinence [8], found evidence to suggest that preoperative PFMT improves early continence rates but not long term continence rates. The Authors analysed seven studies contained sufficient quantitative data on post-operative incontinence suitable for meta-analysis. Only one of them took into account patients undergone RARP [9]. Moreover, a very few studies addressed the attention on the possible role of PFMT in improving sexual function after radical prostatectomy. Recently Geraerts et al. [10] observed that patients with persistent erectile dysfunction (ED), minimum 12 months after radical prostatectomy, experienced a better recovery of erectile function (EF) with PFMT compared with patients without this intervention.

The aim of this study will be to carry out a randomised controlled trial in order to determine a causal relationship between preoperative PFMT and postoperative functional outcomes in patients undergoing RARP. It is an opportunity to examine a comprehensive pre-rehabilitation program for these men that may have a profound influence on surgical preparation by reducing the often chronic nature of complete recovery from this procedure.

Methods/Design

This study will be a 2-arm, single-centre; pilot randomized controlled trial to examine the effect of a preoperative PFMT program versus usual care (UC). The primary objective of this study will be to report estimates of efficacy on functional outcomes for RARP patients. This study will be conducted at one Academic teaching hospital, after receiving the approval from the local research ethics boards.

Participants

We will recruit at least 100 participants (n=50 per site and per group) consistent with recommended sample sizes for a pilot study [11]. We anticipate an attrition rate of 20%. Inclusion criteria: Men aged 40 and 80 years of age with localized PCa (stage cT1- cT2) who have consented for RARP.

Exclusion criteria: Patients that: 1) are diagnosed with a known neurological disease, autoimmune connective tissue disorder; 2) have a prior experience with PFMT by a healthcare provider; 3) have hypertonic pelvic floor muscles upon baseline evaluation.

Hypertonic pelvic floor is determined by the physical examination findings of extra pelvic musculoskeletal and connective tissue examination, as well as the elements of patient history [12]. These patients who exhibit levator ani hypertonicity (tension myalgia) will be excluded as they can experience pelvic, urogenital, and rectal

pain; tightness and spasticity; and adverse effects on sexual, urinary, and bowel function that may be exacerbated with contraction-based pelvic floor training [13].

Participants will be 1:1 randomized to the UC and PFMT groups. Blinded allocation of the participants to their treatment groups will be performed using a generator to create a blocked randomisation list.

Study arms

Both groups will begin participation in their respective study arms at the time of randomization following shortly after RARP scheduling. The duration of the preoperative wait-time (typically 4-8 weeks) will be recorded. All participants signed an informed consent form explaining the nature of the study previously approved by the Ethics Committee of our Institution.

PFMT group

PFMT participants will engage in a PFMX program. The PFMT prescription will begin with instructions on how to engage the pelvic floor delivered by the research coordinator (RC) trained in PFMT. The PFMX prescription will include a gradual increase in repetitions from 60 per day during weeks 1-2, 120 per day during weeks 3-4, and 180 per day during week 5 to the surgical date [14]. The total number of repetitions of the PFMT will be divided equally between the rhythmic contractions (contract and relax over one second) and the sustained contractions (contract and hold for up to 10 seconds). Total daily contractions will be divided into multiple sets over the course of the day, aiming for 10-20 repetitions per set in all positions: sitting, standing, squatting, and going up and down stairs. Participants will be instructed to contract with maximal effort during all PFMT repetitions. Four days after surgery participants will restart the PFMT with escalating repetition volume every 2 weeks. Twelve days after surgery indwelling catheter will be removed. Repetition volume will start at 30-60 repetitions per day during weeks 1-2; 60-120/day during weeks 3-4; and 120-150/day during weeks 5-6, and 150-180/day for weeks 7-26 after surgery [15]. Total daily contractions will be divided into multiple sets over the course of the day, aiming for 10-20 repetitions per set in all positions: sitting, standing, squatting, and going up and down stairs. The RC will communicate with the PFMT participants weekly via phone or email to ensure program compliance, support appropriate progression, and address any barriers to exercise that may prevent ongoing participation.

Usual care (UC)

The UC group will not receive any formal training in PFMT neither preoperatively nor after surgery.

Outcome Measures

Self-report measures will be conducted at: baseline (following RARP booking, prior to beginning group assignment) approximately 4-8 weeks preoperatively, within 1 week prior to RARP, and at 4, 12, and 26 weeks postoperatively. All self-reported measures are available in Italian.

Urinary incontinence

Urinary Incontinence (UI) will be assessed using the 24-h pad test, a 3-day, bladder diary. The 24-h pad test will be used to measure UI by assessing the quantity of urine lost in one day. A urinary leakage pad is measured after a 24-h period and compared to the unused pad weight and is used to assess the severity of UI [16-18].

Continence is defined as a loss of ≤ 2 g of urine or the use of one or less pad per day [18-21]. During the 24-h period that the pad is worn, the participants will complete a frequency volume chart including urination frequency, times of UI, and if the pad was ever removed for a period of time. The 3-day bladder diary is a standard instrument for self-reporting voiding patterns. Items include fluid intake, frequency of toilet voids, episode of urine loss, nocturia, number of pads used, and activity during event for the three-day period. Bladder diaries are widely used in clinical trials assessing UI after prostatectomy [22-26]. Participants will be instructed to complete these 3 days prior to their scheduled assessment appointments.

The ICIQ-Urinary Incontinence (ICIQ-UI) will be administered as an additional self-reported measure of Post-RARP UI. The Impact of UI on QoL will be further assessed using the Incontinence Quality of Life Scale (I-QOL). The I-QOL questionnaire developed by Patrick et al. [27] contains 22 items, each with a five-point Likert-type response scale, yielding a total score and three subscale scores. Higher I-QOL scores indicate better levels of quality of life.

Quality of life

QoL will be measured using the following widely used and psychometrically valid and reliable measures, validated in Italian language: The UCLA-PCI and the Short-Form 36 (SF-36).

The UCLA-PCI is a disease-specific health-related QoL (HR-QOL) instrument that evaluates sexual, urinary, and bowel function, and also measures bother, which reflects any distress caused by dysfunction. The UCLA-PCI has been widely validated in men with and without prostate cancer from several ethnicities and countries, and has been translated into and validated in Italian [28].

The SF-36 is a generic HR-QoL instrument that contains 36 questions assessing eight aspects of HR-QoL, including physical functioning (PF), role-physical functioning (RP), role-emotional functioning (RE), vitality (VI), mental health (MH), social functioning (SF), bodily pain (BP) and general health (GH) [29]. These scales can also be also grouped into physical (PCS) and mental (MCS) components scores. The higher the score, the better the results [29].

Additional urological symptoms are assessed using the valid and reliable, 7-item International Prostate Symptom Score (IPSS) [30,31] with its further item on QoL. Erectile function is assessed using the 5-item International Index of Erectile Function (IIEF) scale, a widely used, psychometrically validated multidimensional self-report instrument evaluating male sexual function [32,33].

Statistics

Participant characteristics will be summarized using descriptive statistics (mean, standard deviation, frequency, median, interquartile range). The equivalence of groups at baseline in terms of demographic and clinical variables will be assessed using independent samples t-tests for continuous variables, the Wilcoxon test for non-normal distributed variables, and chi-square tests for categorical variables. A p value < 0.05 will be considered statistically significant.

Discussion

The primary outcome of this study will be to examine a structured pre-, peri-, and post-surgical exercise program of PFMT for men undergoing RARP for prostate cancer. This trial will advance our understanding of strategies aiming at an early recovery of continence and sexual activity after RARP, and to efficiently and effectively

use the pre-and peri-operative period to optimize post-operative continence and sexual recovery, improving patients' QoL.

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