The influence of typology and posology of exercise for the preoperative strengthening training of pelvic floor in urinary incontinence post RALP

PROTOCOL NAME: The influence of typology and posology of exercise for the preoperative strengthening training of pelvic floor in urinary incontinence post RALP

PROTOCOL IDENTIFYING NUMBER: CLF19/02

PROTOCOL VERSION DATE 29/01/2019

Contact addresses : roberto.gatti@hunimed.eu

Coordinator of the study: Roberto Gatti
+390282245610

Signatures Page

STUDY COORDINATOR SIGNATURE *(where applicable)*

ROBERTO GATTI
Printed name

Physiotherapy service manager and educational coordinator of Physiotherapy degree course
Role & Department

	29/01/2019
Signature	Date

CENTRE SIGNATURE – PRINCIPAL INVESTIGATOR

I read this protocol entitled "The influence of typology and posology of exercise for the preoperative strengthening training of pelvic floor in urinary incontinence post RALP" and I agree to conduct this study, as detailed here, and according to the guidelines of the Good Clinical Practice, by applying the regulations envisaged.
I will provide all the information supplied by the sponsor to the personnel involved in the study, overseen by me, and I will inform them about their responsibilities and obligations.

ROBERTO GATTI
Printed name

Physiotherapy service manager and educational coordinator of Physiotherapy degree course
Role & Department

Via Manzoni 56 Rozzano (Mi) 20089
Address

Signature

29/01/2019
Date

Glossary of abbreviations

RALP: Robotic-assisted laparoscopic prostatectomy

PF: Pelvic Floor

UI: Urinary Incontinence

RP: Radical Prostatectomy

PFME: Pelvic Floor Muscle Exercise

PFMT: Pelvic Floor Muscle Training

STS: Sit To Stand

ICH: Istituto Clinico Humanitas

INDEX

1 Synopsis

Title	The influence of typology and posology of exercise for the preoperative strengthening training of pelvic floor in urinary incontinence post RALP
Coordinator of the study	Roberto Gatti
Protocol number	CLF19/02
Date of the protocol	29/01/2019
Background e rational	The male urinary incontinence is one of the possible complications following radical prostatectomy surgery. In patients undergoing this type of surgery, it represents one of the main problems to be solved, since it has a great impact on quality of life, on physical activity and on social well being of the individual. The recent literature defines strengthening exercises for the pelvic floor as the most effective conservative approach for the postoperative continence recovery, while the effect of a preoperative exercises training is still controversial. At present, studies evaluating the influence of a preoperative rehabilitation program in postoperative urinary incontinence to varying of exercises posology (number of daily repetitions) and of the exercises typology (isometric exercises VS functional exercises) have still not been published. The aim of this clinical study is to investigate possible chances concerning the urinary incontinence in subjects undergoing a robotic-assisted laparoscopic prostatectomy, to varying of posology and typology of preoperative exercises.
Population and inclusion criteria	120 subjects undergoing a RALP (Robotic-assisted laparoscopic prostatectomy) will be recruited. The inclusion criteria will be: RALP surgery planned after approximately 30-40 days from the preoperative session, objectivity of Pelvic Floor Muscle recruitment and contraction at manual perineal testing during preoperative session. Subjects with urinary incontinence before surgery, patients receiving radiotherapy treatment before surgery or patients who have had previous urogenital surgery shall be excluded from the study. Moreover, subjects with cognitive and/or psychiatric deficits and subjects with concurrent neurological conditions, internal conditions or disorders of the musculoskeletal system, which

	may affect the functional or motor recovery, will be excluded from the study.
Study design and duration	The study is a randomized controlled clinical trial. It will begin in March 2019 and the recruitment is expected up to November 2019. Then, data processing, analysis and the writing of a scientific work will be executed.
Objectives	The aim of the study is to investigate how posology and typology of preoperative strengthening training of Pelvic Floor Muscle before RALP surgery can affect the postoperative urinary incontinence. The recruited patient will be randomized and stratified by age in 4 groups according to exercise posology and typology. The primary outcome is to quantify the amount of the urinary leakage for 48h after 45-55 days post-surgery (Pad Test 48h). The secondary outcome is to evaluate urinary symptoms (IPSS and ICIQ-SF) and their impact on quality of life (index of quality of life 0-6), through self-assessment questionnaires compiled during preoperative session (about 30-40 days before surgery) and after 45-55- days (follow-up).
Statistical methods and data analysis	At the end of the data collection, a verification of normality and homogeneity of demographic variables and of outcome measures will be proceeded. Any differences between groups will be investigated through ANOVA test for mixed models with possible post-hoc analysis.
Ethical consideration	The aim of the study is to conduct an investigation in subjects who will undergo a RALP surgery. Participants will receive a treatment similar to treatment already described in literature and free from any adverse events for health.

2 Background and introduction

Prostate cancer is a common male cancer and a major cause of cancer-related death in men **(Lin YH et al., 2011)**.

At present, radical prostatectomy (RP) appears to be the most used therapeutic option for solving this issue **(MacDonald R et al., 2007)**. Despite improvements in surgical techniques, which allow a detailed dissection and a watertight vesical–urethral anastomosis, urinary incontinence (UI) remains a significant problem in several men undergoing radical prostatectomy **(Kjellby-Wendt G et al., 2001)**.

The reported prevalence of patients with post-prostatectomy UI varies between different studies and it is found in more than 80% of patients one month after surgery and in 30% of patients UI is still present after one year **(Chang JI et al., 2016; Zhang AY et al., 2015)**.

UI may dramatically worsen the quality of life (QoL) of a patient who has been successfully cured of prostate cancer **(D.F. Penson et al., 2005)**. Many therapeutic strategies have been adopted for treating UI, ranging from behavioral interventions to pharmacotherapy and surgical therapy **(Bauer RM et al., 2009)**.

Pelvic floor muscle exercise (PFME) is the most common conservative management for UI and it can improve the strength and endurance of striated muscles of the pelvic floor by repeated contractions, partially compensating for the urethral sphincter insufficiency **(Anderson CA et al., 2015)**. PFME is thought to be an economical and safe therapy for patients **(Huebner M et al., 2011)**.

Studies have shown that post-operatory PFME guided by a physiotherapist has favored a rapid recovery of urinary incontinence after RP **(Tienforti D et al., 2012; Manassero F et al., 2007; Filocamo MT et al., 2005)**.

Some studies, nevertheless, support that preoperative PFME can aid patients to recover urinary incontinence early post-surgery. Other studies, however, showed that preoperative PFME had limited benefits in patients after RP **(Aydın Sayılan A et al., 2018; Bales GT et al., 2000; Centemero A et al., 2010)**.

3 Rational of the study

Several studies in literature analyze the effect of a rehabilitation program after RALP surgery on post-operatory urinary incontinence, but there are conflicting results. The most important limitation of these studies is the variability of administered treatment due to a lack of standardization in typology and posology of suggested exercises.

4 General objectives

The study aims to investigate possible changes in terms of urinary incontinence in patients undergoing RALP, to varying of posology and typology of preoperative exercises.

4.1 End-points

4.1.1 Primary endpoint

The primary endpoint is to investigate the amount of urinary leakage during 48h after 45-55 post-operatory days (Pad Test 48h). In order to quantify the amount of leakage the weight of pad used by patients during 48h will be measured.

4.1.2 Secondary endpoint

The secondary endpoint is to evaluate urinary symptoms (IPSS and ICIQ-SF) and their impact on quality of life (index of quality of life 0-6), through self-assessment questionnaires compiled by patients during the preoperative session (about 30-40 days before the surgery) and after 45-55-days, during the follow-up session.

5 Selection criteria of patients

5.1 Inclusion criteria

Inclusion criteria:

- On the list for RALP (Robotic-assisted laparoscopic prostatectomy) surgery expected 30-40 days before preoperative session
- Objectivity of Pelvic Floor Muscle recruitment and contraction at manual perineal testing during pre-operative session

5.2 Exclusion criteria

Exclusion criteria:

- Incontinence before surgery
- Radiotherapy treatment before surgery
- Previous urogenital surgery
- Simultaneous presence of neurological disorders, internal conditions or disorders of the musculoskeletal system that may affect the functional or motor recovery.

Recruited subjects should respect all the mentioned eligibility criteria.

6 Study design

The study is a RCT and it will be held at Humanitas Research Hospital.

6.1 General design

120 subjects on the list for RALP surgery will be recruited. Subjects will be evaluated during the preoperative session (T0) and about 45-55 days before the surgery (T1). The initial assessment shall provide for the compilation of two self-assessment questionnaires concerning urinary symptoms: IPSS (International Prostatic Symptoms Score) and ICIQ-SF (International Consultation on Incontinence Questionnaire- Short Form). Furthermore, the impact of quality of life of patient

(index of quality of life 0-6) will be evaluated, in order to give a numerical indicator to the patient's perception about its condition.

The same questionnaires will be given by a physiotherapist during follow-up session (T1) before 45-55 days post-surgery, when the amount of urinary incontinence through PAD test 48h will be evaluated, that provides for the weighing of used pad by patient during 48 hours before the session and preserved in a zip lock bag to avoid the evaporation of urine.

A properly trained physiotherapist, who will use always the same scale, shall undertake weighing. Patient shall fill out a diary where he will take his activities carried out and the amount of drinks during the test.

Recruited subjects will be divided randomly into 4 groups:

1. ISOMETRIC STRENGTHENING once a day (1RI): patients in this group will have to play 20 tonic contractions of Pelvic Floor Muscle with a duration of 5 seconds each, performed in supine position (with bent knees and feet resting on the bed), in sitting position and in erect position. Every recruited subject will be adequately educated by a physiotherapist (following standardized instructions) during an individual session at pre-hospital (T0), and he will be instructed to continue the same exercises at home once a day (only in the morning) from the day following the session until the day before surgery. The same exercises in the same way will be resumed independently by patient 2 days after the removal of bladder catheter and they will be executed until the follow-up session (T1), about 45-55 days after surgery in order to verify the compliance with the planned program. Every subject should complete a diary where he will take the execution of daily exercises from the pre-hospital session until follow-up (excluding days of hospitalization for surgery).
2. ISOMETRIC STRENGTHENING twice a day (2RI): patients in this group will have to play the same typology of exercises in the same way just described (see above), but twice a day (in the morning and in the evening).
3. FUNCTIONAL STRENGTHENING once a day (1RF): patients in this group will have to play 10 times the postural passage from supine position to sitting position on a bed and 10 times the postural passage from sitting position to erect position (STS), maintaining the contraction of Pelvic Floor Muscle during the execution of each functional act. In sequence, starting from erect position, they will have to play 10 trunk flexion bending their knees (as to pick up an object on the ground), maintaining the contraction of Pelvic Floor Muscle during the execution of each functional movement. Every recruited subject will be adequately educated by a physiotherapist (following standardized instructions) during an individual session at pre-hospital (T0), and he will be instructed to continue the same exercises at home once a day (only in the morning) from the day following the session until the day before surgery. The same exercises in the same way will be resumed independently by patient 2 days after the removal of bladder catheter and they will be executed until the follow-up session (T1), about 45-55 days after surgery in order to verify the compliance with the planned program. Every subject should complete a diary where he will take the execution of daily exercises from the pre-hospital session until follow-up (excluding days of hospitalization for surgery).

4. FUNCTIONAL STRENGTHENING twice a day (2RF): patients in this group will have to play the same typology of exercises in the same way just described (see above), but twice a day (in the morning and in the evening).

Furthermore, a control session with a physiotherapist will be carried out before the surgery, in order to verify the proper execution of exercises learned by recruited subjects.

7 Statistical consideration

7.1 Sample size

This protocol refers to a pilot study, therefore no normative data are available. There is no study investigating the effectiveness of a preoperative Pelvic Floor Muscle Training in subject undergoing Radical Robotic-assisted Prostatectomy in literature.
These studies analyze a sample of about 100 subjects. For this protocol 120 subjects will be recruited. They will be enough to obtain an initial estimate of any changes with parameters considered.

7.2 Analysis

The statistical analysis will be made at the end of the data collection through the software SPSS 20.0. Categorical variables will be described in terms of the proportion, while continuous variables will be described in terms of an average and standard deviation or median and interquartile range.
The verification of assumption of normalcy of demographic variables and of outcome measures through Kolmogorov-Smirnov test will be proceeded. Differences between groups in time will be evaluated through mixed models ANOVA test with possible post-hoc analyses. Statistical significance level will be set at 0.05.

8 Abandonment of the study

Subjects, who during or at the end of each evaluation included in the study protocol decide to give up the study for whatever reason, will be immediately excluded from it.
Moreover, the possibility of abandoning the study also during the period from the preoperative session (T0) to follow-up (T1) will be made explicit to patients, after informing one of the experimenters. The uncompleted evaluations of recruited subjects will be excluded from the analysis of results.

9 Modules and procedures for data collection and management

Data from demographic variables and outcome measures will be included in anonymous form into Excel worksheet (*Annex B*). Only two experimenters will collect these data in order to minimize possible errors and they will be preserved in electronic format, protected by the appropriate password.

10 Ethical considerations

10.1 Patient's protection

The coordinator of the study shall ensure that this study will be conducted according to the principles outlined by Helsinki Declaration (*Annex C*) and according to laws and rules of the Country in order to ensure maximum protection of subjects recruited in the study.

After describing the protocol, the study will be conducted according to the guidelines (ICH) for Good Clinical Practice.
Protocol and its annexes are subjected to review and approval borne by the relevant Independent Ethics Committee (ICE)

10.2 Entity Identifier– Protection of personal data

All data related to the acquisitions, evaluations and all the information related to individuals will be treated in strict confidence and to the extent permissible under laws in force.

Privacy will be protected and no information will be made public. Patient's name and surname will not be asked, subjects will be identified with ID code, as indicated in *Annex B*. Information requested will be therefore date of birth, sex, weight and height. Only and exclusively person actively involved in the study will have access to database.
Each patient will be informed through a proper module related to protection of personal data *(Annex D)* and each one of them will have to sign the informed consent without which the patient cannot be involved in the study.

10.3 Informed consent

All subjects will receive information about the study, methods of performance and its goal. They will also be informed of the strict confidentiality on how their data will be processed. It is submitted that participation will be voluntary and that patient can abandon the study at any time. Each subject will compile the informed consent and only after the compilation data may be included in the collection table *(Annex E)*.

11 Conflict of interest

All members of the study declare that they have no conflict of interest.

12 Ownership of the data

In accordance with Guidelines (ICH) of the Good Clinical Practice and considering that the study is a single institution study, the owner of the data is the Humanitas Research Hospital.

After the completion of the study, the coordinator will prepare a manuscript with the final results on the basis of the statistical analysis. This manuscript, following revision, will be sent to proper

scientific journal. The coordinator of the study will revise all publications, abstract, presentations, manuscripts and slides, including data of this study.

13 Bibliography

- Anderson CA, Omar MI, Campbell SE, Hunter KF, Cody JD, et al. Conservative management for postprostatectomy urinary incontinence. Cochrane Database Syst Rev 2015; 1: CD001843.
- Aydın Sayılan A, Özbaş A. The effect of pelvic floor muscle training on incontinence problems after radical prostatectomy. Am J Mens Health 2018; 12: 1007–15.
- Bales GT, Gerber GS, Minor TX, Mhoon DA, McFarland JM, et al. Effect of preoperative biofeedback/pelvic floor training on continence in men undergoing radical prostatectomy. Urology 2000; 56: 627–30.
- Bauer RM, Bastian PJ, Gozzi C, Stief CG. Postprostatectomy incontinence: all about diagnosis and management. Eur Urol 2009; 55: 322–33
- Centemero A, Rigatti L, Giraudo D, Lazzeri M, Lughezzani G, et al. Preoperative pelvic floor muscle exercise for early continence after radical prostatectomy: a randomized controlled study. Eur Urol 2010; 57: 1039–43.
- Chang JI, Lam V, Patel MI. Preoperative pelvic floor muscle exercise and postprostatectomy incontinence: a systematic review and meta-analysis. Eur Urol 2016; 69: 460–7.
- Filocamo MT, Li Marzi V, Del Popolo G, Cecconi F, Marzocco M, et al. Effectiveness of early pelvic floor rehabilitation treatment for post-prostatectomy incontinence. Eur Urol 2005; 48: 734–8.
- Huebner M, Riegel K, Hinninghofen H, Wallwiener D, Tunn R, et al. Pelvic floor muscle training for stress urinary incontinence: a randomized, controlled trial comparing different conservative therapies. Physiother Res Int 2011; 16: 133–40.
- Lin YH, Yang MS, Lin VC, Yu TJ, Chiang PH. The effectiveness of pelvic floor exercise on urinary incontinence in radical prostatectomy patients. Int J Urol Nurs 2011; 5: 115–22.
- MacDonald R, Fink HA, Huckabay C, Monga M, Wilt TJ. Pelvic floor muscle training to improve urinary incontinence after radical prostatectomy a systematic review of effectiveness. BJU Int 2007; 100: 76–81.
- Manassero F, Traversi C, Ales V, Pistolesi D, Panicucci E, et al. Contribution of early intensive prolonged pelvic floor exercises on urinary continence recovery after bladder neck-sparing radical prostatectomy: results of a prospective controlled randomized trial. Neurourol Urodyn 2007; 26: 985–9.

- Tienforti D, Sacco E, Marangi F, D'Addessi A, Racioppi M, et al. Efficacy of an assisted low-intensity programme of perioperative pelvic floor muscle training in improving the recovery of continence after radical prostatectomy a randomized controlled trial. BJU Int 2012; 110: 1004–10.
- Zhang AY, Bodner DR, Fu AZ, Gunzler DD, Klein E, et al. Effects of patient-centered on persistent urinary incontinence after prostate cancer treatment: arandomized controlled trial. J Urol 2015; 194: 1675–81.

List of annexes

Annex A_ Scheme of study

Annex B_ Data collection sheet

Annex C_ Helsinki Declaration

Annex D_ Informed consent

Annex E_ Privacy statement

Annex H_ Curriculum Vitae Roberto Gatti