PEnile ReHAbilitation After Nerve Sparing Robot-assisted Radical Prostatectomy for Prostate Cancer 2.0, a Multicenter, Randomized Clinical Trial

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This study aims to assess the effect of two different rehabilitation strategies on the recovery rate of ED after nsRP in patients who undergo nsRP.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Sexual function and fertility disorders
Study type	Interventional

Summary

ID

NL-OMON56218

Source
ToetsingOnline

Brief title
PEHAB-II Trial

Condition

- Sexual function and fertility disorders

Synonym
Erectile dysfunction after prostatecancer, impotence

Research involving
Human

Sponsors and support

Primary sponsor: Urologie
Source(s) of monetary or material Support: Memidis Pharma,Via een donatie van een

patiënt aan de AvL Foundation,Viatris

Intervention

Keyword: Multimodal Therapy, Nervesparing prostatectomy, Penile Rehabilitation, Vacuumdevice

Outcome measures

Primary outcome

The primary endpoint is an adequate, unassisted erection at 24 months after surgery. In this, an adequate unassisted erection is defined as an erection sufficient for successful sexual intercourse without the use of medication or devices. Measured by IIEF-EF>/=22 after a one-month drug washout or EPIC-erection score (sum off Q8b, 9 and 10) >=83 for patients who did not participate in penetrative sex.

Secondary outcome

Secondary endpoints include erectile function (assisted, unassisted, time to recovery, penile length), health and sexual quality of life (other sexual functions, climacturia, feelings of masculinity, health related quality of life of both patients and partners, partner interaction from both perspectives and differences between hetero versus gay/bisexual patients during follow-up), Adherence and side-effects and comparing two sexual function questionnaires.

Study description

Background summary

Postoperative erectile dysfunction (ED) is a widely observed side effect of prostate cancer surgery for clinically localized prostate cancer and it has a substantial impact on the quality of life. While nerve-sparing radical

prostatectomy (nsRP) has improved the outcomes of erectile function, ED rates remain high even after well-performed nsRP. It is important to note that ED after nsRP is not primarily caused by complete transection (neurotmesis) but rather by neuronal crushing and/or overstretching (neuropraxia) of the neurovascular bundle running alongside the prostate towards the erectile tissue of the penis. It is suggested that the post-operative care is insufficient to consolidate the effects of nsRP because penile rehabilitation is necessary to activate neural recovery as well as to retain the vasculogenic functions of the penile corpora cavernosa. However, the best penile rehabilitation strategy to reduce post-operative ED remains unclear due to a lack of well-designed randomized studies.

Study objective

This study aims to assess the effect of two different rehabilitation strategies on the recovery rate of ED after nsRP in patients who undergo nsRP.

Study design

This study is a multicentre, randomized, controlled clinical trial.

Intervention

Patients will be randomized 1:1: to arm 1: High intensive therapy using a daily dose of 75-100 mg Sildenafil for 12 month, combined with vacuum device (VED) therapy for 10 minutes a day, five times a week; or to arm 2: Less intensive therapy using 75/100mg Sildenafil on demand (before sexual activity). After these 12 months in therapy, the treatment intensity can be adjusted for the next 12 month until the full neuropraxia recovery time (24 month) has been reached. The treatment option that can be used to intensify the therapy is intracavernosal injection therapy (ICI), in which erections can be obtained quickly by injecting papaverine/phentholamine (Androskat) in the penis. This auxiliary therapy can be an option for those that do not want to wait any longer for the recovery of their spontaneous erections and thus that want to use ICI to obtain erections in the meantime. It is important to note that ICI is not a part of the rehabilitation program and thus is not mandatory. Patients will finish participating in the trial after 24 months follow-up. One month before end of follow-up (23 months) a drug washout will take place. Endpoints will be assessed after 24 months using validated questionnaires as well and composed validated questions.

Study burden and risks

In this study, patients will be evaluated at baseline and every three months thereafter through telephonic appointments, online surveys, and outpatient clinic visits. These outpatient clinic visits will take 20 minutes on average.

Patients and partners will fill out HRQoL questionnaires and questionnaires on sexual functioning online. In order to answer these questions correctly, patients and partners will be advised to participate in sexual activity at least once a month. Answering the questionnaires will take approximately 20 minutes. for patients and 10 minutes for partners. In addition, patients will be asked to provide blood samples once at baseline, to determine testosterone levels, HbA1c, liver enzymes, and lipid profiles. Patients may experience side effects from sildenafil (such as dyspepsia, dizziness, and headache) or the VED (i.e. cold feeling, pain, hematoma, or oedema). These effects are temporary and subside within 25 hours. Participating patients in both arms benefit from free sildenafil and VED, along with the extra attention and guidance provided for sexual recovery, sexual health and erectile function compared to patients that do not participate in the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Pre-screening eligibility criteria
* Age > 18 years and < 75 years
* Patients who have a penis that has developed naturally, without surgical interventions.
* Histologically confirmed PCa
* Scheduled for RP as primary treatment with the intention of at least a one-sided nerve-sparing procedure.
* Non-metastatic disease (cN0M0)
* Pre-operative erections good enough for intercourse (anamnestic)
* Motivated to participate in a penile rehabilitation program
Inclusion criteria
To be eligible to participate in this study, a subject must meet all of the following post- operative criteria:
* All of the above-mentioned pre-screening eligibility criteria
* At least unilateral nerve-sparing or if available FP score =>5
* A pre-diagnostic anamnestic erection that was good enough for intercourse.
* A pre-diagnostic IIEF-EF>=22 with or without PDE5i. For patients without a partner or did not participate in
penetrative sex we use accumulated score of EPIC- erectile function; Q8b, Q9 and Q10 >=83.
* Willing to provide one blood sample to determine testosterone level, Hb1Ac, liver enzymes and lipid profile
* Testosterone levels of at least >9 nmol/l, measured pre or post-operative, blood needs to be obtained before 11 am and before breakfast with the absence of hypo gonadal symptoms such as loss of libido, lack of energy and orgasmic dysfunction.
* A signed informed consent form

Exclusion criteria

6.3 Pre-screening exclusion criteria:
Regarding history of oncological treatment
* Previous pelvic radiation therapy
* Patients on Androgen Deprivation Therapy (ADT)
* Patients with diseases that affect the red blood cells (e.g., sickle cell anaemia), blood cancer (leukaemia) or
bone marrow tumors
Regarding history of cardiovascular diseases
* Patients with heart failure New York Heart Association (NYHA) >= class 3
* Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction
(e.g., aortic stenosis, hypertrophic obstructive cardiomyopathy), or those with

the rare syndrome of multiple
system atrophy manifesting as severely impaired autonomic control of blood pressure.
* Patients with unstable angina pectoris
* Patients using nitride oxide for coronary artery disease
* Patients with hypotension (blood pressure <90/50 mmHg)
* Patients with recent (within the last 6 months) history of stroke or myocardial infarction
* Patients with diseases that affect blood clotting or causes bleeding (i.e. coagulation disorders) or prolonged
erections
Other pre-screening exclusion criteria:
* Patients with neurological diseases; such as CVA, TIA, Parkinson, and polyneuropathy.
* Allergy regarding Sildenafil
* Patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy
(NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure.
* Patients with severe hepatic impairment (based on blood test)
* Patients with known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of
these patients have genetic disorders of retinal phosphodiesterases).
* Patients using alpha-blockers, but they may be eligible to participate after discontinuing alpha-blocker use.
* The inability to speak and read in Dutch
Exclusion criteria
* A potential subject who meets any of the following criteria will be excluded from participation in this study:
* All of the above-mentioned pre-screening exclusion criteria
* Adjuvant radiotherapy or hormonal therapy
* Inability to use VED such as severe penile deformity or too much peripubic, or belly fat causing fitting problems

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-01-2024
Enrollment:	220
Type:	Actual

Medical products/devices used

Generic name:	Vacuum erectile device
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	14-12-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-04-2024
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84375.041.23