EffectiveNess of a multimodal preHAbilitation program in patieNts with bladder canCEr undergoing cystectomy. The ENHANCE randomized controlled trial.

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To study the effectiveness of a multimodal prehabilitation program preceding radical cystectomy in reducing the number and severity of perioperative complications within 90 days, shortening the length of hospitalization and reducing the number of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54317

Source
ToetsingOnline

Brief title
ENHANCE

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
bladder tumor; bladder cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: bladder cancer, cystectomy, physical fitness, prehabilitation

Outcome measures

Primary outcome

The number of perioperative complications (grade 2 or higher) in the first 90 days following surgery.

Secondary outcome

The number of high-grade (grade 3 or higher) complications, length of hospital stay, number of readmissions, improvement over time (pre- to post surgery) in cardiorespiratory fitness, physical functioning, nutritional status and a number of patient-reported outcomes (health-related quality of life, anxiety and depression, fatigue, levels of physical activity), changes in tumor hypoxia and health care costs.

Study description

Background summary

In the Netherlands annually around 6500 patients are diagnosed with bladder cancer. About 20-30% has muscle invasive disease for which radical cystectomy (RC) is an established effective treatment. RC is also the treatment of choice in case of a high-risk tumor and in intravesical chemotherapy refractory bladder cancer. RC is a challenging and costly surgical procedure and results in 50-65% of patients experiencing perioperative complications of which 10-20% are high-grade. Bladder cancer patients often have poor levels of cardiorespiratory fitness, are malnourished, and smoke. This poor fitness and nutritional status may be exacerbated by neoadjuvant chemotherapy. At the same

time, low fitness, malnutrition, smoking, as well as experiencing of anxiety and/or depression before surgery are related to the occurrence of perioperative complications and longer length of hospital stay, leading to higher medical costs. The potential value of a multimodal preoperative psychological counseling in these patients has been understudied and no adequately powered trial has been performed to establish its effectiveness in reducing morbidity and costs.

Study objective

To study the effectiveness of a multimodal prehabilitation program preceding radical cystectomy in reducing the number and severity of perioperative complications within 90 days, shortening the length of hospitalization and reducing the number of readmissions. Furthermore, we will investigate the effects of the prehabilitation program on physical fitness, muscle strength, physical functioning, nutritional status, smoking behaviour, anxiety and depression, fatigue, quality of life, physical activity, tumor tissue characteristics, and healthcare costs.

Study design

A multicenter randomized controlled trial.

Intervention

Patients will be randomized to either an intervention group or to a usual care control group (1:1 allocation). The intervention group will receive a structured multimodal prehabilitation program consisting of a tailored exercise program, nutritional intervention and if relevant smoking cessation and/or psychological counseling. The exercise program is designed to maximize improvement in cardiorespiratory fitness and decrease anxiety and depression within a short timeframe (approximately 3-6 weeks). The intervention consists of a 3 times weekly individually tailored supervised aerobic training (3x/week, resistance training (2x/week) and relaxation exercises (1x/week). Additional instructions for exercising and relaxation at home will be provided. For patients who receive neo-adjuvant chemotherapy treatment, the intervention consists of a 2 times weekly supervised aerobic training combined with resistance exercises during chemotherapy treatment. Similar programs have been demonstrated to be both feasible and effective in a number of older and vulnerable patient populations. Nutritional counseling will be provided by a dietician, including tailored dietary advice aiming at a total protein intake of 1.9 (- max 2.3) g/kg fat free mass per day and a minimum of 25-30 g protein/meal. In addition, patients will be provided with a supplement containing 30 g of protein, 20 microgram of vitamin D and 250 mg of calcium immediately after supervised training and daily in the morning after waking up or before sleep. Smoking cessation assistance will be provided by intensive

in-person counseling and telephone follow-up, and nicotine replacement therapy. The smoking cessation program will involve intensive in-person counseling, telephone follow-up, and nicotine replacement therapy. Patients who screen positive for clinically relevant levels of anxiety and/or depression will be referred to an appropriate medical health professional (i.e., social worker, psychologist or psychiatrist).

Study burden and risks

Participating in the study requires time for the measurements (all patients) and for the training and supervision with regard to nutrition and possible smoking cessation and/or psychological consultation (patients in the intervention group). Patients who start exercising can also experience the normal effects of exercise such as temporary fatigue or muscle pain.

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

patients who have histologically confirmed, primary, bladder cancer (cTa-4N0/N+M0)

Exclusion criteria

Patients with severe cognitive or psychiatric disorders; patients who are operated within 3 week; patients with insufficient command of the Dutch language, which precludes them from following study instructions or completing study questionnaires; patients who have contraindications to safely perform exercise training or testing, and; patients who express the intention to follow a similar exercise training programme regardless of randomisation outcome.

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-08-2022
Enrollment:	148
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	11-07-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-02-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2025
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	NL78792.031.22