Favorable and unfavorable effects of risk-reducing salpingo-oophorectomy (RRSO) in women at high genetic risk of ovarian cancer

Published: 18-07-2018
Last updated: 12-04-2024

Primary Objective: To study long-term effects of premenopausal risk-reducing salpingo-oophorectomy (RRSO) on - cardiovascular status- bone mineral density- cognitionSecondary Objective: To study long-term effects of premenopausal RRSO on - quality…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON50443

Source
ToetsingOnline

Brief title
HARMOny (Health After eaRly Menopause due to Oophorecomy)

Condition

- Other condition
- Menopause related conditions
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
ovariectomy, RRSO

Health condition

Botgezondheid

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Bone health, Cardiovascular disease, Cognition, Risk-reducing salpingo-oophorectomy (RRSO)

Outcome measures

Primary outcome

We will assess long-term physical and mental health of 500 women who underwent premenopausal RRSO compared to 250 women of the same age without RRSO (or RRSO after the age of 55) in a cross sectional retrospective cohort study on

- (subclinical)Cardiovascular disease

- Bone mineral density

- Cognitive functioning

Secondary outcome

Secondary parameters will be differences in the following factors between women with premenopausal RRSO and women without premenopausal RRSO:

- Quality of life

- Sexual functioning

- Urogenital problems

Study description

Background summary

Women at high genetic risk of ovarian cancer (OC) are advised to undergo risk-reducing salpingo-oophorectomy (RRSO) at ages 35-45 years. Currently, in the Netherlands ~500 women/ year opt for RRSO, which minimizes OC risk and may decrease breast cancer (BC) risk as well, due to reduced gonadal hormone levels. Besides favorable effects of RRSO on OC and, potentially, BC risk, RRSO induces immediate menopause, which may have unfavorable health consequences. Early menopause has been associated with increased risks of cardiovascular disease (CVD), lower bone mineral density (BMD), cognitive impairment, and decreased quality of life (QoL). Current evidence regarding these health effects is mainly based on women with a natural early menopause, and it is unknown whether these results hold for women undergoing RRSO at early premenopausal ages.

Study objective

Primary Objective:
To study long-term effects of premenopausal risk-reducing salpingo-oophorectomy (RRSO) on
- cardiovascular status
- bone mineral density
- cognition

Secondary Objective:
To study long-term effects of premenopausal RRSO on
- quality of life
- urogenital problems
- cardiovascular risk factors

Subgroup analysis of the effect of RRSO on CVD, BMD, cognition and Quality of life will be performed according to:
- age at RRSO
- time since RRSO
- hormone replacement therapy
- BRCA1/2 mutation carrier ship
- breast cancer history

Study design

a cross-sectional study of women with premenopausal RRSO compared to women of the same age without premenopausal RRSO. We will invite them to participate in a screening program assessing cardiovascular status, bone mineral density, cognitive functioning and quality of life.

we will assess the long-term effects of premenopausal RRSO on cardiovascular status, bone mineral density and several aspects of quality of life in a subgroup of women who underwent RRSO > 10 years ago and a comparison group. In

this study women will be invited for a medical assessment. During this medical assessment the coronary artery score (CAC score) will be calculated as an indication of (sub)clinical atherosclerosis as will the Pulse Wave Velocity (PWV). Also the Advanced glycation end products (AGEs) will be calculated using autofluorescence of the skin and the breast arterial calcification (BAC) score will be calculated using mammograms. The length and weight of patients will be measured as will the blood pressure and some specific cardiac enzymes in the blood. For the calculation of the BMD a DEXA scan and some specific markers in the blood will be tested. Cognitive function will be assessed using an online test recently developed and for the QoL a questionnaire is filled in. We select 500 women with premenopausal RRSO and 250 women without RRSO of RRSO after 55 years of age.

multivariate linear regression analyses will be performed. Adjustment for confounders (lifestyle factors, reproductive factors, medication use) will be made. Analyses will be performed separately in women with and without BC history (treatment as a confounding factor). Subgroup analyses are planned according to HRT use (type, duration and timing of use), BRCA1/BRCA2 mutation status, age at RRSO, time since RRSO

Women recruited from the UMCG are able to specify whether they want to fill in an online questionnaire or a paper questionnaire. The questionnaire includes questions that are relevant for assessment of osteoporosis and fracture risk, such as fracture history, corticosteroid use, calcium and vitamin D intake, duration of HRT use, physical activity and questions on lifestyle.
We will send two reminders to all eligible non-responding women, one after one month, and one two months after the initial invitation. Women who do not want to participate can send their refusal on the same reply form. A pre-stamped envelope will be enclosed in the envelope containing the invitation letter and information folder. Women willing to participate will be scheduled for a visit in the UMCG. If possible, the DEXA scan will be performed on the same day. Travel and parking cost of participants will be reimbursed if necessary. Participants are able to withdraw from the study at any time for any reason.

Study burden and risks

The cardiovascular and fracture risk assessment will be performed consecutively in one morning or afternoon. All medical tests combined will take 2.5 hours. Test results will be discussed and when medical care is warranted (e.g. increased blood glucose or hypertension) patients will be referred to their general practitioner (e.g. in case of hypertension) or medical specialist if specialized care is indicated (e.g. a cardiologist in case of suspected impaired cardiac function as measured by ECG or NT-proBNP-level). They will be offered standard of care according to the clinical practice guidelines and the guidelines from the European Society for Cardiology. If the test results implicate no further treatment, participants will not be informed about their results.

Assessment of neurocognitive functioning in the current study will take place at home, 1-3 weeks after the study visit in the hospital, to prevent overburdening of participants before the study visit when they are already asked to complete a questionnaire on general health, risk factors and quality of life

We will assess generic HRQOL the SF-36 Health Survey. All raw scale scores were linearly converted to a 0 to 100 scale, with higher scores indicating higher levels of QOL. We will assess cancer-specific distress with the 7-item Intrusion subscale of the Impact of Events Scale, with the frequency of intrusive thoughts about the increased risk of developing breast/ovarian cancer as the stressor. Cancer worries will be measured with 5 items adapted from Lerman. Self-perceived cancer risk will be assessed with 2 items used in previous studies. To assess endocrine symptoms we will employ the 18-item FACT-ES and the Hot Flush rating Scale (HFRS). The Sexual Activity Questionnaire (SAQ) will be used to measure sexual functioning. Urogenital problems will be evaluated using the Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7).

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121 Plesmanlaan 121
Amsterdam 1066 CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121 Plesmanlaan 121
Amsterdam 1066 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Female patients
High genetic risk of ovarian cancer
Risk reducing salpingo-oophorectomy before the age of 46, or (for control group):
High genetic risk for ovarian cancer
Natural menopause after age of 50 years
No RRSO before 55 years of age
No treatment induced menopause before 50 years of age

Exclusion criteria

For both groups:
History of gynecological cancer at time of RRSO
History of cancer at time of testing for BRCA-1 / BRCA-2
Ovariectomy for other reasons in patient history
Cystectomy in patients history
Metastatic disease
Other serious comorbidity, psychiatric disorders, which would interfere with a clinic visit
Not enough understanding of the Dutch language
Non-bioresorbable cardiac stent
Younger age than 55 years
Premature Ovarian Insufficiency

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-02-2019
Enrollment:	750
Type:	Actual

Ethics review

Approved WMO Date:	18-07-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-08-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-10-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-05-2022
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
ClinicalTrials.gov	NCT03835793
CCMO	NL63554.031.17