Vruchtbaarheid, eicelvoorraad en vervroegde overgang bij Nederlandse vrouwen die in hun jeugd kanker hebben gehad .

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25491

Source
NTR

Brief title
VEVO-onderzoek

Health condition

childhood cancer , fertility, ovarian reserve, premature menopause

Sponsors and support

Primary sponsor: VU University Medical Center Amsterdam
Source(s) of monetary or material Support: Dutch Cancer Society (in Dutch: KWF) Cildren CancerFree (in Dutch: KiKa)

Intervention

Outcome measures

Primary outcome

1. Questionnaire part: Reproductive history, pregnancy outcomes, menopausal symptoms and menopause;

2. Clinical part: FSH, Estradiol, inhibin B, AMH,
ovarian reserve.

Secondary outcome

1. Questionnaire part: Co-morbidities, menstrual history, family history of subfertility;

2. Clinical part: Ovarian volume, uterus flow, uterus length.

Study description

Background summary

BACKGROUND:

Because of improvements in the treatment of childhood cancer in the past decades, survival among this group of patients has significantly increased. This has resulted in a rapidly growing group of childhood cancer survivors (CCS). There is much concern, however, about the effects of treatment on reproductive potential. In females there is evidence that both chemo- and radiotherapy may adversely affect ovarian function, ovarian reserve, and uterine function, clinically leading to sub- or infertility, adverse pregnancy outcomes, and/or premature menopause. The available literature suggests that some female CCS may enter menopause as early as the age of 32. With the current Dutch trend to postpone childbearing to the thirties, more insight into the effect of various cancer treatments on ovarian function and reserve is, therefore, essential. Not only to prevent involuntary childlessness but also to prevent menopause-associated conditions such as symptoms of oestrogen deficiency, osteoporosis and cardiovascular disease.

In the literature to date, ovarian function and reserve are assessed by traditional measurements of the pituitary and sex hormones. These markers, however, are of limited value when aiming to assess reproductive potential and risk of premature menopause. New techniques (3D ultrasound measurements of the ovaries and anti-Müllerian hormone (AMH) concentrations), may provide a better insight into ovarian function and reserve. However, to our knowledge, they have rarely been used in CCS.

AIM:

The aim of this study is to assess, in female CCS in the Netherlands, the effects of treatment in general, and the effects of different types of treatment, doses of drugs, radiation sites and

doses, and age at time of treatment on:

1. Ovarian function and actual fertility;

2. Ovarian reserve and (risk of) premature menopause;

3. Uterus function and pregnancy outcome.

This with the intention to:

1. Identify subgroups of female CCS who have an increased risk of premature menopause and, therefore, are potential candidates for early testing of ovarian function and reserve;

2. Optimize the referral of female patients with childhood cancer, who are about to start treatment, to clinical interventions aimed at preserving their reproductive function, such as hormonal manipulation and cryopreservation of ovarian tissue;

3. Contribute to the design of new treatment protocols with maximum treatment efficacy and a minimal risk of reproductive late effects.

MATERIALS AND METHODS:

The study is a multi-center retrospective cohort study, coordinated by the VU university medical center (VUmc) but performed in collaboration with all Dutch Paediatric Oncology and Stem Cell Transplant Centers. These centers are united in a nationwide collaborative group for Late Effects Registration of Childhood Cancer (LATER).
The study population will be selected from an estimated cohort of 2500 female 5-year CCS, treated between 1965 and 2002. At study entry they should be at least 18 years of age. An equally sized group of age-matched female siblings will be used as controls. The study consists of two parts: a questionnaire and a clinical part. In the clinical study, ovarian function and reserve will be assessed from:

1. Blood levels of the hypothalamic-pituitary hormones, sex hormones, inhibin A an B, and AMH;

2. Three-dimensional (3D) ultrasound measurements of ovarian volume and the number of antral follicles in the ovaries. Uterine size and blood flow, also assessed by ultrasound, will evaluate uterine function while actual fertility, pregnancy outcomes and menopausal status will be assessed from the mailed questionnaire.

CLINICAL/SCIENTIFIC RELEVANCE:

Among CCS, there are serious concerns about reproductive potential. This study will provide

an accurate estimate of overall and treatment specific relative and absolute risks of compromised reproductive function, ovarian reserve and premature menopause in female CCS. This increased knowledge will greatly improve the physicians ability to counsel CCS on family planning. However, not only female survivors of childhood cancer will potentially benefit from this study. Also females which are about to undergo cancer therapy may benefit since proven high risk populations can be offered clinical interventions aimed at preserving a women's reproductive function, such as hormonal manipulation, cryopreservation and transplantation of embryos or ovarian tissue, and conservative fertility-sparing surgery. All with the aim of improving the quality of life.

Study objective

To assess the effects of treatment in general, and the effects of different types of treatment, doses of drugs, radiation sites and doses, and age at time of treatment on:

1. Ovarian function and actual fertility;

2. Ovarian reserve and (risk of) premature menopause;

3. Uterus function and pregnancy outcome.

Study design

Timing of clinical measurements (blood sample and ultrasound measurement): Day 2-5 of natural menstrual cycle or day 7 of hormone-free interval in case of use of oral contraceptives.

Intervention

Questionnaire, provision of a blood sample, and transvaginal ultrasound measurement of the reproductive organs.

Contacts

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Eligibility criteria

Inclusion criteria

1. Female;

2. Treated for malignancy or a central nervous system tumour before the age of 18;

3. Treated between 1965 and 2001, 5-year survivors;

4. At least 18 years at study entry.

Exclusion criteria

1. Being unable to speak or read Dutch;

2. Having severe mental sequelae;

3. Being pregnant or lactating at time of study.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2006
Enrollment:	2000
Type:	Anticipated

Ethics review

Positive opinion

Date:	31-05-2011
Application type:	First submission

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
NTR-new	NL2782
NTR-old	NTR2922
Other	METC VUmc / CCMO ABR form : 06/249 / NL15106.029.06;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

Van den Berg MH, van Dulmen-den Broeder E, Overbeek A, Twisk JW, Schats R, van Leeuwen FE, Kaspers GJ, Lambalk CB.
Comparison of ovarian function markers in users of hormonal contraceptives during the hormone-free interval and subsequent natural early follicular phases. Hum Reprod. 2010 Jun;25(6):1520-7.