

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

Gepubliceerd: 31-05-2011 Laatste bijgewerkt: 18-08-2022

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)...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON25491

Bron

NTR

Verkorte titel

VEVO-onderzoek

Aandoening

childhood cancer , fertility, ovarian reserve, premature menopause

Ondersteuning

Primaire sponsor: VU University Medical Center Amsterdam

Overige ondersteuning: Dutch Cancer Society (in Dutch: KWF)

Children CancerFree (in Dutch: KiKa)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Questionnaire part: Reproductive history, pregnancy outcomes, menopausal symptoms and menopause;
2. Clinical part: FSH, Estradiol, inhibin B, AMH, ovarian reserve.

Toelichting onderzoek

Achtergrond van het onderzoek

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 and 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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Being unable to speak or read Dutch;
2. Having severe mental sequelae;
3. Being pregnant or lactating at time of study.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blinding:	Open / niet geblindeerd

Controle: Geneesmiddel

Deelname

Nederland
Status: Werving gestart
(Verwachte) startdatum: 01-12-2006
Aantal proefpersonen: 2000
Type: Verwachte startdatum

Ethische beoordeling

Positief advies
Datum: 31-05-2011
Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten

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.