The EARLY study: Early detection of acute and early-onset cARdiovascuLar toxicitY in children with cancer using a multiparametric approach.

Published: 05-02-2020
Last updated: 10-04-2024

1. To investigate the feasibility to perform advanced echocardiographic measurements2. To describe the incidence and variation of cardiac damage during and shortly after treatment using detailed advanced echocardiographic measurements and ECG at...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Observational invasive

Summary

ID

NL-OMON49327

Source
ToetsingOnline

Brief title
The EARLY study

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
cardiomyopathy, heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie

Source(s) of monetary or material Support: KiKa

Intervention

Keyword: cancer, cardiovasculair toxicity, children, early detection

Outcome measures

Primary outcome

Outcome definitions for the pilot study

1.Echocardiography systolic dysfunction at pretreatment, 3-4 months after start treatment and 1-year post start treatment:

• A change in left ventricular ejection fraction (EF) (echocardiography), defined as a decline in EF of >10% from baseline measurement or a decrease to a value <50% or symptomatic heart failure

• A change in left ventricular fractional shortening (echocardiography), defined as a decline in fractional shortening of >10% from baseline measurement or to a value <28% or symptomatic heart failure

• A change in left ventricular global longitudinal strain (GLS) measurements (echocardiography), defined as >15% decline in GLS from baseline measurement

2.Presence of myocardial fibrosis (MRI) at pretreatment, 3-4 months after start treatment and 1-year post start treatment expressed by increased myocardial T1 values and/or ECV (extracellular volume).

Secondary outcome

1. Abnormal blod biomarkers pretreatment, after 3-4 months of treatment, 1 year after start of treatment

2. ECG abnormalities pretreatment, after 3-4 months of treatment, 1 year after

start of treatment

Study description

Background summary

Early detection of (subclinical) cardiotoxicity is crucial, to allow for timely intervention and prevention of further progression of cardiac disease. Anthracyclines and radiotherapy of the chest and mediastinum including the heart are both cornerstones in the treatment of children with cancer (CC), including Hodgkin Lymphoma (HL), osteosarcoma (OS), Ewing sarcoma (ES) and soft tissue sarcoma (STS). Irradiated patients are also prone to develop accelerated coronary artery disease, valvular and pericardial disease, conduction abnormalities and arrhythmias, especially if treated with high-dose thoracic radiotherapy. In CC patients treated with an anthracycline-based chemotherapy, approximately 10% develop overt congestive heart failure 40 years after treatment, as a result of anthracycline exposure. Prospective information on the incidence, the extent and prognostic value of subclinical cardiotoxicity in children during treatment for CC is scarce. Echocardiography is the current tool for detecting cardiac disease related to cardiotoxicity - given its low costs, widespread availability, and reproducibility - but was limited in the past to detection of only overt systolic dysfunction. Recently introduced advanced echocardiography techniques using strain measurements by myocardial deformation analysis, have demonstrated the potential to detect subclinical cardiac dysfunction, even before systolic dysfunction becomes apparent. In addition, cardiac MRI has recently emerged as an important non-invasive imaging tool for myocardial tissue characterization. Myocardial tissue mapping by MRI allows for quantification of myocardial fibrosis and scar tissue as a response to cardiac damage by cardiotoxicity, while myocardial deformation analysis provides subtle functional assessment of the heart, with delineation of the maladaptive changes in response to myocyte injury. Cardiac biomarkers and ECG analysis can provide complementary information about the cardiac disease status, while genetic testing may help with prediction of potentially increased susceptibility for the development of cardiotoxicity of the individual patient. Therefore, a multimodality approach using advanced echocardiography and MRI, together ECG, will allow for a comprehensive assessment of potential risk factors and disease course of early cardiac disease in CC patients, and will hopefully provide insights for early detection and early start of treatment in CC treated with anthracyclines and/or radiotherapy in the cardiac region.

Study objective

1. To investigate the feasibility to perform advanced echocardiographic

measurements
2. To describe the incidence and variation of cardiac damage during and shortly after treatment using detailed advanced echocardiographic measurements and ECG at different time points
3. To assess the association between abnormalities measured in objective 1 with anthracycline dose, chest irradiation dose, disease profile, age at diagnosis, and gender.
4. To collect blood for future assessment of biomarkers and pharmacogenetics.Subgroup of 30 children with cancer with anthracyclines
5. To investigate the feasibility to perform cardiac MRI during MRI*s that are planned for tumor response evaluation.
6. To describe the incidence and variation of cardiac damage during and shortly after treatment using MRI markers of myocardial fibrosis at different time points, and the association with anthracycline dose, chest irradiation dose, disease profile, age at diagnosis, and gender.
7. To investigate the association between MRI abnormalities and echo parameters.

Study design

Prospective follow-up pilot-study in children with cancer from diagnosis to 1 year post diagnosis.

Study burden and risks

Patient burden
Cardiac evaluation for this study will be closely intertwined with the routine oncological evaluation documented in the international cancer treatment protocols, to minimize the burden on the study participants. Echocardiography, MRI and ECG are routinely obtained for the first time point of the study (at baseline). The supportive care guidelines state that an echocardiogram should be performed when a cumulative dose of anthracyclines (doxorubicine and daunorubicine 240 mg/m2; epirubicine 400 mg/m2; idarubicine and mitoxantrone 60 mg/m2) is reached. The cardiac MRI evaluation will be incorporated in the routine MRI for oncological evaluation (extra duration 15-20 minutes of cardiac scanning), which implies only a limited burden on the study participants. MRI at time points 3-4 months and 1 year after treatment are for research purposes. Echocardiography and ECG will be done simultaneously and will approximately take one hour. Blood samples for future use for cardiac biomarkers and genetic testing will be drawn at the same time when the patient will need blood sample collection routinely for treatment evaluation. All CC patients included into this study will have a central venous access.

Contacts

Public
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584CS
NL
Scientific
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584CS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1) 100 children with cancer receiving anthracyclines according to their treatment protocol
2) A subgroup of 30 children, aged > 8 years, diagnosed with Hodgkin Lymphoma, Ewing Sarcoma, Osteosarcoma or Soft Tissue Sarcoma who have MRI evaluation as part of their tumor response evaluation.
3) a signed informed consent

Exclusion criteria

Children with

1) severe comorbidity
2) congenital heart disease
3) a history of thoracic radiation or chemotherapy for other malignancies
4) general contraindications for MRI for the patients in the MRI study group.
5) Patients who need anaesthesia for MRI scanning

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-11-2020
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	05-02-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-08-2020
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-09-2021
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	NL71056.041.19
Other	NTR nummer: NL7980