Cardiopulmonary toxicity of thoracic radiotherapy.

Published: 07-03-2018
Last updated: 12-04-2024

The main objective is to test if PH occurs in patients treated with thoracic radiotherapy and identify dose metrics and other risk factors for the development of PH after thoracic radiotherapy. In addition, changes in systolic and diastolic...

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

Summary

ID

NL-OMON48574

Source
ToetsingOnline

Brief title
CLARIFY

Condition

- Cardiac disorders, signs and symptoms NEC
- Pulmonary vascular disorders
- Vascular disorders NEC

Synonym
Cardiopulmonary toxicity; pulmonary hypoertension

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Cardiopulmonair, Lung- and esophageal carcinoma, Radiotherapy, Toxicity

Outcome measures

Primary outcome

The following primary endpoints will be assessed:

Primary aim is to confirm that PH occurs in patients receiving thoracic radiotherapy and assess incidence and time course. Therefore we decided to use high-risk pulmonary hypertension as assessed by echocardiography at one year after radiotherapy as primary endpoint. Following the ECS/ERS guidelines (25), a patient is classified as high risk of PH when meeting one of the following criteria:

- tricuspid valve Doppler velocity 2.9-3.4m/s with other signs of PH (see below)

- tricuspid valve Doppler velocity >3.4m/s

Other signs of PH are:

- Pulmonary artery acceleration time (<105 ms)

- Early pulmonary valve diastolic velocity (>2.2 m/s)

- Doppler notching of right ventricular outflow tract signal (y)

- Inferior Caval Vein collapsibility (>21 mm and <50% collapse)

- Left ventricle eccentricity index (>1.1 in systole)

- RV dilatation (RVEDV>45mm)

Secondary outcome

The following secondary endpoints will be assessed:

- Intermediate risk of PH:

o tricuspid valve Doppler velocity <2.8m/s in combination with other signs of PH

o tricuspid valve Doppler velocity 2.9-3.4m/s without *other signs of PH*

- Right ventricle systolic dysfunction

- Right ventricle diastolic dysfunction

- Left ventricle systolic dysfunction

- Left ventricle diastolic dysfunction

- Change in NT pro BNP

- Acute and late cardiac and pulmonary toxicity: Common Toxicity Criteria for Adverse Events version 4.0.

- Patient-rated outcome is assessed using the EORTC quality of life core questionnaire (EORTC QLQ-C30) and additionally the shortened version of EORTC QoL -LC13.

Study description

Background summary

Radiotherapy improves locoregional control and survival of thoracic tumour patients. However, the associated exposure of normal tissues, often leads to side effects and possibly even reduces survival. Indeed, there is growing evidence that overall survival after radiotherapy for lung and oesophageal cancer is related to the radiation dose to heart and lungs. This suggests that thoracic radiotherapy causes mortality, which is currently not recognized as radiation-induced toxicity. So the question arises how to explain this treatment-related mortality.
Interestingly, we demonstrated in rats that thoracic irradiation can lead to pulmonary hypertension (PH). Histopathological analysis showed that radiation-induced PH closely resembles the pulmonary arterial hypertension (PAH) subtype. Moreover, in a clinical pilot study we confirmed early signs of PH including dose-dependent reductions in blood flow towards the lungs in radiotherapy patients.
In general PH significantly affects survival. Moreover, the PAH subtype is the most-rapidly progressive and lethal subtype. However, medical treatment can

significantly slow down PAH progression, providing opportunities for secondary prevention. Yet, hard evidence that radiation-induced PH is a clinically relevant phenomenon in patients treated for thoracic tumours, is lacking.

Study objective

The main objective is to test if PH occurs in patients treated with thoracic radiotherapy and identify dose metrics and other risk factors for the development of PH after thoracic radiotherapy. In addition, changes in systolic and diastolic myocardial function of the systemic and pulmonary circulation after radiotherapy will be investigated.

Study design

Prospective multicenter cohort study.

Study burden and risks

We will perform a prospective cohort study in 320 patients with lung and oesophageal cancer treated with standard (chemo-)radiotherapy. In these patients we will assess parameters of cardiovascular function using echocardiography and serum biomarkers prior to radiotherapy and at 6, 13, 26 and 52 weeks after radiotherapy. All patients will also be invited for further characterization of vascular and cardiac damage with cardiac MR prior to treatment and at 13 and 52 weeks after treatment and in case of cardiovascular abnormalities are observed during echocardiography. Also physician-rated toxicities and patient-rated outcome measures will be assessed as part of our prospective standardized follow up programs (METC nr 2014.379 and METc nr 2013.101)
To establish treatment-dependence, signs of PH will be related to lung dose. To estimate the impact on health, signs of pulmonary hypertension will be related to survival, toxicity and QoL.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patients with oesophageal cancer in the mid or distal oesophagus and patients with NSCLC stage IIA-III or NSCLC stage IV with limited brain metastases (treatable with surgery or stereotactic radiosurgery) or SCLC limited disease (stage I-IIIB)
• Scheduled for external-beam radiotherapy with curative intention.
• WHO 0-2.
• Age >= 18 years
• Written informed consent.

Exclusion criteria

• Heart failure in the last 2 months
• Pulmonary embolism in the last 2 months
• COPD gold IV
• BMI >35
• History of thoracic radiotherapy
• Noncompliance with any of the inclusion criteria
- For MRI part: Contra indications for MRIFor MRI part:
• contra-indications for MRI

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-09-2018
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	07-03-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL62680.042.17
Other	volgt