The yield of a yearly surveillance program for the early detection of pancreatic cancer and its precursor lesions in high-risk individuals

Published: 03-06-2013
Last updated: 24-04-2024

Within the framework of a longitudinal follow-up study, we aim to determine the excess number of detected and surgically resected high-grade premalignant lesions and early stage pancreatic cancers resulting from yearly testing using EUS in a cohort...

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

Summary

ID

NL-OMON54674

Source
ToetsingOnline

Brief title
Early detection of pancreatic cancer in high-risk individuals

Condition

- Other condition
- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
cancer of the pancreas, Pancreatic ductal adenocarcinoma

Health condition

pancreatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 1. Cancer susceptibility, 2. Pancreatic ductal adenocarcinoma, 3. Early detection of cancer, 3. Precancerous condition

Outcome measures

Primary outcome

The resectability, stage distribution and survival of pancreatic cancer cases

in the screened high risk population as compared to the general population.

Secondary outcome

(I) The number of screen detected and resected high-grade dysplastic lesions

(II) The number of intensified follow-up periods

(III) The yield of EUS as a screen tool for pancreatic cancer and it*s

precursor lesions: e.g. detection rate of solid and cystic lesions

(VI) The number of cases that wrongfully underwent surgery, due to false

positive tests

(V) The natural course of development of lesions that are identified during

surveillance.

(IV) Identify potential biomarkers that can predict the development of

high-grade dysplasia or early pancreatic cancer

Study description

Background summary

With a mean survival after diagnosis of <6 months and a 5-year survival of <6%, pancreatic cancer has one of the poorest prognosis of all human cancers. Since this poor prognosis is mainly caused by the late occurrence of symptoms, one of the most promising means to fight pancreatic cancer death is early detection at a stage when the cancer is not yet symptomic or, preferably, at its benign precursor stage. In particular when this early detection is tailored towards a well-defined population of individuals that carry a significantly increased risk of developing pancreatic cancer (relative life-time risk: 2.3-132!) the potential health gains are enormous.
Preliminary data (including the results of our own ongoing pancreatic cancer surveillance study) is starting to show that endoscopic ultrasonography (EUS) and magnetic resonance imaging (MRI) are promising techniques to detect non-invasive precursor lesions and asymptomatic early stage pancreatic cancer in high-risk individuals. However, we currently lack data driven evidence showing that the benefits of screening and identification of early stage lesions outweigh the negative side effects of (over)treatment and costs. In order to remedy this lack of knowledge, longer-term follow-up studies are urgently needed.

Study objective

Within the framework of a longitudinal follow-up study, we aim to determine the excess number of detected and surgically resected high-grade premalignant lesions and early stage pancreatic cancers resulting from yearly testing using EUS in a cohort of high-risk individuals compared to the natural disease development and manifestation.

Study design

Multicenter prospective study
Surveillance entails an endoscopic ultrasonography. At baseline also a magnetic resonance imaging will take place. The frequency of screening is dependent of the findings of both screening tests and the consensus agreement of the expert-panel. The frequency will be (1) annually in case of normal findings or small cystic lesions, (2) after 6 months in case of the detection of a cyst with a diameter ranging from 10 to 30 mm without the presence of malignant features or (3) after 3 months in case of the detection of a lesion of unknown clinical significance. Whenever a lesion is detected with a high suspicious of being either a malignant or high-grade premalignant lesion, the lesion will be surgically resected.

Study burden and risks

Burden: (1) yearly screening investigations (EUS (+ at baseline MRI)), (2) yearly blood sampling and collection of feces and saliva. Risk: (1) complications directly related to the screening procedure (EUS/MRI), (2) screening related drawbacks being over-diagnoses, false positive test results, and false negative test results Benefits: (1) early disease detection and thereby reduction of pancreatic cancer related mortality, gains in life years and preventing people from dying of pancreatic cancer. Group-relatedness: not applicable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Eligible are individuals who, after evaluation by a clinical geneticist, have an estimated >10-fold increased risk of developing pancreatic cancer, this includes:
(1) Carriers of CDKN2A gene mutations (excl. mutation in exon 1b), regardless of the family history of pancreatic cancer
(2) Peutz-Jeghers Syndrome patients (diagnosis based on a proven LKB1 gene mutation and/or clinical diagnosis), regardless of the family history of pancreatic cancer
(3) Carriers of gene mutations in BRCA1, BRCA2, PALB2, ATM, p53, or Mismatch Repair Gene with a family history of pancreatic cancer in at least 2 family members (at least 1 PA proven, and at least 1 also a mutation carrier)

Exclusion criteria

1) Personal history of pancreatic cancer
(2) Age younger than 18 years
(3) Individuals unable to provide informed consent either due to mental retardation or language barrier
(4) Severe medical illness: WHO 1 to 5
(5) PRSS1 gene mutation carrier
(6) Contra-indication for EUS, due to anatomic abnormalities/surgery or patients whish.
Individuals who already participate in the study with MRI-only (no EUS) will be excluded if they

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-06-2013
Enrollment:	700

Type:	Actual

Ethics review

Approved WMO Date:	03-06-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL40489.078.13