Fluorescence in situ hybridization in the early diagnosis of cholangiocarcinoma in patients with primary sclerosing cholangitis

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To evaluate the outcome of FISH testing with a set of biomarkers with regard to the prognostic value and the diagnostic accuracy for both sporadic cholangiocarcinoma and PSC related cholangiocarcinoma. Subsequently we want to develop a valid...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON37613

Source
ToetsingOnline

Brief title
FLIPPER

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified

Synonym
Primary Sclerosing Cholangitis, Progressive inflammation of the bilde ducts more likely to develop into cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,US Endoscopy

Intervention

Keyword: Cholangiocarcinoma, Fluorescence In Situ Hybridisation, Primary Sclerosing Cholangitis

Outcome measures

Primary outcome

* Sensitivity, specificity, positive prognostic value (PPV) and negative

prognostic value (NPV) of different FISH markers for the detection of

(PSC-related) CCA.

Secondary outcome

* Sensitivity, specificity, PPV and NPV of conventional cytology.

* Sensitivity, specificity, PPV and NPV of different FISH markers while

preserving the specificity of cytology.

* Sensitivity, specificity, PPV and NPV of FISH when FISH is positive and

conventional cytology is neither positive nor suspicious for cancer.

Study description

Background summary

Patients with primary sclerosing cholangitis (PSC) are at increased risk for the development of cholangiocarcinoma (CCA). The risk is approximately 0.5%-1.5% per year. Most patients are diagnosed with advanced disease which has a poor prognosis. To distinguish a fibrotic stenosis from a malignant stricture is a challenge for both the radiologist and the pathologist. On imaging modalities CCAs are often extremely difficult to differentiate from benign dominant strictures. The diagnostic approach is currently based on a combination of imaging modalities, biliary brush cytology and analysis of a few

serum tumour markers. So if there is any suspicion of malignancy an endoscopic retrograde cholangiopancreaticography (ERCP) will be performed to obtain cytology. However the interpretation of cytology is complicated because of the inflammation associated with PSC. Conventional cytology has a poor sensitivity which varies between 18%- 62.5% which means that a certain amount of patients with a cholangiocarcinoma will have a false-negative test.
Fluorescence in situ hybridization (FISH) that can detect chromosomal and specific gene aberrations have shown promise in identifying CCA in PSC patients. However only a few FISH markers have been studied and this technique needs to be optimized for clinical practice.
Recently, we developed a novel assay using biomarkers in combination with cytology which in several long term prospective follow up studies proved to efficiently identify Barrett patients with a 10 time increased risk to develop dysplasia or cancer. By histology these Barrett patients were classified as having no dysplasia. In this biomarker assay fluorescence in situ was also applied to brush specimen.
With our knowledge of previous studies we would like to develop a valid clinical tool, consisting of a set of genetic markers that will be assessed by FISH on brush cytology specimen. These markers will be used for identifying (PSC-related) CCA.

Study objective

To evaluate the outcome of FISH testing with a set of biomarkers with regard to the prognostic value and the diagnostic accuracy for both sporadic cholangiocarcinoma and PSC related cholangiocarcinoma. Subsequently we want to develop a valid clinical tool, consisting of a set of the most promising genetic markers that can be used for predicting which PSC patients have a high risk for developing CCA and indentifying CCA in a cohort of PSC patients.

Study design

We will conduct a pilot study in which all consecutive patients with 1) PSC and 2) 35 known cholangiocarcinoma that will undergo ERCP per clinical practice or for surveillance purposes from May 2012 until May 2014 will be included.
30 patients with gallstone disease, undergoing ERCP for stone extraction will be used as a control population. (see also *sample size calculation*)
Apart from routine brush-cytology, one extra cytology specimen will be obtained for FISH analysis with different probe sets.
This pilot study can be considered as an exploratory/ marker discovery phase in which a wide panel of potential biomarkers will be tested on a relatively small cohort of PSC patients. Depending on the results of this pilot study, we will consider the set-up a multi-center trial in the future, in order to enlarge our study population.

Study burden and risks

We will perform a pilot study (comparative diagnostic and prognostic) and we will only include patients who are already planned fur undergoing ERCP indicated per clinical practice. One extra cytology specimen will be obtained during this ERCP. This means that the endoscopic procedure will take some extra time, which will be no more than 5 extra minutes. All the PSC patients will be asked to fill in a short questionnaire (see also document F1) which will take about 5 minutes to complete. Other than this no extra tests or examinations will take place.
Endoscopic brush cytology has a very low risk of complications (such as haemorrhage or bleeding). Therefore we don*t expect that the ERCP-associated complication rate will increase by the acquisition of one additional cytology specimen on behalf of participation in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients from the AMC PSC surveillance cohort with PSC who will undergo ERCP indicated per standard practice.

Exclusion criteria

Inability to pass a guidewire through the stricture

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2012
Enrollment:	125
Type:	Actual

Medical products/devices used

Generic name:	the Infinity□- bile duct brush
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	16-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL39490.018.12