A care path for the detection of advanced NAFLD-fibrosis: the Nijmegen-Leiden-Amsterdam 2-tiered care path study

Published: 01-08-2022
Last updated: 06-04-2024

The aim of the study is to improve case finding of advanced cases of NAFLD (>=F3 fibrosis), whilst simultaneously reducing unnecessary referrals for mild cases (

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

Summary

ID

NL-OMON53438

Source
ToetsingOnline

Brief title
NLA2 study

Condition

- Other condition
- Hepatic and hepatobiliary disorders
- Diabetic complications

Synonym
fatty liver, Non-alcoholic fatty liver disease

Health condition

obesitas

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: MLDS

Intervention

Keyword: Advanced liver fibrosis, Care path, Non-alcoholic fatty liver, Non-invasive diagnostics

Outcome measures

Primary outcome

- The diagnostic accuracy of the three different sequential care path

algorithms to detect underlying advanced (>=F3) liver fibrosis, assessed using

sensitivity, specificity, predictive values and area under the receiver

characteristics (AUROC) curve;

- The diagnostic performance of the three different sequential care path

algortithms, ed as the increase in correct and the decrease in unnecessary

referrals when using these care paths to detect underlying advanced (>=F3)

NAFLD-fibrosis compared to regular care.

Secondary outcome

- The cost effectiveness of the different diagnostic modalities/care path

algorithms compared to each other and to regular care;

- Number of patients coded for NAFLD by hospital specialists and GPs before and

after initiation of the NLA2 study (measure of awareness);

- The diagnostic accuracy of the three individual non-invasive tests

(FIB4-score, VCTE and ELF-test) to detect underlying advanced (>=F3) liver

fibrosis, assessed using sensitivity, specificity, predicitive values and

AUROC-curves;

- The diagnostic performance of the three individual non-invasive tests

(FIB4-score, VCTE and ELF-test), defined as the increase in correct and the

decrease in unnecessary referrals when using these non-invasive tests to detect

underlying advanced (>=F3) NAFLD-fibrosis compared to regular care.

Study description

Background summary

Non-alcoholic fatty liver disease (NAFLD) is a disease of alarmingly increasing prevalence. Progression along the NAFLD spectrum often goes unnoticed since it is often asymptomatic. Awareness among health care workers and implementation of care paths to detect progressing NAFLD stages are limited. Without clear guidance papers or robust care pathways for risk stratification, the current diagnostic approach for NAFLD is highly variable, leading to both underdiagnosis of advanded stages of disease, and unnecessary referrals for mild stages of disease. This calls for a comprehensive care path consisting of non-invasive alternatives to detect those patients with severe cases of NAFLD. Particularly the use of a sequential, two-tiered care path algorithm is promising as it has the ability to detect underlying advanced cases of fibrosis, and has previously been shown to be cost-effective. This was shown by dr. Ankur Srivastava, who designed a pathway consisting of FIB4-score and ELF-test that led to a reduction of unnecessary referrals to the hepatologist by 80%, whilst improving the detection of advanced fibrosis and cirrhosis 5- and 3-fold, respectively (8). In this study we propose the investigation of several two-tiered sequential care path algorithms, comprised of the FIB4-score, VCTE and the ELF-test, for the detection of advanced stages of NAFLD-fibrosis: the Nijmegen-Leiden-Amsterdam NAFLD-NASH 2-tiered care path study: NLA2-study.

Study objective

The aim of the study is to improve case finding of advanced cases of NAFLD (>=F3 fibrosis), whilst simultaneously reducing unnecessary referrals for mild cases (NAFLD-related complications, and to assess the cost-effectiveness of the different proposed care paths compared to current regular care.

Study design

This is a care innovation study, with an estimated duration of three years. We intend to commence the study at three academic medical centres namely in

Nijmegen, Leiden and Amsterdam, with the intention to include other non-academic hospitals after the initial roll-out. The study has both a prospective and a retrospective part. The prospective part consists of participants who are deemed by their treating physician to be at risk of severe NASH fibrosis. Participants will be invited to attend a study visit at the local hospital.

This study visit will consist of, among others: anthropometric measurements, blood pressure measurement, blood sampling and VCTE. The diagnostic testing for potentially underlying advanced (>=F3) liver fibrosis consists of the FIB4-score, VCTE and the ELF-test. A blood sample will be stored for additional biomarker testing. Based on predefined cut-offs for the FIB4-score and liver stiffness measurement (LSM) (measured using VCTE), participants will be classified as being at low or high risk of advanced (>=F3) fibrosis (see figure 1). The ELF-test will be analysed in bulk and will thus not be used for risk assessment. Participants classified at low risk will remain under the care of their treating physician. Participants classified at high risk of advanced (>=F3) fibrosis will be referred to a hepatologist.

Read-outs of the electronic health records (EHR) of all participants will be performed at 24 months after inclusion in the study, and at six months for those classified at high risk. Read-outs will be performed to assess the correctness of the risk assessment and subsequent referral to the hepatologist.

The three different sequential, two-tiered care path algorithms will be evaluated upon completion of the study. The diagnostic accuracy, defined as sensitivity, specificity, predictive values and AUROCs, of the three different care path algorithms will be calculated. The diagnostic performance will be expressed as the percentage of correct referrals and the percentage of unnecessary referrals of the different care path algorithms and the individual non-invasive tests, compared to regular care.

Study burden and risks

All tests are non-invasive tests and pose minimal burden on and minimal to no risk to participants. There is the possibility that severe cases of NAFLD, including cirrhosis, will be diagnosed as a result of the study procedures. This would result in participants remaining under care of a hepatologist for screening of HCC and esophageal varices and could imply repetitive invasive and uncomfortable procedures such as esophagogastroduodenoscopy. Benefits from participation include comprehensive diagnostic workup for potentially underlying severe NAFLD, which is currently highly variable. Moreover, on the population level, the implementation of a clear care path for the detection of advanced (>=F3) NAFLD-fibrosis would allow for the identification of those patients who would benefit from additional treatment options (e.g. bariatric surgery) or intensification of treatment regiments. This would decrease the number of patients progressing to end-stage liver disease, such as cirrhosis

and HCC, and would decrease both liver related and overall mortality.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age >= 18 years;
- Suspected by treating physician to suffer from a severe stage of NAFLD-fibrosis.

Exclusion criteria

- Previous diagnosis of advanced (>=F3) liver fibrosis;

- Any other known chronic liver disease (alcoholic steatohepatitis, hepatitis B, hepatitis C, autoimmune hepatitis, hemochromatosis, Wilsons disease, alpha-1-antitrypsin deficiency);
- Drugs that may cause drug-induced hepatic steatosis (see protocol, table 1);
- Present excessive alcohol use, defined as > 2 units/day for women and > 3 units/day for men;
- A psychiatric, addictive or any other disorder that compromises the subject*s ability to understand the study content and to give written informed consent for the participation in the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-11-2022
Enrollment:	730
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2023

Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	12-05-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL81357.018.22