Optimizing diagnosis of splanchnic vein thrombosis with MR Direct Thrombus Imaging.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Embolism and thrombosis
Study type	Observational non invasive

Summary

ID

NL-OMON52628

Source
ToetsingOnline

Brief title
Rhea study

Condition

- Embolism and thrombosis

Synonym
abdominal vein thrombosis, Splanchnic vein thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ISTH

Intervention

Keyword: Diagnosis, MR Direct Thrombus Imaging, Splanchnic vein thrombosis

Outcome measures

Primary outcome

The sensitivity and specificity of MRDTI for the diagnosis of acute and chronic

SVT

Secondary outcome

The secondary endpoints are

1) optimized MRDTI scan sequences for SVT;

2) the assessment of interobserver agreement between the reviewers.

Study description

Background summary

Splanchnic vein thrombosis (SVT) includes portal vein thrombosis, mesenteric vein thrombosis, splenic vein thrombosis and the Budd-Chiari syndrome (Riva et al, Thromb Res 2017). There is no validated clinical algorithm for the diagnosis of SVT and there are no specific laboratory tests. D-dimer cannot be used due to the high rate of false positive results, especially in patients with cirrhosis, cancer, or underlying inflammatory conditions, present in more than half of the total SVT population (Dai et al, Int J Clin Exp Med 2015). Whereas Doppler ultrasound is the imaging test of choice for most forms of SVT, its sensitivity is only 90%, as is the sensitivity of CT angiography (Riva et al, Thromb Res 2017; Garcia-Pagán et al, J Hepatol 2015). MR angiography has been reported to have 90-100% sensitivity for SVT, but this technique is limited by the need to administer a contrast agent. Moreover, it may take >60 minutes to complete the scan.
Importantly, many of SVT diagnoses in clinical practice (up to 30%) are incidental findings in asymptomatic patients (Thatipelli et al, Clin Gastroenterol Hepatol 2010). Whereas the diagnosis of symptomatic SVT is often challenging, the correct diagnosis of acute versus chronic incidental SVT is even more difficult, as neither of the current available imaging tests is helpful in determination of the age of the clot. Due to this impossibility to determine whether the incidentally observed thrombosis is acute, chronic or

even an imaging artefact, the vast majority of patients with incidental SVT are treated with -often lifelong- anticoagulants. It is widely acknowledged that this practice likely results in overdiagnosis and unjust exposure to anticoagulant therapy with associated risk of bleeding.
An alternative imaging technique for more accurate diagnosis of SVT is MR Direct Thrombus Imaging (MRDTI). This technique is in an advanced stage of development (Theia study, NCT02262052, supported by TSN grant 2013-02) and is close to implementation in clinical practice. The method is based on the formation of methemoglobin in a fresh thrombus leading to shortening of the T1 signal. It does not require contrast dye. Both the diagnostic accuracy (sensitivity 97-100%, specificity 100%) as well as the inter-observer agreement of MRDTI for first and recurrent DVT of the leg were reported to be excellent (kappa 0.89-0.98) (Fraser et al, Ann Intern Med 2002; Tan et al, Blood 2014). Moreover, it was shown to accurately differentiate acute from chronic thrombosis (Tan et al, Blood 2014).

Study objective

The primary objective of this study is to explore the diagnostic accuracy of MRDTI in the diagnostic management of acute and chronic SVT in a prospective diagnostic proof of concept study. The secondary objectives include optimizing MRDTI sequences for imaging of SVT and assessing the interobserver agreement of the readers of MRDTI for suspected SVT.

Study design

This study is a prospective diagnostic proof of concept study to explore the diagnostic accuracy of MRDTI in the diagnostic management of incidental SVT. This will be achieved by performing MRDTI scans to adjust and optimize the DTI scan sequence in 3 patients with confirmed, symptomatic SVT. If a reproducible clearly positive DTI signal is achieved in all three patients, the study can proceed with the inclusion of cohort 1 and 2, i.e. 35 patients with confirmed acute SVT (cases) and in 35 patients with confirmed, non-symptomatic chronic SVT remains (controls). All scans will be evaluated post-hoc by expert readers blinded for the final diagnosis. It is predetermined that at least five patients of each SVT site (PVT, MVT, SpVT and BCS) and at least five patients of each SVT risk factor (oncologic, post-surgical and inflammatory/infectious) will be included. To make sure that cohort 1 is generally similar to cohort 2, the last 10 patients with acute SVT will be included by matching with the last 10 included controls, according SVT site and risk factor.
This is not a management study: before inclusion in the study, a final diagnosis and management plan, i.e. initiation of anticoagulant treatment or not, is made and discussed with the patients. The MRDTI findings are not used for this decision processto change this. When At the moment venous thrombosis at any anatomical site is diagnosed during follow-up, treatment with therapeutically dosed anticoagulants will be initiated without delay, according

to current guidelines.

Study burden and risks

This is an observational study; patients do not have direct benefits of participating in this study other than helping in increasing our knowledge of the subject under study. The burden of the study is limited and includes a MRDTI test, which is a non-invasive imaging test, without the use of ionizing radiations and iodinated contrast agents and a telephonic follow up. The MRDTI scan will only take a few minutes, as will the 90-day telephonic follow up. Patients are not expected to experience harm from study participation.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with confirmed acute SVT; definitions provided in paragraph 4.2 in the Rhea study protocol (Cases, group 1)
- Patients with confirmed non-symptomatic chronic SVT, defined by incident SVT with chronic thrombi on 2 serial imaging tests with at least 3 months interval (controls, group 2)
- Aged 18 years and older
- Willing and able to give informed consent

Exclusion criteria

- MRI contra-indication (including but not limited to a cardiac pacemaker or subcutaneous defibrillator; vascular clips in the cerebral vessels; metal splinter in the eye, a hearing aid that cannot be removed; a neurostimulator that cannot be removed; a hydrocephalus pump)
- A medical condition, associated illness or co-morbid circumstances that precludes completion of the study procedures (MRI and 90-day follow-up assessment), including but not limited to life-expectancy less than 3 months, inability to lie flat, morbid obesity preventing use of MR and claustrophobia.
- Patients with decompensated liver disease with Child-Pugh class C cirrhosis (since MRDTI evaluation will be inadequate in these patients)
- Patients with suspected tumour thrombus

Study design

Design

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

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	22-03-2019
Enrollment:	50
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	13-11-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	17-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-08-2022

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.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	NL65303.058.18
Other	NTR: TC = 7061