The detection of focal liver lesions with contrast-enhanced ultrasound

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

Summary

ID

NL-OMON32981

Source
ToetsingOnline

Brief title
Letucontrast 01

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
liver tumours

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: contrast-enhanced ultrasound, liver, tumours

Outcome measures

Primary outcome

To compare diagnostic efficacy of contrast-enhanced sonography to MRI in patients with focal liver lesions. The diagnostic criterion will be the ability to diagnose benign versus malignant focal liver lesions.

Our overall aim is that CEUS will be incorporated as a diagnostic tool in protocol (-s) for focal liver lesions and in screening algorithms for metastatic liver disease. Both the time to diagnosis and costs per patient are expected to decrease.

Secondary outcome

To perform a cost-effectiveness study.

Study description

Background summary

Medical imaging techniques have played an evolving role in the diagnosis of focal liver lesions. Non-enhanced ultrasound is usually the first-line investigation, due to its low cost, non-invasiveness, repeatibility and easy access. MRI is nowadays mostly used to establish the definitive diagnosis, however, there are important limitations (expensive, nephrogenic systemic sclerosis, claustrophoby). Another method - CT - has also its limitations (allergy, irradiation, renal insufficiency). New ultrasound contrast agents with tissue harmonic imaging gained appropriate diagnostic accuracy. Microbubbles can be detected wherever they lie and regardless of whether they are moving or stationary. This means that they can be detected also in the microcirculation. The diagnostic pattern is based on the vascular pattern and consists of enhancement in the arterial, portal and late phases. When patterns of contrast enhancement on sonography are compared with those on CT or MRI, a high level of

agreement in type and pattern of enhancement is seen. The use of contrast-enhanced ultrasonography (CEUS) as a reliable alternative for characterisation of liver tumors (as hepatocellular carcinoma) has recently been endorsed by the American and European associations of liver disease.
In everyday clinical practice, doctors face cases in which the focal liver lesions have not been fully characterized, although it has been determined to be benign or malignant, which is often what the referring physician and the patient really need to know. For this purpose, CEUS has a diagnostic accuracy around 90% for all focal liver lesions.
In both situations (characterization and benign/malignant differentiation), the clinical question could be answered, partially or completely, without requiring the patient to undergo other imaging studies. Therefore, CEUS can - in unknown percentage of patients - replace CT, MRI, or biopsy, providing a definitive answer for the patient.

Study objective

Our primary objective is the development of an algorithm for liver tumour diagnosis using CEUS. This provides us with a more flexible, readily available and cheaper method without compromising specificity and sensitivity. We will compare diagnostic efficacy and costs of both methods (MRI). The diagnostic outcome criterion is the ability to diagnose benign versus malignant lesions.
The innovative step would be, that CEUS could be routinely used as the first step in the diagnostic algorithm for the characterization of focal liver lesions detected on baseline ultrasound and being performed during the same examination. Further studies are necessary to evaluate the cost-effectiveness of this approach.

Study design

Patients referred to the Erasmus MC specialized liver-tumor outpatient clinic will be enrolled. This is a specialized service for patients with focal liver lesion (-s). The idea is to minimize the diagnostic work-up to 4 days. CEUS is the only additional examination implemented by the study and serves as a second imaging method.
Single center, blinded study. Ultrasound blinded to MRI results and vice versa. Ultrasound blinded also to blood tests results.
CEUS agent used will be SonoVue (Bracco SpA), administered IV as 5-mL boluses through the antecubital vein in 2-3 seconds. Hitachi sonography system will be used. The vascularity and pattern of SonoVue enhancement of the lesion compared with the adjacent liver parenchyma and vessels during the hepatic arterial, portal venous, and late phases will be evaluated. Two trained physicians will review stored US pictures and videos.
Results of MRI, lab results or - if needed - results of biopsy will be used for diagnosis. Lesions diagnosed as benign will be further followed by a serial examinations for at least 6 months.

Biopsy will not serve as the reference standard in all of the cases. Intraoperative ultrasound will not be used in all patients. CT will be used only as a third imaging method where MRI is not conclusive and biopsy/FNAB is not possible to obtain.

Study burden and risks

CEUS agents are very safe and the examination does not need radiation exposure. They could be used in patients allergic to MRI/CT agents, with renal insufficiency and in pediatric population. They are not recommended in patients with acute cardiac diseases, as non-stabile angina pectoris among others. There has been a thorough search for adverse events in 2nd generation of contrast ultrasound agents. Post marketing surveillance has covered more than 2 million injections and the disputable death of 4 registered cardiac patients after application of Definity would have meant a risk 1:500 000. A 2006 study of more than 23,000 injections of Sonovue showed no deaths and 2 serious adverse events, giving a measured serious adverse event rate of less than 1:10,000 . These number reflect the general safety of US contrast agents. The inconveniences to the patient will be 1) intravenous cannule placing (which would be placed at liver tumor clinic for blood examination anyway) and 2) painless abdominal ultrasound examination (20 minutes with an immediate result).

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 >18 years old, with at least one focal liver lesion identified but not completely characterized.

Exclusion criteria

Patients who are critically ill or medically unstable, with previous hypersensitivity to contrast for ultrasound or MRI, left to right cardiac shunts, severe pulmonary hypertension, chronic obstructive pulmonary disease, unstable angina or dysrhythmias, and pregnant or nursing mothers.

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):	18-08-2009
Enrollment:	160

Type:	Actual

Ethics review

Approved WMO Date:	14-08-2009
Application type:	First submission
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	NL26779.078.09