A treatment algorithm for Hepatic Angiomyolipomas: a long-term follow-up study and a systematic review

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The aim of this study is to get insight into the long-term clinical course of HAML*s in order to develop a treatment algorithm. Primary Objective: The main study parameters are recurrence, growth or development of new HAML tumors.

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

Summary

ID

NL-OMON44998

Source
ToetsingOnline

Brief title
Managment of Hepatic Angiomyolipoma's

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
benign liver tumor, Mesenchymal tumor

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: Angiomyolipoma, Hepatic, Management

Outcome measures

Primary outcome

Number of recurrences, growth (size of tumor) or new HAML tumors.

Secondary outcome

Not applicable.

Study description

Background summary

Hepatic angiomyolipoma (HAML) is a rare mesenchymal liver tumor that belongs to a group of perivascular epithelioid cell tumors called PEComa. It is composed of blood vessels, smooth muscle and adipose cells. The proportions of these tissues can vary greatly (1). Previous observations demonstrate that most patients are asymptomatic and are discovered incidentally during regular health check-ups or follow-up examinations for other diseases (2-4). If patients do present themselves with symptoms they usually complain of abdominal discomfort (5).The natural history of HAML*s has not yet been clarified (1, 5). There is an association with tuberous sclerosis in more than 50% of the AML*s in the kidney, but this has been estimated to be only 5-15% in the liver (1). HAML*s usually occur in non-cirrhotic livers and are not accompanied by serological abnormalities (2, 4). Also they occur more frequently in women, however sex-hormones do not seem to play a role in the pathogenesis and growth of HAML (2, 6).

On imaging HAML*s have various features closely related to the proportions and distribution of the different tissue components. Mature adipose tissue and central thick feeding blood vessels are the most important distinctive characteristics. HAML*s with domineering fat are easy to diagnose but the low- and non-fat HAML*s have less typical manifestations and may easily be misdiagnosed as other benign or malignant tumors of the liver (2). Thus, the diagnosis of HAML based on imaging can be very difficult due to heterogeneity (4). Therefore, pathological examination and HMB-45 staining, a histopathological biomarker of AML, remain an important step towards the diagnosis (4, 5).

The majority of the tumors are believed to be clinically benign, however an increasing number of cases and aggressive changes including growth in size, recurrence after surgical resection, metastasis and invasive growth patterns into the parenchyma and along the vessels have been reported (1). Meanwhile, there are numerous therapeutic strategies available but the best treatment option for hepatic AML has remained controversial (4). Many researchers advocate surgical resection over a non-surgical approach. However a non-surgical approach is also being recommended, especially for patients who are asymptomatic and have small tumors. A non-surgical approach involves close follow-up with repeated imaging, preferably with MRI (5).

Despite the growing number of reports on HAML, little is known about the long term follow-up outcomes after a surgical or non-surgical treatment approach. Recent reports on possible malignant cases have led to our interest in performing research on patients who have previously been diagnosed with HAML and have received either a surgical or a non-surgical treatment in one of the academic medical centres in the Netherlands and Belgium. The aim of this study is to gain insight into the long-term clinical course of HAML*s. We will investigate whether there is recurrence, growth, development of new tumors or metastasis in patients previously diagnosed with HAML. The results could lead to the development of a treatment algorithm.

Study objective

The aim of this study is to get insight into the long-term clinical course of HAML*s in order to develop a treatment algorithm.

Primary Objective: The main study parameters are recurrence, growth or development of new HAML tumors.

Study design

The study will be a cross sectional cohort study. All patients who have previously been diagnosed with HAML can be included in this study. These patients will be contacted by post and asked to undergo a MRI scan in one of the academic medical centers. The inclusion period will end 3 months after sending out a reminder after 1 month to all potential participants. Depending on the primary treatment (surgical and non-surgical), we will evaluate whether the HAML*s recur, grow or whether new HAML tumors develop.

Study burden and risks

There are no known harmful side-effects with temporary exposure to the strong magnetic field used during an MRI scan (7). Potential AE*s associated with MRI are related to the administered contrast agents (usually gadolinium based). The frequency of all acute adverse events ranges from 0.07% to 2.4% with the vast

majority of mild reactions (e.g. coldness at injection site, nausea, headache, dizziness). Allergic responses (e.g. urticaria, rash hives) are very unusual and vary from 0.004% to 0.7%. Severe, life-threatening anaphylactoid reactions are even more rare and range from 0.001% to 0.01%. The frequency of acute adverse reactions is higher in patients with previous reactions and second reactions can be more severe than the first, thus those patients are excluded from this study. Gadolinium agents are considered to have no nephrotoxicity at approved dosages. However patients with end stage renal disease have the potential to develop nephrogenic systemic fibrosis, thus those patients are excluded from this study as well (8).
If an anaphylactic reaction does occur, though chances are exceedingly rare, the radiology personnel in each participating center is trained to respond to life-threatening reactions. The principles of advanced cardiac life support will be followed (e.g. stabilisation of airway, cardiac function, blood pressure and administration of epinephrine).

A potential benefit is the development of a treatment algorithm. This may lead to refined treatments or confirm that the initial chosen treatment is still the best option for the patients.

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

Eighteen years or older;
Diagnosis of HAML either by MRI, biopsy or after tumor resection;
Previous MRI scan with baseline characteristics for patients who received a non-surgical treatment.

Exclusion criteria

Contrast allergy;
MRI contraindication (e.g. pacemaker, metal)
Renal failure.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-07-2016
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO Date:	07-07-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-03-2017
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	NL54364.078.15