Expedite and facilitate diagnostic work up of transient ischemic attack and minor ischemic stroke: dynamic 320-detector row CT angiography of cardiac and carotid sources of emboli compared to currrently used diagnostic procedures

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Main study objective of this study is:To evaluate whether the 320-detector volumetric CT technology can replace carotid duplex scanning and TEE in the diagnostic workup in TIA/IS patients. Specific aims of this main study objective are:1. To assess...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON43919

Source
ToetsingOnline

Brief title
Evaluation of TIA / ischemic stroke with 320-detector row volume CT scanner

Condition

- Central nervous system vascular disorders
- Embolism and thrombosis

Synonym
TIA / ischemic stroke

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CTA, diagnosis, ischemic stroke, TIA

Outcome measures

Primary outcome

o TTE/TEE and cardiac CT images: The prevalence of minor and major cardioembolic sources as identified by cardiac CTA will be determined and compared to the prevalence as found by TTE/TEE. False positive, false negative, positive and negative predictive value of the 320-detector row volume CT scanner for detection of cardiac and aortic sources of emboli will be evaluated. Main study parameter will be presence of intra-cardiac thrombus. Secondary study parameters are anatomical abnormalities, presence and extent of atherosclerotic plaque in the thoracic aorta and ventricular function. For ventricular functional analysis, the end-diastolic volume, end-systolic volume and ejection fraction will be calculated with use of reconstructed axial image series every 5% of the R-R interval.

o Carotid ultrasound and CTA carotid arteries: accuracy of CT angiography of carotid arteries for degree of carotid stenosis (> 50% (males) and > 70% (females)) will be evaluated (in comparison with carotid ultrasound scanning). Main study parameter will be degree of stenosis. Degree of carotid stenosis

will be calculated according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (25). For carotid ultrasound, a carotid index (peak internal carotid artery velocity (m/s) / peak common carotid artery velocity (m/s)) of will be used to define degree of stenosis. Peak systolic velocity and end-diastolic velocity will be used to confirm degree of stenosis. For CT angiography, degree of cross-sectional stenosis will be calculated in percent as: percent stenosis = (1-dmin/dnorm) x 100%, according to NASCET criteria).

o CT angiography intracranial vessels/whole brain CT perfusion: Occurrence of intracranial vessel stenosis will be assessed. Further, degree of stenosis will be assessed in 15 prespecified large intracranial arterial segments per study (Samuels et al. 643-46). Determination of percent stenosis will be calculated using the method for the Warfarin-Aspirin Symptomatic Intracranial Disease Study: percent stenosis = [(1-(Dstenosis/Dnormal))] x 100, where Dstenosis = diameter of the artery at the site of the most severe degree of stenosis and Dnormal = the diameter of the proximal normal artery (Samuels et al. 643-46). Degree of stenosis will be subdivided into 5 subgroups: I normal (0-9%); II mild (10-29%), III moderate (30-69%), IV severe (70-99%) and V occluded (no flow detected). Presence/absence of collateral flow will be evaluated on dynamic CT angiography. Occurrence of hemodynamic alterations will be assessed on CT perfusion images. Color-coded perfusion maps of cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP) and mean transit time (MTT) will be calculated using standard CT perfusion software on a Vitrea work

station. Perfusion parameters will be evaluated using region of interest (ROI) analysis. Absolute and relative (compared to the contralateral hemisphere) values of MTT, CBV and CBF will be assessed to identify presence and degree of hemodynamic alterations.

Secondary outcome

see primary study parameters/outcome of the study

Study description

Background summary

Patients who suffer from a TIA or IS are at high risk of early (recurrent) stroke, the majority occurring within the first weeks after the initial event. The main goal of the diagnostic evaluation is to identify patients with symptomatic carotid disease who will benefit from carotid endarterectomy and to identify patients with TIA/IS caused by a cardiac embolus. Early diagnostic evaluation and rapid initiation of treatment reduces the risk of early (recurrent) IS substantially. Carotid ultrasound and TTE/TEE are used to screen for large artery atherosclerosis and cardiac sources of emboli, but have well-known limitations (e.g. interobserver variability and major patient discomfort). TEE identifies a cardiac embolic source with an absolute indication for oral anticoagulation in appr. 20% of patients with TIA/IS without pre-existent indication for anticoagulation. Despite this, TEE is usually replaced by the non-invasive TTE and both are only performed in selected patients and usually not at first presentation of the patient. Further, changes in intracranial vessels and hemodynamic factors may account for 10-15% of causes of (recurrent) TIA/IS, but are usually not screened for. CT angiography provides an alternative: accurate diagnosis of severe carotid stenosis, diagnosis of cardiogenic thrombus, and intracranial stenosis > 50% has been shown in earlier studies. With the introduction of the 320-detector row CT scanner (16 cm coverage) a comprehensive imaging protocol has become possible, permitting screening for causes of TIA/IS in the heart, aorta and carotid arteries together with dynamic evaluation of intracranial vessels and whole brain perfusion, all in one examintaion.

Study objective

Main study objective of this study is:
To evaluate whether the 320-detector volumetric CT technology can replace

carotid duplex scanning and TEE in the diagnostic workup in TIA/IS patients.
Specific aims of this main study objective are:
1. To assess the yield of cardiac CT for detecting minor and major cardioembolic sources in the acute stage of patients presenting with TIA/IS.
2. To determine whether accuracy of CT angiography of carotid arteries for degree of carotid stenosis (>50A% and > 70%) is comparable with that of carotid ultrasound scanning.
3. To determine false positive, false negative, positive and negative predictive value of the 320-detector row volume CT scanner for detection of cardiac and aortic sources of emboli compared to TTE/TEE.

Study design

This is a prospective crossectional study. 200 patients, age > 50 years, will be included in this study. Approximately 43 to 54 patients visit our TIA/IS out-patient clinic per week; therefore, we expect to require an inclusion period of approximately one to 1.5-2 years. Patients who have experienced a TIA or IS usually visit our TIA/IS out-patient clinic within 72 hours after the event. Within 24 hours of admission, patients are seen by a vascular neurologist. As part of the routine work-up, blood analysis and carotid ultrasound will be performed in the morning; in the afternoon, unenhanced CT and * if carotid ultrasound shows a carotid stenosis or is inconclusive * CT angiography of the carotid arteries will be is performed. All patients will be informed about this study by their treating vascular neurologist. When the inclusion criteria are met and patients are willing to participate, a written informed consent will be obtained. In patients who have given informed consent unenhanced CT, whole brain CTP/CTA, CTA of thoracic aorta and carotid CTA will be performed in the afternoon. TTE or TEE will be performed within 72 hours after the visit to our TIA/IS-outpatient clinic. In patients who already use oral anticoagulation or in patients with proven atrial fibrillation or a significant carotid stenosis TTE/TEE will not be performed, since these patients already have an indication for oral anticoagulation, and findings of TTE/TEE will not change therapeutic management.

Study burden and risks

Identification of etiology of TIA/IS is important, since the cause of TIA/IS affects prognosis, outcome and management. Identification of major cardiac risk factors, e.g. thrombi in left atrium, is imperative since these findings will have implications in terms of choice of (anticoagulant) treatment that reduces the risk of stroke. TEE is the standard reference to identify cardiac sources of emboli, showin abnormalities even in TIA/IS patients without pre-existent indication for anticoagulation. However, TEE is often replaced by non-invasive TTE since major patient discomfort is inherent to the TEE procedure. Moreover, both TTE and TEE are only performed in selected patients and often not performed at first presentation of the patient resulting in a delay in the

start of oral anticoagulation in case of a cardiac embolus. Rapid an accurate classification of degree of carotid stenosis is important as the benefit of surgery depends on this. Carotid ultrasound is widely used to screen for stenosis, but this procedure provides limited information, is investigator dependent and requires skilled operators. Further, intracranial vessel pathology and hemodynamic disturbances account for 10-15% of causes of TIA/IS, but are usually not screened for. With the 320-detector row volume CT scanner it has become possible to provide a *one-stop-shop* diagnostic work up of the cardiac, carotid and intracranial region implying a major improvement for large number of TIA/IS patients in terms of patient comfort, logistics and (probably) reproducibility.
Estimated radiation dose for the entire scan protocol will be approximately 13 mSv. We will only include patients > 50 yrs. Radiation risks for the patients will be in the order of one in the hundred thousand (category IIa) or in the order of one in ten thousand (category IIb).
With the intravenous application of iodinated contrast media, there is a minimal chance of developing an adverse reaction to iodine contrast media. Patients who have a history of anaphylactic reactions to iodine based contrast media will not be included in this study. Experienced, well-trained radiographers and radiologists are present during the CT investigation; this personnel will act immediately if an allergic reaction occurs.
Further, there is a small risk of developing contrast-induced nephropathy. Therefore, the GFR will be determined prior to contrast injection. Patients showing a GFR < 50 ml/min will be excluded from the study due to the increased risk of developing contrast induced nephropathy.

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

All patients who visit our TIA/IS out-patient clinic within 72 hours after the TIA or IS will be registered. Patients who meet the inclusion criteria will be invited to participate in this study. A total of 200 consecutive patients will be included in this study. Appr. 4 to 5 patients visit our TIA/IS out-patient clinic per week: we expect to require an inclusion period of appr. 1.5 to 2 years.
Specific inclusion criteria:
1. Age > 50 years
2. Voluntary participation
3. Having given their written informed consent
4. Willing to accept use of all anonymized data, including publication, and the confidential use and storage of all data.

Exclusion criteria

1. Age * 50 years
2. Allergy to intravenous application of iodinated contrast media
3. Glomerular filtration rate (GFR) of less than 50 mL/min.
4. Patients with a different diagnosis (intracerebral hemorrhage or stroke mimics)
5. Patients arriving > 72 hours after symptom onset

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-12-2011
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	08-03-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Not approved

Date:	19-06-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO

Date:	31-03-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO

Date:	20-12-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL34204.058.10