The diagnostic value of additional research in giant cell arteritis

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This study aims to investigate the sensitivity and specificity of the history and physical examination for the diagnosis of giant cell arteritis, compared with the superficial temporal artery biopsy, and get more insight into the positive and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Headaches
Study type	Observational invasive

Summary

ID

NL-OMON39789

Source
ToetsingOnline

Brief title
The diagnostic value of additional research in giant cell arteritis

Condition

- Headaches
- Vascular disorders NEC

Synonym
giant cell arteritis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Elisabeth Ziekenhuis
Source(s) of monetary or material Support: geen geldstroom

Intervention

Keyword: giant cell arteritis, ultrasonography

Outcome measures

Primary outcome

Sensitivity, specificity and positive predictive value of history and physical examination in patients with suspected giant cell arteritis compared with the biopsy of the temporal artery

Sensitivity and specificity of ultrasonography of the temporal arteries compared with the biopsy of the temporal artery

Secondary outcome

The duration of ultrasonographic abnormalities, that persist after starting steroid therapy.

Change of ultrasonographic abnormalities in time, after start of therapy with corticosteroids

Change of ultrasonographic abnormalities in recurrent symptoms or increase in inflammatory parameters.

Study description

Background summary

For the diagnosis of giant cell arteritis the criteria established by the American College of Reumatology in 1990 are often used. However, these criteria

(Annex 2A) are research criteria and are not always applicable in clinical practice. In the presence of 3 of 5 criteria a sensitivity of 93.5% and a specificity of 91.2% is achieved. However, if these criteria are used in clinical practice, these numbers will be lower, and reaches a sensitivity of 75% and a specificity of 92%. For the population these criteria have a positive predictive value of only 29% . Clinicians should therefore be cautious in applying these criteria in clinical practice. A combination of history, physical examination and additional research is needed for diagnosis. Additional criteria are hereby desirable. Jaw claudication (positive likelihood ratio 4.2, 95% confidence interval 2.8 to 6.2) and diplopia (positive likelihood ratio 3.4, 95% confidence interval 1.3 to 8.6), for example, are not included in these criteria, but are strong positive predictors for the diagnosis. Already proposed criteria by Alberts et al, in which a risk assessment is made, seem more applicable in clinical practice. (Appendix 2B) Meisner et al have proposed an alternative on the same base. Regarding these criteria, an algorithm for clinical practice can be made. This algorithm describes what should be done for further diagnosis and / or treatment.

The additional diagnostic tests includes blood tests, in which an elevated ESR and CRP can be seen. The ESR has a sensitivity of 76-82%, but only a specificity of 9%. A normal ESR is seen in 0-20% of the patients. 60% of patients have a ESR> 100 mm / h, 89% ESR> 50mm/ h, 95% a ESR> 40 mm / hour. The CRP has a sensitivity up to 97.5%. The CRP may be solely increased , without increasing ESR. Also, anemia, thrombocytopenia and elevation of liver enzymes are seen (20-30%).
For diagnosis, the biopsy of the superficial temporal artery is still the gold standard. The biopsy should be at least 2-3 cm in length because of the probability of false negative results. The probability of a positive biopsy is dependent on the length of the biopsy, and is 19% with a biopsy specimen of less than 5 mm, increasing to 89% at a biopsy of more than 20mm. Partly due to the presence of skip lesions. The sensitivity of the biopsy, 87%, specificity increases to 100%. A false negative result is seen in 5-44% of patients, depending on biopsy length. If a biopsy is negative, a contralateral biopsy can be contributing, the sensitivity of the procedure would thus be increased 12.7% compared to a unilateral biopsy. The chance that a biopsy on the contralateral side is contributing is small, 1-3%, and is therefore not recommended. The complication rate of biopsy is low, 0.5% .

The use of corticosteroids prior to biopsy rarely influences the outcome of the biopsy. After starting corticosteroids a positive biopsy can be seen at least 14 days after start of therapy. In 40% of patients the biopsy was positive even after 4 weeks of treatment with corticosteroids. If giant cell arteritis is suspected therapy with corticosteroids should therefore be initiated immediately.

Currently, the research criteria of the American College of Reumatology are still widely used. Given the varying sensitivity, specificity and positive

predictive value of these criteria in the general population, we examine whether there are other predictive factors for the diagnosis of giant cell arteritis. We will focus here on data from the clinical history and abnormalities on physical examination.

There is increasing awareness about the additional value of ultrasonography of the temporal arteries in the diagnosis of giant cell arteritis. By ultrasonography halo's can be seen, increased flow and stenosis and occlusions. Halos have a sensitivity ranging from 40-86% and a specificity ranging from 78-100%. There is a positive predictive value of 75-92% and a negative predictive value of 64-96%. It is important that the presence of halos increase the chance of diagnosing giant cell arteritis strongly, with an odds ratio of> 65. The specificity increases to 100%. The thickness of this halo is also important, a halo of> 1mm enhances the chance of diagnosing temporal arteritis. Ultrasonography may be false positive by infection, malignancy, vasculitis, and absent flow in the adjacent vein. Ultrasonography can be false-negative in the early (if no vascular edema) and in the late phase of inflammation (decreased vascular edema).

There are studies that suggest that the use of ultrasonography instead of a doing a biopsy does not lead to an increase in morbidity. In a patient with a high suspicion of giant cell arteritis and halos at ultrasonography examination, a biopsy should no longer be indicated. This is particularly true for the presence of bilateral halos. If ultrasonography has indeed the same (or better) diagnostic value as a biopsy, this would be a great advantage for clinical practice because no more invasive surgery has to happen, or only when in doubt about the diagnosis. Ultrasonography is not stressful for the patient, quicker accessible and cost effective. Hellman and Hunder already proposed an algorithm for the diagnostic approach of giant cell arteritis in 2005 (Annex 3A). Recent meta-analyzes have shown that ultrasonography is not yet superior to the biopsy.
It is also known that ultrasonography of the larger vessels, including carotid artery, subclavian artery and femoral artery show abnormalities, particularly vascular edema / halos, indicating vasculitis. This is described in 29% of the patients with a giant cell arteritis. If these vessels are also examined in suspected giant cell arteritis, the sensitivity of the examination can be increased.

We would like to investigate what the additional value of ultrasonography, of the temporal arteries, is compared with the biopsy. If ultrasonography shows abnormalities appropriate to diagnose giant cell arteritis, a biopsy must be taken, guided by ultrasonographic abnormalities. This should increase the sensitivity of the biopsy. Research has already shown that the probability of a positive biopsy is increased with an ultrasound guided biopsy. With a strong suspicion of giant cell arteritis and a negative ultrasound examination, a biopsy will still be performed, given the chance of false-negative ultrasound examination. In 1 in 10, biopsy proven giant cell arteritis, ultrasonography

can be negative. This means that all patients will undergo a biopsy and ultrasonography of the temporal artery.
The literature has shown that ultrasonographic abnormalities are seen for 16 (7-56) days after starting treatment with corticosteroids. We would like to investigate how long abnormalities can be seen after starting treatment in our population. We would also like to investigate how the ultrasonographic abnormalities change during treatment or by recurrent symptoms increase in inflammatory parameters .

By using new criteria and other complementary imaging techniques a risk assessment can be made. By implementing this risk assessment in the already existing algorithm of Hellmann and Hunder it is possible to improve clinical practice with a new algorithm for clinical practice. Meisner et al in 2011 have already made a proposal for practice (Annex 3B).

Study objective

This study aims to investigate the sensitivity and specificity of the history and physical examination for the diagnosis of giant cell arteritis, compared with the superficial temporal artery biopsy, and get more insight into the positive and negative predictors of the disease. The additional value of ultrasonography of the temporal arteries in suspected giant cell arteritis will also be examined. We will examine the sensitivity and specificity of ultrasonography compared with the superficial temporal artery biopsy. We will also examine the duration that the ultrasonographic abnormalities persist after starting therapy. The behaviour of ultrasonographic abnormalities under therapy (decrease and disappearence) and recurrent symptoms or increase in blood disorders (increased inflammatory parameters) will also be followed.

Study design

In this prospective, cohort study, we will examine all patients aged over 50 years with a newly developed unilateral headache (temporal or occipital) and / or visual complaints (ie loss of vision, amaurosis fugax, diplopia, or blindness), where there is suspicion of giant cell arteritis. Patients seen in the St. Elisabeth Hospital Tilburg and TweeSteden hospital by a neurologist, internist, rheumatologist or ophthalmologist, patients seen in the Atrium Medical Center Heerlen by a neurologist and patients seen in the Gelderse Vallei Hospital Ede by a neurologist, are included. Initially, 125 patients with suspected giant cell arteritis are prospectively studied.

Flowchart:
1. All patients aged over 50 years with a newly developed unilateral headache and / or visual difficulties which the suspicion of giant cell arteritis seen by the neurologist, internist, rheumatologist or ophthalmologist.
*

2. ultrasonography of the temporal artery on both sides (every patient)
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3. After ultrasonography, the patient is referred to the neurology clinic where he urgently (same or next business day) will be seen by the 'principal investigator' (Drs TWH Alleman, St. Elisabeth Hospital, Tilburg, drs. JMP Rovers, Gelderse Vallei Hospital, Ede or drs. P. Janssen, Atrium Medical Center, Heerlen). The patient is informed about the study.
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4. An additional history and physical examination is performed.
*
5. Blood tests according to protocol
*
6. Temporal artery biopsy on the symptomatic side, if possible ultrasound guided (signed), within 5 working days. All biopsies will be assessed by the pathologist, blinded to any clinical information and duplex results.
*
7. When giant cell arteritis is diagnosed, than further treatment according to the local guidelines
*
8. If ultrasonography of the temporal arteries shows presence of halos, a control ultrasonography is performed after 4 weeks and 8 weeks after initiation of therapy with corticosteroids. This will be repeated every 8 weeks until the halos are disappeared. If there is an exacerbation of giant cell arteritis (increased symptoms or increased inflammatory parameters) a control ultrasonography will be performed (focussed on the place where in previous research the halos were seen).
*
9. Outpatient control after the last ultrasonography, according to the local guidelines
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10. Analysis

Study burden and risks

This is a prospective multicenter cohort study, where patients with suspected giant cell arteritis are examined. Given the regular therapy occurs (blood examination, biopsy and ultrasonography), the patient is not exposed to additional risks.
However, all patients undergo additional ultrasonography investigation after initiation of therapy, by 4 weeks and 8 weeks. And then every 8 weeks until the halos have disappeared. This is not an invasive procedure, but can be perceived as a burden. Further follow up will be according to the standard guidelines.

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

suspicion of giant cell arteritis in a patient older than 50 years with at least 2 additonal points:
- increased ESR and/or CRP
- new onset headache, temporal or occipital
-visual deterioration, blindness, diplopia
-jaw claudication
-tender temporal artery, pressure sensitive

Exclusion criteria

another form of vasculitis

incompetence

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2012
Enrollment:	125
Type:	Actual

Medical products/devices used

Generic name:	ultrasonography
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-07-2012
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Approved WMO

Date:	20-05-2014
Application type:	Amendment
Review commission:	METC St Elisabeth Ziekenhuis (Tilburg)

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	NL40526.008.12