

Structural and Functional Microcirculatory Aspects of Patients with (suspected) Connective Tissue Disease and Pulmonary Arterial Hypertension

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The proposed project focuses on: a) implementation of an improved, standardized method for performing quantitative nailfold capillaroscopy to visualize morphological patterns and evaluate its diagnostic use in patients with (possible) CTD and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Connective tissue disorders (excl congenital)
Study type	Observational non invasive

Summary

ID

NL-OMON30520

Source

ToetsingOnline

Brief title

Microcirculation in CTD and PAH

Condition

- Connective tissue disorders (excl congenital)
- Pulmonary vascular disorders

Synonym

elevated pressure in the main blood vessel of the lung, Pulmonary arterial hypertension

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Stichting Medicinae Interna (SMI)

Intervention

Keyword: Connective tissue disease, Hypertension, Microcirculation, Pulmonary

Outcome measures

Primary outcome

a) Prevalence and severity of structural and functional derangements in the microcirculation in patients with UCTD complicated by PAH compared with patients with UCTD but without PAH

b) Correlation of the degree and type of structural abnormalities of the microcirculation and severity of endothelial dysfunction with the phenotype of PAH

c) Effect of vasoactive agents that influence vascular function used in the treatment of PAH such as prostanoids, endothelin-1 antagonists, and PDE-5 inhibitors on microcirculatory structure and function in patients with PAH and its correlation with clinical effectivity.

Secondary outcome

not applicable

Study description

Background summary

Pulmonary arterial hypertension (PAH) is described as a group of disorders characterized by a progressive increase of the pulmonary vascular resistance leading to right ventricular failure and premature death. PAH includes idiopathic PAH (IPAH), familial PAH (FPAH) and PAH secondary to connective tissue diseases (CTD). Microvascular dysfunction may be a common denominator linking PAH with CTD. A CTD with a high prevalence of PAH is systemic sclerosis (SSc), a disorder typically characterized by structural impairment of the microcirculation as assessed with capillary microscopy in the nailfold, and a possible impairment of endothelium-(in)dependent microcirculatory function in the skin as assessed with iontophoresis combined with laser Doppler fluxmetry. In several PAH centres including our centre, a group of patients with PAH can be distinguished displaying signs and symptoms suggestive of CTD that lack the characteristics of any classifiable disease, called undifferentiated connective tissue disease (UCTD). Whereas most (~80-90%) of the patients with systemic sclerosis exhibit peripheral structural impairment of microvascular function, this is only true for a minority (~14%) of patients with UCTD. Presently it is unknown whether patients with UCTD and PAH are characterized by impaired peripheral microvascular function. It is also not known whether patients with UCTD and impaired microvascular function are at increased risk for developing PAH. This would enable early identification of these patients, which is of paramount importance given the severe prognosis of CTD-related PAH. This is especially relevant now that it is recognized that several newly developed vasoactive agents have effects on vascular remodelling, including prostanoids, endothelin-1 antagonists, and PDE-5 inhibitors. Another unknown issue is whether assessment of morphological and functional derangements can be of aid in differentiating phenotypes of patients with PAH, monitoring microvascular disease progression and/or treatment response, and predicting prognosis in these patients.

Study objective

The proposed project focuses on: a) implementation of an improved, standardized method for performing quantitative nailfold capillaroscopy to visualize morphological patterns and evaluate its diagnostic use in patients with (possible) CTD and suspected PAH and its use in monitoring disease progression and response to therapy; b) assessment of the relationship between, on the one hand structural, and on the other functional characteristics of the microcirculation, and the subtype and severity of PAH; c) investigate whether newly developed treatments have an effect on skin microcirculation, and if such an effect correlates with the clinical and/or hemodynamic response to these new therapies in patients with PAH.

Study design

Observational, cross sectional.

Because of its readily accessibility, the skin and nailfold capillaries will be used to investigate the microcirculation. Noninvasive tools used in this study to investigate microcirculatory structure and function respectively, are capillary microscopy of the nailfold, and iontophoresis with acetylcholine (to assess endothelial dependent vasoactivity) and nitroprusside (to assess endothelial independent vasoactivity) combined with laser Doppler techniques.

Study burden and risks

As stated above non-invasive tools will be used:

a) Capillaroscopy:

-no restrictions

-no risk

-investigation will take ~45 minutes

b) Iontophoresis combined with laser Doppler:

-participants have to refrain from eating, smoking and beverages at least 4 hours

-except for local transitory redness of the skin (fading away within approximately 30 minutes) in some cases, no risks are expected

-investigation will take ~45 minutes

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

-Age 18-80

-Healthy

-Raynaud's phenomenon

-connective tissue disease (with or without pulmonary hypertension)

-Pulmonary hypertension (primary, familial, secondary to CTD)

Exclusion criteria

-age <18 years or >80 years

-for healthy controls: smoking, skin disease affecting the fingers/nails, diabetes mellitus, hypertension, symptoms/signs/past medical history of connective tissue disease or pulmonary disease

Study design

Design

Study type: Observational non invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

Recruitment

NL

Recruitment status: Pending

Start date (anticipated):	01-12-2006
Enrollment:	300
Type:	Anticipated

Ethics review

Approved WMO	
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL14990.029.06