Cross-sectional cohort study to analyse the relation between advanced glycation end-products (AGEs) and diastolic function in patients with diabetes mellitus with and without chronic heart failure.

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Aim is to establish the relation between plasma and tissue AGE levels and the severity of diastolic/vascular dysfunction and its relation with symptoms in patients with type 2 DM with and without CHF, and in patients with CHF without DM. Primary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational non invasive

Summary

ID

NL-OMON33946

Source
ToetsingOnline

Brief title
DIABAGES

Condition

- Heart failures
- Diabetic complications

Synonym
Diastolic heart failure, heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Advanced Glycation End-products, Chronic heart failure, Diabetes mellitus, Diastolic function

Outcome measures

Primary outcome

diastolic function

serum and plasma AGEs

Secondary outcome

NYHA-functional class

6MWT (6 Minutes Walk Test)

Minnesota Living with Heart Failure questionnaire

Arterial compliance using Pulse Wave Analysis (PWA)

Study description

Background summary

In patients with diabetes mellitus (DM) the risk of developing heart failure (HF) is strongly increased. The prevalence of LV diastolic dysfunction in asymptomatic patients with type 2 DM is significantly higher than in patients without type 2 DM. In patients with systolic heart failure, diastolic function and not systolic function was related to NYHA functional class. Patients with DM also develop vascular dysfunction, which may further contribute to the development of chronic HF (CHF). In patients with DM and CHF, symptoms seem to be more severe compared to similar CHF patients without DM. One possible explanation might be that patients with DM the levels of advanced glycation

end-products (AGEs) are increased compared to non-diabetic patients. AGEs are modifications of protein, formed by oxidative or non-oxidative reactions. The formation of AGEs affects the physiological properties of proteins in the matrix, such as turnover and elasticity. AGEs also cause complex vascular, myocardial, structural, and functional changes via the interaction with AGE-receptors. In patients with diabetes, enhanced AGE accumulation is associated with the development of diabetic complications. One of the diabetic complications associated with AGE accumulation is the development of diabetic cardiomyopathy. The first manifestation of diabetic cardiomyopathy is asymptomatic diastolic dysfunction that progresses to systolic dysfunction. In addition to the development of diabetic cardiomyopathy, patients with diabetes also develop vascular dysfunctions. One explanation for this could be that formation of AGE-crosslink results in increased arterial stiffening.

We hypothesize that patients with CHF and diabetes are more symptomatic and have a more impaired diastolic and vascular function than patients with CHF without diabetes, which is related to accumulation in tissue and serum AGEs.

Study objective

Aim is to establish the relation between plasma and tissue AGE levels and the severity of diastolic/vascular dysfunction and its relation with symptoms in patients with type 2 DM with and without CHF, and in patients with CHF without DM.

Primary Research Question
1. To establish the relation between plasma and tissue AGE levels and the severity of diastolic and vascular dysfunction and symptoms in CHF patients with DM compared with age-matched CHF patients without DM.

Secondary Research Questions
1. To establish AGE levels in patients with DM with and without CHF, and patients with CHF without DM compared with age matched normal controls.
2. To establish the relation between plasma and tissue AGE levels and the severity of vascular dysfunction in CHF patients with DM compared with age-matched CHF patients without diabetes and age matched healthy controls.
3. To establish the relation between plasma and tissue AGE levels, diastolic dysfunction and the severity of heart failure measured as NYHA functional class and levels of NT-pro-BNP in CHF patients with and without type 2 DM.
4. To establish the relation between vascular function and the severity of heart failure measured as NYHA functional class and levels of NT-pro-BNP in CHF patients with and without type 2 DM.
5. To establish the relation between plasma and tissue AGE levels on quality of live (QoL) measured with the Minnesota

Living Heart Failure score.
6. To establish the relation between diastolic function and exercise capacity measured in six minutes walk test (6MWT).

Study design

In this cross-sectional study we will include patients with type 2 DM with and without CHF and patients with CHF without DM. In parallel a control group will be included. Diabetic patients without CHF will be screened from patients visiting the Internal Medicine outpatient clinic or Diabetes centre for routine diabetes care. Patients with CHF with and without DM will be screened from the Cardiology outpatient clinic. Control patients will be screened from the partners of the patients included from both outpatient departments and Diabetes centre.

Patients will be informed about the presence of this study by their treating physician. Patients will be informed in writing about the purpose, the study design, study duration, draw-backs and risks, and the consequences of preliminary ending of the study. Patients will receive at least one week to think about the participation to the current research. If they are willing to participate, patients will be asked to sign written informed consent and are scheduled for the study visit at the outpatient clinic followed by collection of blood, an echocardiographic examination, Minnesota Living with Heart Failure Questionnaire, 6 Minutes Walk Test, and non-invasive measurements of vascular function. Patients will be studied in the morning after an overnight fast and abstinence from tobacco, caffeine and alcohol and before any medication is taken. At any time during the study patients are allowed to stop their participation without any consequences. Medical care will resume normally.

Study burden and risks

Patients are scheduled for the study visit at the outpatient clinic where they will be physically examined by the research physician and asked at the current condition, followed by collection of blood, an echocardiographic examination, Minnesota Living with Heart Failure questionnaire (MLHF), six-Minute Walk Test (6MWT) and non-invasive measurements of vascular function. This will take about 2-2.5 hour.
All measurements except collection of blood are non-invasive and therefore have a minimum risk of complications.

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

General
• Signed Informed consent
• Age > 18 years;Diabetes patients with chronic heart failure
• Type 2 DM according to ADA criteria
• Stable CHF diagnosed according to ESC criteria
• Duration of HF > 3 months
• NYHA functional class II-IV ;Diabetes patients without chronic heart failure
• Type 2 DM according to ADA criteria
• No evidence of heart failure;Patients with chronic heart failure without DM type 2
• No type 2 DM (fasting glucose <6.9 mmol/l)
• Stable CHF diagnosed according to ESC criteria
• Duration of HF for > 1 month
• NYHA functional class II-IV;Normal controls
• No type 2 DM (fasting glucose < 6.9 mmol/l)
• No presence of HF

Exclusion criteria

• Sustained/Accepted atrial fibrillation
• Severe Valvular Disease
• Pacemaker use (ICD allowed with backup pacing <= 40 bpm)
• Fitzpatrick type VI skin colour

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2009
Enrollment:	200
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL25189.042.08