Eur J Vasc Endovasc Surg (2016) ■, 1–9

# The DanCavas Pilot Study of Multifaceted Screening for Subclinical Cardiovascular Disease in Men and Women Aged 65–74 Years

T.V. Kvist [a,*], J.S. Lindholt [a,b], L.M. Rasmussen [a], R. Søgaard [c], J. Lambrechtsen [d], F.H. Steffensen [e], L. Frost [f], M.H. Olsen [a], H. Mickley [g], J. Hallas [h], G. Urbonaviciene [f], M. Busk [e], K. Egstrup [d], A.C.P. Diederichsen [a,g]

[a] Elitary Research Centre of Individualised Medicine in Arterial Disease (CIMA), Odense, Denmark
[b] Department of Cardiothoracic and Vascular Surgery, Odense University Hospital, Odense, Denmark
[c] Department of Public Health and Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
[d] Department of Cardiology, University Hospital Odense Svendborg, Svendborg, Denmark
[e] Department of Cardiology, Vejle Hospital, Vejle, Denmark
[f] Department of Cardiology, Diagnostic Centre, Regional Hospital Silkeborg, Silkeborg, Denmark
[g] Department of Cardiology, Odense University Hospital, Odense C, Denmark
[h] Institute of Pharmacology, University of Southern Denmark, Odense C, Denmark

**WHAT THIS PAPER ADDS**

This study adds to the existing literature in that it evaluates the effect of screening for subclinical cardiovascular disease by using computed tomography to assess both aortic and iliac aneurysms, coronary artery calcification, heart rhythm, and by ankle–brachial index peripheral arterial disease. Because of the screening preventive measures were initiated in a high number of individuals. The individuals tested in this study form the basis for a large ongoing randomised controlled multicenter clinical trial involving 46,000 individuals, in which the effects of the intervention will be evaluated.

**Objective/Background:** This pilot study of a large population based randomised screening trial investigated feasibility, acceptability, and relevance (prevalence of clinical and subclinical cardiovascular disease [CVD] and proportion receiving insufficient prevention) of a multifaceted screening for CVD.

**Methods:** In total, 2060 randomly selected Danish men and women aged 65–74 years were offered (i) low dose non-contrast computed tomography to detect coronary artery calcification (CAC) and aortic/iliac aneurysms; (ii) detection of atrial fibrillation (AF); (iii) brachial and ankle blood pressure measurements; and (iv) blood levels of cholesterol and hemoglobin A1c. Web based self booking and data management was used to reduce the administrative burden.

**Results:** Attendance rates were 64.9% ($n = 678$) and 63.0% ($n = 640$) for men and women, respectively. In total, 39.7% received a recommendation for medical preventive actions. Prevalence of aneurysms was 12.4% (95% confidence interval [CI] 9.9–14.9) in men and 1.1% (95% CI 0.3–1.9) in women, respectively ($p < .001$). A CAC score $> 400$ was found in 37.8% of men and 11.3% of women ($p < .001$), along with a significant increase in median CAC score with age ($p = .03$). Peripheral arterial disease was more prevalent in men (18.8%, 95% CI 15.8–21.8) than in women (11.2%, 95% CI 8.7–13.6). No significant differences between the sexes were found with regard to newly discovered AF (men 1.3%, women 0.5%), potential hypertension (men 9.7%, women 11.5%), hypercholesterolemia (men 0.9%, women 1.1%) or diabetes mellitus (men 2.1%, women 1.3%).

**Conclusion:** Owing to the higher prevalence of severe conditions, such as aneurysms and CAC $\geq 400$, screening for CVD seemed more prudent in men than women. The attendance rates were acceptable compared with other screening programs and the logistical structure of the screening program proved successful.



Article history: Received 17 March 2016, Accepted 14 October 2016, Available online XXX

**Keywords:** Aortic aneurysm, Cardiovascular prevention, Computed tomography, Coronary calcium score, Peripheral arterial disease, Screening

## INTRODUCTION

Atherosclerotic cardiovascular disease (CVD) develops throughout life. By the time symptoms occur it has usually progressed to an advanced stage. The European Society of Cardiology (ESC) reports that 38% of deaths in men and 42% in women below the age of 75 years are caused by CVD. In particular, coronary heart disease remains a leading cause

* Corresponding author. Elitary Research Centre of Individualised Medicine in Arterial Disease (CIMA), Sdr. Boulevard 29, DK-5000 Odense C, Denmark.

*E-mail address:* thomasvedelkvist@gmail.com (T.V. Kvist).



http://dx.doi.org/10.1016/j.ejvs.2016.10.010

Please cite this article in press as: Kvist TV, et al., The DanCavas Pilot Study of Multifaceted Screening for Subclinical Cardiovascular Disease in Men and Women Aged 65–74 Years, European Journal of Vascular and Endovascular Surgery (2016), http://dx.doi.org/10.1016/j.ejvs.2016.10.010

of premature death.[1] Screening for traditional risk markers has proven unsuccessful in reducing mortality and morbidity.[2–4] However, adding new imaging modalities more closely related to CVD improves the risk discrimination, which is why the need for a clinical randomised trial has been discussed intensively.[5–9]

This pilot study assessed the preliminary results of the first 2060 people enrolled in the ongoing population based Danish Cardiovascular Screening trial (DANCAVAS), which includes 45,000 people.[10] This study incorporates several different markers for CVD and aims to devise a screening program which, in time, will abide by the World Health Organization's screening criteria.[11]

Aneurysms are mostly asymptomatic until rupture, at which point mortality is in the range of 75%. It has been established that ultrasound based screening can reduce the mortality by up to 66%.[12,13] Cost-effectiveness of screening for abdominal aortic aneurysms (AAA) has been thoroughly discussed and has been validated.[14] By replacing the ultrasound screening with a non-contrast thoraco-abdominal computed tomography (CT) scan, the screening for AAA will not only incur an additional cost, but it will also uncover thoracic aortic aneurysms (TAA) and iliac aneurysms, along with an estimation of the coronary artery calcification score (CAC). The value of CAC has been established by its capability in improving traditional cardiovascular risk stratification, such as the Framingham Risk Score or the HeartScore systems.[7,8,15–17] Other markers included in the study are ankle–brachial index (ABI) as a marker for peripheral arterial disease (PAD) and atrial fibrillation (AF) as a marker for cardiac overload and an increased risk of stroke. The prevalence of PAD is estimated to be up to 18% in a population of 60–90 year olds, which increases with higher age.[18] Even if asymptomatic, PAD is a powerful indicator for mortality by CVD.[19] AF is a prominent risk factor for ischaemic stroke and is presently underdiagnosed.[20]

### Objective

The objective of this study was to investigate the prevalence of unknown subclinical CVD and the feasibility, acceptability, and relevance of multifaceted screening across several specialties in a random sample of men and women from the general Danish population aged 65–74 years.

## METHODS

### Study population

A random sample of 1044 men and 1016 women from the general Danish population were invited to participate. Participants were from the Northern part of Funen and the city of Odense (approximately 230,000 citizens),[21] and were aged 65–74 years. The participants were randomly recruited from the national civil registry based on equal distribution of sex, area of residence, and year of birth. Invitation was performed from September 2014 to September 2015. Non-responders were re-invited once. No exclusion criteria were applied. The individuals were the first of 45,000 included in the DANCAVAS main study. Details of randomization and power calculations can be found in Appendix S1.

Booking was performed through an in-house constructed secure web based self-booking system, by phone, or by e-mail. The web based self-booking system was hosted by a secure hospital server, and was connected to the personal identity registry, which was updated daily on death and change of address. This secured optimal re-invitation and follow-up. The system allowed participants to select their preferred date and time. Login was performed using a reference number included in the letter of invitation along with the participant's civil registration number as the password. The same system was used for the booking of follow-up consultations. The screening examinations were arranged at 10 min intervals in the following order: (i) informed consent and interview; (ii) CT scan; (iii) blood pressure measurements; and (iv) blood sampling.

All participants signed informed consent forms on the day of the screening. The project was approved by the Southern Denmark Region Committee on Biomedical Research Ethics (S-20140028) and the Data Protection Agency.

### Interview

An interview was conducted with a thorough review of a questionnaire, which was sent along with the letter of invitation. The questionnaire evaluated the following: relevant history of CVD, AF, history of smoking, family history of CVD, symptoms of PAD, dyspnea, palpitations or chest pain, and quality of life. CVD was classified as presence of prior stroke, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass graft operation, prior heart valve surgery, prior aneurysm, or prior PAD. A score of 2 or more, classified by the New York Heart Association criteria,[22] was diagnostic for dyspnea. Evaluation of chest pain was done according to the guidelines of the ESC.[23] Medication was classified as thrombocyte aggregation inhibitor, anticoagulant, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor, antiarrhythmic, thiazide, $\beta$-blocker, angiotensin converting enzyme (ACE)/AT-2, calcium blocker, potassium-saving diuretic, loop diuretic, oral antidiabetic, insulin, $\beta$-agonist, inhalation steroid, oral steroid, non-steroidal anti-inflammatory drug, and others.

Blood samples were tested for total cholesterol and hemoglobin A1c (HbA1c). Levels $>$ 8 mmol/L and $>$ 48 mmol/mol were diagnostic for hypercholesterolemia and diabetes mellitus (DM), respectively. Details about the standard of the blood sample analysis and the cutoff for hypercholesterolemia can be found in Appendix S1.

Participants' height and weight were measured in order to calculate the body mass index.

### CT

To assess CAC and the presence of aneurysms, non-contrast full body CT scans were performed using a Siemens Somatom Definition Flash 128 slice Dual Source scanner. The scan

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