

Study protocol

Title : Impact of a coronary artery calcium-guided primary prevention of major coronary heart disease for asymptomatic coronary artery disease in diabetes: a prospective cohort study

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Background

The patients with type two diabetes mellites increased gradually and heart disease and cerebral vascular disease is the fourth leading cause of mortality.

According to the National Health Insurance Research Database (NHIRD) till 2014, incidence of coronary heart disease is 25.2% and heart failure is 3.77% . Multiple complication including chronic kidney disease and cerebrovascular diseases were also well-known.

A systematic review study of scientific evidence from across the world in 2007-2017 revealed cardiovascular disease (CVD) affected 32.2% overall; 29.1% had atherosclerosis, 21.2% had coronary heart disease (CAD), 14.9% heart failure, 14.6% angina, 10.0% myocardial infarction and 7.6% stroke. CVD representing 50.3% of all deaths is a major cause of mortality among people with type 2 Diabetes mellitus (T2DM) (1).A study in Asian population revealed patients with diabetes had a 1.89-fold risk of all-cause death and 2.0-fold risk of cardiovascular death compared with patients without diabetes(2) . However, most diabetes with CAD are asymptomatic.

Coronary artery calcium (CAC) score measured by multi-detector computerized tomography is a reliable measure of subclinical atherosclerosis.

The presence, extent and progression of CAC have been shown to predict adverse cardiovascular events better than traditional risk factors and global risk scoring (3-7) . Our previous study in 2020 revealed CAC score could predict long-term cardiovascular outcomes in asymptomatic patients with T2DM (8). 2019 AHA/ACC Guideline on the Primary Prevention of Cardiovascular Disease and 2019 ESC/EAS Guidelines for the management of dyslipidaemias recommend CAC score as a decision making aid for personalized risk management in primary prevention (9,10). This prospective cohort study will investigate the impact of a coronary artery calcium-guided primary prevention of major coronary heart disease for asymptomatic coronary artery disease in T2DM.

Objective

To evaluate benefits of primary prevention of major coronary heart disease for asymptomatic coronary artery disease in T2DM based on the coronary artery calcium score

Our proposal

1. Based on CAC score, primary early prevention could reduce incidence of major coronary heart disease (CHD) including cardiac mortality, acute myocardial infarction, coronary revascularization

2. based on CAC score, primary early prevention could reduce all cause mortality, cardiac mortality, cardiovascular disease, heart failure, ischemic stroke, heart failure associated hospitalization and chronic kidney disease and related clinical cost effect.

Method

Population:

The investigators will enroll 1500 asymptomatic T2DM patients who will receive Coronary artery calcium (CAC) imaging using 256 sliced multi-detector computerized tomography (MDCT) scanner as research group and 500 patients as control group from Lan-Yan Diabetes Shared Care Network (public health bureau, clinics, and regional hospital in Yilan County).

Inclusion criteria: more than 40 years old T2DM patients have any one cardiovascular risk as follows

1. total cholesterol > 200 mg/dl or low density lipoprotein (LDL) > 100 mg/dl
2. blood pressure $> 140/90$ mm/Hg or taking anti-hypertension agents
3. history of smoking
4. family history of early coronary heart diseases
5. proteinuria

Exclusion criteria: history of cardiovascular diseases such as coronary heart disease, stroke, heart failure etc, pregnant

CAC Scores Measurement

Coronary artery calcium (CAC) imaging was performed using an 256 sliced multi-detector computerized tomography (MDCT) scanner (Philips Brilliance 256) equipped with high-resolution detectors.

Intervention for study group

Based on 2019 AHA/ACC Guideline on the Primary Prevention of Cardiovascular Disease and 2019 ESC/EAS Guidelines for the management of dyslipidemias and result of CAC score(9-12), the investigators will recommend the in-charged doctor to control the cardiovascular risk factors more aggressively. The study protocols are as follows

If CAC score >0 , Treadmill ECG or Thallium²⁰¹ Scan would be arranged. If Treadmill ECG or Thallium²⁰¹ show significant ischemia, further study such as CT angiography or coronary angiography will be arranged.

If CAC score > 100 , Aspirin 100mg QD will be suggested to decrease the cardiovascular risk in patients with low risk of bleeding. Previous studies revealed aspirin for patients with CAC score >100 at low bleeding risk indicated net benefit (13-17).

If CAC score > 400 , statin therapy will be suggested to control lipidemia aggressively and target LDL level <70 mg/dL (9-12) °

The investigators will follow up these patients every 6 month, record their results of blood tests and medication for 5 years. Primary endpoint is major coronary heart disease including cardiac mortality, acute myocardial infarction and coronary revascularization. Second endpoint include all caused death, death due to cardiovascular disease, heart failure, stroke, admission for heart failure, chronic kidney disease and stroke, and cost related to AMI, coronary heart disease, heart failure, stroke, chronic kidney disease etc.

Control group

The investigators will enroll 500 age, gender, risk factor matched T2DM patient from our hospital. The doctor in charge will give usual care according to the Diabetes associate of Taiwan clinical practice guidelines for diabetes care.

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