Impact of diabetes duration on the extent and severity of coronary atheroma burden in type 2 diabetic patients: evaluation by Coronary CT angiography

THESIS

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List of Abbreviations

Abbreviation	Full term
ABCA1	ATP-binding cassette transporter, subfamily A, member 1
ABOS	atheroma burden obstructive score
ACS	Acute Coronary Syndrome
AGE	Advanced Glycation End-product
Akt	Protein kinase B
apoB	apolipoprotein B
apoCIII	apolipoprotein CIII
ASCVD	Atherosclerotic cardiovascular disease
ATP	Adenosine triphosphate
BMI	Body Mass Index
bpm	Beat per minute
CABG	Coronary Artery Bypass Grafting surgery
CACS	Coronary artery calcium score
CAD	Coronary artery disease
CCS	Coronary Calcium Score
CCTA	Coronary Computed Tomography Angiography
CE	Cholesteryl Ester
CETP	Cholesteryl Ester Transfer Protein
CHD	Coronary Heart Disease
CT	Computed tomography
CTA	Computed tomographic angiography
CVD	Cardiovascular disease
DM	Diabetes Mellitus
DNA	Deoxyribonucleic acid
DSCT	Dual Source Computed Tomography
EC	Endothelial cells
ECG	Electrocardiogram
ER	Endoplasmic reticulum
ERK	Extracellular signal-regulated kinase
FFA	Free Fatty Acids
Gd_2O_2S	Digadolinium dioxide sulfide

GlcNAc	N-Acetylglucosamine
H_2O_2	Hydrogen peroxide
HbA1C	Glycated haemoglobin
HDL	High-density lipoprotein
HF	Heart Failure
HL	Hepatic Lipase
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
HU	Hounsfield units
IL	Interleukin
JNK	C-Jun N-terminal kinase
LAD	Left anterior descending artery
LCX	Left circumflex artery
LDL	Low-density lipoproteins
LM	Left main coronary artery
LPL	lipoprotein lipase
LRR	Leucine-Rich Repeat
MAPK	Mitogen-Activated Protein Kinase
MCP-1	Monocyte Chemoattractant Protein-1
MDCT	Multidetector Computed Tomography
MET	Estimated metabolic equivalent of exercise
MI	Myocardial Infarction
ms	Millisecond
mSv	Millisievert
NACHT	Neuronal apoptosis inhibitor protein
NALP3	Domains-containing protein 3
NF-κβ	Nuclear Factor–kappa beta
NO	Nitric oxide
NOS	Nitric oxide synthase
Nox	Nitogen oxide
O-GlcNAc	O-linked N-acetylglucosamine
OM	obtuse marginal branch
PCI	Percutaneous Coronary Intervention
PDA	Posterior descending artery
PI3K	Phosphoinositide 3-kinase
PKC	Protein kinase C
PYD	Pyrin Domain
RAGE	Receptor for Advanced Glycation End-products

RCA	Right coronary artery
RNS	Reactive nitrogen species
ROS	Reactive Oxygen Species
sd-LDL	Small-dense low-density lipoprotein
SIS	Segment involvement score
SPSS	Statistical Package for the Social Sciences
SSS	Segment stenosis score
TG	triglyceride
TGRL	triglyceride-rich lipoprotein
TNF-α	Tumor Necrosis Factor-α
VCAM-1	Vascular Cell Adhesion Molecule 1
VD	vessel disease
VLDL	Very low-lipoprotein
VSMC	Vascular Smooth Muscle Cells

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Introduction

Reducing atherosclerotic cardiovascular disease (ASCVD) burden in diabetes mellitus (DM) is a major clinical imperative that should be prioritized to reduce premature death, improve quality of life, and lessen individual and economic burdens of associated morbidities, decreased work productivity, and high cost of medical care **(Cecilia et al., 2016).**

Atherosclerotic cardiovascular disease remains the principal cause of death and disability among patients with diabetes mellitus, especially in those with type 2 diabetes mellitus in whom it typically occurs 14.6 years earlier, **(Booth et al., 2006)** with greater severity, and with more diffuse distribution than in individuals without diabetes mellitus **(Beckman et al., 2013).**

Furthermore, about two-thirds of deaths in people with diabetes mellitus are attributable to cardiovascular disease: of these, ≈ 40% are from ischemic heart disease, ≈ 15% from other forms of heart disease, principally congestive heart failure, and ≈ 10% from stroke. Among those with diabetes mellitus, excess risks of death from any cause and of ASCVD mortality are particularly prominent in those with younger age, higher burden of glycaemia, and greater renal complications, in comparison with those without **(Tancredi et al., 2015).**

Although the incidences of diabetes mellitus–related complications including cardiovascular disease have decreased over the past 2 decades, patients with diabetes mellitus continue to have significantly increased risk for vascular complications in comparison with individuals without diabetes mellitus **(Gregg et al., 2014)**.

An estimated 382 million people worldwide have diabetes mellitus, and this number is expected to reach 592 million by the year 2035, **(Guariguata et al., 2014)**. Key manifestations of ASCVD in diabetes mellitus include advanced atherosclerosis manifest as coronary artery disease (CAD), ischemic stroke, peripheral vascular disease, and heart failure. Understanding the mechanisms, strategies for and challenges with managing ASCVD and heart failure risk in diabetes mellitus, as well as the potential cardiovascular risks and benefits of glucose-lowering drugs, is important for managing cardiovascular disease in diabetes mellitus **(Cecilia et al., 2016).**

Coronary computed tomography angiography (CCTA) has emerged as a non-invasive imaging modality for the detection or exclusion of CAD, with prior studies observing a high prevalence of CAD in asymptomatic type 2 diabetic patients using CCTA that is associated with worsened outcomes **(Chow et al., 2011).**

Several studies have investigated the association of diabetes duration and CAD prognosis in the pre-CCTA era, these outcome-based analyses lacked information regarding the prevalence, extent, and severity of CAD. Prior CCTA studies have examined CAD findings and Prognosis in type 2 diabetic patients but have limitations of single-center study and small cohorts of diabetic patients **(Hadamitzky et al., 2010).**

The CONFIRM registry clearly demonstrated that diabetic patients had a higher prevalence, extent, and severity of CAD compared with matched non-diabetics, but also had a limitation of the lack of information on the longitudinal nature of the diabetic process on CAD burden and prognosis **(Rana et al., 2012).**

Aim of the work

The aim of this work is to explore the association between diabetes duration on both the extent and severity of coronary atheroma burden using coronary computed tomography angiography (CCTA) in type 2 diabetic patients.