Original Articles

Reduced Incidence of Severe Coronary Atherosclerosis in Obese Subjects With Type 2 Diabetes – An Obesity Paradox?

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Abstract

An obesity paradox wherein a lower incidence of cardiovascular (CV) morbidity and mortality is seen in overweight/obese patients compared with patients with a 'normal' body mass index (BMI) has been reported in patients with type 2 diabetes mellitus (T2DM). We evaluated the relationship between BMI and coronary atherosclerosis in a cohort of subjects with T2DM who were asymptomatic for CV disease using computed tomography coronary angiography. Subjects were followed up for a composite endpoint of all-cause death, non-fatal myocardial infarction or late coronary artery revascularisation. Of the 258 patients enrolled, 226 were eligible for follow-up over a median of 22.8 months. In patients with a normal BMI (<25 kg/m2), 53% had ≥1 significantly stenotic plaque compared with 26% of patients with a BMI >30 kg/m2 at baseline. Subjects with a BMI ≥35 kg/m2 were 82% less likely to present with significant coronary artery plaque at baseline compared with those with a BMI <25 kg/m2 (p=0.01). The risk of a composite CV endpoint event in the overweight/obese group (>25 kg/m2) was approximately 70% lower than in subjects with normal weight. In conclusion, higher BMI may be associated with a lower prevalence of coronary atherosclerosis in patients with T2DM.

Keywords

Diabetes, Atherosclerosis, Computed Tomography Coronary Angiography, Obesity

Introduction

The World Health Organization has indicated that 39% of adults over the age of 18 years are overweight (body mass index [BMI] >25 kg/m^2) and 13% are considered to be obese (BMI > 30 kg/m^2).[1] The prevalence of obesity is even greater in the United Kingdom where 28% of all adults are classified as being obese.[1]

Obesity is associated with an increased risk of insulin resistance and type 2 diabetes mellitus (T2DM),[2,3] as well as other individual risk factors for cardiovascular (CV) morbidity and mortality, such as hypertension and dyslipidaemia.[4,5] In particular, patients with T2DM are 2–6-fold more likely to have coronary artery disease (CAD) than the general population.[6,7]

Overweight and obese patients with T2DM have a higher risk of being hospitalised for CV reasons.[8] However, some studies have suggested that an obesity paradox exists whereby overweight or obese patients with T2DM have a lower risk of CV and all-cause mortality than patients with a normal weight (body mass index [BMI] 18–25 kg/m^2).[8,9] In particular, a nadir in the risk of mortality has been suggested to exist in patients with a BMI of 28–31 kg/m^2.[10,11] Furthermore, in studies where a definitive obesity paradox has not been observed, the relative risk of mortality versus patients with normal weight has remained flat until BMI is >35 kg/m^2.[11,12] This effect has also been observed within British populations.[13,14] However, the acceptance of the obesity paradox in patients with T2DM remains controversial given that a linear increase in the risk of all-cause mortality in patients with T2DM with increasing BMI has been observed elsewhere.[15]

However, few investigations examining the relationship between BMI and characteristics of the vasculature that may precipitate major CV events and death in patients with T2DM have been performed. This study aimed to investigate the relationship between BMI and coronary artery atherosclerosis in patients with T2DM who were asymptomatic for CV disease.

Methods

Patients diagnosed with T2DM were recruited from hospital diabetes clinics and a CV screening clinic in North-West London (Barnet Hospital, Central Middlesex Hospital, Royal Free Hospital and the North-West London CV Screening Community Clinic) as part of the Progression of Coronary Atherosclerosis in Asymptomatic Diabetic Subjects: Evaluation of the Role of Computed Tomography Coronary Angiography (CTCA) and Markers of Endothelial Function and Vascular Inflammation (PROCEED) study. All patients

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attending these clinics aged ≥35 years old with a diagnosis of T2DM for ≥1 year, were invited to participate in the study. All patients included in the study provided written informed consent before enrolment. This study is registered with ClinicalTrials.gov (Clinicaltrials.gov identifier: NCT02109835). Ethical approval was obtained from National Research Ethics Service, UK.

All patients underwent a non-contrast coronary artery calcium (CAC) scan. Subjects with a CAC score of > 1000 Agatston units (AU) did not undergo CTCA because they were presumed to have significant coronary stenosis and measuring coronary stenosis would be difficult due to partial volume artefacts.

Validation Cohort

Once the obesity paradox was observed in the PROCEED study participants, a validation cohort comprising 173 consecutive patients with a known history of T2DM and who had undergone a clinically indicated CTCA at the same centre was evaluated. Only patients with no known history of CAD were included in the validation cohort. Patients with a history of percutaneous coronary intervention or coronary artery bypass graft surgery were excluded. All the patients included in the analysis had provided informed consent for this analysis. As this cohort of patients included a significant percentage of patients with symptoms of angina, or angina equivalent, stenosis >70% was considered to be significant.

CTCA scan protocol

All scans were acquired using a dual source computed tomography scanner (Somatom Definition, Forchheim, Germany). The scan protocol consisted of: 1) topogram; 2) prospectively gated, non-contrast scan according to a standard protocol; 3) test bolus scan to determine the circulation time; and 4) contrast-enhanced CTCA.

All images were acquired during a single breath-hold in inspiration. Images were acquired with a gantry rotation time of 330 ms, detector collimation of 2 x 32 x 0.6 mm (with double sampling in the z axis, using flying focal spot technology), pitch of 0.2–0.5 (adapted to heart rate) with retrospective electrocardiogram (ECG) gating and ECG-controlled tube-controlled modulation. A triple phase contrast protocol was used with a bolus of contrast (Iomeron 400, Bracco, Italy) at a rate of 5.5–6.0 mL/s.

Image Reconstruction and Analysis

CTCA images were reconstructed in mid-diastole in subjects with a heart rate <70 beats per minute (bpm) and in end-systole in subjects with a heart rate >70 bpm. If unsatisfactory, additional reconstructions were made to pick the best quality data set. Images were reconstructed with a slice thickness of 0.75 mm and increment of 0.5 mm using B26 heart view convolution kernel. Images were then transferred to a dedicated workstation (Leonardo, Siemens, Forchheim, Germany). Axial slices, multi-planar reconstructions and maximum intensity projections were used to evaluate the patency of coronary arteries.[16]

All images were analysed by two readers (SV and AJ each with over 7 years' experience in CTCA). Segmentation was based on the American Heart Association 18 segment model as recommended by the Society of Cardiovascular Computed Tomography. All contrast opacified vessels with a diameter greater than 1.5 mm were included in the analysis. Degree of stenosis was assessed based on the percentage reduction in luminal diameter compared with reference vessel diameter.

CTCA Image Quality

Image quality was scored on a Likert scale from 1–4: 1 = excellent with no vessel margin blurring and without any other artefacts; 2 = vessels with mild vessel margin blurring and minimal artefacts; but with good image quality; 3 = vessels which were diagnostic for the presence of significant plaque, but in the presence of either significant image noise or poor signal and/or contrast:noise ratios that would preclude the accurate analysis for presence of minor plaque; and 4 = vessels which were non-diagnostic for any reason. Patients with ≥1 vessel with an image quality score of 4 were given an overall image quality score of 4 and were excluded from the final analysis.

Study measures

The primary measure was the relationship between BMI and the number of significant plaques. The secondary measure was the relationship between BMI and the presence of significant coronary artery plaque (stenosis ≥50%). For the purpose of comparing the relationship between BMI and outcome, subjects were classified as having normal weight (BMI <25 kg/m^2); being overweight (BMI 25–29.9 kg/m^2); obese (class I) (30–34.9 kg/m^2) or obese (class II) (≥35 kg/m^2).

Safety Follow-up

Safety follow-up was performed by email and telephone for up to 2 years after baseline investigations were performed. An adverse CV event was defined as all-cause death, non-fatal myocardial infarction (MI) or late coronary revascularization. Late coronary revascularization was defined as any revascularization procedure that was undertaken ≥60 days after the baseline investigations. Given the relatively low number of expected adverse CV events, the safety analysis compared subjects with normal weight (BMI <25 kg/m^2) versus overweight/obese patients (BMI >25 kg/m^2).

Statistical Analysis

Baseline demographic, clinical and laboratory data was obtained from all patients. Baseline characteristics were described using frequencies and percentages for categorical variables. For continuous variables, mean and standard deviation (SD) was used if the variable was normally distributed and median and inter-quartile range (IQR) if not normally distributed. Independent two-sided Student's t test was used to examine the difference between two independent groups for a normal

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distributed variable. Categorical variables were compared using a X^2 test.

All analyses were performed using regression methods. Correlation between BMI and the number of coronary artery plaques was assessed using Spearman's rank correlation coefficient. The relationship between BMI and significant plaque, considered as a binary measure (yes/no), was explored using logistic regression and is presented in the form of an odds ratio.

Adverse events were assessed as time to event and analysed using a Cox proportional hazards regression model. Patients who did not report an adverse CV event were censored at the time of last follow-up.

Following an unadjusted analysis for each endpoint adjusted analyses were performed using multiple regression. Traditional risk factors found to have some association with the outcome ($p<0.1$) were included in the multiple regression analysis. The exception was for adverse CV events, where due to the small number of events, the number of factors in the analysis was limited by only considering those with a p value <0.05.

Data was analysed using STATA (StataCorp LLC, College Station, TX, USA). P values <0.05 were considered to be statistically significant.

Results

In total, 258 patients were enrolled in the PROCEED study. Twenty patients had a CAC score >1000 AU and did not undergo CTCA. A further 12 patients had a CTCA image quality score of 4 and were not included in the final analysis. Accordingly, 226 patients were included in the final analysis.

Subjects participating in this study were predominantly male (55%), had a median BMI of 28.4 (IQR: 25.4–32.6), and a median duration of diabetes of 13 years (IQR: 8–19). The study population was largely comprised of Asian subjects (54%), predominantly of South Asian ethnicity. Traditional CV risk factors were well controlled for the entire cohort with a mean total cholesterol of 4.09 mmol/L, low-density lipoprotein cholesterol (LDL-C) of 2.15 mmol/L, high-density lipoprotein cholesterol (HDL-C) of 1.3 mmol/L and mean systolic blood pressure (SBP) of 137 mm Hg (Table 1).

A higher prevalence of hypertension (p=0.02) was noted in the higher BMI categories, but no significant difference was noted in the SBP between the four categories. Patients in the higher BMI categories had a higher waist-to-hip ratios ($p<0.001$) and lower HDL-C levels compared with those in the lower categories (p=0.002). A higher percentage of Asian subjects were classified as having normal weight versus the higher BMI categories. This trend was reversed for Caucasian, and to a lesser extent in Afro-Caribbean, subjects, although the number of Afro-Caribbean subjects was low (Table 1). No difference in statin use was observed across patient subgroups.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AU, Agatston units; BMI, body mass index; CAC, coronary artery calcium; DPP-4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide 1; HbA_{1c}, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation

BMI and Coronary Plaque

Total CAC score (R=-0.04; p=0.004) and the number of coronary plaques in the PROCEED population was negatively correlated with BMI (R=-0.12; p=0.03) (Figures 1 and 2). When assessed by weight category, a higher proportion of patients with normal weight had ≥1 epicardial artery with significant stenosis, with a decreasing prevalence with increasing BMI (Figure 3). In particular, 51.0% (25/51) of patients with a normal BMI had significant plaque compared with <30% of obese patients (obese class I, 28.3% [17/60]; obese class II, 25.8% [8/31]).

Both unadjusted and adjusted analyses indicated a significant negative association between BMI and significant

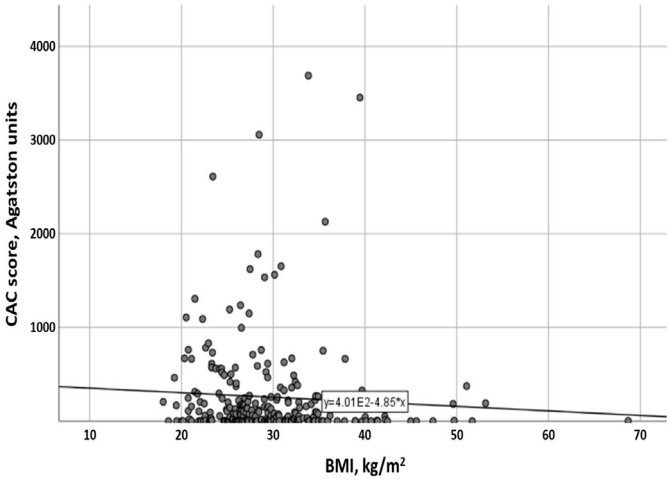


Figure 1. Scatter plot of CAC score versus BMI in the PROCEED population
BMI, body mass index; CAC, coronary artery calcium

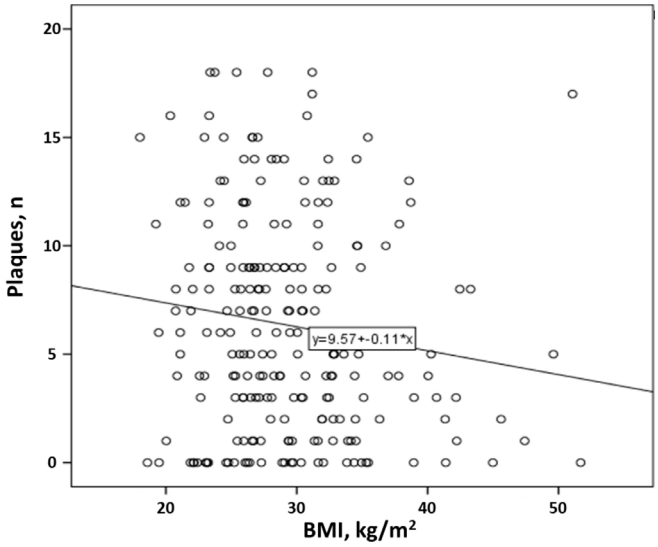


Figure 2. Scatter plot of coronary artery plaque versus BMI in the PROCEED population
BMI, body mass index

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Table 1. Baseline demographics and characteristics of subjects enrolled in the PROCEED study

	PROCEED Population (N=226)	Normal BMI (n=49)	Overweight (n=86)	Obese (Class I) (n=60)	Obese (Class II) (n=31)	p Value
Age, mean (SD) years	60.3 (8.5)	61.5 (8.6)	61 (8.6)	59.4 (8.2)	57.9 (8.4)	0.19
Sex, male (%)	125 (55)	28 (57)	54 (63)	31 (52%)	12 (39)	0.14
BMI, median (IQR) kg/m2	28.4 (25.4–32.6)	–	–	–	–	
Waist-hip ratio, mean (SD)	0.96 (0.08)	0.92 (0.07)	0.96 (0.07)	0.98 (0.07)	0.97 (0.09)	<0.001
Ethnicity, n (%)						0.01
Asian	122 (54)	36 (74)	51 (59)	23 (38)	12 (39)	
Caucasian	74 (34)	9 (18)	23 (27)	28 (47)	14 (45)	
Afro-Caribbean	30 (13)	4 (8)	13 (15)	9 (15%)	5 (16)	
Duration of diabetes, median years (IQR)	13 (8–19)	14 (7.5–20)	12 (8–18)	12.5 (7.3–19.8)	13 (8–18)	0.61
HbA1c, median mmol/mol (IQR)	64.0 (51.9–78.0)	59.6 (49.2–72.9)	63.0 (51.9–78.0)	69.4 (57.1–81.9)	69.0 (56.3–82.0)	0.33
Microvascular disease, n (%)	113 (50)	25 (51)	44 (51)	28 (47)	16 (52)	0.90
Retinopathy, n (%)	94 (42)	23 (47)	32 (37)	25(42)	14 (45)	0.65
Hyperlipidaemia, n (%)	171 (76)	39 (80)	64 (74)	44 (73)	24 (77)	0.74
Hypertension, n (%)	165 (73)	27 (55)	69 (80)	46 (77)	23 (74)	0.02
Current smoker, n (%)	18 (8)	3 (6)	7 (8)	6 (10)	1 (3)	0.48
Statin use, n (%)	167 (74)	37 (76)	60 (70)	45 (75)	25 (81)	0.64
Family history of premature ischaemic heart disease, n (%)	41 (18)	9 (18)	17 (20)	10 (17)	5 (16)	0.90
SBP, mean (SD) mm Hg	136.8 (16.0)	133.6 (18.8)	137.0 (16.8)	138.6 (13.8)	137.6 (12.5)	0.43
eGFR, mean (SD) mL/min/1.73m2	81.2 (19.0)	80.9 (19.4)	79.5 (17.9)	79.2 (16.8)	89.8 (23.7)	0.05
CAC, median (IQR) AU	69.5 (0–262.7)	134.5 (0.8–619.4)	96.6 (0.9–223)	52.8 (0.1–248.5)	7 (0–220)	0.06
Total cholesterol, mean (SD) mmol/L	4.1 (0.9)	4.2 (0.9)	4.1 (1.1)	3.9 (0.8)	4.2 (0.7)	0.17
LDL-C, mean (SD) mmol/L	2.2 (0.9)	2.2 (0.8)	2.2 (1.0)	2.0 (0.7)	2.3 (0.8)	0.26
HDL-C, mean (SD) mmol/L	1.3 (0.4)	1.5 (0.4)	1.3 (0.4)	1.2 (0.4)	1.3 (0.3)	0.002
Triglycerides, median (IQR) mmol/L	1.37 (1.0–1.5)	1.1 (0.8–1.7)	1.3 (1.0–2.0)	1.4 (1.0–2.0)	1.5 (1.0–2.1)	0.53
Total cholesterol:HDL-C ratio, mean (SD)	3.4 (1.2)	3.0 (1.0)	3.5 (1.3)	3.4 (1.1)	3.6 (1.1)	0.09
Antidiabetic medication, n (%)						
Metformin	205 (91)	44 (90)	78 (91)	55 (92)	28 (90)	0.97
Sulphonylureas	73 (32)	12 (24)	31 (36)	19 (32)	11 (35)	0.56
Thiazolidinediones	18 (8)	3 (6)	8 (9)	5 (8)	2 (6)	0.91
GLP-1 agonists	31 (14)	1 (2)	9 (10)	13 (22)	8 (26)	0.002
DPP-4 Inhibitors	46 (20)	9 (18)	18 (21)	12 (20)	7 (23)	0.97
Insulin	126 (56)	27 (55)	41 (48)	38 (63)	20 (65)	0.17
ACEi/ARB, n (%)	139 (62)	25 (51)	57 (66)	41 (68)	16 (52)	0.15

Normal BMI = BMI <25 kg/m2; Overweight = BMI 25–29.9 kg/m2; Obese (Class I) = BMI 30–34.9 kg/m2; Obese (Class II) = BMI ≥35 kg/m2

plaque in the PROCEED population (p=0.03 and 0.01, respectively). The adjusted analysis suggested that subjects with T2DM whose BMI was ≥35 kg/m^2 were 82% less likely to have coronary plaque than those with a BMI <25 kg/m^2 (Table 2).

BMI and Coronary Plaque in the Validation Cohort

A total of 173 consecutive patients were included in the retrospective analysis of a validation cohort with a mean (SD) age of 60.3 (9.7) years, BMI of 30.6 (5.8) kg/m^2, SBP of 141.7 (17.4) mm Hg and median CAC score of 66 [IQR: 0–315.8].

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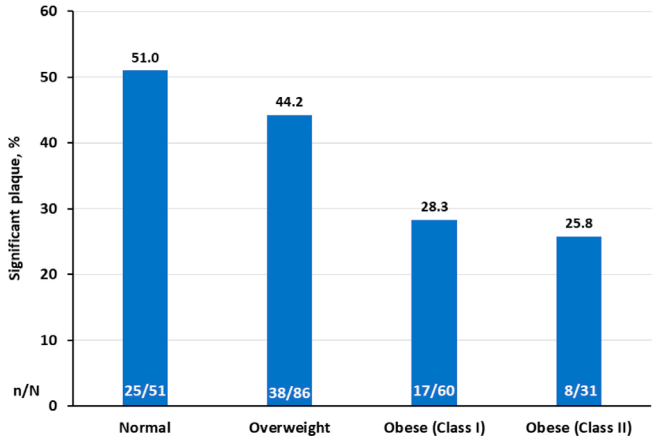


Figure 3. Scatter plot of coronary artery plaque versus BMI in the PROCEED population

Full demographic characteristics are provided in Table 3. In a univariate analysis, BMI trended toward significance in the validation cohort with a reduction in the odds of significant stenosis being present for every 5 kg/m² increase in BMI (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.45–1.03; p=0.07), but in a multivariate analysis, which included age and CAC-based percentile rank, BMI significantly reduced the odds of significant stenosis by 48% (OR, 0.52; 95% CI 0.3–0.9; p=0.02).

BMI and Adverse Cardiovascular Events

A total of 11 adverse CV events were reported after following up patients for a median of 22.8 months in the PROCEED population. An unadjusted model comparing patients with normal weight versus overweight/obese patients trended towards a significantly lower risk of adverse CV events (hazard ratio 0.32 [95% CI 0.10, 1.05]; p=0.06), while an adjusted model showed borderline significance (0.27 [95% CI 0.07, 1.01]; p=0.05) (Figure 4).

Table 3. Baseline characteristics of the validation cohort

	Validation Cohort (n=173)
Age, mean (SD) years	60.3 (9.7)
Sex, male n (%)	126 (71.6)
BMI, median (IQR) kg/m²	29 (26.3–33.3)
Ethnicity **Asian** **Caucasian** **Afro-Caribbean**	 69 (39.2) 98 (55.7) 6 (3.4)
Hyperlipidaemia, n (%)	127 (72.2)
Statin use, n (%)	116 (67.1)
Hypertension, n (%)	114 (64.8)
Current smoker, n (%)	25 (14.2)
Family history of premature ischaemic heart disease, n (%)	57 (33)
SBP, mean (SD) mmHg	141.7 (17.4)
Prevalence of >50% stenosis	80 (45.5)
Prevalence of >70% stenosis	33 (18.8)
CAC score, median (IQR) AU	65.5 (0.7, 315.5)
Insulin use, n (%)	37 (21.4%)

AU, Agatston units; BMI, body mass index; CAC, coronary artery calcium; IQR, interquartile range; SBP, systolic blood pressure; SD, standard deviation

Table 2. Models showing the association between BMI categories and prevalence of significant coronary plaque.

Analysis	BMI Category	Odds Ratio (95% CI)	p value
Unadjusted	Normal BMI Overweight Obese (Class I) Obese (Class II)	1 (reference) 0.67 (0.33, 1.35) 0.34 (0.15, 0.75) 0.30 (0.12, 0.82)	0.03
Adjusted*	Normal BMI Overweight Obese (Class I) Obese (Class II)	1 (reference) 0.42 (0.16, 1.07) 0.25 (0.09, 0.72) 0.18 (0.05, 0.65)	0.01

Normal BMI = BMI <25 kg/m2; Overweight = BMI 25–29.9 kg/m2; Obese (Class I) = BMI 30–34.9 kg/m2; Obese (Class II) = BMI ≥35 kg/m2

*Adjusted for age, gender, ethnicity, SBP, duration of diabetes, HDL-C and total cholesterol:HDL-C ratio

BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure

Discussion

In the PROCEED study of subjects with T2DM who were asymptomatic for CV disease recruited from centres across North West London, patients with a higher BMI were found to have a significantly lower prevalence of plaque lesions causing at least 50% stenosis. This was then verified in a retrospective analysis of a separate validation cohort of patients undergoing clinically indicated CTCA.

Subjects who were overweight or obese were also approximately 70% less likely to experience a MACE during the 2-year follow-up period in the PROCEED study. While being overweight or obese is generally considered to be a risk factor for CV events, the results of this study are consistent with studies evaluating the relationship between BMI and mortality in patients with T2DM.[8-11,13,14]

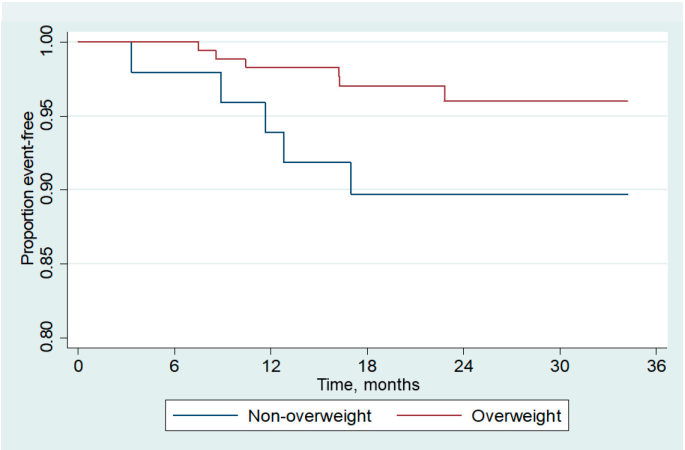


Figure 4. Adverse cardiovascular events

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Interestingly, the validation cohort, which comprised patients with a clinical indication for CTCA, had similar rates of CAD to those in the PROCEED population who were considered to be asymptomatic. It could have been reasonably expected that symptomatic patients would have a higher pre-test probability of significant CAD compared with the aysmptomatic PROCEED cohort. This suggests that symptomology may be non-specific for predicting CAD in patients with T2DM.

Many hypotheses have attempted to explain this apparent paradox. Several studies have suggested that smoking may be a key confounding factor,[13-15,17] but the low prevalence of smoking (<10%) in this study does not appear to be sufficient to account for the effect and was not identified as a significant potential confounding factor in univariate analyses. Furthermore, weight loss may occur in patients with T2DM as a result of comorbidities that could increase the risk of death, confounding the outcome for patients classified as 'normal weight', especially following a relatively short-term follow-up, as in this study.[17]

BMI may also be a poor marker of obesity in the PROCEED study, especially visceral adiposity, which increases the risk of CAD compared with subcutaneous adiposity, because BMI cannot adequately discriminate between adiposity and lean muscle mass.[18] For example, the obesity paradox appears to be more pronounced when using measurements of waist circumference compared with BMI.[11] It is also possible that patients with a higher BMI are more likely to be prescribed antidiabetic, antihypertensive and statin medications to control hyperglycaemia, SBP and lipid profile, respectively, indirectly resulting in a favourable additive, pleiotropic effect.[19-21] Lead-time bias also cannot be ignored; patients who are obese, are more likely to be less physically active and therefore manifest symptoms of exertional dyspnoea or chest discomfort, prompting early referral for investigations. In this cohort of patients, there was no significant association of BMI with age, duration of diabetes or SBP and most importantly, all subjects were asymptomatic for CV disease.

The concept of an obesity paradox also raises questions about the validity of different anthropomorphic measures as risk factors for CV disease. For example, a BMI of more than 25 in women and 26.5 in men was significantly associated with CV mortality in a large prospective study involving nearly 1.2 million subjects, whereas the graded association between BMI and the risk of a MI was lost adjusting for other risk factors.[22] Another study of >13,500 patients using CTCA found BMI was significantly associated with an increased prevalence of any plaque and significant plaque in a multivariate analysis.[23] In contrast, successive quintiles of waist-to-hip ratio were significantly associated with risk of MI, even after adjusting for other risk factors, with patients in the top quintile being 75% more likely to have an MI compared with patients in the lowest quintile.[24]

All chronic conditions in which the obesity paradox has been described, such as heart failure, are essentially catabolic states and it is possible that obesity, or more specifically adiposity, acts as a metabolic sink, preventing muscle wasting and protein catabolism. Subcutaneous adipose tissue produces a soluble tumour necrosis factor receptor that binds the pro-inflammatory cytokine tumour necrosis factor α (TNFα), possibly negating its deleterious effects on the vasculature, as well as the myocardium.[25] Similarly, increased leptin levels, which are correlated with increased BMI, are a significant, but non-linear predictor of CV events in patients with T2DM.[26] Leptin may attenuate the effect of TNFα, leading to improved CV outcomes and survival, but a BMI threshold may be reached wherein patients become leptin-resistant and any beneficial effect is lost.[26]

The limited geographical location of centres participating in this study, and the predominantly South Asian ethnicity of subjects enrolled, reflecting the population demographics of the catchment area, as well as the high prevalence of T2DM in this ethnic group, and may limit the generalisability of the results of this study. The study was also not powered to detect the difference in CV event rates between patients in the different BMI categories.

While CTCA has high sensitivity for detecting CAD, its specificity is modest, particularly in patients with higher levels of coronary artery calcification compared with the gold standard of invasive catheter coronary angiography. As a result, data from patients with poor image quality studies were excluded.

Assessing and comparing coronary artery stenosis across sample populations with differing BMI values is also challenging. Firstly, vessel size increases with BMI and thus a larger plaque burden is requisite for it to categorised as significantly stenotic. Secondly, images from patients with a lower BMI generally have a lower image noise:signal ratio, resulting in better image quality. Therefore, it is possible that small, non-significant plaques were more easily identified in subjects with a lower BMI.

In conclusion, increasing BMI was associated with a lower risk of coronary artery calcification, stenosis and MACEs patients with T2DM who were asymptomatic for cardiovascular disease. This suggests that there may be a paradox between the apparent increased risk of CV morbidity and mortality generally associated with obesity in patients with T2DM that requires further investigation.

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Disclosures

AL is the Editor of the International Journal of Cardiodiabetes. JN is an Assistant Editor of the International Journal of

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Cardiodiabetes. RR is an Associate Editor of the International Journal of Cardiodiabetes. SV, AJ and DN are on the Editorial Board of the International Journal of Cardiodiabetes.

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