



Original Article

Body composition analysis components as markers for coronary artery diseases in type 2 diabetic patients



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المخلص

أهداف البحث: الهدف من الدراسة هو دراسة قدرة مكونات تحليل تكوين الجسم على التنبؤ بمرض الشريان التاجي لدى السكان الهنود الآسيويين المصابين بالسكري من النوع الثاني.

طرق البحث: تم إجراء دراسة الحالات والشواهد هذه بمشاركة 50 شخصاً من مرضى السكري النوع الثاني المصابين بمرض الشريان التاجي في مجموعة التجربة مع 50 شخصاً آخرين من مرضى السكري النوع الثاني كمجموعة تحكم أعمارهم بين 40-70 عاماً من السكان الهنود الآسيويين من زائري قسم أمراض القلب في أحد مراكز الرعاية الصحية المتقدمة في مدينة مانيبال بالهند. تم تأكيد تشخيص مرض الشريان التاجي عن طريق اختبارات تخطيط كهربية القلب والتغيرات في تصوير الأوعية التاجية. تم تقييم القياسات الجسمانية. كما تم تحليل مكونات الجسم باستخدام جهاز بوديستات 1500 أم دي دي.

النتائج: أدت زيادة الدهون بمقدار وحدة واحدة إلى ازدياد احتمالات الإصابة بأمراض الشريان التاجي بمقدار 4.434 مرة لدى مرضى السكري من النوع الثاني. وأدى انخفاض الكتلة العضلية بمقدار وحدة واحدة إلى ازدياد احتمالات الإصابة بأمراض الشريان التاجي بمقدار 4.976 مرة. كما أدت زيادة مؤشر كتلة الدهون في الجسم بمقدار وحدة واحدة إلى ازدياد احتمال الإصابة بأمراض الشريان التاجي بمقدار 1.747 مرة.

الاستنتاجات: تعتبر زيادة كتلة الدهون وانخفاض الكتلة العضلية في الجسم من العلامات المهمة للتنبؤ بمرض الشريان التاجي بين مرضى السكري من النوع الثاني.

الكلمات المفتاحية: مرض السكري النوع الثاني؛ مرض الشريان التاجي؛ تحليل تكوين الجسم؛ مؤشر كتلة الدهون في الجسم؛ دراسة الحالات والشواهد

Abstract

Objectives: The objective of the current study is to investigate the potential of body composition analysis components for predicting coronary artery disease (CAD) in the Type 2 diabetic Asian Indian population.

Methods: This case-control study was performed by recruiting 50 type 2 diabetic patients with CAD along with 50 controls. The participants recruited were those between the ages of 40–70 who visited the Department of Cardiology at a tertiary care referral centre in Manipal, India. The diagnosis of CAD was confirmed by electrocardiogram tests and coronary angiogram changes. An anthropometric evaluation was conducted, and body composition analysis was conducted using Bodystat 1500MDD equipment.

Results: In type 2 diabetics, for a unit increase in fat, the odds of CAD increased by 4.43 times. For a unit decrease in lean mass, the odds of CAD increased by 4.98 times. For a unit rise in body fat mass index, the odds of CAD increased by 1.75 times.

Conclusion: In Type 2 diabetics, increased body fat mass with decreased lean tissue mass were valuable markers of CAD. Future studies can examine the benefits of different types of nutritional and exercise interventions targeted at improving muscle mass and reducing fat content in the

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body with an aim to reduce the occurrence of CAD in patients diagnosed with T2DM.

Keywords: Body composition; Body fat mass index; Case control; Coronary artery disease; Type 2 diabetes

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Introduction

According to a recent report, approximately 88 million adults in South Asia are living with diabetes and these numbers are expected to double by 2045.¹ Coronary artery disease (CAD) accounts for the primary cause of death in India.² The WHO outlined preventive strategies for non-communicable diseases (NCDs) in 2013, stating that a 25% mortality reduction would result from halting the surge in diabetes and obesity.³ As cardiovascular diseases form a substantial part of NCDs in India, the current National Health Policy aims to decrease one-fourth of early deaths from cardiovascular disease by 2025.⁴ The risk of developing CAD in patients with diabetes is two-to four-fold greater than in non-diabetic patients.⁵ There is evidence of higher rates of mortality and morbidity in patients with type 2 diabetes mellitus (T2DM) with CAD resulting in more than 50% of deaths.⁶ Focusing on the conventional cardiovascular risk factors (CVRFs) has proven beneficial in decreasing the mortality in both the general and the diabetic population.^{7–9}

In the global scenario, T2DM, which is observed in adults, is most often related to adiposity.¹⁰ Further, lean Asian Indians are more prone to develop insulin resistance at a younger age, predisposing them to develop T2DM and CAD.¹¹ The current epidemic of CAD may have resulted from the exposure of a genetically prone population to physical inactivity and changes in dietary habit. Obesity is an established risk factor contributing to CAD.⁹ Hence, screening for CAD and its risk factors could play a vital role in prescribing specific health promotion and disease prevention measures, particularly for diabetic populations.

High adiposity and visceral accumulation of fat are linked with insulin resistance, glycometabolic disorders, and a higher risk of developing T2DM and CVD.¹² Loss of skeletal tissue has been reported to play a role in the pathogenesis of metabolic syndrome and T2DM.^{12,13} The associations of concurrent skeletal muscle mass depletion, in combination with fat accumulation and cardio-metabolic disorders, are not yet well-understood.

Sophisticated and high-accuracy radiological techniques like dual-energy X-ray absorptiometry (DEXA) and computed tomography (CT) are regarded as the gold standards for the exact measurement of lean-to-fat mass ratio, but they are not suitable for routine screening because of the prerequisite of skilled technicians and higher costs.¹⁴

Recent evidence based on body composition parameters from our laboratory using the Bodystat 1500MDD machine based on the principle of bioelectrical impedance analysis

(BIA) has demonstrated that the estimation of body fat percentage, along with dry lean weight, can assist the identification of glycometabolic disorders.¹⁵ Few studies have been conducted on markers for identifying cardiometabolic diseases, such as CAD in T2DM patients in the Indian scenario. The investigators hypothesise that body composition analysis components would be adequate markers of CAD risk in diabetic Asian Indians. The objective of the current study was to determine whether body composition parameters like body fat, lean body mass, body fat mass index, and fat-to-muscle ratio, measured using the Bodystat 1500MDD machine, can be used as markers to predict the occurrence of CAD as confirmed by coronary angiograms in South Asian T2DM patients.

Materials and Methods

Study design

The data used in this study comprised of cases and controls visiting the Cardiology Department of a tertiary referral center in Manipal, India. Skilled technical experts from the collaborating Department of Physiology conducted data collection from 1st June to 30th November 2017. The study participants included adults aged 40–70 years. Patients with self-reported thyroid dysfunction, those with a history of carcinoma, chronic infections like Tuberculosis, or Acquired immunodeficiency syndrome were excluded from the study. The study was conducted with the implementation of Good Clinical Practice guiding principles, respecting the ethical standards acknowledged in the Declaration of Helsinki (1983), and written informed consent provided by the participants.

Sample characteristics

The definition of patients with CAD¹⁶ included:

- a) Electrocardiogram (ECG) performed during preoperative cardiac evaluation suggesting ischaemic changes.
- b) Raised levels of Creatinine kinase, Troponin-T levels ≥ 0.1 .
- c) Coronary angiogram suggestive of $\geq 50\%$ stenosis in any epicardial coronary artery

Patients who were diagnosed to have T2DM using the American Diabetes Association (ADA) criteria, at least 5 years before the onset of this study were eligible to participate.

T2DM patients with CAD confirmed on coronary angiography were recruited during their follow-up after discharge. Patients were presented with a fact sheet about the study and assured of their right to withdrawal from the study at any point in time.

Controls who matched the baseline characteristics were recruited from the cardiology department. These were T2DM patients who underwent ECG, had no evidence of CAD as confirmed by coronary angiogram, and who had no history of being diagnosed with or treated for CAD.

Anthropometric evaluation and body composition analysis

Skilled technical experts carried out the anthropometric evaluation after the subjects' heavy clothing and footwear were removed. Bodyweight was converted towards the closest 0.1 kg, contiguous with body stature to the closest 0.5 cm, using anthropometric measurement tools— an electronic weighing scale (ESSAE, India, DS-415 series) and height measuring scale (Prestige stadiometer, India, HM006A) in corresponding erect stance. Body mass index (BMI) was computed using the ratio of body mass (kg) by height (m²). Waist circumference (WC) was recorded in the erect posture, at the intermediate point in the middle of the iliac crest and the least palpable rib by means of a flexible tape. Hip circumference (HC) was recorded at the broadest segment of the buttocks. The waist to hip ratio (WHR) was derived by the division of WC by HC.

All the participants underwent a non-invasive evaluation of their body composition by the means of the Bodystat 1500MDD device, which provides details regarding various body fluid divisions.¹⁵ The method employed involves bioelectrical impedance analysis of the entire body. The technique involves placing electrodes at the hand-to-foot tetra polar positions. Participants were instructed to lie down in supine posture with the abduction of their upper and lower limbs, which were not in touch with the body surface. The device offers information on Total Body Water (TBW) through a stream of flux at 400 µA at a pre-set frequency of 50 kHz. Lean Tissue is therefore estimated from TBW using hydration fraction. Fat mass is estimated by subtracting total lean mass from body weight.¹⁵

Body composition indicators derived as body fat mass (Kg) and lean mass (Kg) were represented as body fat mass in percentage (Body Fat mass %) and lean mass in percentage (Lean mass %), respectively. The fat-free mass index in Kg/

m² (FFMI) and Body fat mass index in Kg/m² (BFMI) were derived from the manufacturer's pre-set analytical equations. The variables obtained also consisted of Dry Lean Weight in Kg (DLW in Kg). Total Body Water as a percentage of total body weight (TBW %) was categorised into Extracellular water as a percentage of total body weight (ECW %) and Intracellular water as a percentage of total body weight (ICW %).¹⁵ Fat-to-Muscle Ratio was estimated as the fraction of fat mass to lean muscle mass.¹⁷

Statistical analysis

The statistical information was analysed using SPSS statistical software package, version 15.0 (SPSS Inc., Chicago, IL, USA). Statistical information that consisted of normally distributed continues variables is represented as means along with standard deviation (SD). The values, which had skewed distribution, were log-transformed and represented as median with interquartile range (IQR). Data displaying normal distribution were evaluated by an independent sample t-test and data that posed a skewed distribution were analysed using a Mann Whitney U test. The Chi-Square test was adopted for comparing the proportion involving binary groups. Univariate analysis was used to assess independent factors associated with CAD. The statistical test results were considered significant if the P value was <0.05. Stepwise backward logistic regression was executed with the implementation of adjusted odds ratio (aOR) and 95% confidence interval (95% CI) to explore predictors of CAD as the dependent variable and independent variables acquired from univariate analyses.

Results

The average age of males was 57.1 ± 7.57, and that of controls was 56.89 ± 9.35. [Table 1](#) outlines the

Table 1: Baseline Characteristics and Body composition Analysis Parameters of Type 2 Diabetic Patients with and without CAD.

Characteristic		Case (CAD) n = 50	Control (No CAD) n = 50	p value
Age (years) mean ± SD		57.1 ± 7.57	56.9 ± 9.35	0.433
Gender (male) n (%)		50 (25/50)	50 (25/50)	0.841
BMI (Kg/m ²) mean ± SD		24.7 ± 3.74	24.6 ± 4.11	0.323
WC (cm), male, mean ± SD		85.3 ± 10.8	85.4 ± 9.56	0.480
WC (cm), female, mean ± SD		86.7 ± 10.5	83.3 ± 9.44	0.300
WHR male, mean ± SD		0.97 ± 0.50	0.96 ± 0.05	0.200
WHR female, mean ± SD		0.96 ± 0.03	0.93 ± 0.36	0.100
Body fat mass (%) mean ± SD		38.3 ± 10.3	30.5 ± 6.43	<0.001
Lean mass (%) mean ± SD		61.8 ± 10.5	69.5 ± 6.52	<0.001 ^a
DLW (Kg) mean ± SD		6.54 ± 5.13	9.57 ± 5.19	0.002 ^a
TBW (%) mean ± SD		52.0 ± 7.78	55.1 ± 6.30	0.015 ^a
ECW (%) mean ± SD		23.7 ± 2.03	24.5 ± 2.14	0.070
ICW (%) mean ± SD		28.3 ± 5.69	31.6 ± 3.81	<0.001 ^a
BFMI (Kg/m ²) mean ± SD		9.74 ± 3.79	7.43 ± 2.00	<0.001 ^a
FFMI (Kg/m ²) mean ± SD		16.9 ± 3.14	15.2 ± 3.21	0.048
FMR mean ± SD		0.66 ± 0.28	0.52 ± 0.39	0.025
History of smoking, n (%)	Yes	8 (4/50)	4 (2/50)	0.233
	No	92 (45/50)	96 (45/50)	
History of alcohol consumption, n (%)	Yes	22 (11/50)	2 (1/50)	<0.001 ^a
	No	78 (38/50)	98 (46/50)	
Family history (1st degree relatives with CAD), n (%)	Yes	10 (5/50)	17 (8/50)	0.329
	No	90 (44/50)	83 (39/50)	

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Table 1 (continued)

Characteristic		Case (CAD) n = 50	Control (No CAD) n = 50	p value
History of hypertension, n (%)	Yes	43 (21/50)	47 (22/50)	0.690
	No	57 (28/50)	53 (25/50)	
History of hyperlipidaemia, n (%)	Yes	45 (22/50)	11 (5/50)	<0.001 ^a
	No	55 (27/50)	89 (42/50)	

Abbreviations: BMI - body mass index; WC - waist circumference; WHR - waist hip ratio; Body Fat mass % - fat mass as % body weight; Lean mass % - lean mass as % body weight; DLW (kg) - dry lean weight in Kilograms; TBW% - total body water as % body weight; ECW %; extracellular water as % body weight; ICW% - intracellular water as % body weight; BFMI - body fat mass index; FFMI - fat free mass index; FMR - fat to muscle ratio.

^a P value < 0.05 considered significant.

Table 2: Logistic regression for the predictors of CAD in type 2 diabetics.

Covariates	P-value	Adjusted Odds Ratio (aOR)	95% C.I. (Lower, Upper)
Body Fat mass %	0.023	4.434	(1.226–16.039)
Lean mass %	0.022	4.976	(1.260–19.655)
Dry lean weight (kg)	0.825	0.957	(0.648–1.414)
Total Body water %	0.214	1.271	(0.871–1.853)
Intracellular water %	0.190	0.696	(0.405–1.196)
BFMI	0.067	1.747	(0.962–3.175)
FFMI	0.053	0.867	(0.547–1.374)

Variables entered in step 1: Fat, Lean Mass, Dry lean weight, Total body water, Intracellular water, ICW, BFMI, FFMI.

Abbreviations: C.I - Confidence interval.

anthropometric characteristics and body composition analysis components of the T2DM patients with and without CAD. The cases and controls were age- and gender-matched. The baseline characteristics were similar in CAD cases and controls. Of the 100 patients, 50 were males and 50 were females. Body composition analysis parameters that were significantly higher in cases compared to controls include body fat mass %, fat-muscle ratio, and BFMI. Values that were significantly lower in cases compared to controls were lean mass percentage, DLW (kg), TBW%, and ICW%. **Table 2** shows the logistic regression model that was utilised to derive aOR with 95% CI for potential predictors in correlation to the presence of CAD in T2DM patients. The body composition components included in the adjusted model were fat mass %, lean mass %, DLW (kg), TBW, ICW, BFMI, and FFMI. In the multivariate analyses, the presence of CAD in Type 2 Diabetics was significantly associated with increased fat mass in combination with decreased lean mass. For a unit increase in fat, the odds of CAD increased 4.43 times and for a unit decrease in lean mass, the odds of CAD is increased 4.98 times.

Discussion

In this case–control study, we analysed 50 Type 2 Diabetics with and without CAD to identify body composition variables that can aid in the screening of CAD in the Asian Indian population. Body composition indices like fat percentage were significantly elevated in T2DM patients with CAD. Traditional anthropometric measures such as high BMI, high waist

circumference, high waist-hip ratio, along with a history of smoking, hypertension, and family history of CAD are considered risk factors for CAD. No significant difference in values and occurrences for these parameters were observed among cases and controls in our study. However, the occurrence of CAD was associated with higher measures of body fat accumulation, such as a higher proportion of the body mass made of fat (i.e. fat mass percentage), higher height normalised index of body fat (i.e. BFMI), which was obtained by dividing the weight of body fat by the square of the subject's height. Concurrently, it was associated with a lower measure of percentage of body devoid of fat (i.e., lean mass percentage). The reduced lean mass percentage coincided with a decrease in the associated components, such as the percentage of body weight attributable to water (i.e. TBW %), the percentage of body weight made of water present inside cells (i.e. ICW %), and DLW, which is essentially lean mass devoid of all water.¹⁵ Obesity is a recognised risk factor for CAD, which enhances lipid metabolism dysfunction, glucose metabolic dysregulation, and increases C-reactive protein (CRP) levels.⁹ Adipose tissue is an endocrine organ contributing to the synthesis of inflammatory biomarkers like Interleukin 6, along with tumour necrosis factor- α , which may contribute to the pathophysiology of CAD.¹⁸

Skeletal muscle contributes to glucose regulation.¹⁹ A higher fat-to-muscle ratio suggests lower muscle mass in CAD patients in our study. The emerging concept of sarcopenic obesity is the cumulative depletion of skeletal muscle mass in combination with the rise in fat mass, and has been proposed to be a contributing factor for CAD.²⁰ One study

reported higher cardiovascular disease risk factors in the sarcopenic obese elderly population.²¹ The pathophysiology of the association of sarcopenic obesity and cardiometabolic risks remains to be explored. Higher levels of cytokines like IL-6 and CRP, produced by macrophages, are linked with the loss of lean tissue.²² Elderly populations with raised levels of inflammatory markers, like TNF α , reported a progressive deficit of lean muscle mass and strength.²³ Previous studies have noted that there is raised CRP concentration in South Asian women—almost twofold compared to their European counterparts.²⁴ A recent study reported that elevated CRP levels result in reduced size of human myotubes with decrease in muscle protein production.²⁵ Raised CRP levels would lead to a reduction of phosphorylation of Akt, the upstream regulator of the motor pathway that contributes to muscle growth.²⁶ The muscle cells also exercise an endocrine role by producing myokines with positive cardiovascular effects.²⁷

While assessing body composition parameters for their utility as a marker for CAD in diabetes using the regression model, we found the combination of higher body fat mass % together with decreased lean mass % to be the strongest predictors for the occurrence of CAD in T2DM patients. For a unit increase in fat, the odds of CAD are increased by 4.434 times, while for a unit decrease in lean mass, the odds of CAD are increased by 4.976 times. For a unit increase in BFMI, the odds of CAD are increased by 1.7 times. There is strong evidence for the link between fat mass and cardiometabolic risk factors. Many studies have reported the vital role of adipose tissue in contributing to cardiovascular risks via different pathways. Adipose tissue accumulation together with insulin resistance results in excessive free fatty acids in the blood and deranged hepatic fat metabolism which contributes to dyslipidemia.²⁸ Excess fat tissue derived inflammatory mediators contributes to insulin resistance and the consequent hyperglycemia leads to vascular endothelial dysfunction promoting atherosclerotic plaque formation.²⁹ The atrophy of lean tissue combined with decreased anabolic hormones (IGF-1, Testosterone, Ghrelin) contributes to the pathogenesis of T2DM.³⁰ Sarcopenic obesity in T2DM is due to reduced response to insulin for the synthesis of muscle proteins.³¹ Our study shows that sarcopenic obesity is associated with the occurrence of CAD in T2DM patients, independent of the other risk factors of CAD, making it a useful marker for screening for risk of CAD in diabetic patients.

The BMI is unable to distinguish between fat mass, which is a risk factor for CAD, and lean mass, which is protective. A person with lower BMI could have sarcopenia rather than lower fat percentage and an overweight person may have higher lean percentage rather than excess adiposity. Our study emphasises that lean mass percentage is an important predictor of CAD, which is not accurately analysed by BMI. Our study draws attention towards the “Asian Paradox,” which proposes a higher cardiovascular risk even at lower BMI.³² The results of our study also demonstrate that BMI cannot distinguish between low lean mass or high-fat content and hence, does not provide any additional information in patients with CAD. Our results emphasise the need for

conducting body composition analysis in screening for CAD. Since the relative risk of CAD is linked (20–50%) with higher mortality in the Asian Indian population in comparison to other populations,³³ it necessitates the presence of robust screening strategies along with health education and awareness to improve health.

Bioelectrical impedance analysis (BIA) is a more cost-effective and convenient method that has been validated in several studies and has been found to yield comparable body composition results to the standard method of DEXA scan.³⁴

The strengths of the current study include standardised repeated anthropometric and body composition evaluation performed by skilled technical experts. Integrating cost-effective body composition analysis measurements could assist in the screening of CAD and predicting the risk of CAD in diabetic patients. While the occurrences of obesity and of T2DM have been considered independent risk factors for CAD, the higher risk of CAD in diabetic patients with altered body compositions is reported for the first time in this study.

Limitations

The chief limitation of our study is the sample size: a larger sample would be essential to consolidate our findings that body composition parameters are valuable markers of CAD in T2DM patients. The authors utilised a case–control study design, although a prospective cohort outline would have been more appropriate. Our analysis of altered body composition to predict CAD can be validated with a larger sample and would be a valuable tool for population screening.

Conclusions

Our study confirms that an increased body fat percentage in combination with decreased lean mass percentage are valuable markers for predicting the occurrence of CAD in T2DM patients. Future studies should examine the benefits of nutritional and exercise interventions, which are targeted at improving muscle mass and reducing fat content in the body, with an aim to reduce the occurrence of CAD in patients diagnosed with T2DM.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

This institute based original study was approved on 9/5/2017 by the Ethics Committee of the Kasturba Medical College and Kasturba Hospital, Manipal (IEC 299/2017).

Authors contributions

PD and DP conceived and designed the study, conducted research, provided research materials, and collected and organised the data. DP and VKRN analysed and interpreted the data. DP, PD, and VKRN wrote the initial and final drafts of the article. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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