# Predictors of Cardiovascular Disease in Patients with Type 2 Diabetes Mellitus

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## Abstract

**Aims:** Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients with type 2 diabetes mellitus (T2DM). Although patients with T2DM and CVD share common risk factors, the link between these diseases remains unclear. This study intends to identify the predicting risk factors of CVD in Malaysian T2DM patients.

**Methods:** We conducted an analytical cross-sectional study on 313 patients diagnosed with T2DM at selected tertiary hospitals upon prior ethical approvals. Systematic random sampling method was applied in patient selection. Socio-demographic data was assessed using a pre-tested interviewer-administered structured questionnaire. Diet (by 24-hour dietary recall), physical activity level [via International Physical Activity Questionnaire (IPAQ)], smoking and alcohol consumption status were ascertained. Anthropometric and blood pressure measurements were performed according to standard procedures. Clinical and laboratory characteristics on cardiovascular risk factors (medical history, treatments, glycaemic control, and lipid profile) were collected from medical records, clinical examination and face-to-face interview. All statistical analyses were performed by using SPSS Statistics Version 21.0.

**Results:** The mean age of study subjects was 55.7±9.2 years, with a mean diabetes duration of 10.1±8.1 years (CVD patients 11.5±8.7 years, non-CVD patients 9.2±7.6 years); 52.1% subjects were females; and 47.0% were Malays. Approximately one third (36.1%) of the subjects were suffering from CVD. Multivariate logistic regression analysis showed age (B=0.056, adjusted $OR_{95\% CI}$=1.058, $p$=0.004), lower HDL-C level (B=-1.466, adjusted $OR_{95\% CI}$=0.231, $p$=0.003), working status of self-employment (B=1.381, adjusted $OR_{95\% CI}$=3.978, $p$=0.002) in comparison to retirement, low (B=1.164, adjusted $OR_{95\% CI}$=3.203, $p$<0.001) and moderate physical activity levels (B=1.172, adjusted $OR_{95\% CI}$=3.227, $p$<0.001) compared to high physical activity level were significantly associated with higher CVD risk, upon adjustment for potential covariates.

**Conclusion:** Increased age, lower HDL-C, low and moderate physical activity levels, and working status appeared to be significant predictive factors of CVD among the T2DM patients studied.

**Key words:** Cardiovascular disease, type 2 diabetes mellitus, predictors, tertiary hospitals

## Introduction

Diabetes mellitus (DM) is one of the most common non-communicable diseases globally.[1] It has been predicted that approximately 366 million people having DM worldwide in 2011 and this is expected to increase to 552 million of the adult population by 2030.[1] Type 2 diabetes mellitus (T2DM) accounts for the vast majority of DM, which is 90–95% of all cases.[2,3] More than 60% of the world's population with DM lives in Asia, being the world's most populous region.[1,4-6] It is foreseen that the number of individuals with DM in each Asian country will escalate substantially in the coming decades. Similarly in Malaysia, DM is a growing concern with its marked increase in prevalence rate. The prevalence of DM among adults 30 years and above in Malaysia was elevated for nearly three-fold within 15 years from 8.3% in 1996 to 20.8% in 2011.[7] Malaysia ranked ninth among Asian countries with high DM estimates (11.6% of comparative prevalence), and this figure is projected to reach 13.8% in year 2030.[6]

Cardiovascular disease (CVD) is the principal cause of mortality in patients with T2DM worldwide, accounting for up to 60-80% of the deaths.[3,8] Epidemiological studies indicated that individuals with T2DM have a 2–4 times higher risk of CVD mortality than non-diabetic individuals, and CVD mortality among diabetics without prior myocardial infarction (MI) is similar to non-diabetics with prior MI.[9] The risks of CVD onset are known to be multi-factorial and resulting from a complex and dynamic interaction of genes, environment and lifestyle over time. It is believed that any attempt at stemming the tide of increasing morbidity and mortality of CVD should start with critical evaluation of T2DM patients who as a result of their diabetes are already at greater risk of progressing to CVD. In this regard, identification of predictors of increased cardiovascular risk in diabetic patients is of considerable interest clinically in order to establish more effective preventive strategies. The mindset and strategy changes may well help curtail the rampage of CVD on the Malaysian population with T2DM. To the best of our knowledge, the risk factors associated with CVD in patients with T2DM have never been

previously addressed in Malaysia. Therefore, this study aims to evaluate the predicting risk factors contributing to CVD among patients with T2DM in tertiary hospital settings.

## Materials and Methods

### *Research Design and Patients*

This is an analytical cross-sectional study designed to determine the predictors of CVD in patients with T2DM at two tertiary government hospitals. Medical Specialist and Endocrinology Clinics at Hospital Serdang, Malaysia served as the clinical settings and source of participants for the present study. Subjects were also recruited from Physician Clinic at Hospital Kuala Lumpur (HKL), the largest hospital under Ministry of Health Malaysia as well as one of the largest hospitals in Asia[10]. A systematic random sampling method was applied to select patients. Prior to study entry, patients with T2DM were evaluated according to the inclusion and exclusion criteria justified. Generally, eligible patients were those previously diagnosed with T2DM. Whereas the exclusion criteria were patients with type 1 diabetes mellitus (T1DM), gestational DM, embolic or haemorrhagic strokes; malignant disease; psychiatric illness or dementia; pregnant or lactating female; bed-ridden and disabled wheelchair individuals. Upon invitation to participate in this study, informed consent was obtained from each patient prior to completing an approximately 1-hour interview.

Subjects were interviewed and completed a standardised questionnaire that included socio-demographic backgrounds, aspects of personal medical and family health history, and lifestyle variables comprised of dietary intake, physical activity level, smoking status and alcohol consumption behaviour. The intakes of past 24-hour foods and beverages of subjects were assessed using the interactive 24-hour dietary recall method on a face-to-face interviewed basis. The foods consumed were then recorded and entered into the Nutritionist Pro$^{TM}$ diet analysis software (Version 2.5, Axxya Systems, USA) for energy and nutrient analysis. Physical activity (PA) status was ascertained using the 7-item International Physical Activity Questionnaire (IPAQ) short form as an index of weekly energy expenditure using frequency (times per week), duration (in minutes per time) and intensity across all domains of leisure-time, occupation and transportation, and household tasks, which summate to total PA.[11] The subjects were required to report the number of days, hours and minutes they engaged in PA of different intensities in each PA domain including time spent sitting. Weekly minutes of walking, moderate-intensity and vigorous-intensity activity were computed separately by multiplying the number of days/week (frequency) by the duration on an average day. Reported minutes per week in each category were then weighted by a metabolic equivalent (MET; multiples of resting energy expenditure) resulting in a PA estimate independent of body weight, expressed as metabolic equivalents (METs) multiplied with time in minutes per week (METs*minutes*week$^{-1}$, abbreviated METs-min/week). The summary indicator[11] was used to categorise the subjects into three levels of PA: "low" (physically inactive), "moderate" and "high" levels of PA. Cigarette smoking behaviour of subject was categorised as current-smoker, ex-smoker or non-smoker. Subjects were considered as current smokers if they had smoked during the previous 12 months, ex-smokers if they had quit smoking and non-smokers when they had never smoked. Meanwhile, subjects were asked to identify themselves as current-drinker ($\geq$1 drink of any type per month for more than 1 year; one drink is considered to contain 10 g alcohol), former drinker (subjects consuming at least 12 drinks of any type over a subject's lifetime but not currently

drinking alcohol), or non-drinker (<1 per month or never consumed alcohol) during the interviews.

Patients' medical records on glycaemic control composed glycated haemoglobin ($HbA_{1C}$) and fasting plasma glucose (FPG), and blood lipid profiles including serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides were accessed. The diabetes treatment and use of cardio-protective medications was also ascertained. Physical examination included anthropometric [body mass index (BMI; calculated as weight in kg divided by height in $m^2$) and waist-hip-ratio (WHR; determined as waist circumference divided by hip circumference)] and blood pressure measurements were performed according to standardised protocols. The diagnoses of cardiovascular events, T2DM, hypertension, dyslipidaemia, peripheral neuropathy, diabetic retinopathy, and nephropathy were based on self-reports, confirmed by hospital medical records and further clinical examinations carried out at the time of the survey.

### *Diagnosis of CVD*

Taken overall, CVD consisted of coronary artery disease (CAD), non-fatal ischaemic stroke, transient ischaemic attack (TIA) and clinically significant peripheral vascular disease (PVD), in which CVD was defined by the presence of one or more of the above described outcomes. Two main categories of diseases were identified in this research study: (i) CVD and (ii) non-CVD. The presence of CVD was established based on physical examination and personal medical history. On the other hand, detailed information about each subject's medical history was collected during face-to-face interview. Coronary artery disease was defined using the following representative criteria[12]: 1) history of definite MI verified by typical symptoms, a positive exercise stress test, consistent changes in cardiac enzyme levels, or coded electrocardiogram (ECG) evidence in the medical record, and confirmed by the study adjudication committee formed by physicians. Angina pectoris was defined as experience of typical repeated effort-dependent episodes of chest pain or oppression relieved at rest, or by use of nitroglycerine as validated by exercise-positive electrocardiogram and/or angiography; 2) prior cardiac intervention confirmed by evidence in the medical record of the standard treatments of symptomatic CAD – percutaneous transluminal coronary angioplasty (PTCA) (coronary angioplasty or stent) or coronary revascularization (CABG); 3) other CAD determined as >70% stenosis confirmed by angiography; 4) heart failure that was secondary to atherosclerotic disease; and 5) receiving CAD-related medication such as coronary vasodilator due to MI or angina pectoris. Stroke events were defined as a constellation of focal or global neurological deficits that were sudden or rapid in onset and for which there was no apparent cause other than a vascular accident on the basis of a detailed clinical history, neurologic examination, and ancillary diagnostic procedures such as computed tomography (CT) and magnetic resonance imaging (MRI).[13] Stroke events were classified as cerebrovascular accident (CVA) (neurological deficit that was present for more than 24 hours) or TIA (neurologic deficit resolving completely within 24 hours). No cases of intracranial haemorrhage (including subarachnoid haemorrhage) were included in this study. The stroke events were also verified from local hospitals' discharge diagnoses and medical records, as well as self-reported disease history. Peripheral vascular disease was assessed as positive intermittent claudication by the WHO/Rose questionnaire,[14] gangrene of the lower extremities and revascularization or amputation procedures. Any patient who was asymptomatic or had negative investigations based on medical record review was classified as no CVD.

### *Ethical approvals*

The study protocol conforms to the principles of the Ethical Guidelines of the Declaration of Helsinki (World Medical Association Declaration of Helsinki). Approvals to conduct this study were obtained from the Medical Research and Ethics Committee of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia and Ministry of Health Malaysia (Code: NMRR-10-483-5703). All patients were aware of the nature of the study and gave informed consent prior to commencement of interview. Participation was completely voluntary in the study.

### *Statistical analyses*

All statistical analyses were performed by using IBM SPSS Statistics Version 21.0 (SPSS Inc., Chicago, IL, USA). Univariate analyses of all variables were run to inspect the distribution of the data and check for outliers. Descriptive statistics such as frequencies, percentages, means, ranges and standard deviation (SD) were used to describe the data. Categorical variables are expressed as absolute number and percentage. All continuous variables were expressed as means±SD. In the bivariate analysis, mean levels of risk factors were compared between subjects with and without CVD, in which the associations or difference between socio-demographic, anthropometric, biochemical, clinical, and lifestyle variables, and the prevalence of CVD were explored by chi-square ($\chi^2$) test and independent *t*-test. A multivariate analysis using binary logistic regression was used to calculate odds ratios (ORs) and their 95% confidence intervals (CIs). All the variables with a $p$ value <0.05 in the bivariate analysis were investigated with the binary logistic regression model to identify the potential independent risk factors associated with CVD. A $p$ value of <0.05 was regarded as statistically significant, and has been used to decide upon the rejection of the null hypothesis. This cut-off point was chosen to ensure that all possibly related variables were included in the logistic regression model.

## Results

### *Medical backgrounds of subjects*

Table 1 represents the prevalence of CVD and its components in the study. The prevalence of CVD among the subjects was 36.1%, with one or more cardiovascular events ever been experienced. The prevalence of CAD, cerebrovascular disease and PVD was 30.7%, 10.2% and 5.1%, respectively. Among the CAD patients, 10.9% ever experienced MI and 22.0% had angina pectoris. A total of 4.5% and 9.4% CAD patients underwent CABG and PTCA, respectively. There were 9.6% subjects with history of ischaemic stroke and 4.5% documented with TIA. Neuropathy (41.5%), nephropathy (17.6%) and retinopathy (15.0%) were identified among the subjects.

### *Characteristics of subjects*

A total of 313 patients with T2DM who fulfilled the eligibility criteria participated in the present research upon written informed consent. A response rate of 100% was achieved when all the T2DM patients approached showed enthusiasms and interests in the interviews, and complete data were obtained. Table 2 demonstrates socio-demographic, anthropometric, biochemical and clinical characteristics of the subjects. Generally, the mean age of the study subjects was 55.7±9.2 years (ranged 30-78 years), and majority of them were above 50 years old. The average duration of diabetes of the subjects in this study was approximately 10 years, men and women were equally represented, with majority were Malays, followed by Indians and Chinese. The majority was of low educational status, having completed only secondary school (44.1%) or less (23.0% primary school and 9.6% no formal education, respectively); married (81.2%) and retired (27.8%). Compared to non-CVD patients, subjects with CVD were more likely to be older and having longer duration of diabetes. The disease significantly affected more men (58.4%) than women (41.6%) ($\chi^2$=7.788, $p$=0.005).

The mean BMI of the subjects was 29.0±5.0 kg/m$^2$, with CVD patients being 28.5±4.2 kg/m$^2$ and non-CVD subjects 29.2±5.4 kg/m$^2$, respectively. Higher mean value was observed in patients with CVD compared to non-CVD subjects with regards to WHR level, exhibiting a statistically significant difference between the CVD and the other group ($t$=3.202, $p$=0.002). The mean value for glucose measures of $HbA_{1c}$ and FPG was 8.7±2.1% and 8.8±3.6 mmol/L, respectively. Moreover, the mean total cholesterol, LDL-C, HDL-C and triglycerides levels were 4.9±1.3 mmol/L, 2.9±1.1 mmol/L, 1.2±0.3 mmol/L and 1.8±1.2 mmol/L respectively. Although patients with CVD demonstrated higher FPG and $HbA_{1c}$ levels than their non-CVD counterparts, there were no statistically significant differences between the glycaemic controls. Likewise, there was no significant difference in total cholesterol and LDL-C levels between groups ($p$>0.05). Result shows that HDL-C was significantly lower ($t$=-3.749, $p$<0.001) while triglycerides were significantly higher ($t$=2.498, $p$=0.013) in T2DM patients with CVD than in those without CVD, despite the fact that their use of medications for dyslipidaemia was much more common than in patients without CVD. Majority of the subjects suffered from at least one other chronic (non-diabetic) medical condition such as dyslipidaemia and hypertension. There was a significant difference found in antihypertensive therapy ($\chi^2$=13.37, $p$<0.001) and lipid-lowering agent use ($\chi^2$=3.98, $p$=0.046) respectively between patients with and without CVD.

In terms of lifestyles, the mean total energy intake of the subjects was 1674±694 Kcal per day, and subjects with CVD were noted to consume higher total calories ($t$=3.275, $p$=0.001). Likewise, the mean carbohydrate, protein and total fat intake of CVD patients were significantly higher than for non-CVD subjects ($p$<0.05). There was a very tremendous significant difference between subjects with and without CVD in terms of the IPAQ categories ($\chi^2$=28.006, $p$<0.001) as clearly tabulated in Table 2. Smoking status and pattern of alcohol consumption were found to be associated with increased CVD prevalence among the patients with T2DM.

***Relationship between predicting risk factors and cardiovascular disease***

Table 3 outlines the significant predictors of CVD among the T2DM patients estimated using multivariate logistic regression analysis in conjunction with the forward stepwise method. The variables with $p$ values < 0.05 in the bivariate analyses: age, diabetes duration, gender, ethnicity, employment, dietary intakes (total energy intake, carbohydrates, protein, total fat), physical activity, smoking, alcohol consumption, WHR, HDL-C, triglycerides, hypertension, and dyslipidaemia were included in the model. The crude and adjusted ORs with their 95% CI are

presented in Table 3. Older age patients were 1.058 times slightly more likely to develop CVD (adjusted $OR_{95\%\ CI}$=1.058 [1.018–1.099]). Logistic regression analysis also strongly suggests that subjects with lower HDL-C displayed higher odds of CVD (adjusted $OR_{95\%\ CI}$=0.231 [0.087–0.613]), where a unit (mmol/L) increase in HDL-C level resulted in a decrease in the odds of CVD by 0.231 folds, which fits well to the other publications and illustrates the close overlap of T2DM and CVD with decreased HDL-C. In addition, it was revealed that those self-employed subjects were more likely to develop CVD compared with retired subjects (adjusted $OR_{95\%\ CI}$=3.978 [1.626–9.733]). Whereas those with low PA (adjusted $OR_{95\%\ CI}$=3.203 [1.671–6.140]) and moderate PA levels (adjusted $OR_{95\%\ CI}$=3.227 [1.708–6.099]) exhibited almost triple odds of CVD compared to subjects with high PA level, after controlling for other risk factors.

## Discussions

In Malaysia, CVD is the leading cause of death in government hospitals in both men and women, accounting for 25.4% of total deaths.[15] The CVD rates among patients with T2DM in the present study are high, where as much as 30.7% CAD, 10.2% cerebrovascular disease and 5.1% PVD were identified. The total CVD prevalence was somewhat higher than that conducted in Spain where CVD complications were found in 25% of their diabetic patients, with CAD as the most frequent finding (14%), followed by CVA and PVD complications (7% and 6%, respectively).[16] On top of that, cardiovascular complications also appear to be higher in the present study as compared with a similar study carried out in Italy in which the total CVD rate was 31.7%.[17] Whereas in Germany, 15.2% of their T2DM patients had atherosclerotic vascular disease (AVD), and 7.6% of the patients reported a previous MI and 4.3% a stroke.[18] The differences being, perhaps, influenced by study design, sample population selection, screening procedures, and higher prevalence of DM in Asia. In another prospective open-observational study included 930 outpatients with T2DM and hypercholesterolemia that was also conducted in Spain, 13.8% had a history of angina, 13.5% of acute MI, 5.2% of stroke, and 7.9% of PAD,[19] which rather concurred the present finding.

Multivariate logistic regression analyses showed that age, HDL-C level, working status, and PA level were significant independent predictors of CVD. Unsurprisingly, increasing age was associated with an increased likelihood for CVD in the present study. This result corroborates earlier local recent findings that age at onset of DM emerged as one of the significant predictors of cardiovascular disorders.[20] Indeed, it is commonly known that advancing age always served to be one of the most powerful independent risk factors for CVD.[21] This might be due to the combined effects of age-related changes in the vascular system as well the duration of exposure to adverse risk factors. Therefore effects of ageing and the senior citizens should continue to receive focus in routine diabetes care.

The present study provides strong evidence that HDL-C is a robust predictor of CVD, confirming the conclusions of a recent comprehensive report on the protection of HDL-C against CVD by Cooney et al. (2009). In this analysis of the large size SCORE dataset contained data on HDL-C for 104,961 individuals, a strong, graded, independent, inverse relationship between HDL-C and both CVD and CAD mortality was demonstrated, withstanding adjustment for other CV risk factors, including factors known to be associated with HDL-C level, including BMI, triglycerides, DM, smoking and family history of CAD.[22] In the Japan Cholesterol and Diabetes Mellitus Study, a prospective cohort study of 4,014 type 2 diabetic patients (mean age

67.4±9.5 years) to clarify the relationship between lipid levels and ischaemic heart disease (IHD) and cerebrovascular disease in diabetic individuals, lower HDL-C was also found to be an important risk factor for CVD.[23] Our results are also in line with the other publication by Drexel et al. (2005) that concluded the decisive role of the dyslipidaemic features (low HDL/high triglycerides) in cardiovascular risk prediction in patients with T2DM.[24] Increased HDL-C is known to protect against the development of CVD through a number of mechanisms including increasing reverse cholesterol transport, anti-inflammatory and antioxidant mechanisms.

As expected, those self-employed subjects in this study were more likely to develop CVD compared with retired subjects, despite adjusting for other variables. Several explanations for this association are possible. Self-employment was associated with more job control, larger social networks, higher stress level,[25,26] greater hostility and lower optimism in comparison with retired individuals that might contribute to the development of CVD.[27] These factors can independently affect the circulatory system via changes in circadian rhythms, hormonal regulation and cardiovascular dynamics.[28] Several other confounding factors might affect the association between the respective employment status and CVD. Many of the risk factors and behaviours that are linked with CVD, such as smoking, alcohol consumption, dietary intake, obesity and past medical history, might differ between self-employed and retired subjects. In fact, significant differences in these factors were detected between the two groups in our analysis. However, the multivariate model demonstrated that working status had a stronger association with the risk of CVD than several other factors, including smoking, alcohol consumption, some of the nutrient intakes, WHR, hypertension and dyslipidaemia. This emphasizes that working status, self-employment as compared to retirement is an important social determinant of health, at least for CVD, among the patients with T2DM.

Besides that, the findings in this study are consistent with the scientific evidence established by Professor Jeremiah Morris, the "Father of Physical Activity Epidemiology"[29] that "vigorous exercise is a natural defence of the body, with a protective effect on the aging heart against ischaemia and its consequences", and reaffirms that physically active is an effective and safe way to prevent CVD events in T2DM patients. More specifically on PA intensity, the results in this study are firmly in agreement with Swain and Franklin (2006) whom completed a review of the cardioprotective benefits of vigorous- versus moderate-intensity aerobic exercise in the sense that exercise performed at a vigorous intensity conferred greater cardioprotective effects than PA performed at a moderate intensity. Epidemiological studies identified in this review consistently found a greater reduction in risk of CVD with vigorous PA than with moderate-intensity PA, and reported more favourable risk profiles for individuals engaged in vigorous, as opposed to, moderate-intensity PA. Not one single epidemiological study reported greater benefits for moderate rather than vigorous-intensity PA.[30] Likewise, evidence from clinical trials also supported a crucial role for high-intensity PA.[31]

A second explanation of the observed phenomenon of the significant relationship between CVD and PA levels in this study, from another standpoint, which one could argue is, it has less to do with the consequences of habitual inactivity itself that with the effects of having pre-existing cardiovascular events. It appears that the sedentary lifestyle behaviour might be negatively influenced by enforced physical postoperative inactivity in patients after cardiac surgery.[32] Yet the very symptoms which are used as indicators of physical inability may themselves be products of inactivity. Often chronic illnesses, for example CVD, are sufficient excuses for inactivity. Fears concerning the presumed harmful effects of exercise and the belief that effective exercise must be overly strenuous are other reasons cited for the low levels of activity among them.[33,34] This may consequently produce mild forms of symptoms related to diminished

work capacity, circulatory problems, dizziness and lethargy which act as a disincentive to becoming more active, creating a vicious cycle of deteriorating physical functioning and decreased PA.

It is now widely believed that besides physical functional ability, exercise appears to have positive psychological benefits, including reduced anxiety and tension, and increased feelings of relaxation and overall well-being among individuals. Just as any other preventive or rehabilitative treatment is prescribed on an individual basis, so too should exercise be.[35,36] While health problems are not contra-indications to beginning or continuing exercising, they are important considerations when deciding on an appropriate exercise regimen. These cardiac surgical patients as well as other T2DM patients at high CVD risk should be provided practical advice or approval concerning their suitability for participation in safe and beneficial exercise. The factors that may be considered in the design and implementation of exercise programs in order to ensure patient safety, for instance, are potential silent myocardial ischaemia, loss of proprioception in diabetics, resting tachycardia, and orthostatic hypotension associated with specific diabetic vascular complications.[37] Public health messages, health care professionals, and health care system should aggressively promote PA during occupation, commuting, leisure time and daily life, preferably, together with the medical considerations associated with exercising for this group of vulnerable patients with reduced cardiovascular efficiency. This is not only a task for health personnel, but all patients should take a lead in the process towards the primary prevention of T2DM and subsequent CVD and other diabetic complications.

## Conclusions

In this group of T2DM patients, CVD patients tend to be older, having longer DM duration, shorter years of education, lower personal and household monthly income, higher WHR, elevated HDL-C level, and higher triglycerides as indicated by bivariate analysis. There are also significant differences between CVD and non-CVD patients in the gender, ethnicity, employment, hypertension, dyslipidaemia, nutrient intakes (calories, carbohydrate, protein, and total fat), physical activity level, smoking status and alcohol consumption. In conclusion, the predictive findings in this study suggest that advancing age, unfavourable low HDL-C level, self-employment, and low and moderate PA levels are strongly and independently associated with a higher risk of CVD in patients with T2DM. The importance of secondary and tertiary preventions focusing on the risk factors to minimise the potential deterioration of metabolic control and quality of life accompanied CVD coexisted T2DM should be emphasized. More resources to forge a better partnership between diabetes healthcare providers and patients in the area of awareness, comprehensive diabetes service and patient co-operation in therapy are highly recommended. Also, public health messages, health care professionals and the health care system should strongly promote lifestyle modifications comprised of regular PA and healthy nutritional habits during daily life and prevent further diabetic complications. Prevention of CVD in patients with T2DM should start from the prevention of DM itself.

This study has thrown up some considerably limitations in need of further investigation. Firstly, this is a cross-sectional study, hence, the temporal relationship between CVD and the risk factors could not be established. Future longitudinal studies are needed to provide stronger evidence on the associations between CVD and its risk factors. However, appropriate analysis of cross-sectional data may represent a valuable initial step in identifying the relations between CVD and its risk factors. Secondly, the study subjects were hospital-based patients with DM of

a relatively long duration; it is likely that these subjects have more diabetic complications and a more difficult metabolic control and treatment than expected in a group of patients with T2DM followed up by general practitioners in primary care settings, therefore, inferences beyond a similar group cannot be made.

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**Table 1:** Prevalence of cardiovascular disease and its components (*n*=313)

| | *n* (%) |
|---|---|
| Cardiovascular disease | |
| No | 200 (63.9) |
| Yes | 113 (36.1) |
| Coronary artery disease | 96 (30.7) |
| Myocardial infarction | 34 (10.9) |
| Angina pectoris | 69 (22.0) |
| Coronary artery bypass grafting (CABG) | 14 (4.5) |
| Percutaneous transluminal coronary angioplasty (PTCA) | 29 (9.4) |
| Cerebrovascular disease | 32 (10.2) |
| Ischaemic stroke | 30 (9.6) |
| Transient ischaemic attack | 14 (4.5) |
| Peripheral vascular disease | 16 (5.1) |

**Table 2:** Socio-demographic, anthropometric, biochemical and clinical characteristics of the patients (*n*=313)

| Characteristics | All (*n*=313) | CVD absent (*n*=200) | CVD present (*n*=113) | *p* value |
|---|---|---|---|---|
| Age (years) | 55.7±9.2 | 54.7±9.7 | 57.4±8.1 | 0.013* |
| 30-39.9 | 19 (6.1) | 16 (8.0) | 3 (2.7) | 0.068 |
| 40-49.9 | 53 (16.9) | 38 (19.0) | 15 (13.3) | |
| 50-59.9 | 118 (37.7) | 76 (38.0) | 42 (37.2) | |
| 60-69.9 | 112 (35.8) | 62 (31.0) | 50 (44.2) | |
| ≥70 | 11 (3.5) | 8 (4.0) | 3 (2.7) | |
| Known diabetes duration (years) | 10.1±8.1 | 9.2±7.6 | 11.5±8.7 | 0.021* |
| Gender | | | | 0.005** |
| Male | 150 (47.9) | 84 (42.0) | 66 (58.4) | |
| Female | 163 (52.1) | 116 (58.0) | 47 (41.6) | |
| Ethnicity | | | | 0.015* |
| Malay | 147 (47.0) | 106 (53.0) | 41 (36.3) | |
| Chinese | 80 (25.6) | 47 (23.5) | 33 (29.2) | |
| Indian | 86 (27.5) | 47 (23.5) | 39 (34.5) | |
| Marital status | | | | 0.417 |
| Married | 254 (81.2) | 165 (82.5) | 89 (78.8) | |
| Single/Widowed/Divorced | 59 (18.8) | 35 (17.5) | 24 (21.2) | |
| Education level | | | | 0.054 |
| No formal education | 30 (9.6) | 20 (10) | 10 (8.9) | |
| Primary school | 72 (23.0) | 41 (20.5) | 31 (27.4) | |
| Secondary school | 138 (44.1) | 83 (41.5) | 55 (48.7) | |
| College/University | 73 (23.3) | 56 (28) | 17 (15.0) | |
| Employment | | | | 0.009** |
| Employed (Public sector) | 40 (12.8) | 32 (16.0) | 8 (7.1) | |
| Employed (Private sector) | 48 (15.3) | 31 (15.5) | 17 (15.0) | |
| Self-employed | 46 (14.7) | 23 (11.5) | 23 (20.4) | |
| Housewives | 74 (23.6) | 53 (26.5) | 21 (18.6) | |
| Unemployed | 18 (5.8) | 7 (3.5) | 11 (9.7) | |
| Retired | 87 (27.8) | 54 (27.0) | 33 (29.2) | |
| Total energy intake (Kcal/day) | 1674±694 | 1579±590 | 1843±824 | 0.001** |
| Carbohydrate (g/d) | 230.2±96.9 | 218.1±84.9 | 251.8±112.5 | 0.003** |
| Protein (g/d) | 65.8±31.4 | 62.7±28.4 | 71.3±35.7 | 0.020* |
| Total fat (g/d) | 54.3±30.0 | 50.8±24.0 | 60.6±37.9 | 0.006** |
| PA level | | | | <0.001*** |
| Low PA (%) | 72 (23.0) | 34 (10.9) | 38 (12.1) | |
| Moderate PA (%) | 71 (22.7) | 35 (11.2) | 36 (11.5) | |
| High PA (%) | 170 (54.3) | 131 (41.9) | 39 (12.5) | |
| Smoking (%) | | | | 0.004** |
| Current | 31 (9.9) | 14 (7.0) | 17 (15.0) | |
| Former | 64 (20.4) | 34 (17.0) | 30 (26.6) | |
| Never | 218 (69.7) | 152 (76.0) | 66 (58.4) | |
| Alcohol consumption (%) | 16 (5.1) | 7 (3.4) | 9 (8.0) | 0.025* |

| | | | | |
|---|---|---|---|---|
| Current | 17 (5.4) | 7 (3.5) | 10 (8.8) | |
| Former | 280 (89.5) | 186 (93.0) | 94 (83.2) | |
| Never | | | | |
| BMI (kg/m$^2$) | 29.0±5.0 | 29.2±5.4 | 28.5±4.2 | 0.259 |
| WHR | 0.9±0.1 | 0.9±0.1 | 1.0±0.1 | 0.002** |
| Hypertension (%)† | 251 (80.2) | 148 (74.0) | 103 (91.2) | <0.001*** |
| Dyslipidaemia (%)† | 279 (89.1) | 173 (86.5) | 106 (93.8) | 0.046* |
| $HbA_{1c}$ (%) | 8.7±2.1 | 8.6±2.0 | 8.9±2.2 | 0.202 |
| FPG (mmol/L) | 8.8±3.6 | 8.7±3.5 | 9.0±3.9 | 0.575 |
| SBP (mmHg) | 137.9±18.9 | 138.8±17.7 | 136.5±20.9 | 0.302 |
| DBP (mmHg) | 80.7±11.8 | 81.4±11.4 | 79.4±12.6 | 0.154 |
| Total cholesterol (mmol/L) | 4.9±1.3 | 4.9±1.1 | 5.0±1.6 | 0.527 |
| LDL-C (mmol/L) | 2.9±1.1 | 2.9±0.9 | 3.0±1.4 | 0.465 |
| HDL-C (mmol/L) | 1.2±0.3 | 1.2±0.4 | 1.1±0.3 | <0.001** |
| Triglycerides (mmol/L) | 1.8±1.2 | 1.7±1.2 | 2.1±1.3 | 0.013* |

Data presented as *n* (%) or mean±SD

*$p$<0.05, **$p$<0.01, ***$p$<0.001 according to independent *t* test and chi-square ($\chi^2$) test
SD: standard deviation; CVD: cardiovascular disease; PA: physical activity; BMI: body mass index; WHR: waist-to-hip ratio; $HbA_{1c}$: glycosylated haemoglobin; FPG: Fasting plasma glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.
† Being treated

**Table 3:** Results from stepwise logistic regression model of CVD predictors in patients with T2DM (*n*=313)

| Variables | B | Crude OR (95% CI) | Adjusted OR (95% CI) | *p* value |
|---|---|---|---|---|
| Age (years) | 0.056 | 1.033 (1.007-1.061) | 1.058 (1.018-1.099) | 0.004** |
| High-density lipoprotein cholesterol (mmol/L) | -1.466 | 0.235 (0.101-0.551) | 0.231 (0.087-0.613) | 0.003** |
| Working status | | | | 0.014* |
| Public sector | 0.026 | 0.409 (0.168-0.994) | 1.026 (0.355-2.966) | 0.962 |
| Private sector | 0.949 | 0.897 (0.431-1.868) | 2.583 (0.972-6.864) | 0.057 |
| Self-employed | 1.381 | 1.636 (0.795-3.369) | 3.978 (1.626-9.733) | 0.002** |
| Housewives | 0.196 | 0.648 (0.333-1.261) | 1.216 (0.574-2.576) | 0.609 |
| Unemployed | 1.197 | 2.571 (0.907-7.289) | 3.312 (0.980-11.188) | 0.054 |
| Retired | 0 | 1[a] | 1[a] | - |
| Physical activity level | | | | <0.001*** |
| Intense/High | -1.114 | 0.266 (0.148-0.478) | 0.328 (0.172-0.626) | 0.001** |
| Moderate | 0.051 | 0.920 (0.477-1.774) | 1.053 (0.520-2.130) | 0.887 |
| Low | 0 | 1[a] | 1[a] | - |
| Constant | -3.091 | | 0.045 | 0.015 |

*$p$<0.05, **$p$<0.01, ***$p$<0.001

CI: confidence interval; CVD: cardiovascular disease; T2DM: type 2 diabetes mellitus

The following variables which demonstrated $p$ values < 0.05 in the bivariate analyses were entered into the model: age, diabetes duration, gender, ethnicity, employment, dietary intakes (total energy intake, carbohydrates, protein, total fat), physical activity, smoking, alcohol consumption, waist-to-hip ratio, hypertension, dyslipidaemia, high-density lipoprotein cholesterol, and triglycerides.

[a] Reference category