Proliferative Diabetic Retinopathy in Patients with Type 2 Diabetes Correlates with the Presence of Atherosclerosis Cardiovascular Disease

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Research

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Abstract

Background: Atherosclerosis cardiovascular disease (ASCVD) is the main cause of morbidity and mortality in Type 2 diabetes mellitus (T2DM). As most diabetic patients with ASCVD are asymptomatic, it is most neglected in clinical practice. For this reason, identifying high-risk ASCVD population with intensified treatment is very important. In recent years, the relationship between diabetic retinopathy (DR) and ASCVD has caused much academic concern, but the results are inconsistent. Moreover, whether all grades of DR increase the risk of ASCVD remains controversial. Most importantly, very few data can be found in China.

Objective: Our aim is to discuss whether all grades of DR increase the risk of ASCVD after adjustment for the traditional cardiovascular risk factors and to assess the independent contribution of DR to cardiovascular events in patients with T2DM, hoping to provide more evidence for early identification of ASCVD.

Research design and methods: A total of 425 T2DM patients with complete physical and biochemical data were included in the study. The grade of DR was assessed with two 45°color digital retinal images. Based on the presence of history of ASCVD, 425 T2DM patients were divided into 2 groups: ASCVD group and non-ASCVD group.

Results: Patients with ASCVD had a significantly higher level of age, fasting plasma glucose (FPG) and glycated haemoglobin (HbA1c) and higher proportion of history of ASCVD, female sex and lower level of alcohol, calculated glomerular filtration rate (eGFR) than non-ASCVD patients. Their trend to develop DR with ASCVD was significantly higher than patients with non-ASCVD (χ^2 =5.805, P =0.016). DR was an independent statistical indicator of the presence of ASCVD [odds ratio (OR) (95% CI): 2.321 (1.152-4.678), P =0.018]. Furthermore, when DR was divided into non-proliferative retinopathy (NPDR) and proliferative retinopathy (PDR) according to its severity, only PDR was significantly associated with incident ASCVD [OR (95% CI): 8.333 (1.813-38.304), P =0.006]. After adjusting for traditional ASCVD risk factors, such an association still existed [OR (95% CI): 7.466 (1.355-41.137), P =0.021].

Conclusion: DR associates strongly with ASCVD in the Chinese population with T2DM. With the severity of DR increasing, the risk of ASCVD also grows. After adjustment for traditional risk factors, PDR is still an independent risk marker for ASCVD.

Introduction

Diabetic retinopathy (DR) is one of the most common and severe microvascular complications of diabetes mellitus (DM). According to the WHO study, the number of diabetic patients worldwide has reached 366 million in 2011, and by 2025, this figure is expected to jump to more than 500 million, and about one-third of them will develop DR (1). Increasing DR severity is associated with an increased risk of vision impairment or loss and risk of vision-threatening proliferative disease over time (2).

DM, defined by elevated glycemic markers, is a major risk factor for atherosclerosis cardiovascular disease (ASCVD), which is the most common cause of death among adults with diabetes mellitus (3), and thus is considered to have an ASCVD risk equivalent. ASCVD is the leading cause of mortality and morbidity among the DM population, accounting for 70% of all deaths (4) (5). However, persons with DM are at increased risk of silent myocardial ischemia and myocardial infarction (MI): up to one-third of patients with DM who experience an acute MI do not manifest chest pain (6). These patients often do not have timely and effective treatment in the event of emergency with high fatality rate. As a result, early recognition of such high-risk ASCVD population is very important.

The association between DR and ASCVD in patients with type 2 DM (T2DM) has attracted considerable attention, as traditional risk factors for ASCVD, such as hypertension, hyperlipidemia, duration of hyperglycemia and magnitude of glycemia control are well known risk factors for progression and development of DR (7). And, similar pathophysiological processes may be contributed in ASCVD and DR. Previous studies have reported the fact that DR presence increases the risk of ASCVD, such as stroke (8) (9)and coronary heart disease (CHD) (10) (11). However, some studies (12, 13) pointed out that this correlation is weakened after adjustment for traditional ASCVD risk factors. What remains disputed is whether each stage of DR is associated with increased risk of ASCVD. Furthermore, present studies focused mainly on European and American people, leading to limited data on Asian people, especially Chinese. The aim of this study is to discuss whether the presence or severity of DR is associated with ASCVD independent of traditional cardiovascular risk factors and to evaluate the independent effect of DR on cardiovascular events in patients with T2DM.

Research Design And Methods

Study population

The study participants were diagnosed DM patients from geriatric and endocrine ward in Beijing Tongren Hospital, chosen during January 2018 and June 2020. 447 received examinations including a physical examination, blood glucose and lipid measurements, renal function tests and ophthalmic examination. After excluding subjects with cataracts, glaucoma, age related retinopathy or other eye diseases, impaired renal function [calculated glomerular filtration rate (eGFR) <60 ml/min], cancer, chronic obstructive pulmonary disease (COPD), T1DM, secondary diabetes and chronic pancreatitis, 425 participants with T2DM were available for the follow-up test that divided them into two groups, 65 with ASCVD and 360 without.

Data collection

All participants received a standardized examination. Data regarding age, smoking, alcohol consumption, physical activity, educational level, and history of diabetes, hypertension and ASCVD were obtained with detailed medical records. Body Mass Index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference (WC) was measured at the level of the umbilicus in cm. Blood

pressure (BP) was measured 3 times when participants were seated, and the average of the last 2 measurements was adopted. Blood samples were collected after an overnight fast for the determination of plasma glucose, HbA1c, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) concentrations and serum creatinine (Scr). GFR was estimated by using the modified MDRD formula for Chinese patients (14): eGFR (ml/min/1.73m^2) = 175 × Scr$^{-1.234}$ × age$^{-0.179}$ × 0.79 (if female).

Definition of clinical and biochemical variables

Various non-fatal ASCVD were determined according to a patient's self-report. CHD can be defined with a history of myocardial infarction, at least one coronary stenosis more than 50% by coronary angiography or coronary CTA, a surgical history of revascularization(including percutaneous coronary intervention(PCI) or coronary artery bypass grafting(CABG)). The definition of stroke included a history of language or physical dysfunction continuing for more than 24 h and ischemic or hemorrhagic stroke diagnosed using imaging examination [computed tomography or magnetic resonance imaging]. ASCVD referred to a history of CHD or stroke, as defined above. Diagnosis of hypertension was based on meeting any of three criteria: systolic blood pressure (SBP) of ≥140 mmHg, diastolic blood pressure (DBP) of ≥90 mmHg or current use of antihypertensive drugs (15). Central obesity is based on WC cutoff ≥ 80 cm in women and ≥ 90 cm in men according to the IDF ethnicity-specific definitions for Asian (16). Overweight and obesity are respectively identified as BMI 24-28 kg/m^2 and BMI equal to or over 28 kg/m^2 according to the Working Group on Obesity in China (WGOC) (2002) (17). Smokers were defined as those who had smoked ≥1 cigarette/day for at least 1 year. Drinkers were defined as those who had consumed ≥30 g of alcohol/week on average for at least 1 year. Regular leisure-time physical activity was defined as participation in moderate or vigorous activity for 30 minutes or more per day at least 3 days a week. Educational level was also recorded and categorized into two groups: low (illiteracy, primary, and secondary education), and high (high school education, college or university education). The family history of ASCVD goes for first-degree relatives (biological mother, father, brothers, or sisters).

Assessment of retinopathy

All participants received eye examinations by an ophthalmologist and had a bilateral retinal photograph taken of the fundus through dilated pupils. Two 45u color digital images of the retina were taken of each eye by a technologist using a Topcon TRC-NW7SF fundus camera (Topcon, Tokyo, Japan), an ophthalmic digital imaging system. The first image was centered on the macula, and the second on the optic nerve. The photographs were graded by two qualified ophthalmologists from the Eye Center of Capital Medical University, Beijing Tongren Hospital according to the international clinical diabetic retinopathy severity scale (18): (i) no diabetic retinopathic changes (NDR); (ii) mild non-proliferative diabetic retinopathy (NPDR); (iii) moderate NPDR; (iv) severe NPDR; and (v) proliferative diabetic retinopathy (PDR). The degree of DR was determined according to the grading in the most affected eye. The ophthalmologists grading the photographs were blinded to the patients' characteristics.

Statistical analysis

All statistical analyses were conducted with the software package SPSS version 22.0 for Windows. For the continuous variables with a normal distribution, mean±SD was reported and the independent t-test was used to compare subjects with no diabetic retinopathy (NDR) with any stage of diabetic retinopathy (DR). For the discrete variables or the continuous variables without a normal distribution, the median (P25–P75) was reported, and a Mann-Whitney rank test was used to examine the differences between the groups. In the meantime, distribution of discrete/qualitative variables was compared by Pearson chi-square test. Multivariable logistic regression analysis was used to estimate crude and adjusted odds ratios (ORs) (95% CIs) to allow for differences between groups with respect to demographic and risk factors and control for potentially confounding variables. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 425 T2DM patients with (n=65) or without (n=360) ASCVD comprised the study groups, with 165 men and 260 women and average age of 58.72±6.82. The total prevalence of DR was 11.29%, 9.65% with NPDR and 1.64% with PDR respectively.

The demographic and biochemical parameters of the two groups are shown in Table 1. Compared with the non-ASCVD group, patients with ASCVD were older, with higher levels of FPG and HbA1c and higher proportion of female and family history of ASCVD, while their level of eGFR and proportion of alcohol are lower. At the same time, there were no statistical differences between the two groups in duration of diabetes, the proportion of smoking, high educational level, physical activity, central obesity, generalized obesity, hypertension and the levels of SBP, DBP, TC, TG, HDL-C, LDL-C (Table 1).

Of the 360 subjects without ASCVD, 35 (9.7%) had DR. However, 13 cases (20.0%) were registered in the ASCVD group of 65 subjects, showing that the trend to DR in ASCVD group was significantly higher than in non-ASCVD group (Pearson χ^2 =5.805, P =0.016), as is illustrated in Fig 1A. Furthermore, when DR was divided into NPDR and PDR based on its severity, a higher proportion of subjects with NPDR (9, 13.8%) and PDR (4, 6.2%) were found in the ASCVD group than from non-ASCVD group [32 subjects (9.0%) with NPDR (Pearson χ^2 =1.975, P =0.160) and 3 subjects (0.9%) with PDR (Pearson χ^2 =10.368, P =0.001)], and the difference of prevalence of PDR in two groups was statistically significant (Fig 1B).

Logistic regression analysis was performed to identify the risk factors of ASCVD. Age [odds ratio (OR) (95% CI): 1.814 (1.257-2.616), P =0.001], female sex [OR (95% CI): 1.971 (1.091-3.562), P =0.025], family history of ASCVD [OR (95% CI): 1.850 (1.085-3.155), P =0.024] and HbA1c [OR (95% CI): 1.198 (1.050-1.368), P =0.007] were relative risk factors and alcohol [OR (95% CI): 0.440 (0.222-0.872), P =0.019] eGFR [OR (95% CI): 0.990 (0.827-0.980), P =0.015] was relative protection factors of ASCVD (Table 2). Next, we found that DR [OR (95% CI): 2.321 (1.152-4.678), P =0.018] was significantly associated with ASCVD, and such a link was only true for PDR [OR (95% CI): 8.333 (1.813-38.304), P =0.006] when DR was divided into

NPDR and PDR. With an adjustment for age, sex, family history of ASCVD and duration of DM, PDR was significantly associated with and an independent risk factor for ASCVD [OR (95% CI): 9.430 (1.963-45.299), P =0.005]. Moreover, the association was not affected by an additional adjustment for smoking, alcohol, educational level, physical activity, obesity (central or general obesity), history of hypertension, SBP, DBP, HbA1c, LDL-C and eGFR [OR (95% CI): 7.466 (1.355-41.137), P =0.021] (Fig 2).

Discussion

In this study, the prevalence of ASCVD was 15.29% in T2DM patients. Age, female sex, the family history of ASCVD and hyperglycemia were risk factors of ASCVD, similar to previous research results. Coexisting diseases with T2DM, such as hypertension and hyperlipidemia are defined ASCVD risk factors, while DM itself is considered to have a CAD risk equivalent. ASCVD is the main cause of morbidity and mortality in diabetic patients, accounting for the biggest burden of DM directly or indirectly. The 2007-2008 China National Diabetes and Metabolic Disorders Study reported that the defined total of ASCVD prevalence was 1.44%, including 0.83% of stroke and 0.63% of CHD in Chinese adults over 20 years of age (19). The Da Qing impaired glucose tolerance (IGT) and Diabetes Study found the leading cause of death for patients with diabetes is ASCVD after 23-year follow-up (20).

It is very important for ASCVD to be detected and intervened timely. Due to the fact that the sensory nerve becomes insensitive and even lost in patients with diabetes, symptoms of ASCVD become asymptomatic or atypical. A variety of cardiovascular risk assessment tools having been proposed to assess the risk of developing ASCVD are available, such as Framingham risk score (FRS), Adult Treatment Panel III (ATP-III), EURO- the Systematic Coronary Risk Evaluation (SCORE), Reynolds risk score (RRS), QRISK2 and the Chinese ten-year appraisal method for ischemic cardiovascular disease (ICVD), etc. But the suitability of these screening assessment tools are limited because the ethnic, region, environment, and the way of life of patients are different. Moreover, computed tomography (CT) and angiography can detect the evidence of stenosis or occlusion of vasculars directly, but these clinical application can result in radiation exposure and sometimes unnecessary invasive diagnosis and treatment. Therefore, it’s necessary to look for a kind of both simple and non-invasive methods to identify ASCVD early in clinical.

In spite of growing controversy，more evidence shows that microvascular diseases in T2DM has a predictive value on developing ASCVD. Micro- and macrovascular complications of T2DM have a “common soil”. Since the Framingham Heart Study and the Framingham Eye Study had reported the association between DR and the occurrence of cardiovascular events, people gradually realized the importance of DR beyond visual damage. The Atherosclerosis Risk in Communities (ARIC) study also found that DR was associated with an increased risk of ischemic stroke [hazard ratio (HR), 2.34; 95% confidence interval (CI), 1.13 to 4.86] over an average follow-up of 7.8 years in the middle-aged persons with diabetes, independent of other risk factors (8). Another ARIC study (21) showed that after controlling for traditional cardiovascular risk factors, participants with retinopathy had more than 2.5-fold higher risk of developing heart failure (HF) than those without retinopathy (HR 2.71; 95% CI 1.46 to 5.05). This association remained significant after further adjustments for glycemic control, carotid atherosclerosis,

and serum markers of endothelial dysfunction (HR 2.20, 95% CI 1.08 to 4.47). Recently, A meta-analysis showed that DR was significantly associated with increased risk of stroke [risk ratio (RR), 1.74; 95%CI 1.35 to 2.24], compared with patients without DR. Furthermore, DR was associated with a marginal increased risk of HF in patients with DM (RR 2.24; 95% CI 0.98 to 5.14) (9). Retinopathy proved to be an independent risk marker for CVD in patients with T2DM (22).

However, there is limited knowledge regarding whether this association is observed consistently in Asian populations, especially in Chineses. There exist differences in the epidemiologic and risk associations of ASCVD between white and Asian populations. There is a potential need for an ethnicity-specific risk model of ASCVD. Furthermore, what remains disputed is whether each stage of DR is associated with increased risk of ASCVD. A report from Finland showed that during the 7-year follow-up, only in patients with PDR at baseline, the risk of CHD events was statistically significantly higher compared with patients without DR (OR 2.31, 95% CI 1.21 to 4.40) (23). However, the Japan Diabetes Complications Study (JDCS) (24), comprised 2,033 patients with T2DM, comfirmed that the presence of DR was found consistently to be associated with an increased risk of stroke and CHD after 8 years of follow-up, and further elucidated that even mild to moderate NPDR had a higher risk of CHD (HR 1.69; 95% CI 1.17-2.97) and stroke (HR 2.69; 95% CI 1.03-4.86) after adjusting for traditional cardiovascular risk factors. In our research, those T2DM patients with an eGFR <60 ml/min/1.73m^2 were excluded specifically to avoid the confounding factor of renal insufficiency, which was associated with an increased risk of atherosclerosis. We found that the presence of DR was significantly associated with an increased risk of ASCVD in Chinese with T2DM. Furthermore, the incidence of ASCVD increased along with the severity of DR. After adjustment for age, sex and other traditional risk factors, PDR rather than NPDR was significantly associated with and an independent risk factor for ASCVD. In the presence of PDR, risk of ASCVD was 7-fold in T2DM patients and PDR offered risk information beyond that provided by those established risk factors.

DR is closely related with ASCVD in epidemiology, similar pathophysiological processes may be also contributed in DR and diabetes-accelerated atherosclerosis. First, traditional risk factors for ASCVD, such as hypertension, hyperlipidemia, duration of hyperglycemia, magnitude of glycemic control and metabolic syndrome (MetS) are well known risk factors for progression and development of DR (7, 25). Secondly, neovascularization (retinal angiogenesis) is a key hallmark of PDR, and angiogenesis is also a common feature observed in advanced atherosclerotic lesions (26, 27). Early pathological changes of macro- and microvascular have similarities, perhaps microcirculation change can accelerate the progress of macrovascular lesions. In addition, more and more evidence support a major role for the unifying mechanism in the pathogenesis of diabetic macrovascular, as well as microvascular, complications (28). These mechanisms what are hexosamine pathway, activation of protein kinase C, oxidative stress, pathological effects of the renin-angiotensin-aldosterone system (RAAS), advanced glycation end product (AGE) formation, inflammation and modification of circulating macromolecules, etc, not only influence the development of DR, also affect the progress of atherosclerosis (29).

Our study has several limitations that must be taken into account. First of all, it may have unpredictable selection bias. Secondly, ASCVD patients in this article are confirmed cases by hospital, so that some potential ASCVD patients may be missed. This might lead to an underestimation of the prevalence of ASCVD in T2DM patients. Thirdly, as these associations are cross-sectional, the study design is incapable of estimating causal relation directly; therefore, our findings may suggest that PDR is an indicator, but not predictor of ASCVD. The adverse effects of DR on ASCVD in Chinese population should be confirmed further in a larger cohort study with a broader spectrum of potential confounding factors. However, we have no reasons to believe these would substantially bias the associations reported herein.

In conclusion, all our data confirm that DR associates strongly with ASCVD in the Chinese population with T2DM. With the severity of DR increasing, the risk of ASCVD also increases. After adjustment for traditional risk factors, PDR is an independent risk marker for ASCVD. Retinal blood vessel is the only microvascular which can be directly observed, it would certainly be exciting to assess whether the retinal microvasculature can be used as a ‘window’ into the state of the cardiovascular complications in patients with diabetes. DR is not only one of the most common microvascular complications of diabetes, but also a “warning sign” for ASCVD. Based on this research findings, we hope that clinicians should pay more attention to systemic vascular risk of the patients with DR, especially PDR, and suggest to incorporate PDR to clinical cardiovascular risk stratification in patients with diabetes.

Abbreviations

ASCVD: atherosclerosis cardiovascular disease; DR: diabetic retinopathy; NDR: no DR; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; DM: diabetes mellitus; BMI: body mass index; WC: Waist circumference; FPG: fasting plasma glucose; HbA1c: glycated haemoglobin; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein; LDL-C: low-density lipoprotein cholesterol; eGFR: calculated glomerular filtration rate; OR: odds ratio; CI: confidence interval.

Declarations

Acknowledgments

Not applicable.

Authors’ Contributions

LG designed the experiments, collected and analyzed the data before writing the manuscript. WZ did the experiments, and was a contributor in collecting data. JKY and MZQ also helped design the study and revise the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Ethics approval and consent to participate

The study was conducted with the approval from the Ethics Committee of Beijing Tongren Hospital, Capital Medical University, and adhered to the tenets of the Declaration of Helsinki. Written consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Clinical characteristic of studied subjects with and without ASCVD.

	Total	non-ASCVD	ASCVD	P value
Number (%)	425	360 (84.71)	65 (15.29)	
Age (year)	58.72±6.82	58.27±6.68	61.21±7.12	0.001
Female (%)	260 (61.2)	212 (58.9)	48 (73.8)	0.023
Smoking n (%)	112 (26.4)	101 (28.1)	11 (16.9)	0.061
Alcohol n (%)	125 (29.4)	114 (31.7)	11 (16.9)	0.016
High educational level n (%)	26 (6.1)	22 (6.1)	4 (6.2)	0.989
Physical activity n (%)	332 (78.1)	281 (78.1)	51 (78.5)	0.942
Family history of ASCVD n (%)	187 (44.0)	150 (41.7)	37 (56.9)	0.023
Central obesity n (%)	311 (73.2)	257 (71.4)	54 (83.1)	0.050
General obesity				0.890
Overweight n (%)	191 (44.9)	162 (45.0)	29 (44.6)	
Obesity n (%)	132 (31.1)	113 (31.4)	19 (29.2)	
Duration of DM (y)	10.39±3.24	10.34±3.16	10.69±3.70	0.416
FPG (mmol/l)	8.61±2.64	8.50±2.58	9.22±2.95	0.042
HbA1c (%)	7.36±1.75	7.25±1.68	7.94±2.04	0.004
Hypertension n (%)	328 (77.2)	275 (76.4)	53 (81.5)	0.363
SBP (mmHg)	150.56±20.17	150.30±20.20	152.06±20.11	0.518
DBP (mmHg)	87.16±11.19	87.37±11.25	85.98±10.86	0.360
TC (mmol/l)	5.37±1.14	5.37±1.13	5.37±1.19	0.977
TG (mmol/l)	2.31±1.96	2.33±2.05	2.19±1.36	0.588
LDL-C (mmol/l)	2.71±0.54	2.71±0.53	2.73±0.59	0.802
HDL-C (mmol/l)	1.45±0.29	1.45±0.29	1.47±0.32	0.589
eGFR (ml/min/1.73m^2)	92.42±17.68	93.31±17.73	87.53±16.69	0.015

Data are means±SE or raw numbers (%). Continuous data were used for univariate general linear models and categorical data were analyzed by χ^2 tests.

Table 2 Odds ratios of metabolic factors for ASCVD.

	B	SE	Wald	OR	95%CI	P value
Age (per 10 years)	0.595	0.187	10.141	1.814	1.257-2.616	0.001
Sex (f/m)	0.679	0.302	5.053	1.971	1.091-3.562	0.025
Smoking (y/n)	-0.649	0.351	3.423	0.522	0.263-1.039	0.064
Alcohol (y/n)	-0.822	0.350	5.526	0.440	0.222-0.872	0.019
High education (y/n)	0.007	0.561	0.000	1.007	0.335-3.026	0.989
Physical activity (y/n)	0.024	0.327	0.005	1.024	0.539-1.946	0.942
Family history of ASCVD (y/n)	0.615	0.272	5.103	1.850	1.085-3.155	0.024
Central obesity (y/n)	0.677	0.351	3.723	1.967	0.989-3.913	0.054
General obesity						
Overweight (y/n)	-0.111	0.334	0.110	0.895	0.466-1.721	0.740
Obesity (y/n)	-0.174	0.363	0.228	0.841	0.412-1.714	0.633
Duration of DM (y/n)	0.031	0.039	0.661	1.032	0.957-1.113	0.416
FPG (per 1 mmol/l)	0.158	0.090	3.068	1.171	0.981-1.396	0.080
HbA1c (per 1 %)	0.181	0.068	7.174	1.198	1.050-1.368	0.007
Hypertension (y/n)	0.311	0.343	0.824	1.365	0.697-2.674	0.364
SBP (per 10 mmHg)	0.051	0.066	0.597	1.052	0.925-1.197	0.440
DBP (per 5 mmHg)	-0.037	0.060	0.368	0.964	0.857-1.085	0.544
TC (≥4.68 mmol/l)	-0.080	0.302	0.071	0.923	0.510-1.668	0.790
TG (≥1.70moll/l)	-0.029	0.274	0.011	0.971	0.568-1.660	0.915

LDL-C (≥2.60 mmol/l)	0.622	0.362	2.959	1.864	0.917-3.788	0.085
HDL-C (m≤1.00 mmol/l; f≤1.30 mmol/l)	0.217	0.323	0.453	1.243	0.660-2.341	0.501
eGFR (per 10 ml/min/1.73m^2)	-0.105	0.043	5.910	0.900	0.827-0.980	0.015

Binary univariate logistic regression was conducted to assess the association of ASCVD with different variables using the Entry method; odds ratios (ORs) and the 95% confidence intervals (CIs) given.

Figures

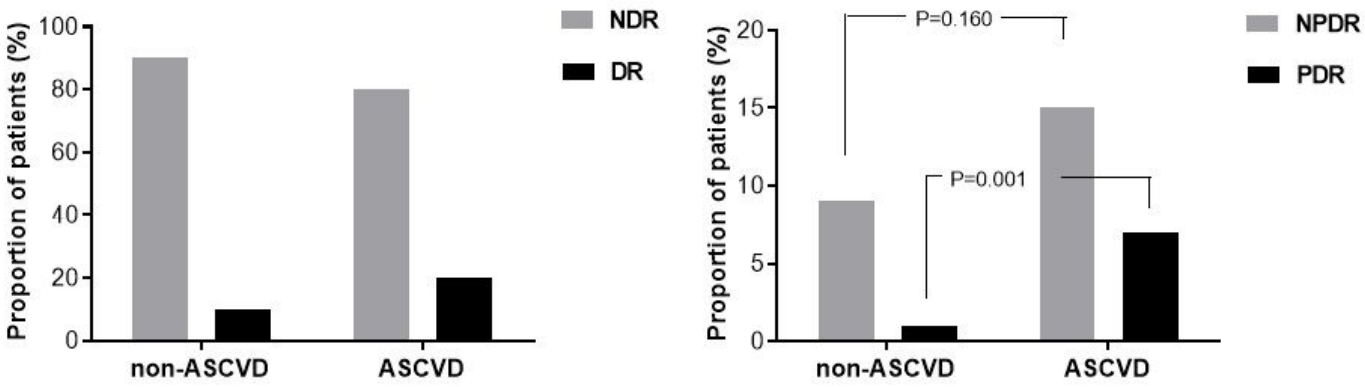

Figure 1

The association of ASCVD with DR or different degree of DR. (A) Comparison of prevalence of DR between ASCVD and non-ASCVD group. The trend to DR in the ASCVD group was significantly higher than in the non-ASCVD group (Pearson χ2 =5.805, P =0.016). (B) Prevalence (%) of patients with different degree of DR (NPDR and PDR) in relation to ASCVD. When DR was divided into NPDR and PDR according to its severity, the prevalence of NPDR between ASCVD and non-ASCVD group had no statistical difference (Pearson χ2 =1.975, P =0.160). However, a higher proportion of subjects with PDR were found in the ASCVD group than from non-ASCVD group (Pearson χ2 =10.368, P =0.001)].

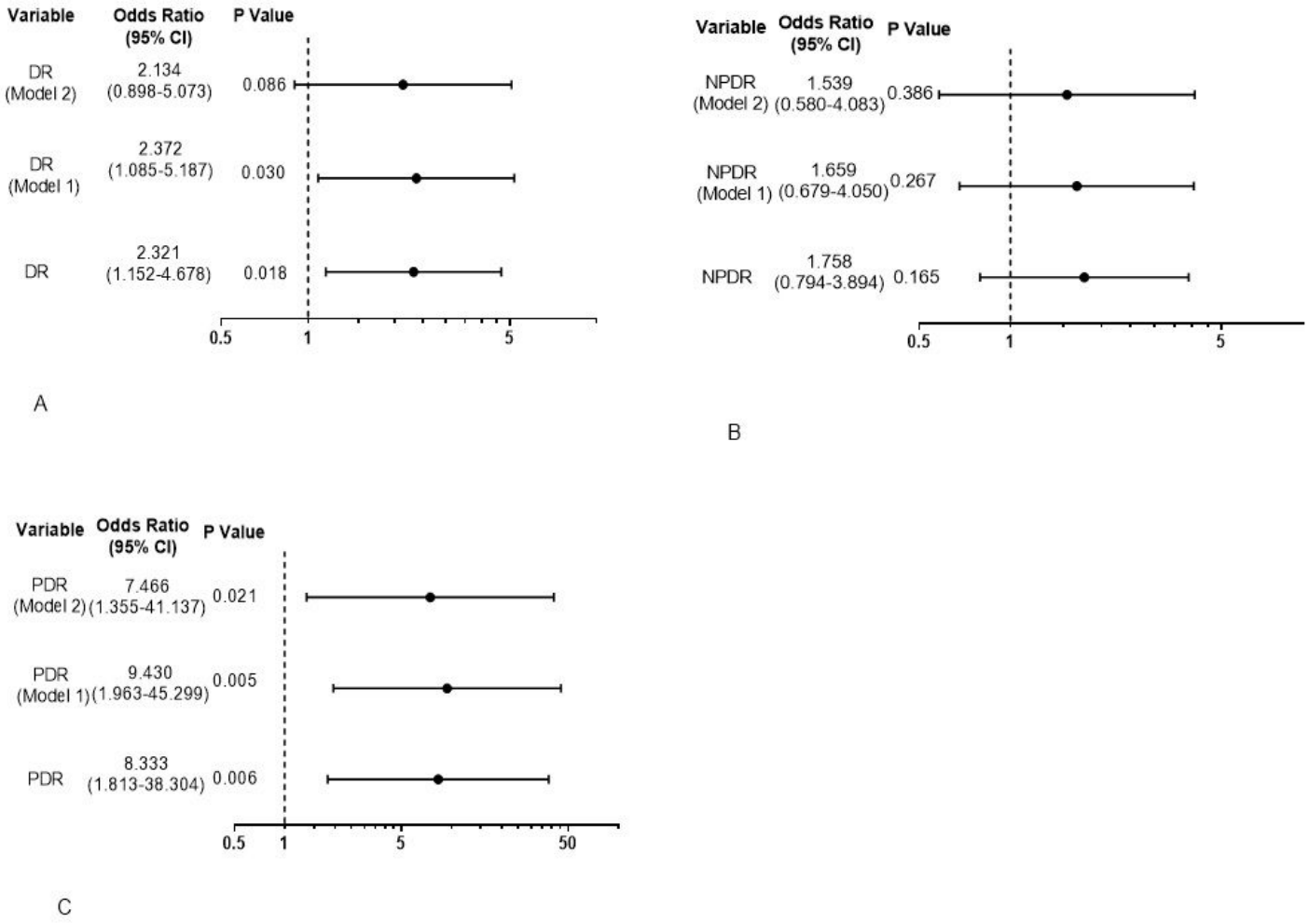

Figure 2

Odds ratios for ASCVD with/without DR and different degree of DR. Binary logistic regression was conducted to assess the association of ASCVD with DR (A) and the different degree of DR: NPDR (B) and PDR (C) using the Entry method; adjusted odds ratios (ORs) and the 95% confidence intervals (CIs) given. Adjustment variables included the basic confounders (age, sex, family history of ASCVD and duration of DM) in Model 1. In Model 2, smoking, alcohol, educational level, physical activity, obesity (central or general obesity), history of hypertension, SBP, DBP, HbA1c, LDL-C and eGFR were also considered other adjustment variables and were thus added to Model 1.