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A prospective cohort study investigating the association between type 2 diabetes and subsequent cardiovascular events in patients with different blood pressure, HbA_{1c}, and lipid levels

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Abstract

Background: Globally, there has been a steady increase in the prevalence of type 2 diabetes, and the risk of cardiovascular disease has increased. The relationship between diabetes and the incidence of cardiovascular disease (CVD) at different blood pressure, glycated haemoglobin A_{1c} (HbA_{1c}), and lipid levels remains uncertain. This study aimed to investigate these associations within a population-based cohort.

Material and methods: We analysed data from the Guiyang subcentre of the China Cardiometabolic Disease and Cancer Cohort Study, which enrolled participants aged 40 years and older between 2011 and 2012. Subsequently, a follow-up visit was conducted during 2014–2016 to assess incident CVD events.

Results: The analysis included a cohort of 7197 adults, of whom 590 were diagnosed with diabetes. Among all the participants, the CVD events linked to diabetes had a multivariable adjusted hazard ratio of 2.37 [95% confidence intervals (CI): 1.38–4.08]. Patients with diabetes had a greater risk of experiencing CVD events if they had high blood pressure [hazard ratios (HR): 1.24, 95% CI: 1.39–4.21] and high lipid levels (HR: 2.19, 95% CI: 1.29–3.70) compared to people with normal blood pressure (HR: 1.23, 95% CI: 0.54–2.82) and lipid levels (HR: 1.26, 95% CI: 0.47–3.41).

Conclusions: Our analysis revealed a significant association between diabetes and an increased risk of subsequent CVD events, which can be mitigated through optimal management of the metabolic profile of cardiovascular risk factors. **(Endokrynol Pol 2024; 75 (5): 517–524)**

Key words: *type 2 diabetes; cardiovascular disease; ideal cardiovascular metabolic profile; prospective cohort study*

Introduction

Cardiovascular disease (CVD) encompasses a group of disorders that impact the heart and blood vessels, resulting in disorders such as coronary artery disease, heart failure, and stroke. There were 153.2 million disability-adjusted life years and 6.9 million diet-related CVD deaths worldwide in 2019, representing increases of 34.3% and 43.8%, respectively, since 1990 [1].

CVD is a result of several risk factors, including poor dietary habits, a sedentary lifestyle, smoking, excessive alcohol consumption, and hereditary predisposition [2–4]. Hypertension [5], diabetes [6], and obesity [7] are significant and important contributors. Early detection and management of risk factors along with medical intervention, when necessary, are crucial in mitigating the impact of CVD on individuals and public health.

The prevalence of type 2 diabetes (diabetes for short) has been steadily increasing on a global scale, presenting a significant public health challenge [8]. The International Diabetes Federation (IDF) projects that 537 million people between the ages of 20 and 79 years will develop diabetes by 2021. Current trends predict that the number of people with diabetes will rise to 643 million by 2030 and 783 million by 2045 [9]. Diabetes significantly increases the risk of developing cardiovascular disease (CVD), indicating a close and complex link between the 2 conditions. The impact of diabetes on the cardiovascular system stems from a combination of factors associated with the metabolic disorder [6, 10–12]. While those who have diabetes are more likely than those without it to get CVD [10, 11], the associations between diabetes and the incidence of CVD in different blood pressure, glycated haemoglobin A1c (HbA_{1c}), and lipid levels are not well-established. We conducted a prospective cohort study in Guiyang, China, to gain a better understanding of how blood pressure, HbA_{1c}, and lipid levels contribute to the development of CVD in diabetes patients. Our study aimed to examine the associations

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between diabetes and CVD risk based on blood pressure, HbA_{1c}, and lipid status.

Material and methods

Study participants

The study participants were recruited from the Guiyang subcentre of the China Cardiometabolic Disease and Cancer Cohort (4C) Study, a multicentre, population-based, prospective cohort study [12, 13]. Between 2011 and 2012, local resident registration systems in Guiyang recruited 10,140 individuals aged 40 years or older. After excluding nonparticipants and those with cardiovascular diseases at baseline, 9672 participants remained. All participants received an in-person visit during the follow-up survey, extending from 2014 to 2016. However, only 7236 participants (74.8%) attended the follow-up visit. At baseline, all study participants had complete data on covariates, with none reporting a history of CVD. We determined whether they experienced a cardiovascular event during the follow-up visit. As depicted in Figure 1, the final analysis comprised 7197 participants. This study was approved by the Shanghai Jiaotong University Medical Ethics Committee at Ruijin Hospital. Each participant in the trial provided written informed consent.

Data collection

We collected data at local community clinics in the mornings. Trained interviewers used standardised questionnaires to gather information regarding the participants' medical history, demographic characteristics, lifestyle factors (including cigarette smoking and alcohol consumption), and family history. We classified the education levels of the participants as follows: junior school or below and high school or further education. Participants were classified according to their marital status as either married or unmarried, including those who were separated, solitary, widowed, or divorced.

We classified each person's smoking status as never, former, or current. Participants who consumed alcohol at least once a week in the past 6 months were considered current consumers of alcohol. Trained nurses assessed the height and body weight of the participants in accordance with a standardised protocol. We computed the body mass index (BMI) by dividing the weight in kilograms by the height in square metres.

The participants' systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automated electronic device (OMRON Model HEM-752 FUZZY, Dalian, China) while they were seated and had remained still for a minimum of 5 minutes, following a 30-minute abstinence from alcohol, coffee, tea, smoking, and exercise. The average of 3 measurements was utilised in the analysis.

After an overnight fast of a minimum of 10 hours, every participant underwent a 2-hour oral glucose tolerance test (OGTT) using 75 grams of glucose. We obtained blood samples at the 0- and 2-hour time points of the experiment. We measured fasting and 2-hour plasma glucose concentrations within 2 hours of blood sample collection using a glucose oxidase or hexokinase method; all procedures adhered to the rigorous quality control regimen. The researchers obtained capillary whole blood samples from the participants' fingertips using the Hemoglobin Capillary Collection System (Bio-Rad Laboratories, Hercules, CA, USA). We then transported and preserved the samples at temperatures ranging from 2°C to 8°C. Four weeks after the collection, we determined the levels of HbA_{1c} using the Variant II Hemoglobin Testing System (Bio-Rad Laboratories) in conjunction with high-performance

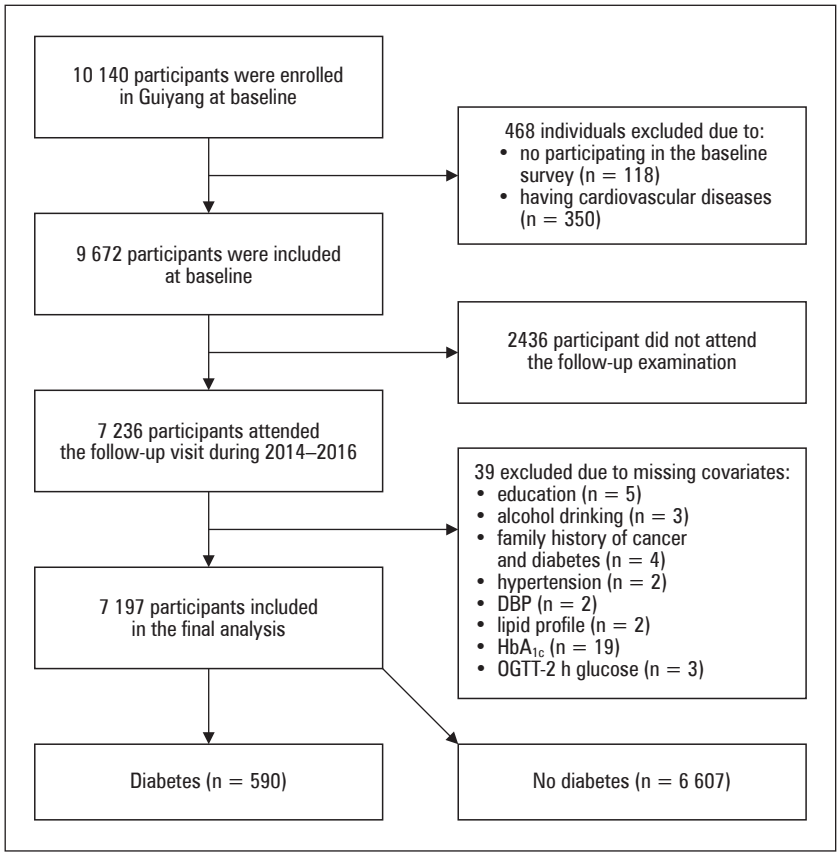

Figure 1. *The flowchart of study participants. DBP — diastolic blood pressure; HbA_{1c} — glycated haemoglobin A_{1c}; OGTT — oral glucose tolerance test*

liquid chromatography at the central laboratory of the Shanghai Institute of Endocrine and Metabolic Disease.
The central laboratory measured the serum levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and total cholesterol using an auto-analyser (ARCHITECT ci16200, Abbott Laboratories, Chicago, IL, USA).

Assessment of diabetes

Based on the American Diabetes Association 2010 criteria [16], participants were defined as diabetic at the baseline as per the following criteria: fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL), OGTT 2-h plasma glucose level ≥ 11.1 mmol/L (200 mg/dL), HbA_{1c} concentration ≥ 6.5%, or a self-reported prior diagnosis of diabetes by medical professionals [16]. The other participants did not have diabetes.

Definition of ideal blood pressure, HbA_{1c}, and lipid level

While the American Heart Association (AHA) has proposed 7 ideal cardiovascular health metrics to promote optimal cardiovascular health in the population [14], our study focused on examining the impact of blood pressure, HbA_{1c}, and lipid levels on CVD. We estimated each participant's glucose metabolism using HbA_{1c} instead of fasting plasma glucose. This modification aligns with the strict HbA_{1c} targets outlined in the most recent clinical practice guidelines from the American Diabetes Association [15]. Based on previous research, our study prioritised the optimal management of the following 3 factors: (1) SBP < 130 mm Hg and DBP < 80 mm Hg [16, 17]; (2) HbA_{1c} < 6.5% [12, 15]; and (3) triglycerides < 1.70 mmol/L, total cholesterol < 5.20 mmol/L, HDL-cholesterol > 1.04 mmol/L, and LDL-cholesterol < 3.37 mmol/L [21–23].

Identification of cardiovascular events

Our study's primary outcome was the composite of incidental fatal or nonfatal CVD events. This composite was composed of outcomes related to heart failure treated in hospitals, stroke, myocardial infarction, and cardiovascular mortality. We have already provided comprehensive definitions of various CVD events [12]. Detailed information on deaths and clinical outcomes was collected from the local vital registers of the National Disease Surveillance Point System and the National Health Insurance System. To ensure precision and uniformity, 2 outcome adjudication committee members independently verified every clinical event and assigned potential reasons for death. Discrepancies were resolved through discussions with fellow committee members. Crucially, the outcome adjudication committee members remained oblivious to each participant's baseline clinical characteristics, thereby enhancing the objectivity and impartiality of the outcome verification process.

Statistical analysis

We summarised the baseline characteristics of participants, classified by diabetes status, using means with standard deviations (SDs) for continuous variables and numbers with percentages for categorical variables. We censored the data pertaining to participants who died, received a CVD diagnosis, or reached the end of their follow-up, whichever occurred first. Each participant's person-time from the date of enrolment to the date of censorship was computed. The differences in baseline characteristics among diabetes status groups were evaluated using a t-test and a chi-squared (X^2) test.
During the follow-up period, we calculated the disparities in subsequent CVD between participants with and without diabetes using the log-rank test and Kaplan–Meier method. The relationship between diabetes and later CVD events was assessed using the multivariable Cox proportional hazards model. We adjusted Model 1 for sex, age, education, and marital status. We further adjusted Model 2 for alcohol drinking, smoking status, BMI, family history of cancer and diabetes, hypertension, hyperlipidaemia, cancer, liver diseases, pancreatitis, gastrointestinal diseases, gallbladder diseases, lung diseases, and renal diseases. The hazard ratios (HRs) and 95% CI were computed for each model to assess the association between diabetes and CVD events. Subgroups were formed based on blood pressure, HbA_{1c}, and lipid levels, and the relationship between diabetes and CVD was examined. We also investigated the association of ideal blood pressure, ideal HbA_{1c}, and ideal lipid levels with CVD events, stratified by diabetes diagnosis.
A 2-sided P value below 0.05 was considered statistically significant. We performed the statistical analyses using the IBM SPSS software, version 25.0 (New York, United States).

Results

Diabetes was diagnosed in 590 (8.20%) of the 7197 participants. The median (25^{th}–75^{th} percentiles) baseline age was 57 (52–63) years, and the median (25^{th}–75^{th} percentiles) follow-up duration was 3.15 (3.07–3.21) years. The baseline characteristics of the study participants are categorised in Table 1 according to whether or not they were diagnosed with diabetes at the commencement of the study. Participants with diabetes at baseline exhibited a higher average age, a greater proportion of males, a larger percentage of individuals with overweight or obesity, a higher likelihood of exposure to both former and present smoking, a higher percentage of having a family history of cancer and diabetes, and a greater proportion of chronic diseases (including hypertension, hyperlipidaemia, liver diseases, gallbladder diseases, gastrointestinal diseases, and renal diseases) compared to the participants without diabetes. We discovered that the participants with diabetes were less likely to have optimal blood pressure, HbA_{1c} level, and lipid levels (Tab. 2).

A total of 134 CVD incidents were reported during 22,587 person-years of follow-up. Ten participants had multiple CVD events; 109 suffered strokes; 21 experienced heart failure; and 14 developed myocardial infarction. As shown in Figure 2, the participants with diabetes exhibited a higher cumulative hazard risk of CVD events during the follow-up period compared to those without diabetes (p < 0.01). After taking into account the potential confounding factors (Supplementary File — Table S1), the multivariable adjusted HR for CVD events linked to diabetes in all the participants was 2.37 (95% confidence interval (CI): 1.38–4.08). Compared to participants without diabetes, diabetes had different risk effects on CVD events: the hazard ratio was 2.24 (95% CI: 1.39–4.21) for people with hypertension, 1.23 (95% CI: 0.54–2.82) for people with normal blood pressure, 2.06 (95% CI: 1.01–4.19) for people with high HbA1c, 2.91 (95% CI: 1.31–6.44) for people with normal HbA1c, 2.19 (95% CI: 1.29–3.70) for people with hyperlipidaemia, and 1.26 (95% CI: 0.47–3.41) for people with normal lipid levels (Tab. 3).

Table 1. *Participants' characteristics between the two groups in terms of whether they were diagnosed with diabetes at baseline*

Characteristic	Diagnosed with diabetes		p-value
	Yes (n = 590)	No (n = 6607)	
Age, years	60.89 ± 7.49	57.46 ± 7.73	< 0.01
Males, n (%)	237 (40.2)	1673 (25.3)	< 0.01
Education, n (%)			0.43
Junior school or below	327 (55.4)	3550 (53.7)	
High school or above	263 (44.6)	3057 (46.3)	
Marital status, n (%)			0.62
Married	499 (84.6)	5,638 (85.3)	
Not married*	91 (15.4)	969 (14.7)	
BMI			0.02
< 23.0 kg/m^2, n (%)	204 (34.6)	2670 (40.4)	
23.0–24.9 kg/m^2, n (%)	158 (26.8)	1658 (25.1)	
≥ 25 kg/m^2, n (%)	228 (38.6)	2279 (34.5)	
Smoking status			< 0.01
Nonsmoker, n (%)	406 (68.8)	5211 (78.9)	
Former smoker, n (%)	63 (10.7)	385 (5.8)	
Current smoker, n (%)	121 (20.5)	1011 (15.3)	
Alcohol drinking			0.01
Non/former drinker, n (%)	445 (75.4)	4656 (70.5)	
Current drinker, n (%)	145 (24.6)	1951 (29.5)	
Family history of cancer and diabetes, n (%)	227 (38.5)	1719 (26.0)	< 0.01
Hypertension, n (%)	176 (29.8)	1075 (16.3)	< 0.01
Hyperlipidaemia, n (%)	135 (22.9)	599 (9.1)	< 0.01
Cancer, n (%)	25 (4.2)	198 (3.0)	0.10
Liver diseases, n (%)	70 (11.9)	364 (5.5)	< 0.01
Gallbladder diseases, n (%)	181 (30.7)	1486 (22.5)	< 0.01
Pancreatitis, n (%)	12 (2.0)	92 (1.4)	0.21
Gastrointestinal diseases, n (%)	38 (6.4)	672 (10.2)	0.04
Renal diseases, n (%)	46 (7.8)	313 (4.7)	0.01
Lung diseases, n (%)	33 (5.6)	286 (4.3)	0.15

Data are presented as a number (%) or mean ± standard deviation (SD). We calculated p-values using either a t-test or a 2-test, depending on the situation.
*Separated, single, widowed, and divorced are examples. The diseases included autoimmune liver disease, fatty liver, viral hepatitis, liver cirrhosis, and gallbladder diseases like cholecystitis, gallstones, and gallbladder polyps. There were also acute pancreatitis and chronic pancreatitis. There were also gastroenteritis and gastroduodenal ulcers in the GI tract, renal calculus, renal cysts, chronic nephritis, and renal syndrome in the kidneys, and emphysema and chronic bronchial diseases in the lungs. BMI — body mass index; SD — standard deviation

Furthermore, we explored the associations between ideal blood pressure, HbA1c, and lipid level with CVD events among all participants, including those with and without diabetes. We found that optimal blood pressure maintenance significantly reduces the incidence of CVD events, especially in individuals with diabetes (HR: 0.35, 95% CI: 0.14–0.86). The effects of optimal blood pressure were not statistically significant in any of the participants, including those without diabetes (Supplementary File — Table S2). Contrary to expectations, ideal HbA_{1c} and lipid levels did not exhibit a reduced risk of CVD events among all participants, those without diabetes, and those with diabetes (Supplementary File — Tables S3 and S4).

Discussion

Through this prospective cohort study involving 7197 adults from the Guiyang subcentre, we have demonstrated once again that those with diabetes are more likely to experience CVD events. Researchers discovered that adults with diabetes were more likely to expe-

Table 2. *Participants' blood pressure, lipid, and glucose levels in relation to whether they were diagnosed with diabetes at baseline*

Index	Diagnosed with diabetes		p-value
	Yes (n = 590)	No (n = 6607)	
Blood pressure			
SBP [mmHg]	127.85 ± 18.32	120.73 ± 18.19	< 0.01
DBP [mmHg]	77.15 ± 10.43	77.03 ± 10.89	0.79
Optimal blood pressure, n (%)	293 (49.7)	3843 (58.2)	< 0.01
Glucose profile			
Fasting glucose [mmol/L]	8.87 ± 2.96	5.93 ± 1.10	< 0.01
OGTT-2 h glucose [mmol/L]	13.85 ± 4.61	8.14 ± 3.04	< 0.01
HbA_{1c} (%)	7.69 ± 1.65	6.08 ± 0.74	< 0.01
Optimal HbA_{1c} level, n (%)	112 (19.0)	5609 (84.9)	< 0.01
Lipid profile			
LDL cholesterol [mmol/L]	2.54 ± 0.86	2.64 ± 0.88	0.01
HDL cholesterol [mmol/L]	1.15 ± 0.34	1.25 ± 0.37	< 0.01
Triglycerides [mmol/L]	2.00 ± 1.52	1.72 ± 1.30	< 0.01
Total cholesterol [mmol/L]	4.52 ± 1.26	4.61 ± 1.24	0.09
Optimal lipid level, n (%)	144 (24.4)	2130 (32.2)	< 0.01

Data are presented as a number (%) or mean ± standard deviation (SD). We calculated p-values using either a t-test or a 2-test, depending on the situation.
DBP — diastolic blood pressure; HbA_{1c} — glycated haemoglobin A_{1c}; HDL — high-density lipoprotein; LDL — low-density lipoprotein; OGTT — oral glucose tolerance test; SBP — systolic blood pressure

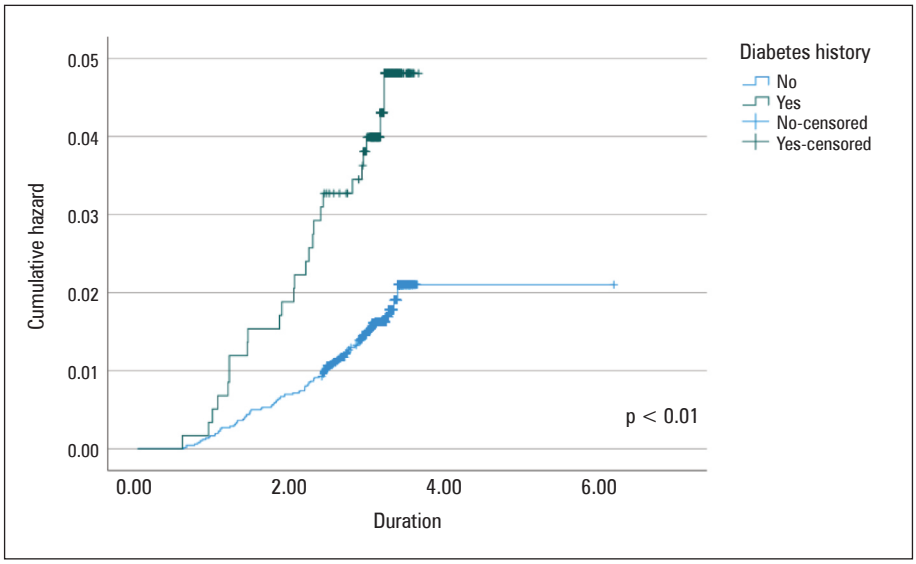

Figure 2. *Cumulative hazard risk of cardiovascular disease with and without diabetes using Kaplan–Meier survival curves*

rience CVD events under conditions of elevated blood pressure and lipid levels [18]. However, adults with diabetes did not have a statistically significant increase in the risk of CVD events when their blood pressure and lipid levels were optimal. Regardless of their HbA1c levels, adults with diabetes face an increased risk of CVD. Among patients with diabetes, only those with optimal blood pressure were associated with a lower risk of CVD compared to those with hypertension. Our results emphasise the significance of optimising the metabolic profile of cardiovascular risk factors to lower the incidence of CVD as an integral component of effective diabetes management [19].

Our findings consistently highlight that participants with diabetes face a notably higher risk of CVD events. This observation aligns with existing evidence pointing to diabetes as a substantial risk factor for CVD development [20–22]. The complex interplay between diabetes

Table 3. *Association of diabetes with cardiovascular disease (CVD) events among the different study participants*

Category	N	Person-years	Cases	HR (95% CI)	
				Model 1	Model 2
Total					
No diabetes	6,607	20,746	109	1.00 (Ref.)	1.00 (Ref.)
Diabetes	590	1,841	25	2.04 (1.31–3.17)	1.80 (1.16–2.81)
High blood pressure					
No diabetes	2,761	8,668	55	1.00 (Ref.)	1.00 (Ref.)
Diabetes	297	923	18	2.73 (1.59–4.66)	2.42 (1.39–4.21)
Optimal blood pressure					
No diabetes	3,846	12,078	54	1.00 (Ref.)	1.00 (Ref.)
Diabetes	293	918	7	1.24 (0.57–2.75)	1.23 (0.54–2.82)
High HbA_{1c} level					
No diabetes	998	3,144	16	1.00 (Ref.)	1.00 (Ref.)
Diabetes	478	1,495	18	2.16 (1.09–4.28)	2.06 (1.01–4.19)
Optimal HbA_{1c} level					
No diabetes	5,609	17,602	93	1.00 (Ref.)	1.00 (Ref.)
Diabetes	112	346	7	3.4 (1.57–7.37)	2.91 (1.31–6.44)
High lipid level					
No diabetes	4,477	14,059	72	1.00 (Ref.)	1.00 (Ref.)
Diabetes	446	1,389	20	2.32 (1.40–3.83)	2.19 (1.29–3.70)
Optimal lipid level					
No diabetes	2,130	6,687	37	1.00 (Ref.)	1.00 (Ref.)
Diabetes	144	453	5	1.46 (0.57–3.75)	1.26 (0.47–3.41)

Model 1 was adjusted for age, sex, education, and marital status using Cox regression. Model 2 was further adjusted for BMI, smoking status, alcohol consumption, and family history of cancer and diabetes, hypertension, hyperlipidaemia, cancer, liver diseases, gallbladder diseases, pancreatitis, gastrointestinal diseases, renal diseases, and lung diseases using Cox regression. CI — confidence interval; CVD — cardiovascular disease; HbA_{1c} — glycated haemoglobin A_{1c}; HR — hazard ratio; Ref. — reference

and cardiovascular health involves various metabolic, inflammatory, and vascular factors [23–25]. Understanding and addressing these intricate mechanisms is crucial for developing effective preventive strategies. The implications of our findings underscore the importance of targeted interventions and heightened vigilance in managing cardiovascular health among individuals with diabetes. It prompts further exploration into customised preventive strategies, highlighting the necessity of all-encompassing care plans that consider the unique challenges that diabetes presents in relation to CVD risk.

Our findings also support a significant finding that optimal management of the metabolic profile of cardiovascular risk factors, particularly lipid and blood pressure levels, could significantly counteract the adverse effects of diabetes on incident CVD events. Previous studies have repeatedly demonstrated that, in adults with diabetes, optimisation of cardiovascular risk variables can result in substantial reductions in severe CVD events [12, 30–33]. Our findings provide similar valuable insights into the potential mitigation of diabetes's adverse effects on incident CVD events. The observed correlation underscores the importance of personalised strategies aimed at achieving and maintaining optimal blood pressure and lipid levels among individuals with diabetes [26–31]. Diabetes remained, unexpectedly, independently associated with the CVD risk even at optimal HbA_{1c} levels. This finding may be largely attributed to the clustering of other cardiovascular risk factors associated with hyperglycaemia [40]. Our team's previous study [12] supports this finding. These findings suggest that, in addition to conventional diabetes therapy, prioritising metabolic control could be essential in lowering the general burden of CVD in this group. While our observations are compelling, the precise mechanisms responsible for these associations remain unclear. Future research into the intricate underlying mechanisms may facilitate the development of tailored and effective interventions for preventing diabetes-related CVD events.

The prospective study design, the well-established definitions of exposure and CVD outcomes, and the thorough analyses involving people with or without optimal blood pressure, HbA_{1c}, and cholesterol levels were among this study's strong points. However, the study has several limitations. First, we only conducted a single follow-up in our cohort for analysis. The comparatively short follow-up time might limit the statistical power to identify CVD events. Second, this investigation could not explain temporal variations in the parameters because it only assessed baseline blood pressure, glucose, and lipid profiles. Third, after controlling for confounding factors such as BMI and smoking, we evaluated the cardiovascular effects of diabetes using only 3 optimal cardiovascular health metrics. Furthermore, the influence of unmeasured and residual variables, including psychological state, drugs, and genetic predisposition, could not be entirely ruled out.

Conclusions

In conclusion, our findings indicate that diabetes significantly increases the risk of developing CVD events. Crucially, this risk can be mitigated through the optimal management of the metabolic profile of cardiovascular risk factors. Our research emphasises the necessity of early intervention to improve metabolic profiles in patients with diabetes to prevent CVD.

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Ethics statement
The Ethical Review Committee of Ruijin Hospital (RUIJIN-2011-14) reviewed and approved the studies involving human participants. The participants provided their written informed consent to participate in this study.

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Conflicts of interest
The authors declare no conflicts of interest to disclose.

Author contributions
Y.Z. conceived and designed the study. Y.Z. and N.P. drafted the manuscript. Y.Z., D.W., and M.Z. conducted the analyses. N.P. contributed to the statistical analysis. Q.Z. and L.S. contributed to the funding acquisition. Q.Z. and L.S. contributed to supervision, had full access to all the study's data, and took responsibility for the integrity and accuracy of the data analysis. All authors approved the final version of the manuscript.

References

1. Dong C, Bu X, Liu J, et al. Cardiovascular disease burden attributable to dietary risk factors from 1990 to 2019: A systematic analysis of the Global Burden of Disease study. Nutr Metab Cardiovasc Dis. 2022; 32(4): 897–907, doi: 10.1016/j.numecd.2021.11.012, indexed in Pubmed: 35067445.
2. Teo KK, Rafiq T. Cardiovascular Risk Factors and Prevention: A Perspective From Developing Countries. Can J Cardiol. 2021; 37(5): 733–743, doi: 10.1016/j.cjca.2021.02.009, indexed in Pubmed: 33610690.
3. Francula-Zaninovic S, Nola IA. Management of Measurable Variable Cardiovascular Disease' Risk Factors. Curr Cardiol Rev. 2018; 14(3): 153–163, doi: 10.2174/1573403X14666180222102312, indexed in Pubmed: 29473518.
4. Levenson JW, Skerrett PJ, Gaziano JM. Reducing the global burden of cardiovascular disease: the role of risk factors. Prev Cardiol. 2002; 5(4): 188–199, doi: 10.1111/j.1520-037x.2002.00564.x, indexed in Pubmed: 12417828.
5. Wang C, Yuan Yu, Zheng M, et al. Association of Age of Onset of Hypertension With Cardiovascular Diseases and Mortality. J Am Coll Cardiol. 2020; 75(23): 2921–2930, doi: 10.1016/j.jacc.2020.04.038, indexed in Pubmed: 32527401.
6. Matheus AS, Tannus LR, Cobas RA, et al. Impact of diabetes on cardiovascular disease: an update. Int J Hypertens. 2013; 2013: 653789, doi: 10.1155/2013/653789, indexed in Pubmed: 23533715.
7. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. Metabolism. 2019; 92: 98–107, doi: 10.1016/j.metabol.2018.10.011, indexed in Pubmed: 30399375.
8. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018; 14(2): 88–98, doi: 10.1038/nrendo.2017.151, indexed in Pubmed: 29219149.
9. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022; 183: 109119, doi: 10.1016/j.diabres.2021.109119, indexed in Pubmed: 34879977.
10. Sarwar N, Gao P, Seshasai SR, et al. Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010; 375(9733): 2215–2222, doi: 10.1016/S0140-6736(10)60484-9, indexed in Pubmed: 20609967.
11. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, et al. Emerging Risk Factors Collaboration. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med. 2011; 364(9): 829–841, doi: 10.1056/NEJMoa1008862, indexed in Pubmed: 21366474.
12. Wang T, Lu J, Su Q, et al. 4C Study Group. Ideal Cardiovascular Health Metrics and Major Cardiovascular Events in Patients With Prediabetes and Diabetes. JAMA Cardiol. 2019; 4(9): 874–883, doi: 10.1001/jamacardio.2019.2499, indexed in Pubmed: 31365039.
13. Wang T, Lu J, Shi L, et al. China Cardiometabolic Disease and Cancer Cohort Study Group. Association of insulin resistance and -cell dysfunction with incident diabetes among adults in China: a nationwide, population-based, prospective cohort study. Lancet Diabetes Endocrinol. 2020; 8(2): 115–124, doi: 10.1016/S2213-8587(19)30425-5, indexed in Pubmed: 31879247.
14. Lloyd-Jones DM, Hong Y, Labarthe D, et al. American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation. 2010; 121(4): 586–613, doi: 10.1161/CIRCULATIONAHA.109.192703, indexed in Pubmed: 20089546.
15. American Diabetes Association. 6. Glycemic Targets: . Diabetes Care. 2018; 41(Suppl 1): S55–S64, doi: 10.2337/dc18-S006, indexed in Pubmed: 29222377.
16. Tian J, Sheng CS, Sun W, et al. Effects of High Blood Pressure on Cardiovascular Disease Events Among Chinese Adults With Different Glucose Metabolism. Diabetes Care. 2018; 41(9): 1895–1900, doi: 10.2337/dc18-0918, indexed in Pubmed: 30002198.
17. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2018; 138(17): e426–e483, doi: 10.1161/CIR.0000000000000597, indexed in Pubmed: 30354655.
18. Leon BM, Maddox TM. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. World J Diabetes. 2015; 6(13): 1246–1258, doi: 10.4239/wjd.v6.i13.1246, indexed in Pubmed: 26468341.

19. Yun JS, Ko SH. Current trends in epidemiology of cardiovascular disease and cardiovascular risk management in type 2 diabetes. Metabolism. 2021; 123: 154838, doi: 10.1016/j.metabol.2021.154838, indexed in Pubmed: 34333002.
20. Dal Canto E, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. Eur J Prev Cardiol. 2019; 26(2_suppl): 25–32, doi: 10.1177/2047487319878371, indexed in Pubmed: 31722562.
21. Brown OI, Drozd M, McGowan H, et al. Relationship Among Diabetes, Obesity, and Cardiovascular Disease Phenotypes: A UK Biobank Cohort Study. Diabetes Care. 2023; 46(8): 1531–1540, doi: 10.2337/dc23-0294, indexed in Pubmed: 37368983.
22. Celis-Morales CA, Petermann F, Hui Li, et al. Associations Between Diabetes and Both Cardiovascular Disease and All-Cause Mortality Are Modified by Grip Strength: Evidence From UK Biobank, a Prospective Population-Based Cohort Study. Diabetes Care. 2017; 40(12): 1710–1718, doi: 10.2337/dc17-0921, indexed in Pubmed: 28986505.
23. Rahman S, Rahman T, Ismail AAS, et al. Diabetes-associated macrovasculopathy: pathophysiology and pathogenesis. Diabetes Obes Metab. 2007; 9(6): 767–780, doi: 10.1111/j.1463-1326.2006.00655.x, indexed in Pubmed: 17924861.
24. Bosevski M, Stojanovska L, Apostolopoulos V. Inflammatory biomarkers: impact for diabetes and diabetic vascular disease. Acta Biochim Biophys Sin (Shanghai). 2015; 47(12): 1029–1031, doi: 10.1093/abbs/gmv109, indexed in Pubmed: 26511092.
25. Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. Can J Cardiol. 2018; 34(5): 575–584, doi: 10.1016/j.cjca.2017.12.005, indexed in Pubmed: 29459239.
26. Adamsson Eryd S, Gudbjörnsdottir S, Manhem K, et al. Blood pressure and complications in individuals with type 2 diabetes and no previous cardiovascular disease: national population based cohort study. BMJ. 2016; 354: i4070, doi: 10.1136/bmj.i4070, indexed in Pubmed: 27492939.
27. Hong S, Park JH, Han K, et al. Blood Pressure and Cardiovascular Disease in Older Patients With Diabetes: Retrospective Cohort Study. J Am Heart Assoc. 2021; 10(22): e020999, doi: 10.1161/JAHA.121.020999, indexed in Pubmed: 34726076.
28. Wan EY, Yu EY, Chin WY, et al. Age-Specific Associations Between Systolic Blood Pressure and Cardiovascular Disease: A 10-Year Diabetes Mellitus Cohort Study. J Am Heart Assoc. 2020; 9(14): e015771, doi: 10.1161/JAHA.119.015771, indexed in Pubmed: 32673523.
29. Huh JiH, Han Kd, Cho YK, et al. Remnant cholesterol and the risk of cardiovascular disease in type 2 diabetes: a nationwide longitudinal cohort study. Cardiovasc Diabetol. 2022; 21(1): 228, doi: 10.1186/s12933-022-01667-6, indexed in Pubmed: 36324177.
30. Wadström BN, Pedersen KM, Wulff AB, et al. Elevated remnant cholesterol and atherosclerotic cardiovascular disease in diabetes: a population-based prospective cohort study. Diabetologia. 2023; 66(12): 2238–2249, doi: 10.1007/s00125-023-06016-0, indexed in Pubmed: 37776347.
31. Weaver OR, Ye M, Vena JE, et al. Non-fasting lipids and cardiovascular disease in those with and without diabetes in Alberta's Tomorrow Project: A prospective cohort study. Diabet Med. 2023; 40(9): e15133, doi: 10.1111/dme.15133, indexed in Pubmed: 37171453.