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THE ASSOCIATION BETWEEN TYPE 2 DIABETES MELLITUS AND CARDIOVASCULAR DISEASES: A SYSTEMATIC REVIEW

Yenny Frida Setiawan*

**Faculty of Medicine, Maranatha Christian University*

***Corresponding Author: -**
yenny31fs@gmail.com

Abstract

Background:

Aim: *The objective of this study is to evaluate the complication of dorsal plication and ventral lengthening technique for penile curvature.*

Methods: *A systematic search strategy was conducted across several electronic reference databases (PubMed, Cochrane Library, ProQuest) and included articles published between 2001–2022. Duplicate publications, review articles, and incomplete articles were excluded.*

Results: *Databases searching identified a total of 254 articles. Of these, 29 articles passed the screening process and resulted in 12 articles for full-text assessment. The 6 articles did not evaluate the outcome of interest. Hence, we found six appropriate studies included in this review.*

Conclusion: *There exists an association between T2DM and CVD. As the incidence of DM continues to rise, it is also possible that the incidence of CVD will increase as a result of both the conventional risk factors for DM and the direct effect of DM on CVD. DM and CVD are on the rise, and their prevalence and progression must be slowed by DM and CVD treatment and control. To improve medical treatment and cardiovascular outcomes for patients with diabetes, additional research is essential to increase understanding of the disease state and its impact on CV function.*

Keywords: *Type 2 diabetes, Cardiovascular Disease, Association, Correlation*

INTRODUCTION

Diabetes mellitus (DM) is a long-term metabolic condition caused by both hereditary and environmental factors that results in inadequate insulin production and/or insulin resistance. DM and cardiovascular disease (CVD) are closely related.[1,2] Compared to individuals without diabetes, adults with diabetes have a greater prevalence of CVD. Even before fasting plasma glucose levels are high enough to diagnose diabetes, this risk gradually rises with rising fasting plasma glucose levels.[3] The incidence of CVD is two to three times higher in persons with diabetes compared to those without diabetes.[4] Additionally, cardiovascular disease is the major cause of premature death among diabetic people.[5] Type 2 DM (T2DM) accounts for approximately 90% of all cases of diabetes, and cardiovascular (CV) events are a major cause of the increased risk of premature death.[6]

More than 70% of hospital admissions for diabetic patients in the United States are due to CVD. CVD includes coronary artery disease (CAD) cerebrovascular disease, heart failure (HF), peripheral artery disease (PAD), congenital heart disease, and others.[7] In the general population, diabetes patients have a 2–4-fold increased risk of coronary artery disease compared to non-diabetic people.[8] In addition, cardiovascular risk (CVR) variables in diabetic patients have a significant role in the overall risk, as 75–80% of diabetic patients suffer from hypertension, 70–80% have elevated LDL-cholesterol levels, and 60–70% are clinically obese. DM has been considered a counterpart of CVD for a long time; nonetheless, this has remained disputed.[9] In this study, we aimed to summarize and evaluate the association between T2DM and CVD.

Method

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to perform this systematic review. We conducted a comprehensive systematic review in 3 online databases (PubMed, Cochrane Library, and ProQuest) during November 15–18, 2022.

"Association" OR “correlation” AND "type 2 diabetes" AND "cardiovascular disease" were used as keywords, with several combinations listed in Table 1. Furthermore, we also reviewed the reference lists among several chosen articles and records from other search engines to identify additional relevant publications.

Table 1. Literature search strategy

Database	Keywords	Results
PubMed	"Association" AND "type 2 diabetes" AND "cardiovascular disease" “Correlation” AND "type 2 diabetes" AND "cardiovascular disease"	
Cochrane Library	"Association" AND "type 2 diabetes" AND "cardiovascular disease" “Correlation” AND "type 2 diabetes" AND "cardiovascular disease"	
ProQuest	"Association" AND "type 2 diabetes" AND "cardiovascular disease" “Correlation” AND "type 2 diabetes" AND "cardiovascular disease"	

Eligibility Criteria

We included studies that assessed the association between type 2 diabetes and cardiovascular disease. Prospective and retrospective studies were both considered eligible. Inclusion of the paper included articles in English, full-text available, evaluating the association between type 2 diabetes and cardiovascular disease. Exclusion criteria included review articles written in languages other than English, nonhuman research, conference abstracts, and studies not evaluating the association between type 2 DM and CVD. Any ambiguity or discrepancies were resolved by discussion among authors. The PRISMA flow diagram was used to guide the study selection process, and all the authors approved the final list of selected papers to be included in this systematic review.

Data Extraction and Outcome

The selected studies are evaluated and extracted according to author and year of publication, study design, the number of study subjects or participants, and the main findings regarding the association between T2DM and CVD.

Results

Databases searching identified a total of 254 articles (Table 1), and they were screened based on the inclusion and exclusion criteria included in the study selection. Of these, 29 articles passed the screening process and resulted in 12 articles for full-text assessment. The six articles did not evaluate the outcome of interest. Hence, we found six appropriate studies included in this review (Figure 1). The summary of the main findings of the selected studies is presented in Table 1. Amon the six studies, 2 studies were genetic studies, ang of these studies, one study was genome-wide analysis. The selected studies included a total of 230193 subjects.

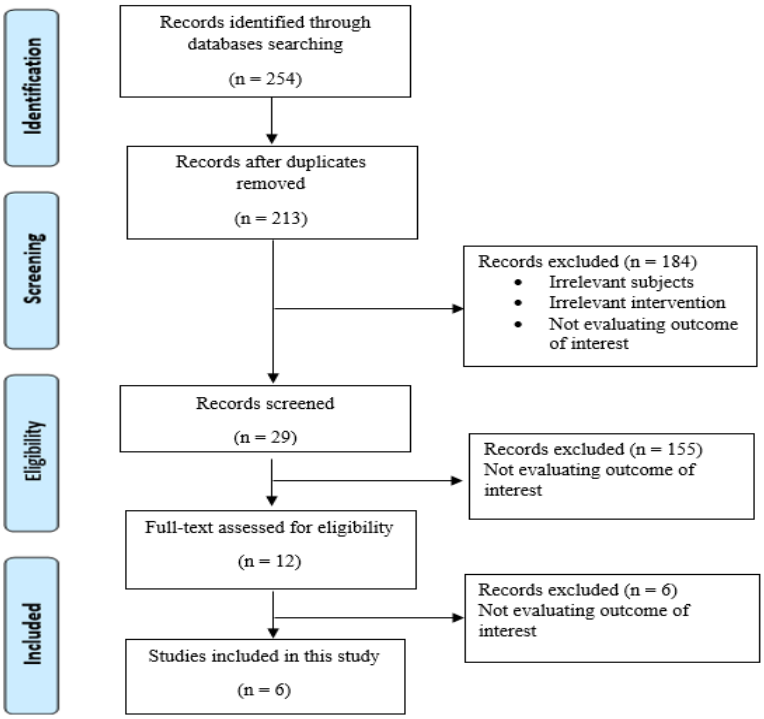

Figure 1. PRISMA flow diagram

Table 1. Summary of included studies

Author	Study design	No. of subjects	Findings
Shah et al.,2015[10]	Cohort	34198	• T2DM was positively associated with PAD (aHR 2·98 [95% CI 2·76–3·22]), ischaemic stroke (1·72 [1·52–1·95]), stable angina (1·62 [1·49–1·77]), HF (1·56 [1·45–1·69]), and non-fatal MI (1·54 [1·42–1·67]), but was inversely associated with abdominal aortic aneurysm (0·46 [0·35–0·59]) and SAH (0·48 [0·26–0.89]), and not associated with arrhythmia or sudden cardiac death (0·95 [0·76–1·19]). • The *p* value of the correlation index between the observed value and the predicted value is 0.01
Bulik-Sullivan et al.,2015[11]	Genome-wide analyses	276 pairs og gene among 24 traits	A positive genetic correlation (rg =0.385) between T2D and CAD.
Gan W., et al 2019[12]	Cohort	160000	• The genetic correlation between T2D and CHD was 0.15 • T2DM genetic risk score (comprising 48 established risk variants) was associated with the presence of carotid plaque (OR 1.17 [95% CI 1.05, 1.29] per 1 unit higher log-odds of T2DM; n=6,819), and elevated risk of ischaemic stroke (IS) (1.08 [1.02, 1.14]; n=17,097), non-lacunar IS (1.09 [1.03, 1.16]; n=13,924) and major coronary event (1.12 [1.02, 1.23]; n= 5,081). There was no significant association with lacunar IS (1.03 [0.91, 1.16], n=3,173) or intracerebral haemorrhage (ICH) (1.01 [0.94, 1.10], n=6,973), although effect estimates were imprecise.
Zhang et al.,2020[13]	Cohort	650	The CV risk factors such as smoking history, diastolic blood pressure, total cholesterol, low-density lipoprotein cholesterol are highly correlated with the risk of T2DM in the elderly (0.987, 0.956, 0.971, and 0.940, respectively), and smoking history has the strongest correlation.
Zhao et al.,2021[14]	Cohort	11,384	Participants with T2DM diagnosed 45 years of age had the highest relative risks of CVD and all-cause death in comparison to matched control subjects, with AHRs of 3.21 (95% CI 1.18–8.72) for CVD, 2.99 (95% CI 1.01–9.17) for stroke, and 4.79 (95% CI 1.95–11.76) for all-cause mortality.
Tseng et al.,2021[15]	Cohort	23,961	Compared with patients with late-onset diabetes (≥60 years), those with earlier onset diabetes had increased risks for CVD, with adjusted ORs (95% CIs) of 1.72 (1.36- 2.17), 1.52 (1.31-1.75) and 1.33 (1.19-1.48) for patients diagnosed aged <40, 40-49 and 50-59 years, respectively.

Discussion

Cardiovascular disease is closely associated with diabetes.[2,7,16] Adults with diabetes have a higher prevalence of cardiovascular disease than those without diabetes. This risk rises proportionately with increasing fasting plasma glucose levels, even before glucose levels are high enough to diagnose diabetes. CVD is one of the leading causes of death for diabetics. T2DM patients have a twofold increased risk of CV mortality compared to healthy people. Therefore, early detection and treatment of CV risks in patients with diabetes is one of the primary objectives of diabetes management.[3] CVD is responsible for at least fifty percent of T2DM-related mortality. The most lethal condition in this group was coronary artery disease, followed by stroke. Similar outcomes have been demonstrated by other models.[17]

According to Einarson et al., approximately 32.2% of people with T2DM are affected by CVD worldwide. CVD is the leading cause of death among individuals with T2DM[5,18], accounting for over half of all fatalities throughout the research period. Stroke and coronary artery disease were the leading factors.[17] Prospective studies have shown that diabetic patients are twice as likely to develop CAD and myocardial infarction MI, proving that type 2 diabetes is an independent risk factor for stroke and heart disease. Indeed, almost 70% of type 2 DM patients 65 years of age die from CVD, although type 2 DM patients without a history of CAD have the same cardiovascular risk as patients with a history of MI.[19,20] Patients with type 2 diabetes represent a group at high risk for CVD, proving that the CVD risk factors examined in this article have a substantial correlation with the presence of type 2 diabetes. Zhang et al., identifies the risk factors that

exacerbate CVD in diabetes: excessive smoking, diastolic blood pressure, total cholesterol, and unstable levels of low-density lipoprotein cholesterol.[13] McAlister found U-shaped associations between baseline or time-varying HbA1c and cardiovascular outcomes, with the lowest risk occurring when HbA1c was approximately 7%. Each one-unit increase in time-varying HbA1c above 7% was associated with an HR of 1.21 (95%CI 1.11-1.33) for first HF hospitalization, 1.11 (1.03-1.21) for all-cause mortality, 1.18 (1.09-1.26) for death or HF hospitalization, and 1.10 (1.02-1.17) for non-HF cardiovascular events. Each one-unit decrease in time-varying HbA1c below 7% was associated with an adjusted HR of 1.35 (95% CI: 1.12-1.64) for first HF hospitalization, 1.37 (1.16-1.61) for death, 1.42 (1.23-1.64) for death or HF hospitalization, and 1.22 (95% CI: 1.06-1.44) for non-HF cardiovascular events.[21]

In a study of patients undergoing coronary angiography for the evaluation of nonacute coronary artery disease, the prevalence of adults with diabetes as indicated by an abnormal glucose tolerance test was 48.6%, and the prevalence of glycemic impairment in diabetic patients plus prediabetic individuals was as high as 62.0%. Moreover, the number of coronary arteries with greater than 50% coronary artery lumen narrowing was greater in patients with diabetes than in nondiabetic individuals among 1045 patients scheduled for coronary artery bypass surgery who had preoperative HbA1c tests. In a separate study, 40% (n = 415) of participants had a known history of diabetes, while 60% (n = 630) did not. Among 630 patients with no known diabetes history, 207 (32.9%) had a normal HbA1c (5.7%), 356 (56.5%) had a HbA1c within the elevated risk range for diabetes (5.7–6.4%), and 67 (10.6%) had a HbA1c in the range for diabetes (6.5% or above). In this investigation, regardless of diabetes history, an elevated HbA1c was related with severe coronary artery disease, as measured by the number of revascularized arteries.[5]

Multiple CV risk factor categories exist for diabetes. One of these distinguishes between glycemic and non-glycemic factors: arterial hypertension, dyslipidaemia, obesity, smoking, chronic inflammation, and microalbuminuria. A further classification identifies traditional (old age, male gender, hypertension, diabetes, dyslipidaemia, smoking, sedentary lifestyle, and family history of cardiovascular disease) and non-traditional risk factors. Their specific impact on CVR has been difficult to assess; examples include insulin resistance, endothelial dysfunction (caused by excessive vasoconstriction and reduced vasodilation), inflammation (high C reactive protein levels, high leukocytes), microalbuminuria, intima-media thickness, and coronary calcium score.[22]

The association between T2DM and CVD is associated with the development of atherosclerosis. The development of atherosclerosis begins with the accumulation of lipoproteins in the artery wall. Foam cells collect and low-density lipoprotein (LDL) particles are oxidized in the subendothelial region, ultimately leading to vascular changes. Acute coronary and cerebrovascular syndromes develop when unstable arterial plaque deposits rupture.[23] Several risk factors for the development of atherosclerosis and cardiovascular disease are frequently coexistent in patients with T2D, including hypertension, insulin resistance, hyperglycemia, obesity, and dyslipidemia. Insulin resistance increases the production of atheroma plaques, diastolic dysfunction, and ventricular hypertrophy, which are all macrovascular disorders. In addition to advanced glycosylated end products and oxidative stress, hyperglycemia increases the development of cardiovascular disease. Both insulin resistance and hyperglycemia contribute to coronary artery disease, cerebrovascular disease, and heart failure.[7,24]

Diabetes has been associated with CVD for decades. Nonetheless, the reasons for this relationship are not fully understood. Due to the fact that the treatment of hyperglycemia alters a number of factors other than circulating glucose levels, clinical and experimental data support the hypothesis that hyperglycemia is not the culprit.[25]

In a clinical trial, intensive diabetes treatment resulted in a reduced incidence of combined major macrovascular and microvascular events (18.1% events in intensive group vs 20.0% events in the control group, p 0.01); and also major microvascular events (9.4% events in intensive group vs 10.9% in controls, p 0.01) due to a decreased incidence of nephropathy (4.1% event in intensive group vs 5.2% event in controls, However, more severe hypoglycemia episodes were observed with intense glycemic control (2.7 vs. 1.5% in controls), and the kind of glucose control had no influence on cardiovascular mortality.[5] Research suggests that a HbA1c reduction of 1% is associated with a 15% relative risk reduction in nonfatal myocardial infarction, but has no significant impact on all-cause mortality. Intensive glycemic management (HbA1c <6.5%) confers a definite cardiovascular advantage for patients with T2D and no evidence of atherosclerosis who have a short duration of disease. In contrast, the potential dangers of strict glycemic control may outweigh the advantages in individuals with a very long duration of diabetes, advanced atherosclerosis, advanced age, or a history of severe hypoglycemia in response to diabetes medication.[5]

Several limitations were identified in this study. First, the included studies were heterogen. Also, the number of studies included in this systematic review was limited; may not represented the whole association between T2DM and CVD. And this research may be susceptible of selection bias due to the extensive search tactics used to obtain the selected studies.

Conclusion

There exists an association between T2DM and CVD. As the incidence of DM continues to rise, it is also possible that the incidence of CVD will increase as a result of both the conventional risk factors for DM and the direct effect of DM on CVD. DM and CVD are on the rise, and their prevalence and progression must be slowed by DM and CVD treatment and control. To improve medical treatment and cardiovascular outcomes for patients with diabetes, additional research is essential to increase understanding of the disease state and its impact on CV function. While a number of studies have contributed to a greater understanding of DM in the field of CVD, additional research is required to improve the recognition and quantification of CV risk in DM patients. How glycemic regulation connects with cardiovascular disease requires further exploration.

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