



(REVIEW ARTICLE)



A review of the research on the cardiovascular risk factors and treatment options for Type II diabetic patients

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Abstract

The rise in the prevalence of diabetes is attributed to changes in human behavior, environment, and lifestyle. The prolonged survival of diabetes patients has been made possible by better care, but this is accompanied by chronic long-term problems brought on by hyperglycemia. Diabetes-related conditions like ketoacidosis or hypoglycemia are fewer common causes of death for diabetics than cardiovascular disease (CVD). Cardiovascular disease is more common in diabetes patients by a factor of 2 to 6 compared to the general population. Additionally, diabetics with CVD have a worse prognosis for survival than those with CVD who don't have diabetes, and their quality of life also declines. As a result, diabetes has been compared to a non-diabetic patient who has a history of heart disease in terms of risk. Identifying patients with a high risk of developing CVD can help prevent or delay cardiovascular events. Chemists must closely monitor these issues to manage CVD prevention and related ones. Patients taking aspirin and clopidogrel for an extended period should be constantly monitored due to the possibility of resistance. Guidelines have been developed to monitor and manage aspirin and clopidogrel in CVD preventive therapy.

Keywords: Blood pressure; cardiovascular disease; Dyslipidemia; Homocysteine Inflammation; Insulin resistance; Microalbuminuria; Obesity; Postprandial Hyperglycemia; Type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic condition with persistent hyperglycemia and glucose intolerance [1]. It develops when the body cannot adequately respond to insulin, followed by an increase in insulin production and an ensuing insulin deficiency. T2DM, which in the twentieth century was primarily confined to elderly adults, is today the biggest worldwide health concern of the twenty-first century [2]. Although its prevalence and incidence have increased quickly in adults, T2DM affects children and adolescents. From 2000 to 2016, diabetes-related premature mortality grew by 5%. Age-standardized rates of diabetes-related fatalities increased by 3% between 2000 and 2019. Cardiovascular (CV) events in people with T2DM are a significant cause of the increased risk of early death and have become a rising threat to human health worldwide. T2DM accounts for roughly 90% of all diabetes cases [3].

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At least 50% of people with T2DM may pass away due to the primary cardiovascular illnesses (CVDs) linked with the condition, which include ischemic heart disease, heart failure, stroke, coronary artery disease (CAD), and peripheral artery disease. As a result, CVDs are pretty concerning for T2DM disease progression and prognosis. Insulin resistance and hyperglycemia, frequently but not always accompanied by impaired lipid metabolism, are characteristics of T2DM. Insulin resistance typically manifests early in the development of T2DM and CVD. Resistance, fibrosis, and diastolic dysfunction [4]. Hypoglycemia has been connected to CVD in T2DM patients and is typically recognized as a negative side effect of glucose reduction. Among T2DM patients, cardiovascular disease (CVD) is a significant cause of death and disability [5].

No nation or healthcare system is safe from the threat of T2DM, and little progress has been made in preventing T2DM up to this point. High-income nations have seen a decline in CVD incidence and death, although only around 10% of the world's population is concentrated in these nations. Uncertainty persists regarding the incidence and death trends of CVD in T2DM patients in middle- and low-income countries [6]. The simultaneous management of T2DM and CVD has also received more attention in light of the clinical burden of CVD consequences in T2DM patients. In this review, we first examine strategies to lessen the risk of CVD in T2DM patients before concentrating more intently on the epidemiology of CVD in T2DM and preventative interventions [7].

2. Relationship between type II diabetes mellitus-related metabolic abnormalities and heart issues

Insulin resistance and deteriorating cell functioning are the two primary underlying defects of type II diabetes. Various factors, such as aging, genetic flaws, environmental factors, and obesity, can cause insulin resistance. Adipocytes emit many free fatty acids (FFAs), and insulin-stimulated glucose elimination is reduced once insulin resistance manifests in several tissues. In addition, higher FFA levels impede insulin's effect on the liver, which causes the hyperglycemic state's gluconeogenesis to grow. Compared to non-diabetic subjects, coronary artery atherosclerosis is more severe and diffuse in diabetic subjects. Due to coexisting diabetic cardiomyopathy, autonomic neuropathy, and the detrimental cardiac and metabolic effects of elevated levels of non-esterified fatty acids, acute MI in people with diabetes carries a double mortality rate that of the average population. These patients' acute MI is often treated with rapid treatment for heart failure, strict monitoring of blood glucose and potassium levels, and other risk factors. Autonomic neuropathy in diabetic people might disguise the symptoms of angina [8].

Patients with DM frequently have several distinct CVD risk factors, including insulin resistance, which may be a shared etiological cause, albeit there is no direct evidence of this. According to the World Health Organisation and the NCEP Adult Treatment Panel (ATP) III, the "metabolic syndrome" combines several CVD risk factors and insulin resistance. Insulin-resistant type II diabetes patients have specific proinflammatory and prothrombotic abnormalities of endothelial cell and vascular functions, as well as impaired glucose regulation, abdominal obesity, hypertension, atherogenic dyslipidemia (characterized by elevated triglycerides [TGs], and low levels of high-density lipoprotein cholesterol [HDL-C]) [9].

The metabolic syndrome also indicates a greater risk of acquiring type II DM in people with standard glucose tolerance. Although each element of the metabolic syndrome increases a person's CVD risk, the effect is amplified when combined. As a result, metabolic syndrome is linked to a threefold increase in the risk of CAD, stroke, and CAD-related mortality. Furthermore, as the metabolic syndrome's component numbers rise, so does the risk of CVD (and also DM) [10].

In many Western nations, the metabolic syndrome affects 25% to 35% of the general population, a significant prevalence rate. Based on information from the 2002 Census of Adults, it is estimated that 47 million people in the United States have metabolic syndrome. The age-adjusted prevalence of the syndrome is 24%, rising with age from 7% in those who participated in the Third National Health and Nutrition Examination Survey (NHANES III) between the ages of 20 and 29 to 44% in those between the ages of 60 and 69. In recent research from NHANES III, the link with DM was underscored by the finding that only 12% of patients with average fasting glucose had metabolic syndrome, compared to over 85% of people with diabetes [11].

2.1. Dyslipidaemia

IR boosts the release of free fatty acids from adipose tissue in T2DM. Higher lipogenesis, higher substrate availability, and decreased apolipoprotein B-100 (ApoB) degradation are the three factors underlying the rise in the generation of very low-density lipoproteins in the liver [12,13]. These modifications result in a lipid profile characterized by low levels of HDL-C, high levels of TGs, increased ApoB production, and small, dense LDL particles. This LDL subtype contributes significantly to atherogenesis because it is more prone to oxidation. Atherogenic dyslipidemia, including low HDL-C and

ApoA, raised fasting and postprandial TG, and elevated small dense LDL particles and ApoB, is a stronger predictor of cardiovascular risk than LDL cholesterol, a low HDL-C, or just one elevated TG [14,15].

2.2. Diabetes type 2: cardiovascular risk and dyslipidemia

Large data from case-control, genetic, and extensive observational investigations demonstrate a causal relationship between the rise of TG-rich particles and their remnants, low HDL-C, and cardiovascular risk [16]. Results from statin studies continue to support the role of low HDL as an independent cardiovascular risk measure in patients with normal LDL-C levels. According to the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study and the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, individuals with dyslipidemia (LDL-C > 2.6 mmol/L, HDL-C 0.88 mmol/L, and TGs 2.3 mmol/L) had significantly higher rates of cardiovascular events [17,18].

The FIELD study identified the non-HDL/HDL-C and total/HDL-C lipid ratios as the strongest predictors of cardiovascular events throughout a five-year monitoring period. The ApoB/ApoA ratio is similarly linked to CVD outcomes. However, it was only as accurate as traditional lipid ratios [19,20,21]. Data from the Emerging Risk Factor Collaboration (ERFC) trial, which included 302430 individuals without a history of cardiovascular disease, showed that, regardless of the presence of diabetes, Apo B and non-HDL-C each had a reasonably similar correlation with coronary heart disease (CHD). According to the ERFC trial, a 22% decrease in the risk of CHD was associated with a rise in HDL-C of 0.38 mmol/L, or 15 mg/dL. In clinical practice, non-HDL-C was the most effective technique for defining the risk associated with TGs' growth [22,23,24]. Our review aims to research the cardiovascular risk factors and treatment options for Type II diabetic patients. This review article discusses Type II diabetic patients' cardiovascular risk factors and treatment options.

3. Methodology

The Rapid Review Guidebook advises using Dr. Dobbin's evidence-informed decision-making (EIDM) process, which consists of the subsequent steps: "Steps for Conducting a Rapid Review" served as the framework. The health Evidence™ tool was used to find and access pertinent research evidence, assess its methodological quality, and synthesize it.

3.1. Search Strategies

Based on a quick review of the research questions, the following key search terms were created: "cardiovascular risk factors and their management in patients with type II diabetes."

3.2. The final search string is as below:

"Type II Diabetics," "Cardiovascular Risk Factors," and "Management."

Scopus, Google Scholar, PubMed, and the Cochrane Library are the four databases adopted to conduct in-depth searches for publications. Google Scholar has been added to give the gray literature a wider audience because the fields of Cardiovascular Risk Factors and people with type II diabetes have produced many publications. Scopus, PubMed, and the Cochrane Library excellently provided peer-reviewed article coverage.

3.3. Eligibility criteria

The literature search included all articles, theses, and review papers on cardiovascular risk factors and type II diabetes that were published before January 2023.

3.4. Data Extraction

Two unbiased medical reviewers reviewed the articles to ensure the selection's objectivity. The two reviewers reached an agreement of 80% on the final list of articles for additional data extraction.

3.5. Results of the literature search

533 total articles were reduced to potentially relevant articles as a result of the initial screening process. Due to their non-English language, title, abstract, and book chapter, irrelevant articles were removed. 172 studies were found based on the inclusion criteria (Figure 1: Preferred Reporting Items for Reviews) (Health Evidence™ tool).

We conducted this review according to Preferred Reporting Items for Reviews (PRISMA) Figure 1.

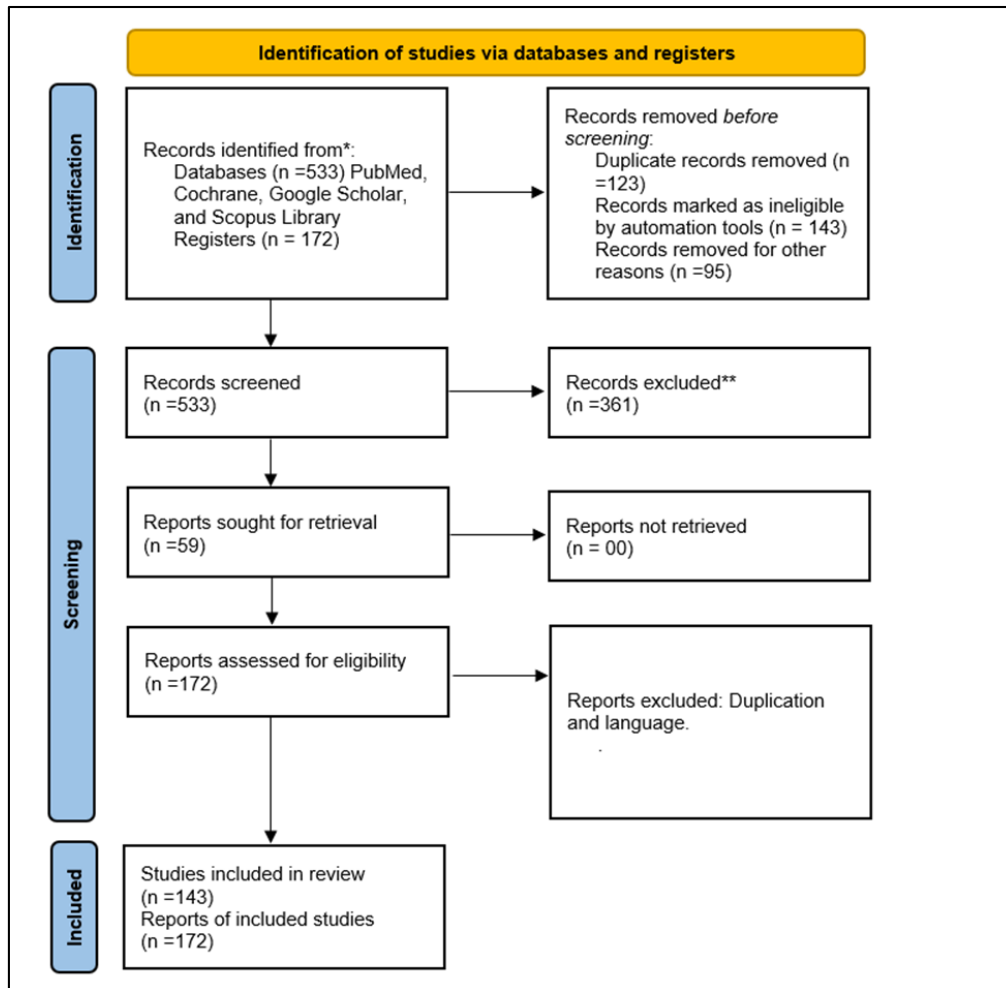


Figure 1 Preferred Reporting Items for Reviews (Health Evidence™ tool) [25] (PRISMA) flow diagram of the literature screening process

4. Result & Discussion

The most common kind of CVD reported was CAD (21.2%), while stroke (7.6%) was the least common [29]. The prevalence of common diseases was higher in men than in women. 50.3% of all T2DM patient fatalities during the review period were attributable to CVD. Age and several risk factors, including obesity and cardiovascular disease, are all linked to it. Therefore, we assessed the relationship between age and obesity in the chosen articles among patients with CVD and T2DM [30].

A well-known CVD risk factor is age. Thirteen (25%) of the 57 articles examined the link between aging and cardiovascular disease; the findings were ambiguous. Only two studies presented findings across multiple age categories, even though nine identified a significant relationship between age and CVD [31]. According to Alonso-Moran's research, the odds ratio for IHD, stroke, heart failure, and MI all successively rose with each additional 5-year age category compared to the reference age range of 35–39. These individual results were all statistically significant ($P < 0.001$) in some way. Similar findings were made by Boonman-de Winter et al., who noted a progressive rise in the prevalence rates of heart failure for all patients across five-year age groups, from 60 to 64 to >80. Other authors reported that older patients had higher prevalence rates than younger patients, despite giving few details on age categories. Four studies, on the other hand, found no age-related differences. In three other studies, age was used as a covariate in a logistic regression without any additional data. Therefore, the effect of age on the prevalence of CVD among those with T2DM has yet to be quantified in many studies [32].

Obesity is associated with CAD, atherosclerosis, and cardiac mortality and has long been recognized as a distinct risk factor for CVD. The relationship between BMI and waist circumference and crucial cardiometabolic risk factors like

hypertension and elevated low-density lipoprotein cholesterol (LDL-C) has also been shown to be crucial. Patients with T2DM with high CV risk are more likely to be overweight and obese [33].

Body mass index (BMI), typically used to define obesity, is calculated by dividing a person's height in meters by the square root of their weight in kilograms. The World Health Organisation (WHO) defines individuals with a BMI of 30 kg/m² as obese. However, using BMI to categorize patients with obesity has its drawbacks. It does not consider the wide range in body fat distribution or fat quality and may not account for associated health risks in various populations and individuals. This has been demonstrated to be accurate for populations in South Asia [35].

According to Raji et al.'s study, Asian Indians have a higher risk of CVD than Caucasians because they have much more total abdominal and visceral fat than Caucasians of the same age, gender, and BMI. Additionally, compared to Caucasians, there is a weaker correlation between increasing BMI and T2DM in Asian populations because the risk for T2DM starts to rise at comparatively normal BMI in Asian populations. Seven studies examined the link between CVD risk and obesity, and BMI. In five of the research that made up this review, a link between obesity and higher rates of CVD prevalence was found [36].

According to WHO recommendations on BMI for Asian populations, one of these research employed lower BMI cut-off points to account for Asian populations. To estimate the prevalence of obesity, abdominal adiposity was assessed using waist circumference measures. Studies indicated a link between rising BMI and CVD; however, one study found that severe obesity in women was associated with a lower risk of stroke. Although the authors do not explain the decreased prevalence of stroke or TIA, differences in vascular risk factors in men, such as ischemic heart disease, age, and smoking, may help. Furthermore, it has been demonstrated that adiposity is linked to higher estrogen levels and that gonadal steroids, most notably estrogen, may confer a protective effect against stroke/TIA in women [37]. Although obesity is recognized as a risk factor for CVD, it is paradoxical in that patients with overweight or obesity have lower mortality rates than those whose BMI is normal or underweight. According to Lee et al., individuals with heart failure who were obese but did not have comorbid diabetes fared better in terms of survival than those who did. According to Tey, there is an inverse relationship between BMI and the risk of dying, with severe obesity associated with a lower probability of dying. Additional research is needed to pinpoint the mechanisms and connections between obesity and the risk of CVD and mortality caused by the condition [38].

4.1. Lipid control

At least in part, CVD is caused by diabetic dyslipidemia, which is present in T2DM patients. Furthermore, diabetic dyslipidemia, which includes high triglycerides, low HDL-C and LDL-C, and low HDL-C, is linked to an increased risk of cardiovascular events, particularly in high-risk populations. Patients with T2DM must consider their metabolic dyslipidemia when determining their CVD risk [39].

4.2. Hypertension

Because the two diseases frequently coexist, hypertension in diabetic patients poses a serious health concern. Over 30% of diabetic patients in Europe suffer from hypertension, which affects them twice as frequently as non-diabetics. By encouraging sodium retention, raising vascular tone, and causing nephropathy, DM puts people at risk for hypertension. Insulin resistance and hyperinsulinemia may contribute to type II diabetes patients' hypertension. Future cardiovascular events in patients with DM and hypertension have been demonstrated to be predicted by aortic stiffness as determined by aortic pulse wave velocity (PWV). It is important to note that in those with type II diabetes, a rise in brachial-ankle PWV is linked to symptomatic cerebral infarction [40,41].

5. Conclusion

The primary goals for patients' glycemia, lipids, and blood pressure control should be incorporated as an individual strategy to prevent CVD in T2DM by the most widely accepted guidelines. Although the prevalence and mortality rates of CVDs in patients with T2DM have decreased, they are still rising. Most T2DM-related CVDs can be avoided by making lifestyle changes and taking adjunctive medications. Precision diabetes therapy has replaced comprehensive medical intervention in T2DM-related CVD management. The GLP-1 agonists, SGLT2 inhibitors, blood pressure, lipid-lowering medications, and T2DM patients with established CVD offer a superior precision therapeutic approach.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors claim that there aren't any conflicts of interest.

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