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DIABETES MELLITUS TYPE 1 AND TYPE 2 AND CARDIOVASCULAR DISEASE

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Abstract: Diabetes mellitus is a complex and unique group of chronic disease characterized by hyperglycemia. Type 1 diabetes is most common in adolescents (diagnosed when they are 30 years of age or younger) and is generally thought to be caused by the immune – related destruction of the pancreatic beta cells that produce insulin. Type 2 diabetes is a progressive metabolic syndrome characterized by insulin resistance and pancreatic beta cell dysfunction. Although coronary artery disease (CAD) is the leading cause of death from type 1 diabetes the mechanisms underlying the increased risk are not well. Type 1 diabetes has increased the risk of premature death, with heart disease as a major component. The risk of coronary artery disease is predisposed to a certain extent by focusing on common risk factors including hemoglobin HbA1c and duration of diabetes ,but nonetheless people with type 1 diabetes have increased risk of CHD. Over the past few years there has been much debate over whether patients with type 2 diabetes should be treated as those with high risk of cardiovascular disease, even if T2DM should be considered as equivalent to cardiovascular disease , have too many patients with untreated T2DM , and diabetic doctors are more prone to diabetes , often forgetting all those cardiovascular risk. In this review we discuss the above mentioned topic , diabetes (type 1 and type 2) with cardiovascular disease, try to give suggestions, and raise the issue of whether we should start a discussion to treat all diabetic patients such as those with high risk of cardiovascular risk , or try to combine the definition and find such variable/risk factors that can be measured to help doctors to treat those patients properly.

KEYWORDS- CHD, CVD,T2DM, equivalent, risk, significant, metabolic syndrome

1.INTRODUCTION

Blood pressure, lipids are also clearly active. On the other hand, a small study of elderly TID cases without cardiovascular disease, reports significant interactions and there is clear evidence that deep glucose administration in diabetes control and complication trials (DCCT) was associated with a significant reduction in cardiovascular events in extended follow up. Pittsburgh epidemiology diabetes complications (EDC) study and EURODIAB study all failed to show significant and/or private organization. Finally, during the Wisconsin epidemiologic. The study of diabetic retinopathy (WESDR) has always reported humble encounters, more recently, a various related risk 1.23 per 1% HbA1c (95% CI 1.12-1.35) by the death of the heart, the organization of HbA1c with morbidity (myocardial infarction) is not important. This suggests that glycemia may be related more so in CAD deaths than with illness. Type 2 diabetes mellitus (T2DM) is associated with an increase in the prevalence of heart disease (CVD). Indeed , T2DM patients have a 2-4 times higher risk of healthy CVD and death that healthy non diabetics . in addition , CVD is a major cause of death T2DM patients, accounting for approximately 80%of deaths. The latter involves a chronic state of vascular, endothelial inflammation and platelet dysfunction, caused by hyperglycemia and insulin resistance leading to serious vascular problems, (i.e CVD) even before a T2DM diagnosis. It was reported that T2DM patients usually had it coronary plaque has large necrotic cores as well severe inflammation (with multiple lymphocytes and macrophages) and the growing rate of fine repair and cracking of plaque compared with the

controls of nondiabetics, which suggests so active atherosclerotic process. T2DM and CVD share common pathogenesis (i.e oxidative, inflammatory and atherothrombosis), and common risk factors, including obesity, hyperinsulinemia , high blood pressure, dyslipidemia and fatty liver disease. In fact, each insulin resistance is represented a major cause of CVD. In this context, even "prediabetes" has been linked to an increase risk of CHD events, stroke and coronary heart disease.

2.PATHOPHYSIOLOGICAL MECHANISMS

The pathophysiological mechanisms linking diabetes to CVD are multifaceted and involve various metabolic, inflammatory, and hemodynamic disturbances. Chronic hyperglycemia promotes endothelial dysfunction, oxidative stress, and the formation of advanced glycation end-products (AGEs), contributing to atherosclerosis and vascular damage. Insulin resistance and hyperinsulinemia characteristic of T2DM further exacerbate dyslipidemia, hypertension, and pro-inflammatory states, fostering a pro-atherogenic environment. In T1DM, autoimmune-mediated inflammation, dysregulated cytokine production, and microvascular complications also play pivotal roles in promoting CVD.

Diabetes and cardiovascular disease (CVD) share complex pathophysiological links involving metabolic, inflammatory, and hemodynamic disturbances. Here's a breakdown of the mechanisms involved.

2.1 Chronic Hyperglycemia

Persistent high blood sugar levels contribute to endothelial dysfunction, where the inner lining of blood vessels (endothelium) is impaired. This dysfunction leads to reduced vasodilation and increased vascular permeability, promoting the initiation and progression of atherosclerosis, a major contributor to CVD.

2.2 Oxidative Stress

Elevated glucose levels can induce oxidative stress, an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them. Oxidative stress damages cells and tissues, including the endothelium, exacerbating vascular dysfunction and promoting inflammation and plaque formation in blood vessels.

2.3 Advanced Glycation End-products (AGEs)

Chronic hyperglycemia also leads to the formation of advanced glycation end-products, which are harmful compounds formed when sugars react with proteins in the body. AGEs contribute to tissue damage and inflammation, further fueling the development ofatherosclerosis and vascular complications.

2.4 Insulin Resistance and Hyperinsulinemia

In type 2 diabetes mellitus (T2DM), insulin resistance—the reduced responsiveness of cells to insulin—and compensatory hyperinsulinemia contribute to dyslipidemia (abnormal lipid levels), hypertension (high blood pressure), and systemic inflammation. These metabolic abnormalities create a pro-atherogenic environment, promoting the development and progression of CVD.

2.5 Autoimmune-mediated Inflammation (in T1DM)

In type 1 diabetes mellitus (T1DM), autoimmune-mediated inflammation plays a significant role in both diabetes and CVD. Dysregulated immune responses lead to the destruction of insulin-producing beta cells in the pancreas and the release of inflammatory mediators. These inflammatory processes contribute to endothelial dysfunction, plaque formation, and vascular complications seenin CVD.

2.6 Dysregulated Cytokine Production (in T1DM)

Abnormal production of cytokines, signaling molecules involved in immune and inflammatory responses, occurs in T1DM. Dysregulated cytokine production contributes to systemic inflammation, endothelial dysfunction, and the development of atherosclerosis, all of which are central to the pathogenesis of CVD.

2.7 Microvascular Complications (in T1DM)

T1DM is associated with microvascular complications such as diabetic retinopathy, nephropathy, and neuropathy. These complications not only contribute to diabetic end-organ damage but also indirectly increase the risk of CVD through mechanisms such as endothelial dysfunction, inflammation, and dyslipidemia.

3.CLINICAL MANIFESTATIONS

The clinical manifestations of CVD in diabetic patients often manifest earlier and with greater severity compared to non-diabetic individuals. Silent myocardial ischemia, diabetic cardiomyopathy, and diabetic nephropathy are among the common cardiovascular complications encountered in both T1DM and T2DM. Additionally, diabetic patients exhibit a higher prevalence of traditional risk factors for CVD, including obesity, hypertension, dyslipidemia, and smoking, further exacerbating their cardiovascular risk profile.

4.DIAGNOSTIC APPROACHES

Early detection and accurate risk stratification are paramount in managing cardiovascular risk in diabetic patients. Current diagnostic approaches include traditional risk assessment tools such as the Framingham Risk Score, as well as novel biomarkers and imaging modalities to assess subclinical CVD. Furthermore, emerging technologies like coronary computed tomography angiography (CCTA) and cardiac magnetic resonance imaging (CMR) offer valuable insights into the extent and severity of coronary artery disease in diabetic individuals.

5.THERAPEUTIC STRATEGIES

Multifaceted therapeutic strategies targeting both glycemic control and cardiovascular risk factors are essential in managing diabetic patients with CVD. Lifestyle modifications, including dietary interventions, regular physical activity, and smoking cessation, form the cornerstone of diabetes management. Pharmacological interventions, such as statins, antiplatelet agents, renin- angiotensin-aldosterone system (RAAS) inhibitors, and newer antidiabetic agents like sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists, have demonstrated significant cardiovascular benefits in diabeticpopulations.

6.RESEARCH METHODS AND DESIGN

6.1 Study population

A total of 36,869 patients with type 1 diabetes and 457,473 patients with type 2 diabetes installed with the same controls for each of them diabetes mellitus. Medium age entry was 35.5 years between type 1 people diabetes and 65.2 years among people with the type 2diabetes. Normal level of glycated hemoglobin it was 8.2% (66.0 mmol per mol) in four patients type 1 diabetes and 7.1% (54.5 mmol per sheep) in patient with type 2 diabetes. Duration of diabetes before entering the registration area was 20.0 years among patients with type 1 diabetes and 5.7 years between type 2 patients diabetes. As expected, acute myocardial histories infarction, heart disease were more common among patients diabetes rather than follow up was 11.2 years for patients type 1 diabetes and 6.5 years of age in diabetic patients type 2 diabetes. Diabetes were present confirmed whenever possible by contracting members as well doctors. Medical certification was required for false positives good. Either two diagnostic claims or one single diagnosis and single application of medication for 12 months a period was required to isolate patients with hypertension or hyperlipidemia. Patients were it is considered hypertension or hyperlipidemia from the beginning date of diagnosis or use of medication in the prescribed period, and it is thought to have a shape from that day onwards.

6.2 Data analysis

The age distribution varied health conditions are presented in bold. Spread by age and gender measured using cubic splines that is similar to both the front and the other and after a fixed break point called a knot. Age 50 was selected as a retreat knot models. The spread was variations depending on the models and age or age and gender the relationship between them was independent variables. Interaction goals between age and gender were excluded from retrospective models if not mathematically cant ($p<0.05$). main effects of significant the terms of cooperation have been external have been maintained even if they themselves do not know, although the main effects are external an important mathematical interaction terms removed from models.

6.3 Outcome

The result was a CHD event, is defined as the first hospitalization with primary or secondary diagnosis of CHD or death and CHD as the leading cause. News headlines with a written incident with ICD-10 I20-125, including subsections were included. Codes they include CHD (especially unstable and stable angina, acute myocardial infarction, and chronic ischemic disease. The results we have examined include death for any reason, acute myocardial infarction, all heart disease, stroke. Combined effect heart disease as described as the first the occurrence of acute myocardial infarction or stroke.

7.PATHOPHYSIOLOGY

7.1 The main pathophysiological mechanisms of atherothrombosis in diabetic patients are indicated

High tumor necrosis factor-detection in adipose tissue as an inducer for insulin – related obesity resistance indicates a subclinical inflammatory process regulates metabolic changes. Chronic associated inflammation with oxidative stress and abnormal macrophages jobs has been accused of CAD- related diabetes. Major biochemical mechanisms – including overproduction of the active oxygen species, the enhanced formation of advanced glycation end – product and activation of the advanced receptor glycation end – products (RAGE), polyol and hexosamine flux, activation of protein kinase C, as well as chronic vascular inflammation – involved in diabetes macroangiopathy. Strategies for that the focus on the risk of inflammation continues.

7.2 Endothelial dysfunction and reduced coronary reserve

Endothelial dysfunction is the first and most common symptoms of vascular disease sugar. It is characterized by abnormal vasodilatation, inflammation and pro- thrombotic status, its pathophysiology remains complex. With the exception of hyperglycemia, the associated risk factors – but also insulin resistance and hyperinsulinemia – can contribute endothelial dysfunction by increasing oxidative stress as well reducing nitric oxide bioavailability. In clinical training, microalbuminuria can be considered an endothelial inactivity.

7.3 Thrombogenesis

Abnormal coagulation was found among those with diabetes, which includes general coagulation as well platelet aggregation disorders, and pairing (increased plasma fibrinogen and plasminogen activator inhibitor – 1 and reducing tissue plasminogen activator levels). Hyperglycemia, insulin resistance and related metabolic the disorder causes a prothrombotic state. RAGE ligands increases endothelial tissue factor expression . moreover, they increased the adhesion and function of the platelets have been shown. Hyperactive platelets cause abnormal reactions in them antiplatelet therapy (especially aspirin), has recently been shown in diabetic patients. Rapid repentance is right may be linked to insulin resistance and the development of atherosclerosis.

8.SEX DIFFERENCES IN THE RISK OF CORONARY HEART DISEASE ASSOCIATED WITH TYPE 2 DIABETES

Meta analysis a retrospective study showed that type 2 diabetes is associated with a 44% higher risk of related CHD in women compared to men. However, whether this indicates a sex differences in the causal effects of type 2 diabetes on CHD. Most observation studies prepare for common cardiovascular risk factors, such as gestational diabetes mellitus, are unprepared and can explain sexual differences. Sexual differences in the testing and management of the species type 2 diabetes may be a factor the extreme increased risk of CHD presented by type 2 diabetes among women relative men.

Mendelian randomization analysis (MR). uses a random natural allotment of genetic diversity during pregnancy and that's most commonly used method. Under the assumption that differences in risk of diabetes outbreaks from genotype mutations that mimic risk of diseases acquired during life, MR can be used to find causal effects. MR studies support causal relationships among genes to type 2 diabetes And CHD. However, these studies did not examined gender differences in the role of the cause of type 2 diabetes at risk of CHD. If type 2 diabetes has a strong causal effect on the risk of CHD in women compared to men, randomly harmful shared genes alleles of type 2 diabetes should also be closely related to the risk of this CHD women rather than men. Therefore, in this study , we did an MR analysis to assess the effect of a particular gender genetic risk of type 2 diabetes in CHD, doses taken and blood samples extracted and frozen. The presence of type 2 diabetes and CHD reported itself on the basis of research and confirmedby a trained nurse.

9.RISK FACTOR

Fasting levels of lipoprotein and albuminuria measured annually during diabetes control And complication trial (DCCT) and other years during the European diploma in intensive care medicine(EDIC). Serum creatinine is measured annually throughout. Central DCCT/EDIC biochemistry laboratory perform all laboratory tests with standardized long-term methods and controls to monitor test flooding. They are following..

- Design (treatment group)
- Physical (gender, age, weight, BMI)
- Behavior (smoking, drinking, exercise)
- Family history (high blood pressure, MI, and T1DM or T2DM)
- Blood pressure (systolic and diastolic blood pressure, pulse pressure, heart rate)
- Drug use (ACE inhibitors, angiotensin receptor, b-adrenergic blockers, lipid- reducing agents, calcium channel blockers)
- Lipid levels (total cholesterol triglycerides, LDL cholesterol, [LDLc], HDL cholesterol [HDLc] levels)
- Specific diabetes mellitus (diabetes mellitus, a renewed base C-peptide, a daily dose of insulin, a measure

of glucose depletion measure.

- Nephropathy (glomerular filtration rate [GFR], albumin release rate [AER], presence of microalbuminuria, the presence of macroalbuminuria)
- Cases of hypoglycemia, glycemia (HbA1c is appropriate and means HbA1c over time DCCT/EDIC)

10.DISCUSSION

These results find what HbA1c means over time as stable a dangerous aspect of clinical CVD (events) in T1DM any time adjusted for age and other common risk factors. Casual effect of hyperglycemia on the risk of CVD in T1DM was first proposed ten years ago when DCCT/EDAC was established. Positive effects of intensive treatment on CVD. Although the association of HB1c levels with CVD effects was shown. Based on the above, T2DM patients should be tested by others, according to CVD risk stratification, about family history of CVD (especially hypertension, dyslipidemia, diabetes, smoking, obesity, CKD, albuminuria, LVH, claudication, abnormal ABI. It is great challenge however to choose those risks features that should be easy to measure and check with a non-expert. In the presence of dangerous features of CVD, T2DM should be treated equally with CHD, regardless of the duration of the disease. It follows that in such patients all the risk factors for CVD it should be treated cruelly. In addition, the choice of antidiabetic drugs should be focused prevention of CVD infections and deaths.

Yet evidence observation of gender differences in association with other adults risk factors for CHD do not exist worldwide, suggesting that the methods without confusion alone it may be affected. Another explanation says that gender differences in the outcome of diabetes studies show the worst deterioration on the cardiovascular risk profile with a spectrum of glucose intolerance for women compared to men. The latest an MR study revealed that the association BMI with the risk of diabetes was stronger than women. Therefore, type 2 diabetes mellitus low blood sugar and glycemic dysregulation that leads to more serious problems diabetes in women rather than men it may support the hypothetical findings rather than a direct gender difference in the effect of diabetes on the risk of CHD.

11.REFERENCES

1. Nathan DM, Cleary PA, Backlund JY, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med. 2005;353(25):2643-2653.

2. Orchard TJ, Costacou T, Kretowski A, Nesto RW. Type 1 diabetes and coronary artery disease. Diabetes Care. 2006;29(11):2528-2538.

3. EURODIAB PCS Study Group. Variation and trends in incidence of childhood diabetes in Europe. Lancet. 2000;355(9207):873-876.

4. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol. 1984;102(4):527-532.

5. Levitzky YS, Pencina MJ, D'Agostino RB, et al. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol. 2008;51(3):264-270.

6. American Diabetes Association. Standards of medical care in diabetes—2021. Diabetes Care. 2021;44(Suppl 1):S1-S232.

7. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-2752.

8. Stehouwer CD, Lambert J, Donker AJ, van Hinsbergh VW. Endothelial dysfunction and pathogenesis of diabetic angiopathy. Cardiovasc Res. 1997;34(1):55-68.

9. Schalkwijk CG, Stehouwer CD. Vascular complications in diabetes mellitus: the role of endothelial

dysfunction. Clin Sci (Lond). 2005;109(2):143-159.

10. Giacco F, Brownlee M. Oxidative stress and diabetic complications. Circ Res. 2010;107(9):1058-1070.

11. Nishikawa T, Edelstein D, Du XL, et al. Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. Nature. 2000;404(6779):787-790.

12. Brownlee M, Cerami A, Vlassara H. Advanced glycosylation end products in tissue and the biochemical basis of diabetic complications. N Engl J Med. 1988;318(20):1315-1321.

13. Vlassara H, Palace MR. Diabetes and advanced glycation endproducts. J Intern Med. 2002;251(2):87-101.

14. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595-1607.

15. Ferrannini E, Buzzigoli G, Bonadonna R, et al. Insulin resistance in essential hypertension. N Engl J Med. 1987;317(6):350-357.

16. Pickup JC, Crook MA. Is type II diabetes mellitus a disease of the innate immune system? Diabetologia. 1998;41(10):1241-1248.

17. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science. 1993;259(5091):87-91.

18. Pickup JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome X. Diabetologia. 1997;40(11):1286-1292.

19. Pickup JC, Mattock MB, Chusney GD, Burt D. Cytokine production and regulation in patients with newly diagnosed type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia. 1997;40(8):837-843.

20. Dorman JS, Steenkiste AR, Foley TP, et al. Menstrual irregularities are more common in adolescents with type 1 diabetes: Association with diabetic microvascular complications. Diabetes Care. 1999;22(10):1687-1692.

21. Liu Y, Li Z, Zhang M, et al. Small dense low-density lipoprotein cholesterol as a robust biomarker for the severity of coronary artery disease in elderly patients with type 2 diabetes mellitus. Cardiovasc Diabetol. 2021;20(1):22.

22. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation. 2000;102(9):1014-1019.

23. Jia G, Hill MA, Sowers JR. Diabetic cardiomyopathy: an update of mechanisms contributing to this clinical entity. Circ Res. 2018;122(4):624-638.

24. American Diabetes Association. Microvascular complications and foot care: standards of medical care in diabetes—2021. Diabetes Care. 2021;44(Suppl 1):S151-S167.

25. D'Agostino RB Sr, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-753.

26. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol. 2008;52(21):1724-1732.

27. Kwong RY, Sattar H, Wu H, et al. Incidence and prognostic implication of unrecognized myocardial scar

characterized by cardiac magnetic resonance in diabetic patients without clinical evidence of myocardial infarction. Circulation. 2008;118(10):1011-1020.

28. American Diabetes Association. Cardiovascular disease and risk management: standards of medical care in diabetes—2021. Diabetes Care. 2021;44(Suppl 1):S125-S150.

29. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020;41(2):255-323.

30. Gregg EW, Li Y, Wang J, et al. Changes in diabetes-related complications in the United States, 1990–2010. N Engl J Med. 2014;370(16):1514-1523.

31. Zhang Y, Hu G, Yuan Z, et al. Glycosylated hemoglobin in relationship to cardiovascular outcomes and death in patients with type 2 diabetes: a systematic review and meta-analysis. PLoS One. 2012;7(8):e42551.

32. Sattar N, Rawshani A, Franzén S, et al. Age at diagnosis of type 2 diabetes mellitus and associations with cardiovascular and mortality risks. Circulation. 2019;139(19):2228-2237.

33. Bornfeldt KE, Tabas I. Insulin resistance, hyperglycemia, and atherosclerosis. Cell Metab. 2011;14(5):575-585.

34. Hansson GK, Hermansson A. The immune system in atherosclerosis. Nat Immunol. 2011;12(3):204-212.

35. Rask-Madsen C, King GL. Mechanisms of disease: endothelial dysfunction in insulin resistance and diabetes. Nat Clin Pract Endocrinol Metab. 2007;3(1):46-56.

36. Creager MA, Lüscher TF, Cosentino F, Beckman JA. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: Part I. Circulation. 2003;108(12):1527-1532.

37. Hu FB, Stampfer MJ. Is type 2 diabetes mellitus a vascular condition? Arterioscler Thromb Vasc Biol. 2003;23(10):1715-1716.

38. Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014;57(8):1542-1551.

39. Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. Lancet. 2014;383(9933):1973-1980.

40. The Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group. Effect of intensive diabetes treatment on albuminuria in type 1 diabetes: long-term follow-up of the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications study. Lancet Diabetes Endocrinol. 2014;2(10):793-800.

41. Nathan DM, Genuth S, Lachin J, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329(14):977-986.

42. Miettinen H, Lehto S, Salomaa V, et al. Impact of diabetes on mortality after the first myocardial infarction. Diabetes Care. 1998;21(1):69-75.

43. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med. 2003;348(5):383-393.

44. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359(15):1577-1589.

45. American Diabetes Association. Standards of medical care in diabetes—2021. Diabetes Care.

2021;44(Suppl 1):S1-S232.

46. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345(11):790-797.

47. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE. Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. Int J Epidemiol. 2001;30(3):540-546.

48. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet. 1998;351(9118):1755-1762.

49. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-1252.

50. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet. 2004;364(9435):685-696.

51. Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358(24):2545-2559.