Review Article
An Overall Glance of Evidence Supportive of One-Hour and Two-Hour Postload Plasma Glucose Levels as Predictors of Long-Term Cardiovascular Events

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Received 18 August 2019; Accepted 28 November 2019; Published 18 December 2019

Academic Editor: Michael Horowitz

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This review summarizes the vast literature describing the long-term epidemiological studies with emphasis on postprandial glucose as a stronger predictor of cardiovascular complications as compared to fasting glucose and HbA1c. Many molecular studies also supported this fact by illustrating that postchallenge hyperglycemia is associated with elevated biomarkers of systemic inflammation in the plasma and thus increasing the chances of vascular damage. Large-scale studies have proved that vascular stiffness, brachial-ankle pulse-wave velocity, carotid intima thickness, and left ventricular hypertrophy have been associated with postprandial glucose as compared to fasting glucose or glycosylated hemoglobin.

1. Introduction

The cardiovascular impact of elevated postprandial glucose has been studied extensively through a significant number of prospective longitudinal, cross-sectional, molecular, and experimental studies in various parts of the world. This concept of relating the postprandial glucose to coronary and cardiovascular events began as early as 1970s with some of the prospective studies at that time. The postprandial state that has been shown to be related to cardiovascular events from time to time was either after 1 hour or 2 hours of ingestion of oral glucose load also known as the oral glucose tolerance test (OGTT). This may be related to the fact that some cases of diabetes (strong risk factor for cardiovascular mortality) can be missed if only fasting blood glucose (FBG) is used in screening [1]. Only few cross-sectional and prospective studies favor glycosylated hemoglobin (HbA1c) being superior to FBG and 2-hour plasma glucose (2hPG) for prediction of ischemic heart disease [2]. In a cross-sectional study, elevated plasma levels on admission, HbA1c, and FBG were found to have low sensitivity to detect undiagnosed diabetes in patients with acute coronary syndrome as compared to OGTT [3]. The EUROASPIRE IV (the European Action on Secondary Prevention through Intervention to Reduce Events) cross-sectional survey of 4004 subjects in 24 European countries showed that OGTT identified a largest number of previously undiagnosed diabetic patients with established coronary artery disease [4]. In a meta-analysis showing that impaired fasting glucose was significantly associated with future risk of coronary heart disease (CHD), the subgroup analyses showed that risk of CHD was only increased in the studies which enrolled participants with increased 2hPG and not in those which excluded them [5].

2. Pioneer Epidemiological Studies

One of the initial investigations showing the relationship of glucose tolerance to the incidence of CHD-associated death and nonfatal myocardial infarction (MI) was two cohort studies consisting of 3,267 and 1,059 Finnish men in 1972 who were followed up over a period of 5 years and the CHD-related death was significantly related to high 1-h postload blood glucose (1hPG) level [6]. Later, another
large prospective study, the Honolulu Heart Program in Hawaii, involving a 20-year follow-up of 457 migrant Japanese patients also found 1hPG to be positively related to MI-related mortality [7]. Also, in the Honolulu program, odds ratio for 1hPG in patients with ankle brachial index <0.9 was 1.3 (p < 0.05) and found to be predictive of peripheral vascular disease 25 years later [8]. The Helsinki Businessmen prospective study in which 610 men joined a multifactorial primary prevention trial of cardiovascular diseases revealed that 1hPG was significantly associated with total mortality along with other traditional risk factors (smoking, blood pressure, and cholesterol) after 28 years of follow-up [9]. The evidence strengthened further in the late 1990s with the Chicago Heart association Detection Project in Industry where a 22-year-long longitudinal study of 26,753 nondiabetic men and women showed that 1hPG level is an independent risk factor for fatal CHD [10].

3. Subsequent Epidemiological Studies
Supportive of Cardiovascular Impact of Postchallenge Hyperglycemia

US National Library of Medicine (Pub Med.gov) was searched with search terms "post load glucose" and "cardiovascular"; "post load glucose" and "coronary"; "post challenge hyperglycemia" and "cardiovascular"; "post challenge hyperglycemia" and "coronary"; "post prandial glucose" and "cardiovascular"; "post prandial glucose" and "coronary"; "OGTT" and "cardiovascular"; and "OGTT" or "coronary". Various epidemiological studies were found to be conducted from 1999 to 2019 suggesting postprandial glucose as a better predictor of cardiovascular disease independent of FBG that have been enlisted in Table 1. The median follow-up in these trials was 7.2 years with a median number of patients 1425 and median rate of 1.5. Graphical presentation of the rate ratios of studies enlisted in Table 1 has been depicted in Figure 1. Epidemiological data from 20 European studies concluded that 31% of the diabetic patients with nondiabetic fasting glucose will remain undiagnosed if only fasting glucose criteria is used and the risk profile of the subjects with impaired fasting glucose depends on 2hPG levels [42]. Thus, the DECODE study (Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe) has emphasized on postchallenge hyperglycemia as the main determinant of risk of cardiovascular disease (CVD) in patients with diabetes [42]. A large prospective Whitehall study involving 17,869 subjects followed up over 33 years established a linear dose-response relationship between postload plasma glucose and CHD mortality risk [14].

3.1. Postprandial State Enhances Atherosclerosis in Arteries and Has Detrimental Effects on Myocardial Function. The epidemiological studies were also supported by experimental studies which indicated that the postprandial state may affect atherosclerosis process in the arteries, thereby increasing the coronary vascular events. In European nondiabetic population of 403 subjects, multivariate analysis showed that carotid intima-media thickness was significantly increased in the top 5th quintile of 2hPG but not the fasting glucose [43]. There was clustering of risk factors such as body mass index, waist to hip ratio, elevated triglycerides, and decreased high-density lipoprotein (HDL-cholesterol) levels in the top quintile of 2hPG as well [43]. Another cross-sectional study of 356 participants from Pittsburgh site of the Cardiovascular Health Study measured the aortic stiffness through aortic pulse wave velocity, and after controlling age and systolic blood pressure, the strongest predictors of aortic stiffness were heart rate and 2hPG (p = 0.063) [44]. In the RIAD study (Risk factors in Impaired glucose tolerance for Atherosclerosis and Diabetes) intima-media thickness of common carotid arteries that was taken as measure of atherosclerosis was associated with 2hPG even when HbA1c was within normal range [45]. This has formed a basis of many studies in 1990s like Diabetes Intervventional Study, Kumamoto study, DIGAMI (Diabetes and Insulin-Glucose infusion in Acute Myocardial Infarction) study, and STOP-NIDDM (Study TO Prevent NIDDM) trial to control the postprandial hyperglycemia in order to prevent CVD [45].

In a randomized study where 61 patients with type 2 diabetes were followed up over 24 months and diastolic myocardial dysfunction (E′), intima media thickness and arterial stiffness were significantly higher in patients receiving only conventional insulin therapy (human insulin b.d.) vs. regimens receiving better postmeal glucose control with intensified conventional insulin therapy (lispro at meals and NPH bed time) and supplementary insulin therapy (regular insulin at meals) [46]. In a cross-sectional study from China involving 671 men and 603 women, it was found that the patients with impaired glucose tolerance after glucose challenge have higher brachial-ankle pulse wave velocity/arterial stiffness, are more insulin resistant, and have worse lipid profile [47]. A cross-sectional study of 767 never treated hypertensive subjects showed that 1hPG of ≥155 mg/dL is a major determinant left ventricular mass index and hence left ventricular hypertrophy in hypertensive patients, that in itself is independent risk factor for cardiovascular morbidity and mortality [48]. In a cross-sectional study including 4938 subjects from China, the ones with impaired glucose tolerance and newly diagnosed diabetes, but not the isolated impaired fasting glucose, had higher brachial-ankle pulse-wave velocity and thus greater arterial stiffness [49]. In a cross-sectional study of 584 newly diagnosed hypertensive individuals, those who had normal glucose tolerance on 2hPG but had 1hPG ≥155 mg/dL had higher indices of vascular stiffness (pulse wave velocity, augmentation pressure, and augmentation index) that correlate with the cardiovascular risk profile [50].

3.2. Molecular Studies Relating Postprandial Effect on the Cardiovascular Profile. An experimental study showed that the concentration of soluble forms of the adhesion molecules sE-selectin and sVCAM-1 (vascular cell adhesion molecule-1), which were hypothesized as early predictors of coronary artery disease, was significantly related to postload glucose
Table 1: Epidemiological studies describing the postprandial hyperglycemia as a predictor of cardiovascular mortality in various parts of the world for the last two decades.

| No. | Type of study | Name of the study | Total number of patients | Duration of follow-up (years) | Subject characteristics | Study outcome measured | Rate ratio | 95% CI | p value |
|-----|---------------|--------------------|--------------------------|-------------------------------|-------------------------|------------------------|------------|--------|---------|
| 1   | Prospective cohort | Sievers et al., 1999 [11] | 1745 | 10.6 | Pima Indians with type 2 diabetes ≥15 years of age | 2-hour postprandial glucose (2hPG) levels were associated with death rate from cardiovascular disease (CVD) | Death rate 1.2 | 1.1–1.4 | 0.007 |
| 2   | Prospective cohort | de Vegt et al., 1999 [12] | 2363 | 8 | Dutch subjects 50–75 years without known diabetes | Postload glucose predictive of increased cardiovascular mortality even within the nondiabetic range | Relative risk (RR) | 3.4 | 1.35–8.53 | <0.05 |
| 3   | Prospective cohort | Meigs et al., 2002 [13] | 3370 | 4 | Subjects from the Framingham offspring study without clinical CVD or medication-treated diabetes | 2hPG is associated with cardiovascular events | RR 1.14 | 1.02–1.27 | Not available |
| 4   | Prospective cohort | Brunner et al., 2006 [14] | 17869 | 33 | London-based male civil servants aged 40–64 years excluding those with known diabetes and with missing glucose measurements | 2hPG associated with coronary heart disease | Hazard ratio (HR) | 3.62 | 2.34–5.56 | Not available |
| 5   | Prospective cohort | Meisinger et al., 2006 [15] | 1160 | 30 | Randomly selected 40–59 year non-diabetic German subjects | 1-hour postload glucose (1hPG) associated with all-cause mortality | HR 1.49 | 1.17–1.88 | Not available |
| 6   | Prospective cohort (1974–1979) | Nigam et al., 2007 [16] | 1691 | 14.7 | Patients with coronary artery disease (CAD) who were enrolled at 15 centers throughout North America | Postprandial hyperglycemia was not associated with cardiovascular mortality in patients with undiagnosed diabetes | HR 0.89 | 0.59–1.36 | Not available |
| 7   | Prospective cohort | Chien et al., 2008 [17] | 2165 | 10.5 | Chinese subjects in Taiwan aged ≥35 years | Postchallenge glucose was associated with major cardiovascular events | RR 2.05 | 1.23–3.42 | ≤0.001 |
| 8   | Prospective cohort | Sarwar et al., 2010 [18] | 18569 | 23.5 | Iceland subjects without history of diabetes and myocardial infarction (MI) | Postload glucose associated with coronary heart disease | HR 1.03 | 1.01–1.05 | Not available |
| No. | Type of study | Name of the study | Total number of patients | Duration of follow-up (years) | Subject characteristics | Study outcome measured | Rate ratio | 95% CI       | p value |
|-----|---------------|-------------------|--------------------------|-------------------------------|-------------------------|------------------------|------------|-------------|---------|
| 9   | Meta-analysis of 26 western prospective cohort studies | Sarwar et al., 2010 [18] | 12652 | Not applicable | Not applicable | Postload glucose associated with coronary heart disease | RR 1.05 | 1.03–1.07 | Not available |
| 10  | Prospective cohort | Kitada et al., 2010 [19] | 422 | 2 | Acute MI (AMI) Japanese patients | 2 hPG was the only independent predictor of long-term major adverse cardiovascular events (MACE) two years after AMI | Odds ratio (OR) 1.85 | 1.07–3.21 | 0.028 |
| 11  | Case control | Shimabukuro et al., 2011 [20] | 287 | Not applicable | Japanese who visited the university hospital to be checked for glucose intolerance or known type 2 diabetes were consecutively recruited | Left ventricle dysfunction associated with impaired glucose tolerance | OR 3.43 | 1.09–11.2 | 0.037 |
| 12  | Prospective cohort (HEART2D trial) | Raz et al., 2011 [21] | 1115 | 2.7 | Patients with type 2 diabetes who survived of AMI | Patients using insulin targeting the postprandial versus fasting hyperglycemia had lower cardiovascular events | HR 0.69 | 0.49–0.96 | 0.029 |
| 13  | Large prospective cohort (EpiDREAM study) | Anand et al., 2012 [22] | 18,990 | 3.5 | 30–85 years multiethnic patients from 21 countries who had impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) levels | 2-hour post OGTT glucose associated with increase in risk of cardiovascular events or death | HR 1.17 | 1.13–1.22 | Not available |
| 14  | Prospective cohort | Tamita et al., 2012 [23] | 275 | 5.3 | Japanese subjects with AMI | Abnormal glucose tolerance associated with MACE | HR 2.65 | 1.37–5.15 | 0.004 |
| 15  | Prospective cohort | Furtado de Souza et al., 2012 [24] | 148 | 36 ± 14 months | Brazilian subjects undergoing diabetes screening attending a primary care unit | 2-hour OGTT results were associated with CVD | OR 1.013 | 1.002–1.025 | 0.024 |
| No. | Type of study | Name of the study | Total number of patients | Duration of follow-up (years) | Subject characteristics | Study outcome measured | Rate ratio | 95% CI | p value |
|-----|---------------|-------------------|--------------------------|-------------------------------|------------------------|------------------------|------------|--------|---------|
| 16  | Finnish and Swedish prospective cohort | Ning et al., 2012 [25] | 3743 men and 3916 women | 16.4 | 25 to 90 years who had fasting plasma glucose (FPG) < 6.1 mmol/l and 2h PG < 7.8 mmol/l and free of CVD | 2hPG associated with coronary heart disease | HR 1.13 in men; 1.33 in women | 0.93–1.37 in men; 0.83–2.13 in women | Not available |
| 17  | Prospective cohort | Henareh and Agewall, 2012 [26] | 123 | 6.03 ± 1.36 | Swedish subjects aged 31–80 years who had suffered a previous MI | 2hPG was a significant predictor of cardiovascular death, recurrent MI, and unstable angina pectoris | HR 1.27 | 1.00–1.62 | <0.05 |
| 18  | Prospective cohort | Silbernagel et al., 2012 [27] | 1772 | 7.7 ± 2.0 | German nondiabetic subjects who were referred for angiography and whose FPG was <126 mg/dl underwent OGTT | Postchallenge glucose undetected by fasting glucose and glycated hemoglobin independently predicted the cardiovascular mortality | HR 1.57 | 1.02–2.43 | 0.041 |
| 19  | Cross sectional (second strong heart study) | Capaldo et al., 2013 [28] | 562 | Not applicable | American nondiabetic and nonhypertensive Indians of 45–74 years of age | Both higher IFG and IGT levels rather than only IFG associated with left ventricular hypertrophy | OR 9.76 | 2.03–46.79 | 0.004 |
| 20  | Prospective cohort | Barzin et al., 2013 [29] | 3794 | 8 | Tehran urban subjects aged ≥40 years without history of diabetes or CVD | Isolated postchallenge hyperglycemia associated with cardiovascular events | HR 1.77 | 1.19–2.64 | 0.005 |
| 21  | Cross sectional | Yang et al., 2013 [30] | 6040 | Not applicable | Chinese prediabetic subjects | CVD events associated with IGT levels compared to IFG levels | OR 2.88 | 1.36–6.01 | 0.0059 |
| 22  | Prospective cohort | Kuramitsu et al., 2013 [31] | 828 | 4.3 | Japanese patients of stable angina undergoing percutaneous intervention (PCI) | Postchallenge hyperglycemia was associated with MACE | HR 1.62 | 1.07–2.53 | 0.023 |
| 23  | Finnish diabetes prevention prospective cohort study | Lind et al., 2014 [32] | 504 | 13 | Finnish individuals with IGT were followed up with yearly OGTT, FPG, and HbA1c | 2hPG was associated with CVD events | HR 2.19 | 1.51–3.18 | ≤0.001 |
| No. | Type of study       | Name of the study               | Total number of patients | Duration of follow-up (years) | Subject characteristics                                                                 | Study outcome measured                                                                 | Rate ratio  | 95% CI       | p value |
|-----|---------------------|---------------------------------|--------------------------|------------------------------|-----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------|--------------|---------|
| 24  | Prospective cohort  | Ritsinger et al., 2015 [33]     | 167 AMI patients and 184 controls | 10                           | Swedish patients up to 80 years with AMI (n = 167) and healthy controls (n = 184) with no previously known diabetes | Patient with AMI having abnormal glucose tolerance after an OGTT performed at the time of discharge had higher cardiovascular mortality | HR 2.3      | 1.24–4.25    | 0.008   |
| 25a | Yorkshire retrospective cohort | George et al., 2015 [34] | 768 | 3 | Patients without pre-existing diabetes mellitus post-MI | IGT associated with increased incidence of MACE | HR 1.54 | 1.06–2.24 | 0.024 |
| 25b | Yorkshire retrospective cohort study | George et al., 2015 [34] | 768 | 3 | Patients without pre-existing diabetes mellitus post-MI | Newly diagnosed diabetes associated with increased incidence of MACE | HR 2.15 | 1.42–3.24 | 0.003 |
| 26  | Prospective cohort  | Faghihi-Kashani et al., 2016 [35] | 2607 | 7.2 | Patients of type 2 diabetes mellitus in Tehran | 2hPG was associated with high incidence of coronary heart disease | HR 1.64 | 1.03–2.61 | Not available |
| 27  | Prospective cohort  | Shahim et al., 2017 [36] | 4004 | 2 | 24 European subjects aged ≥18–80 years hospitalized for a first or recurrent CAD event | 2hPG associated with cardiovascular events | HR 1.38 | 1.07–1.78 | 0.01 |
| 28  | Prospective cohort  | Nielsen et al., 2017 [37] | 4934 | 27 | Swedish subjects without diabetes | 1hPG predicted the cardiovascular death | HR 1.09 | 1.01–1.17 | 0.02 |
| 29  | Prospective cohort  | Chattopadhyay et al., February 2018 [38] | 674 | 4 | Post-MI survivors without known diabetes in England and Wales | Only 2hPG predicted MACE | HR 1.12 | 1.04–1.20 | ≤0.001 |
| 30  | Retrospective cohort | Chattopadhyay et al., August 2018 [39] | 1056 | 40.8 months | Acute coronary event survivors without known diabetes mellitus who had FBG and 2hPG measured predischARGE | 2hPG independently predicted MACE | HR 1.091 | 1.043–1.142 | ≤0.001 |
| 31  | Cross sectional (CATAMERI study) | Fiorentino et al., 2019 [40] | 1010 | Not applicable | Nondiabetic Caucasian individuals with hbA1c <5.7% | 1hPG during OGTT ≥155 mg/dl associated with CAD | OR 6.16 | 1.05–36.32 | 0.04 |
| 32  | Retrospective cohort | Chattopadhyay et al., 2019 [41] | 1056 | 2.8 | MI survivors in East yorkshire and North Lincolnshire | 2hPG predicted MACE-free survival | HR 1.16 | 1.07–1.26 | ≤0.001 |
concentration in 78 men with symptoms of angina and positive exercise stress test who presented for coronary arteriography [51]. In a large observational study, it was found that the oral glucose tolerance test increases biomarkers of systemic inflammation such as hsCRP, IL-6, TNF-alpha, sICAM-1, sVCAM-1, and sE-selectin [52]. Postchallenge hyperglycemia is associated with increased generation of asymmetric dimethylarginine and reactive oxygen species that lead to decreased nitric oxide synthesis which decreases endothelial-dependent flow-mediated dilatation and hence decreased vascular function [53]. In a CODAM (Cohort on Diabetes and Atherosclerosis Maastricht) study, α-dicarbonyl concentrations are correlated with glucose levels during OGTT, not with FBG or HbA1c in individuals with impaired glucose metabolism and type 2 diabetes which are associated with more vascular complications [54].

3.3. Clustering of Cardiovascular Risk Factors with Elevated Postload Glucose. A cross-sectional study of 1475 subjects of Arian ethnicity showed that cardiovascular risk factors like age, body mass index, waist circumference, blood pressure, and lipid profile (not low-HDL cholesterol) were significantly higher in normal glucose tolerance subjects with 1hPG >155mg/dl [55]. In a multicenter cross-sectional GENFIEV (GENetics, PHYsiopathology, and EVolution of Type 2 diabetes) study, 1hPG >155 mg/dl showed lower insulin sensitivity, impaired β-cell function, and worse cardiovascular risk profile (glycosylated hemoglobin, blood pressure, low-density lipoprotein cholesterol, and triglyceride) [56]. In the 2005–2014 National Health and Nutrition examination survey, a cross-sectional survey of 3644 adults with pre-diabetes based on FBG and HbA1c, 6.9% were detected to have diabetes based on 2hPG and were more likely to have hypertension, higher triglycerides, lower high-density lipoprotein cholesterol, and higher albuminur [57]. In a DICAMANO study of 447 overweight/obese subjects with FBG ≤5.5 mmol/l (99 mg/dl) and BMI ≥25 kg/m² who underwent a 75 g OGTT after multivariable adjustment for FBG, smoking, and physical activity level, the odds ratio (95% confidence intervals) was higher for the presence of postprandial hyperglycemia for anthropometric indices of central fat distribution (neck circumference, waist circumference, and waist-to-height ratio) [58].

3.4. Postprandial Glucose Helps to Predict Cardiovascular Disease in Patients with Prediabetes. There has been substantial evidence found by Bergman et al. that led them to support the idea of redefining current diagnostic criteria for prediabetes with elevated 1hPG level. Among patients having normal glucose tolerance during the OGTT, 1hPG was found to be highly predictive for detecting progression to diabetes and micro- and macrovascular complications [59]. As compared with subjects with 1hPG <155 mg/dl, individuals with 1hPG ≥155 mg/dl exhibited a significantly worse cardiometabolic profile, both in the group without diabetes (HbA1c <5.7%) and in the group with prediabetes (HbA1c 5.7–6.4%) [60]. In the Finnish Diabetes Prevention prospective cohort study, when 504 individuals with IGT were followed up over 13 years with yearly evaluations with OGTT, FPG, and HbA1c levels, it was found that 2hPG was
associated with increased risk of CVD. This supports the use of 2 hPG in screening for prediabetes and monitoring glycaemic levels of people with prediabetes [32]. Both IFG and IGT are associated with increased cardiovascular risk as assessed by serum lipid and hsCRP levels but IGT being characterized by a more atherogenic risk profile than IFG [61]. In the EpiDREAM study, the patients from 21 countries who had IGT and IFG levels were followed up over 3.5 years, and 2 hPG was associated with increased risk of cardiovascular events [22]. In a Chinese cross-sectional study involving prediabetic subjects, odds of developing the CVD events were associated with IGT levels rather than IFG levels [30].

4. Conclusion

The concept of relating the postprandial glucose as opposed to fasting glucose to coronary and cardiovascular events began as early as 1970s. This later on formed the basis of large-scale prospective studies that showed that OGTT identifies a largest number of previously undiagnosed diabetic patients with established coronary artery disease. Postprandial glucose was found to be significantly related to myocardial infarction-related mortality in nondiabetic and prediabetic patients. Additionally, studies demonstrated that controlling the postprandial hyperglycemia can prevent cardiovascular disease even in nondiabetic subjects. Biochemical markers of vascular inflammation which were hypothesized as early predictors of coronary artery disease were significantly related to postload glucose concentrations. Cardiovascular risk factors like age, body mass index, waist circumference, blood pressure, and lipid profile were significantly higher in patients with elevated postprandial glucose. The review of these studies suggests the need for reconsideration of factors on the basis of which diabetes is managed in the primary-care clinics. The patients visiting the doctor’s office with their fingerstick log are usually uncertain whether they should check fasting sugars or postprandial. Some of these patients are even unsure about the duration between their meals and checking the sugar. They should be counseled about the importance of each of these blood glucose values (fasting vs. one-hour and two-hour postload glucose) and elevation of which of those values is more detrimental for their cardiovascular health. There has also been suggestion by few authors regarding revising the diagnostic criteria for prediabetes based solely on postprandial glucose for early avoidance of risk factors leading to significant cardiovascular morbidity and mortality.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

B.M. and J.B. researched the data and wrote manuscript. J.H. reviewed and edited the manuscript.

References

[1] W. Wang, E. T. Lee, R. Fabsitz, T. K. Welty, and B. V. Howard, “Using HbA1c to improve efficacy of the American diabetes association fasting plasma glucose criterion in screening for new type 2 diabetes in American Indians: the strong heart study,” Diabetes Care, vol. 25, no. 8, pp. 1365–1370, 2002.
[2] H. Cederberg, T. Saukkonen, M. Laasko et al., “Postchallenge glucose, A1C, and fasting glucose as predictors of type 2 diabetes and cardiovascular disease: a 10-year prospective cohort study,” Diabetes Care, vol. 33, no. 9, pp. 2077–2083, 2010.
[3] M. de Mulder, R. M. Oemrawsingh, F. Stam, E. Boersma, and V. A. Umans, “Comparison of diagnostic criteria to detect undiagnosed diabetes in hyperglycaemic patients with acute coronary syndrome,” Heart, vol. 98, no. 1, pp. 37–41, 2012.
[4] V. Gyberg, D. De Bacquer, K. Kotseva et al., “Screening for dysglycaemia in patients with coronary artery disease as reflected by fasting glucose, oral glucose tolerance test, and HbA1c: a report from EUROASPIRE IV-a survey from the European Society of Cardiology,” European Heart Journal, vol. 36, no. 19, pp. 1171–1177, 2015.
[5] T. Xu, W. Liu, X. Cai et al., “Risk of coronary heart disease in different criterion of impaired fasting glucose: a meta-analysis,” Medicine (Baltimore), vol. 94, Article ID e1740, 2015.
[6] K. Pyorala, “Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: results from two population studies in Finland,” Diabetes Care, vol. 2, no. 2, pp. 131–141, 1979.
[7] K. Yano, J. S. Grove, D. M. Reed, and H. M. Chun, “Determinants of the prognosis after a first myocardial infarction in a migrant Japanese population. The Honolulu heart program,” Circulation, vol. 88, no. 6, pp. 2582–2595, 1993.
[8] J. D. Curby, K. Masaki, B. L. Rodriguez et al., “Peripheral artery disease and cardiovascular risk factors in the elderly,” Arteriosclerosis, Thrombosis, and Vascular Biology, vol. 16, no. 12, pp. 1495–1500, 1996.
[9] T. E. Strandberg, V. V. Salomaa, H. T. Vanhanen, V. A. Naukkarinen, S. J. Sarna, and T. A. Miettinen, “Mortality in participants and non-participants of a multifactorial prevention study of cardiovascular diseases: a 28 year follow up of the Helsinki businessmen study,” Heart, vol. 74, no. 4, pp. 449–454, 1995.
[10] A. J. Orenicia, M. L. Daviglus, A. R. Dyer, M. Walsh, P. Greenland, and J. Stamler, “One-hour postload plasma glucose and risks of fatal coronary heart disease and stroke among nondiabetic men and women: the Chicago heart association detection project in industry (CHA) study,” Journal of Clinical Epidemiology, vol. 50, no. 12, pp. 1369–1376, 1997.
[11] M. L. Sievers, P. H. Bennett, and R. G. Nelson, “Effect of glycaemia on mortality in Pima Indians with type 2 diabetes,” Diabetes, vol. 48, no. 4, pp. 896–902, 1999.
[12] F. de Vegt, J. M. Dekker, H. G. Ruhé et al., “Hyperglycaemia is associated with all-cause and cardiovascular mortality in the Hoorn population: the Hoorn Study,” Diabetologia, vol. 42, no. 8, pp. 926–931, 1999.
[13] J. B. Meigs, D. M. Nathan, R. B. D’Agostino Sr., and P. W. F. Wilson, “Fasting and postchallenge glycaemia and cardiovascular disease risk: the Framingham offspring study,” Diabetes Care, vol. 25, no. 10, pp. 1845–1850, 2002.
[14] E. J. Brunner, M. J. Shipley, D. R. Witte, J. H. Fuller, and M. G. Marmot, “Relation between blood glucose and coronary mortality over 33 years in the Whitehall study,” Diabetes Care, vol. 29, no. 1, pp. 26–31, 2006.
[15] C. Meisinger, G. Wolke, S. Brasche, G. Strube, and J. Heinrich, "Postload plasma glucose and 30-year mortality among nondiabetic middle-aged men from the general population: the ERFORT study," *Annals of Epidemiology*, vol. 16, no. 7, pp. 534–539, 2006.

[16] A. Nigam, M. G. Bourassa, A. Fortier, M.-C. Guertin, and J.-C. Tardif, "Fasting but not postprandial (postmeal) glycemiac predicts the risk of death in subjects with coronary artery disease," *Canadian Journal of Cardiology*, vol. 23, no. 11, pp. 873–878, 2007.

[17] K.-L. Chien, H.-C. Hsu, T.-C. Su, M.-F. Chen, Y.-T. Lee, and F. B. Hu, "Fasting and postchallenge hyperglycemia and risk of cardiovascular disease in Chinese: the Chin-Shan community cardiovascular cohort study," *American Heart Journal*, vol. 156, no. 5, pp. 996–1002, 2008.

[18] N. Sarwar, T. Aspelund, G. Eiriksdottir et al., "Markers of dysglycaemia and risk of coronary heart disease in people without diabetes: reykjavik prospective study and systematic review," *PLoS Medicine*, vol. 7, Article ID e1000278, 2010.

[19] S. Kitada, Y. Otsuka, N. Kokubu et al., "Post-load hyperglycemia as an important predictor of long-term adverse cardiac events after acute myocardial infarction: a scientific study," *Cardiovascular Diabetology*, vol. 9, no. 1, p. 75, 2010.

[20] M. Shimabukuro, N. Higa, T. Asahi et al., "Impaired glucose tolerance, but not impaired fasting glucose, underlies left ventricular diastolic dysfunction," *Diabetes Care*, vol. 34, no. 3, pp. 686–690, 2011.

[21] I. Raz, A. Ceriello, P. W. Wilson et al., "Post hoc subgroup analysis of the HEART2D trial demonstrates lower cardiovascular risk in older patients targeting postprandial versus fasting/premeal glycemia," *Diabetes Care*, vol. 34, no. 7, pp. 1511–1513, 2011.

[22] S. Anand, G. Dagenais, V. Mohan et al., "Glucose levels are associated with cardiovascular disease and death in an international cohort of normal glycaemic and dysglycaemic men and women: the EpiDREAM cohort study," *European Journal of Preventive Cardiology*, vol. 19, no. 4, pp. 755–764, 2012.

[23] K. Tamita, M. Katayama, T. Takagi et al., "Newly diagnosed glucose intolerance and prognosis after acute myocardial infarction: comparison of post-challenge versus fasting glucose concentrations," *Heart*, vol. 98, no. 11, pp. 848–854, 2012.

[24] C. Furtado de Souza, M. Dalzochio, F. J. de Oliveira, J. Gross, and C. Leitão, "Glucose tolerance status is a better predictor of diabetes and cardiovascular outcomes than metabolic syndrome: a prospective cohort study," *Diabetology & Metabolic Syndrome*, vol. 4, no. 1, p. 25, 2012.

[25] F. Ning, L. Zhang, J. M. Dekker et al., "Development of coronary heart disease and ischemic stroke in relation to fasting and 2-hour plasma glucose levels in the normal range," *Cardiovascular Diabetology*, vol. 11, no. 1, p. 76, 2012.

[26] L. Henareh and S. Agewall, "2-h postchallenge plasma glucose predicts cardiovascular events in patients with myocardial infarction without known diabetes mellitus," *Cardiovascular Diabetology*, vol. 11, no. 1, p. 93, 2012.

[27] G. Silbernagel, H. Souri, T. B. Grammer et al., "Isolated post-challenge hyperglycaemia predicts increased cardiovascular mortality," *Atherosclerosis*, vol. 225, no. 1, pp. 194–199, 2012.

[28] B. Capaldo, P. Di Bonito, M. Iaccarino et al., "Cardiovascular characteristics in subjects with increasing levels of abnormal glucose regulation: the strong heart study," *Diabetes Care*, vol. 36, no. 4, pp. 992–997, 2013.

[29] M. Barzin, F. Hosseinpainah, R. Malboosbaf, F. Hajsheikholeslami, and F. Azizi, "Isolated post-challenge hyperglycaemia and risk of cardiovascular events: Tehran lipid and glucose study," *Diabetes & Vascular Disease Research*, vol. 10, no. 4, pp. 324–329, 2013.

[30] Z. Yang, X. Xing, J. Xiao et al., "Prevalence of cardiovascular disease and risk factors in the Chinese population with impaired glucose regulation: the 2007–2008 China national diabetes and metabolic disorders study," *Experimental and Clinical Endocrinology & Diabetes*, vol. 121, no. 6, pp. 372–374, 2013.

[31] S. Kuramitsu, H. Yokoi, T. Domei et al., "Impact of post-challenge hyperglycaemia on clinical outcomes in Japanese patients with stable angina undergoing percutaneous coronary intervention," *Cardiovascular Diabetology*, vol. 12, no. 1, p. 74, 2013.

[32] M. Lind, J. Tuomilehto, M. Uusitupa et al., "The association between HbA1c, fasting glucose, 1-hour glucose and 2-hour glucose during an oral glucose tolerance test and cardiovascular disease in individuals with elevated risk of diabetes," *PLoS One*, vol. 9, no. 10, Article ID e109506, 2014.

[33] V. Rütsinger, E. Tanoglidî, K. Malmborg et al., "Sustained prognostic implications of newly detected glucose abnormalities in patients with acute myocardial infarction: long-term follow-up of the glucose tolerance in patients with acute myocardial infarction cohort," *Diabetes and Vascular Disease Research*, vol. 12, no. 1, pp. 23–32, 2015.

[34] A. George, R. T. Bhatia, G. L. Buchanan et al., "Impaired glucose regulation of newly diagnosed diabetes mellitus diagnosed during admission adversely affects prognosis after myocardial infarction: an observational study," *PLoS One*, vol. 10, no. 11, Article ID e0142045, 2015.

[35] S. Faghihi-Kashani, F. Bonnet, N. Hafezi-Nejad et al., "Fasting hyperinsulinaemia and 2-h glycaemia predict coronary heart disease in patients with type 2 diabetes," *Diabetes & Metabolism*, vol. 42, no. 1, pp. 55–61, 2016.

[36] B. Shahim, D. De Bacquer, G. De Backer et al., "The prognostic value of fasting plasma glucose, two-hour postload glucose, and HbA1c in patients with coronary artery disease: a report from EUROASPIRE IV," *Diabetes Care*, vol. 40, no. 9, pp. 1233–1240, 2017.

[37] M. L. Nielsen, M. Pareek, M. Leösdottir, K.-F. Eriksson, P. M. Nilsson, and H. M. Olsen, "One-hour glucose value as a long-term predictor of cardiovascular morbidity and mortality: the Malmö preventive project," *European Journal of Endocrinology*, vol. 178, pp. 225–236, 2018.

[38] S. Chattopadhyay, A. George, J. John, and T. Sathyapalan, "Two-hour post-challenge glycaemia is a better predictor of adverse outcome after myocardial infarction than fasting or admission glucose in patients without diabetes," *Acta Diabetologica*, vol. 55, no. 5, pp. 449–458, 2018.

[39] S. Chattopadhyay, A. George, J. John, and T. Sathyapalan, "Adjustment of the GRACE score by 2-hour post-load glucose improves prediction of long-term major adverse cardiac events in acute coronary syndrome in patients without known diabetes," *European Heart Journal*, vol. 39, no. 29, pp. 2740–2745, 2018.

[40] T. V. Fiorentino, E. Succurro, F. Andreozzi, A. Sciacqua, F. Perticone, and G. Sesti, "One-hour post-load hyperglycemia combined with HbA1c identifies individuals with higher risk of cardiovascular diseases: cross-sectional data from the CATAMERI study," *Diabetes/Metabolism Research and Reviews*, vol. 35, no. 2, Article ID e0396, 2019.

[41] S. Chattopadhyay, A. George, J. John, and T. Sathyapalan, "Pre-diabetes mellitus newly diagnosed after myocardial infarction adversely affects prognosis in patients without known..."
is fasting glucose sufficient to define diabetes? Epidemiological data from 20 European studies. The DECODE-study group. European Diabetes Epidemiology Group. Diabetes Epidemiology: Collaborative analysis of diagnostic criteria in Europe," *Diabetologia*, vol. 42, pp. 647–654, 1999.

[43] M. Hanefeld, C. Koehler, F. Schaper, K. Euecker, E. Henkel, and T. Temelkova-Kurtchseiw, "Postprandial plasma glucose is an independent risk factor for increased carotid intima-media thickness in non-diabetic individuals," *Atherosclerosis*, vol. 144, no. 1, pp. 229–235, 1999.

[44] R. H. Mackey, K. Sutton-Tyrrell, P. V. Vaitkevicius et al., "Correlates of aortic stiffness in elderly individuals: a sub-group of the cardiovascular health study," *American Journal of Hypertension*, vol. 15, no. 1, pp. 16–23, 2002.

[45] M. Hanefeld, "Postprandial hyperglycaemia: noxious effects on the vessel wall," *International Journal of Clinical Practice. Supplement*, vol. 129, pp. 45–50, 2002.

[46] H. v. Bibra, T. Siegmund, A. Ceriello, M. Volozhyna, and P.-M. Schumm-Draeger, "Optimized postprandial glucose control is associated with improved cardiac/vascular function—omparison of three insulin regimens in well-controlled type 2 diabetes," *Hormone and Metabolic Research*, vol. 41, no. 02, pp. 109–115, 2009.

[47] L. Xu, C. Q. Jiang, T. H. Lam et al., "Impact of impaired fasting glucose and impaired glucose tolerance on arterial stiffness in an older Chinese population: the Guangzhou Biobank Cohort Study-CVD," *Metabolism*, vol. 59, no. 3, pp. 367–372, 2010.

[48] A. Sciacqua, S. Miceli, G. Carullo et al., "One-hour postload plasma glucose levels and left ventricular mass in hypertensive patients," *Diabetes Care*, vol. 34, no. 6, pp. 1406–1411, 2011.

[49] C. H. Li, J. S. Wu, Y. C. Yang, C. C. Shih, F. H. Lu, and C.-J. Chang, "Increased arterial stiffness in subjects with impaired glucose tolerance and newly diagnosed diabetes but not isolated impaired fasting glucose," *The Journal of Clinical Endocrinology & Metabolism*, vol. 97, no. 4, pp. E658–E662, 2012.

[50] A. Sciacqua, R. Maio, S. Miceli et al., "Association between one-hour post-load glucose levels and vascular stiffness in essential hypertension," *PLoS One*, vol. 7, no. 9, Article ID e44470, 2012.

[51] I. Kowalska, M. Straczkowski, M. Szlachowska et al., "Circulating E-selectin, vascular cell adhesion molecule-1, and intercellular adhesion molecule-1 in men with coronary artery disease assessed by angiography and disturbances of carbohydrate metabolism," *Metabolism*, vol. 51, no. 6, pp. 733–736, 2002.

[52] G. Derosa, A. D’Angelo, S. A. T. Salvadeo et al., "Oral glucose tolerance test effects on endothelial inflammation markers in healthy subjects and diabetic patients," *Hormone and Metabolic Research*, vol. 42, no. 1, pp. 8–13, 2010.

[53] E. Mah, S. K. Noh, K. D. Ballard, M. E. Matos, J. S. Volek, and R. S. Bruno, "Postprandial hyperglycemia impairs vascular endothelial function in healthy men by inducing lipid peroxidation and increasing asymmetric dimethylarginine:arginine," *The Journal of Nutrition*, vol. 141, no. 11, pp. 1961–1968, 2011.

[54] D. E. Maessen, N. M. Hanssen, J. L. Scheijen et al., "Post-glucose load plasma a-dicarbonyl concentrations are increased in individuals with impaired glucose metabolism and type 2 diabetes: the CODAM study," *Diabetes Care*, vol. 38, no. 5, pp. 913–920, 2015.