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Research Article

Glucose: An Ongoing Risk Factor for Myocardial Infarction

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Abstract

Background: Myocardial infarction (MI) remains a major cause of mortality and morbidity around the world. Evidence on the relationship between diabetes mellitus (DM), glucose (Glu), and MI remains limited. This study aimed to examine the association between high blood glucose in participants with the acute coronary syndrome (ACS), chronic coronary syndrome (CCS), and MI.

Method: A total of 239 samples were collected including 70 healthy individuals, 70 patients with ACS, 70 patients with CCS, and 29 patients who had suffered a MI. The Pearson correlation test was used to evaluate the significance of the relationship between clinical parameters and MI, and the one-way ANOVA test was performed to analyse the significant differences between the study groups. Statistical significance was determined by P-values less than 0.05.

Results: In Patients groups compared to healthy, there were significant differences in high-density lipoprotein (HDL), Glu, Total Cholesterol (TC), age, Systolic blood pressure (SBP), DM, and hypertension ($p < 0.05$). Additionally, the patient group had a higher Glu level and a larger ratio of DM patients than the healthy group, which may have contributed to the development of MI.

Conclusion: In conclusion, DM and elevated blood Glu levels are linked to the onset of MI. To confirm our findings, a larger cohort study is required in the future.

Keywords: Glucose; Diabetes Mellitus; Myocardial Infarction; Acute Coronary Syndrome; Chronic Coronary Syndrome.

Introduction

The statistical report of the American Heart Association, updated in 2021, indicates that CVD is associated with substantial global health and economic burden [1]. The incidence and mortality of coronary heart disease (CHD) are also increasing and have become the key cause of death and disease in China [2-3]. Coronary atherosclerosis, as the basis of CHD, usually occurs concurrently with carotid atherosclerosis [4]. Coronary atherosclerosis is the basis of coronary artery stenosis, in which abnormal lipid metabolism, the coagulation system, inflammatory factor stimulation, and other risk factors damage endothelial cells promoting an inflammatory reaction and lipid deposition, thus, accelerating plaque formation [5-6]. Studies have shown that peripheral vascular atherosclerosis is predictive of CVD with the

highest mortality rates [7-8].

Although diabetes is a known risk factor for CAD, however, the risk of higher blood glucose in diabetes is unclear [9-10]. Pathologic consequences from modest elevations of glucose are plausible since impaired glucose tolerance and impaired fasting glucose have been associated with macrovascular disease and greater mortality 11. Patients presenting with ACS frequently have glucose intolerance [12], and it has been reported that glucose intolerance, but not impaired fasting glucose could be associated with CAD [13]. In contrast, meta-analysis indicates that glucose above a threshold of 100 mg/dl may also be a significant risk [14]. Since impaired fasting glucose is increasingly common, affecting >35 million adults in the United States [15], and CAD affects a majority of older adults, associations between these common, morbid, and potentially fatal conditions are of clinical importance.

Adverse consequences from hyperglycaemia may reflect the effects of glucose as well as hyperinsulinemia. Glycaemic effects include elevations in reactive oxygen species and the formation of advanced glycation products [16]. Hyperinsulinemia has been associated with mitogenic effects on vascular smooth muscle cells [17]. Because elevated blood glucose is a common and potentially treatable condition, characterization of whether higher blood glucose may contribute to CAD is of clinical consequence [18].

The goal of the current investigation was to ascertain whether increasing blood sugar levels in diabetics enhance the risk of MI. The significance of glucose and other clinical variables were assessed using different test between hyperglycaemia and other CAD risk factors such as age, obesity, hypertension, and hyperlipidaemia.

Materials and Methods

Ethics Statement

The study was approved on 13 May 2021 by the Ethics Committee of Northwest Minzu University and the Gansu Provincial People's Hospital (Approval No: XBMZ-YX-2021008), both in Lanzhou, China. All participants were informed of the study's purpose and provided informed consent following the Declaration of Helsinki.

Recruitment of Patients and Volunteers

The diagnostic records of the patients were collected from June 2021 to September 2021 from the cardiology ward, of the Gansu provincial hospital while the healthy volunteers were selected from the Physical examination centre Lanzhou Second hospital, Lanzhou City, Gansu Province, China. A total of 239 subjects were examined in this study including (70 healthy individuals, 70 ACS, 70 CCS, and 29 MI patients). A flow chart of the patient selection process is shown in (Figure 1). All patients and healthy subjects completed questionnaires that included information.

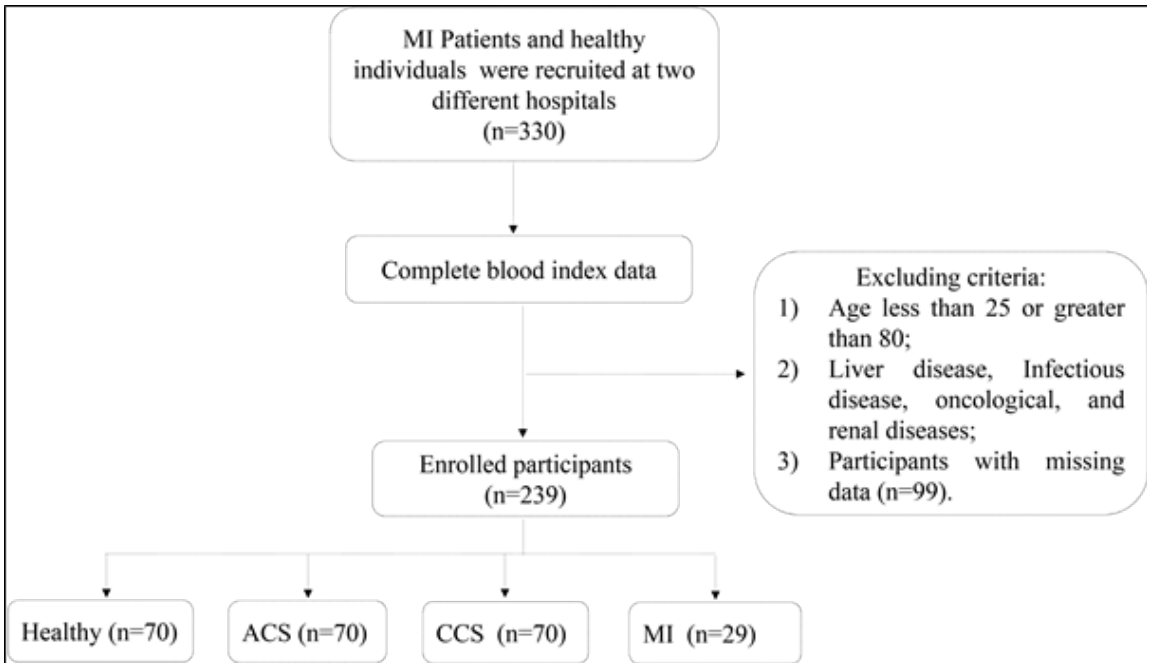

Figure 1: Flow chart of the study.

Excluding Criteria

Patients without MI, ACS, and CCS, age less than 25 years, infectious disease within 1 week before the inclusion, immunocompromised patients, antibiotic treatment within 1 month before the inclusion, chronic viral infection including (hepatitis B and C, human immunodeficiency virus (HIV), human T-lymphotropic virus (HTLV), cytomegalovirus (CMV), syphilis, Chagas disease, and malaria), typed, intestinal bowel disease, renal failure, and pregnancy or the subject with missing data were excluded.

Blood Samples Collection

Fasting venous blood samples were obtained from all participants on the second day of hospitalization. Clinically certified team members drew blood samples in Vacutainer EDTA Blood Collection Tubes. Reagents and materials were disinfected and wore lab clothes, masks, and disposable gloves to avoid contamination of foreign DNA. For each volunteer 3 ml blood sample was collected in the morning following overnight fasting conditions. Plasma was collected by centrifugation and stored at -80°C until further process.

Clinical data collection

All subject's demographic and clinical data were recorded by trained medical staff. This included information on age, sex, smoking, drinking, medical history, and prior medication history, all of which were investigated using a standard structured questionnaire. SBP and diastolic blood pressure (DBP) were measured by trained physicians using an electronic device. Hypertension was defined as an elevated SBP ≥ 130 mmHg or a DBP ≥ 80 mmHg 29. The levels of Glu, TC, TG, HDL, and LDL were measured directly by an automatic haematology analyser. Quality control was conducted by the laboratory according to standard procedures.

Statistical Analyses

Descriptive data were expressed as mean values and percentages for continuous variables and frequencies for categorical variables. One-way ANOVA and Tukey's multiple comparisons post-hoc tests were used for clinical parameters such as HDL, LDL, TG, GLU, TC, SBP, and DBP. The correlation between healthy and disease groups was assessed by using the Pearson correlation. All the statistical analysis of clinical data was conducted using Prism version 9.0, and R studio. P-values of less than 0.05 were regarded as statistically significant.

Results

Baseline characteristics of the studied groups

A total of 239 volunteers were included in this study, including 173 males, and 66 females, ranging in age from 25 to 80 years. All patients experienced ACS, CCS, and MI. The clinical indexes such as age, gender, and body mass index (BMI) were compared between four groups Table 1. The patients with MI, ACS, and CCS were older than healthy individuals (59 ± 13; 61.18 ± 12.1; 62.58 ± 11.16; 41.2 ± 10.1). Based on a one-way ANOVA test significant differences were found in Age, BMI, SBP, HDL, fasting blood glucose, TC, hypertension, DM, and smoking among groups ($p < 0.05$). The remaining variables such as sex, DBP, TG, and LDL were not statistically significantly different among all groups ($p < 0.05$).

Variables	Healthy (n= 70)	ACS (n= 70)	CCS (n= 70)	MI (n= 29)
Age (years)	**41.2 ± 10.1**	**61.18 ± 12.1**	**62.58 ± 11.16**	**59 ± 13**
Sex (male/female)	**44/26**	**55/15**	**51/19**	**23/6**
Body mass index (kg/cm^2)	**24.37 ± 3.80**	**23.75 ± 2.94**	**25.97 ± 3.05**	**24.92 ± 3.95**
Systolic blood pressure (mmHg)	**118.85 ± 15.32**	**131.58 ± 20.08**	**127.6 ± 20.91**	**122.8 ± 25.84**
Diastolic blood pressure (mmHg)	**74.21 ± 11.78**	**78.42 ± 11.94**	**74.94 ± 15.22**	**71.55 ± 15.97**
Smoking (yes/no)	**17/53**	**13/57**	**21/49**	**15/14**
Diabetes mellitus (yes/no)	**3/67**	**20/50**	**21/ 49**	**4/25**
Hypertension	**128.81 ± 14.46**	**141.18 ± 18.30**	**136.64 ± 27.59**	**141.8 ± 19.31**
Triglycerides (mmol/L)	**1.64 ± 1.06**	**1.71 ± 1.17**	**1.71 ± 0.89**	**1.52 ± 0.83**
High-density lipoprotein (mmol/L)	**1.12 ± 0.30**	**0.97 ± 0.19**	**1.06 ± 0.25**	**1.06 ± 0.24**
Low-density lipoprotein (mmol/L)	**2.40 ± 0.71**	**2.49 ± 0.85**	**2.36 ± 1.34**	**2.70 ± 1.13**

Blood Glucose (mmol/L)	**5.17 ± 0.57**	**7.55 ± 3.87**	**7.11 ± 2.68**	**8.05 ± 2.20**
Total cholesterol (mmol/L)	**4.14 ± 0.73**	**3.66 ± 1.36**	**3.70 ± 0.98**	**3.93 ± 1.09**

Table 1: General characteristics of acute coronary syndrome, chronic coronary syndrome, myocardial infarction, and Healthy groups.

The values are presented as mean ± SD and numbers. **Abbreviations:** ACS, acute coronary syndrome; CCS, chronic coronary syndrome; n, number.

Comparison of clinical factors among four groups

The clinical characteristics of all groups were compared in (Table 2), including age, followed by sex, height, weight, BMI, SBP, DBP, smoking, DM, hypertension, TG, HDL, LDL, and TC.

Healthy vs ACS

One-way ANOVA analysis of clinical variables in the ACS patients group showed that age, SBP, hypertension, DM, HDL, blood glucose, and TC were significantly different between ACS and healthy groups. The results showed that the patients with ACS were older than the healthy group, also a significantly higher ratio of patients with hypertension, and DM was observed in the patient's group. In addition, the SBP and blood Glu were found significantly higher in the patient's group than in the healthy group ($p > 0.05$), however, the HDL and TC levels were observed significantly lower in the patients' group than in the healthy. P-values of less than 0.05 were considered statistically significant.

Healthy vs CCS

Comparing the clinical characteristics of healthy and CCS groups showed that the age, BMI, DM, and Glu were significantly different between both groups. The CCS patients were found older than healthy individuals, also a high level of glucose was observed in patients in the ACS group ($p < 0.05$). In addition, a high ratio of DM patients was observed in the CCS group.

Healthy vs MI

We further measured and compared the clinical parameters between healthy MI groups. Our study found significant differences between Age, smoking, DM, and Glu levels between healthy and MI groups. The patients with MI were older than healthy individuals, also the ratio of smokers, patients with DM, and a higher level of glucose were observed in patients in the MI group. Statistical significance was considered as P-values less than 0.05.

Characteristics	Healthy vs ACS	Healthy vs CCS	Healthy vs MI
Age	**0.000***	**0.000***	**0.000***
Sex	0.16	0.54	0.34
Body mass index	0.70	**0.02***	0.88
Systolic blood pressure	**0.001**	0.49	0.79
Diastolic blood pressure	0.25	0.98	0.80
Smoking	0.86	0.86	**0.02***
Hypertension	**0.003***	0.11	**0.02***
Diabetes mellitus	**0.001***	**0.001***	0.68
Triglycerides	0.98	0.97	0.95
High-density lipoprotein	**0.003***	0.51	0.72
Low-density lipoprotein	0.95	0.99	0.56
Blood Glucose	**0.000***	**0.001***	**0.000***
Total cholesterol	**0.04***	0.08	0.81

Table 2. P-values across ACS, CCS, MI, and Healthy groups.

P-values were shown among four groups by comparing their clinical characteristics using the One-way ANOVA test. The significant difference was mentioned in bold font with a star. P-values less than 0.05 were considered statistically significant.

Correlation analysis factors affecting the prognosis of patients with ACS, CCS, and MI

We further calculated all prognostic risk variables for ACS, CCS, and MI using Pearson correlation analysis. The association of all clinical variables was evaluated among groups.

Healthy vs ACS groups

Further investigation between clinical factors of healthy and ACS groups was done. The negative correlation of BMI with age, TG with TC, A negative correlation between BMI and Glu with DM, while the positive correlation of BMI with weight, SBP with diastolic blood pressure, hypertension, LDL and HDL, and LDL with TC were observed in ACS group, shown in (Figure 2). P-values less than 0.05 were considered statistically significant.

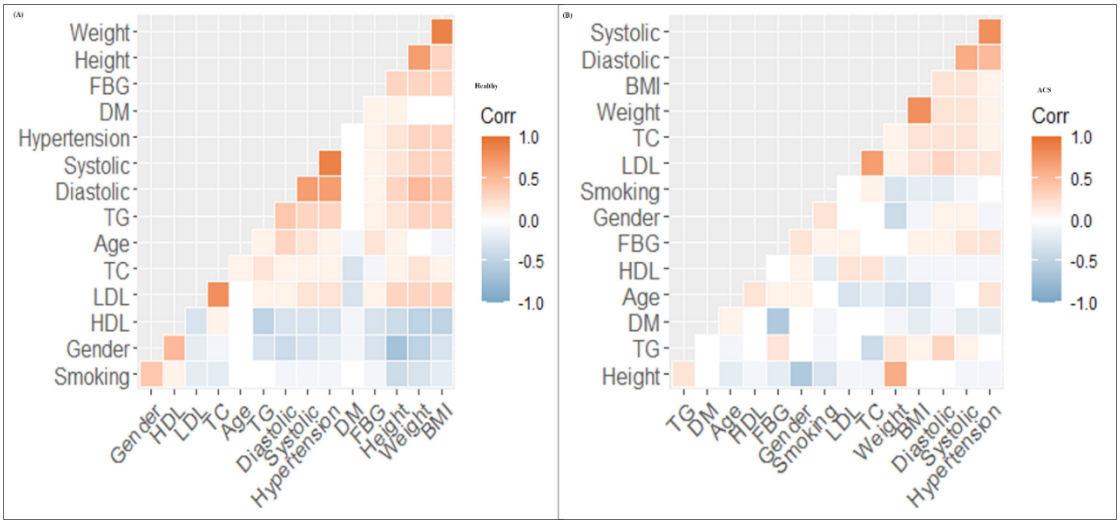

Figure 2: Represent the correlation among clinical variables between each other of healthy and ACS groups.

Abbreviations: FBG, fasting blood glucose; DM, diabetes mellitus; TG, triglycerides; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Healthy vs CCS groups

The results between healthy and CCS groups showed a negative correlation between DM with Glu, HDL with BMI, and TG, although a positive correlation was observed between BMI with TG, SBP with DBP, hypertension, and TG, and LDL with TC in patients with CCS group (Figure 3). Statistics were considered significant with P-values below 0.05.

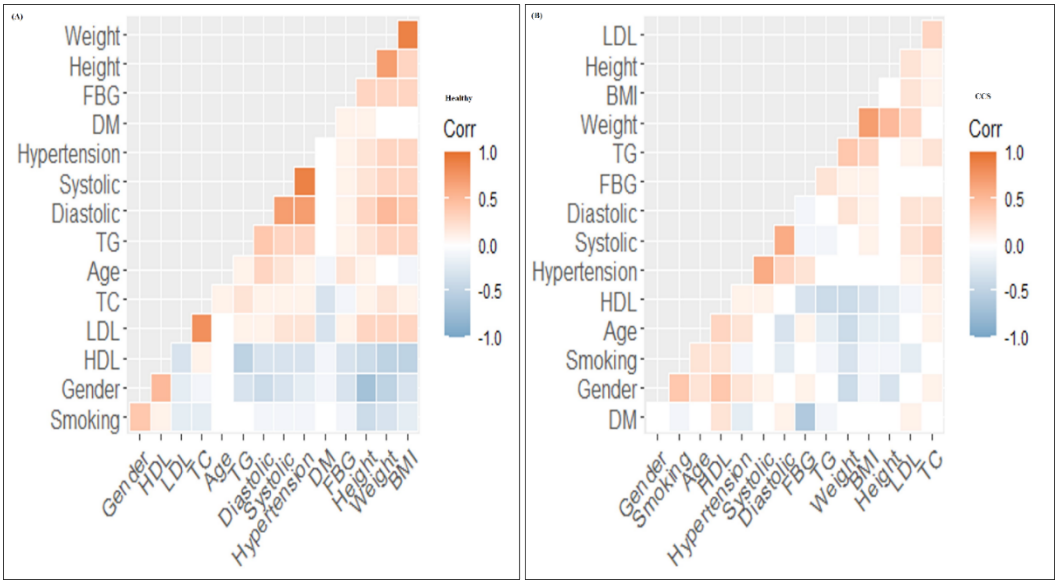

Figure 3: Shows the correlation among clinical variables between each other healthy and CCS groups.

Healthy vs MI groups

Furthermore, the results of the Healthy and MI groups revealed a negative correlation between Age with LDL, while the positive association between gender with smoking, SBP with DBP, and LDL with HDL were observed in the MI group, depicted in (Figure 4).

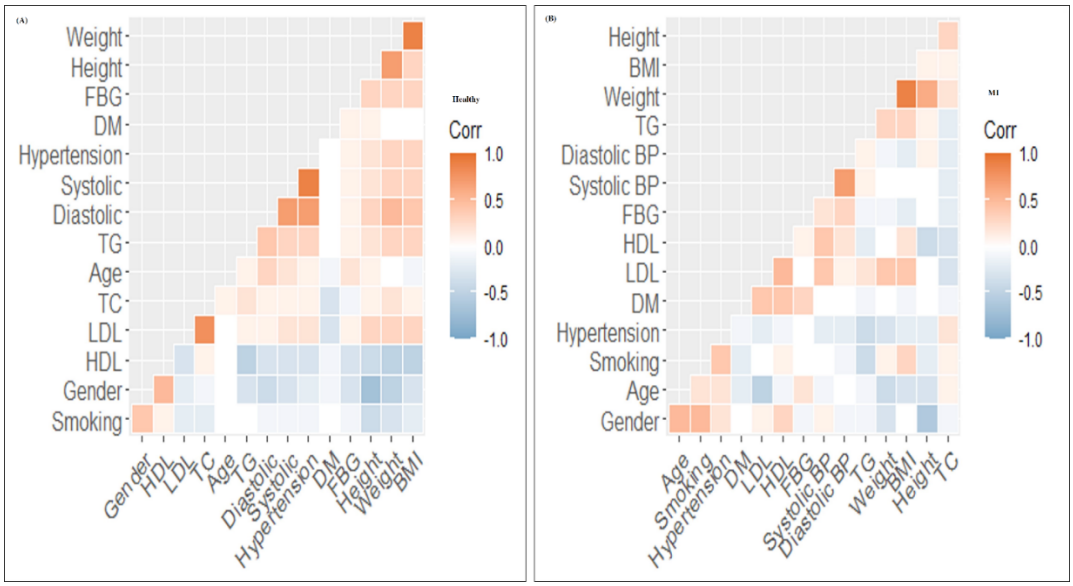

Figure 4: Demonstrates the relationship between the clinical parameters of the healthy and MI groups.

Abbreviations: FBG, fasting blood glucose; DM, diabetes mellitus; TG, triglycerides; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Discussion

Disruption of glucose and MI have been suspected to be related for many years [19-20]. A previous study found that glucosuria and high blood Glu levels are common in patients with AMI [21-22]. The most likely cause of the observed high glucose was an increase in Glu apparently due to adrenergic stress during the acute phase of MI, resulting in temporarily disrupted carbohydrate metabolism with hyperglycaemia related to the severity of the infarction [23-24]. However, subsequent investigations have not confirmed this as the prime cause. Another early finding suggested that the relationship between increasing blood glucose levels and increasing cardiovascular risk existed continuously and began even at blood glucose levels that were currently recommended diagnostic criteria for normal [25]. A recent meta-analysis of 102 studies, including 698,782 individuals, 8.49 million person-years at risk, and 52,765 fatal or non-fatal outcomes, provided strong support for this hypothesis. Based on the analyses, patients with a known history of diabetes had an adjusted hazard ratio of 2.00 (95% CI 1.83-2.19) for non-fatal and fatal CHD, 2.27 (1.95-2.65) for non-fatal and fatal ischemic stroke, and 1.73 (1.51-1.98) for the total number of other vascular deaths [26]. The risk ratios for CHD were higher in women than in men, higher in people aged 40 to 59 compared to people older than 70, higher in people with the lowest tertial than the highest tertial of SBP, and higher for fatal than non-fatal events [27-28]. Additionally, a relationship between fasting glucose and vascular risk was present at a level of 5.6 mmol/L [26,29]. Even after the information derived from several conventional risk factors was added, this relationship persisted. As a result, people who are already at a lower risk due to other factors seem to be particularly affected by rising blood glucose levels.

For decades, researchers have been interested in the connection between glucose abnormalities (impaired glucose tolerance and T2D) and ACS (AMI and unstable angina) [29-30]. Early studies were less reliable when examining the possible correlation between hyperglycaemia and acute coronary events because of some limitations [31]. A small number of patients were examined in these studies using either oral or intravenous glucose tolerance tests on selected populations [32]. The tests, which were not repeated over time, were carried out when there were no established diagnostic standards for diabetes and impaired glucose tolerance. The Glu and MI study was carried out on 181 patients with acute MI but without any previously known glucose perturbations to further explore this relationship [29]. Before being allowed to leave the hospital, or roughly five days after the start of the symptoms, they were all required to take an oral glucose tolerance test. Only 33% of the patients in this group had completely normal glucose tolerance, according to the test, while 35% had impaired glucose tolerance and 31% had type 2 diabetes that had gone undiagnosed [33-34]. The Euro Heart and China Heart Surveys later confirmed these findings, recruiting both stable and unstable CAD patients. Both studies found that the majority of patients without a history of glucose perturbations did have abnormal glucose metabolism, which is primarily made up of newly discovered diabetes and impaired glucose tolerance in ratios that are roughly similar to those found in the Glu and MI trial [35-36]. In 4961 patients with CAD who were recruited for the Euro Heart Survey on Diabetes and the Heart at 110 centres in 25 European countries, 31% had known diabetes, 12% had newly detected diabetes, 25% had impaired glucose tolerance, and 3% had impaired fasting glucose, leaving only 29% with normal glucose regulation [37]. Later, it was observed that patients with peripheral and cerebral vascular disease displayed a similar pattern [38]. The latter investigation, like the Glu and MI study, compared outcomes in patients with CAD with healthy, age- and sex-matched individuals from the general population, of whom approximately 65% had normal glucose regulation, 24% had impaired glucose tolerance, and 11% had diabetes [39]. This demonstrates unequivocally that there is a significant relationship between these two conditions and that people with CVD are very likely to have diabetes and prediabetes [35]. Observations from the Euro Heart Survey on Diabetes and the Heart also showed that without an oral glucose tolerance test, a sizable portion of patients with diabetes and impaired glucose tolerance would have gone undiagnosed [29,40]. The importance of detecting glucose perturbation is strongly underscored by the fact that patients with normal glucose tolerance have a considerably better outcome during follow-up than those with abnormal glucose metabolism.

Strengths and limitations

The study successfully revealed the significant association between higher plasma glucose levels and DM with CVD. There are still some limitations in this study. First, this study is a single-centre observational study. Due to the small size of patients' clinical characteristics, the results of this study need to be verified by a multi-centre study. In addition, further long-term follow-up studies are needed to understand the effect of plasma glucose levels on long-term prognosis.

Conclusion

To summarize the current state of knowledge, it can be said that screening for Glu perturbations in patients with CAD provides information crucial for patient management, that oral Glu tolerance testing is necessary when screening patients with CVD for Glu perturbations and that screening for Glu perturbations in patients with diabetes and prediabetes is very common [41]. Despite being acknowledged in current management guidelines for patients with diabetes and cardiovascular disease and despite a

growing understanding of the significance of glycemia, the medical community has been reluctant to diagnose prediabetic conditions, and the implementation of guideline recommendations is far from being completed.

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Ethics Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Medical Ethics Committee of Northwest Minzu University, Gansu, China. Informed consent was obtained from all subjects involved in the study.

Conflict of Interest

The authors declared that they have no conflict of interest.

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