Type of discrepancy between glycosylated hemoglobin and fasting plasma glucose is associated with in-hospital outcomes in patients with acute coronary syndrome and diabetes: findings from the Improving Care for Cardiovascular Disease in China - Acute Coronary Syndrome (CCC-ACS) Project

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Research

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Abstract

Background

The aim of this study is to investigate the association between types of discrepancy between glycosylated hemoglobin (HbA1c) and fasting plasma glucose (FPG) and in-hospital outcomes in patients with acute coronary syndrome (ACS) and diabetes, based on Improving Care for Cardiovascular Disease in China - acute coronary syndrome project.

Methods

CCC-ACS project is a national, hospital-based quality improvement project. Patients with ACS, diabetes and complete HbA1c and FBG value at admission were included in this study. Patients were divided into consistent group and discrepancy group based on the HbA1c and FBG value at admission. Consistent group included patients with HbA1c < 6.5% and FBG < 7.0 mmol/L, or patients with HbA1c $\geq$ 6.5% and FBG $\geq$ 7.0 mmol/L. Discrepancy group included patients with HbA1c $\geq$ 6.5% and FBG < 7.0 mmol/L, or patients with HbA1c < 6.5% and FBG $\geq$ 7.0 mmol/L. Discrepancy group was further divided into increased HbA1c group (HbA1c $\geq$ 6.5% and FBG < 7.0 mmol/L) and increased FBG group (HbA1c < 6.5% and FBG $\geq$ 7.0 mmol/L).

Results

A total of 7,762 patients were included in this study. Patients in consistent group and discrepancy group were 5,490 (70.7%) and 2,272 (29.3%) respectively. In discrepancy group, increased HbA1c group accounted for 77.5% (1,761/2,272), and increased FPG group accounted for 22.5% (511/2,272). After adjusting for confounders by multivariate logistic regression model, patients in increased FPG group had a significantly 1.6-fold increased risk of heart failure (OR, 1.62; 95% CI, 1.08-2.44), a 1.6-fold increased risk of composite of cardiovascular death and heart failure (OR, 1.63; 95% CI, 1.09-2.43), and a 1.6-fold increased risk of composite of MACCE and heart failure (OR, 1.56; 95% CI, 1.08-2.24).

Conclusions

Patients with an increased level of FPG but normal HbA1c had a higher risk of in-hospital cardiovascular adverse outcomes than those with an increased level of HbA1c but normal FPG. These patients should be given more attention and closer monitoring in clinical practice in order to improve the in-hospital outcomes.

1. Introduction

Cardiovascular disease is the leading cause of both death and premature death in China, being the cause of 40% of deaths in the Chinese population [1]. Acute coronary syndrome (ACS) is an acute manifestation of cardiovascular disease with a high risk of mortality, which can lead to critical conditions such as cardiogenic shock and cardiac arrest. Patients with ACS and diabetes usually have worse clinical

outcomes than those with normal blood glucose [2–8], regardless of in-hospital or long-term outcomes. Indicators commonly used for evaluating blood glucose include intravenous blood glucose, glycosylated hemoglobin (HbA_{1c}), and glycosylated serum albumin. Intravenous blood glucose was firstly used in the diagnosis of diabetes, including fasting plasma glucose (FPG), oral glucose tolerance test and random blood glucose. In 2013, the American Diabetes Association approved the use of HbA_{1c} to diagnose diabetes [9]. In addition to diagnostic value, FPG and HbA_{1c} are also associated with clinical outcomes. Several studies have shown that abnormal blood glucose is an important factor associated with clinical outcomes in patients with ACS and diabetes [10–17].

However, we noticed that some patients have a discrepancy between HbA_{1c} and FPG in clinical practice. This condition may be related to factors such as acute stress, renal dysfunction, anemia that may affect FPG and HbA_{1c}. It may be an increased FPG with normal HbA_{1c}, or an increased HbA_{1c} with normal FPG. We are confused that which one indicates worse in-hospital outcomes in this case, no matter what causes the discrepancy. There are few studies focusing on this issue.

The Improving Care for Cardiovascular Disease in China - Acute Coronary Syndrome (CCC-ACS) project is a national, hospital-based quality improvement project with an ongoing database, aiming to increase adherence to ACS guidelines in China and to improve patient outcomes. We conducted this study based on CCC-ACS project to investigate the types of discrepancy between HbA_{1c} and FPG and its relationship to in-hospital outcomes.

2. Methods

2.1 Research design

The datasets used and analyzed during the current study are available from the principal investigator of CCC-ACS on reasonable request. Details of the design and methodology of the CCC-ACS project have been published [18]. In briefly, it is a national, hospital-based quality improvement project with an ongoing database, aiming to increase adherence to ACS guidelines in China and to improve patient outcomes. It was launched in 2014 as a collaborative initiative of the American Heart Association and Chinese Society of Cardiology. 240 hospitals were recruited representing the diversity of ACS care in hospitals in China, including 150 tertiary hospitals in phase I and phase II, 82 secondary hospitals and 8 tertiary hospitals in phase III (from July 2017) and phase IV (from November 2018). Clinical data were collected via a web-based data collection platform (Oracle Clinical Remote Data Capture, Oracle Corporation). Trained data abstractors entered the data elements abstracted from medical charts. Eligible patients were consecutively reported to the CCC-ACS database for each month before the middle of the following month. Around 5% of reported cases were randomly selected and compared with the original medical records. An audit by a third party was performed to ensure that cases were reported consecutively rather than selectively.

2.2 Research population

A total of 104,516 inpatients with ACS, identified using their principal diagnosis at discharge, were enrolled from 240 hospitals across China from November 2014 to December 2019. Patients with diabetes and complete HbA_{1c} and FPG value at admission were included in this study. Only patients from July 2017 to December 2019 were included in this study because that the FPG value at admission was not included in the database before July 2017. Patients were divided into consistent group and discrepancy group based on the HbA_{1c} and FPG value at admission. Consistent group included patients with HbA_{1c} < 6.5% and FPG < 7.0 mmol/L, or patients with HbA_{1c} ≥ 6.5% and FPG ≥ 7.0 mmol/L. Discrepancy group included patients with HbA_{1c} ≥ 6.5% and FPG < 7.0 mmol/L, or patients with HbA_{1c} < 6.5% and FPG ≥ 7.0 mmol/L. Discrepancy group was further divided into increased HbA_{1c} but normal FPG group (HbA_{1c} ≥ 6.5% and FPG < 7.0 mmol/L) and increased FPG but normal HbA_{1c} group (HbA_{1c} < 6.5% and FPG ≥ 7.0 mmol/L). Institutional review board approval was granted for the aggregate data set for research and quality improvement by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. No informed consent was required.

2.3 Definition of variables

diabetes was defined as having a history of diabetes, or receiving glucose-lowering agents before hospitalization, or diabetes listed in the medical records as the secondary discharge diagnosis, or HbA_{1c} ≥ 6.5% at admission. Hypertension was defined as having a history of hypertension, or receiving antihypertensive medication, or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg at admission. The ACS classification was based on the primary diagnosis of discharge in the medical record. Non-ST-segment elevation ACS (NSTEMI) was defined as non-ST-segment elevation myocardial infarction (STEMI) or unstable angina. All the laboratory testing values were the values tested first time after admission. The estimated glomerular filtration rate (eGFR) was calculated according to the equation developed by the Chronic Kidney Disease Epidemiology Collaboration [19]. The medication was prescribed after admission.

2.4 In-hospital outcomes

The outcomes of this study included major adverse cardiovascular and cerebrovascular event (MACCE), heart failure, composite of cardiovascular death and heart failure, composite of MACCE and heart failure, and death from any cause. MACCE was defined as cardiovascular death, cardiac arrest, cardiogenic shock, recurrent myocardial infarction, stent thrombosis, and stroke.

2.5 Statistical analysis

Continuous variables were presented as mean and standard deviation (SD) or median and interquartile range (IQR) when distribution and variance met the conditions. The categorical variables were presented as a percentage. The comparison between groups of continuous variables was performed by unpaired t-test or Mann-Whitney U test (Kruskal-Wallis), and the chi-square test was used to compare the categorical variables. Multivariate logistic regression model was used to determine the association between the types of discrepancy and in-hospital outcomes by controlling potentially confounders. Candidate adjustment

factors included age, gender, blood pressure, heart rate, eGFR, hemoglobin, heart function, type of ACS, medical history, glucose-lowering drug use, in-hospital management, and referral status. The heterogeneity of effects on the in-hospital outcomes across subgroups was estimated using random effects meta-analysis. For data with missing value less than 15% (Additional file 1: Table S1), sequential regression multiple imputation method implemented by IVEware software version 0.2 (Survey Research Center, University of Michigan, Ann Arbor, MI, USA) was used to impute the missing value. All P values were 2-tailed and a $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS 23.0 (SPSS Inc., Chicago, IL) and Stata/IC 15.1.

3. Results

3.1 Characteristics of patients in discrepancy group

A total of 7,762 patients were included in this study (Additional file 1: Fig. S1). The mean age was 64.4 (± 11.6) years, males accounted for 68.8%. The mean hemoglobin was 135.1 (± 21.3) g/L and mean eGFR was 81.7 (± 25.4) ml min⁻¹ (1.73 m)⁻². 53.3% of patients were treated with at least one class of oral glucose-lowering drug or insulin. The patients in consistent group and discrepancy group were 5,490 (70.7%) and 2,272 (29.3%) respectively. Patients in discrepancy group were more likely to have lower eGFR (Additional file 1: Fig. S2). In discrepancy group, increased HbA_{1c} but normal FPG group accounted for 77.5% (1,761/2,272), and increased FPG but normal HbA_{1c} group accounted for 22.5% (511/2,272). The baseline characteristics for patients in increased HbA_{1c} but normal FPG group and increased FPG but normal HbA_{1c} group were shown in Table 1. Patients in increased FPG but normal HbA_{1c} group were more likely to have lower eGFR, higher heart rate, poorer heart function, have STEMI and hypertension, and be treated with glucose-lowering agents.

Table 1
Characteristics of patients with discrepancy between HbA_{1c} and FPG.

	Increased HbA _{1c} group (n = 1761)	Increased FPG group (n = 511)	P value
Age (years, mean [SD])	65.4(11.2)	65.4(10.9)	0.947
Male (n [%])	1184(67.2)	348(68.1)	0.713
Systolic blood pressure (mmHg, mean [SD])	135.0(22.8)	135.0(25.2)	0.895
Diastolic blood pressure (mmHg, median [IQR])	78.0(70.0, 87.0)	78.0(70.0, 89.0)	0.442
Heart rate (bpm. Median [IQR])	78.0(68.0, 87.0)	80.0(70.0, 90.0)	< 0.001
Current smoker (n [%])	508(28.8)	153(29.9)	0.047
Family history of CHD (n [%])	71(4.0)	21(4.1)	0.937
Hypertension (n [%])	1300(73.8)	403(78.9)	0.021
Previous acute myocardial infarction (n [%])	214(12.2)	58(11.4)	0.623
Previous coronary artery bypass grafting (n [%])	16(0.9)	4(0.8)	0.789
Atrial fibrillation history (n [%])	53(3.0)	14(2.7)	0.751
Heart failure history (n [%])	58(3.3)	19(3.7)	0.640
Cerebrovascular disease history (n [%])	185(10.5)	57(11.2)	0.675
Peripheral artery disease history (n [%])	31(1.8)	10(2.0)	0.769
Killip class (n [%])			0.289
I or II	1505(85.5)	427(83.6)	
III or IV	256(14.5)	84(16.4)	
Types of ACS (n [%])			< 0.001
STEMI	716(40.7)	276(54.0)	

HbA_{1c}, glycosylated hemoglobin; FPG, fasting plasma glucose; SD, standard deviation; IQR, interquartile range; CHD, coronary heart disease; ACS, acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation acute coronary syndrome; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; ACE, angiotensin-converting enzyme.

	Increased HbA _{1c} group (n = 1761)	Increased FPG group (n = 511)	P value
NSTE-ACS	1045(59.3)	235(46.0)	
HbA _{1c} (% , mean [SD])	8.2(14.7)	5.8(0.8)	< 0.001
FPG (mmol/L, mean [SD])	5.6(1.2)	9.5(2.6)	< 0.001
eGFR (ml min ⁻¹ [1.73m] ⁻² , mean [SD])	79.1(25.1)	76.4(27.3)	0.046
Hemoglobin (g/l, mean [SD])	132.1(20.4)	132.4(23.6)	0.192
Total cholesterol (mmol/L, median [IQR])	4.3(3.5, 5.1)	4.3(3.5, 5.1)	0.721
HDL-cholesterol (mmol/L, median [IQR])	1.0(0.8, 1.2)	1.0(0.8, 1.2)	0.931
LDL-cholesterol (mmol/L, median [IQR])	2.6(2.0, 3.2)	2.5(2.0, 3.2)	0.326
Triglyceride (mmol/L, median [IQR])	1.6(1.1, 2.4)	1.5(1.0, 2.3)	0.027
Oral glucose-lowering agents or insulin use before admission (n [%])	809(45.9)	288(56.4)	< 0.001
Therapy during hospitalization (n [%])			
Percutaneous coronary intervention	1170(66.4)	337(65.9)	0.836
Aspirin	1644(93.4)	482(94.3)	0.432
P2Y ₁₂ inhibitors	1603(91.0)	473(92.6)	0.276
Statins	1653(93.9)	477(93.3)	0.669
β-blockers	1146(65.1)	291(56.9)	0.001
ACE inhibitor/angiotensin receptor blocker	917(52.1)	248(48.5)	0.159
Patients with referral (n [%])	587(33.3)	172(33.7)	0.891
HbA _{1c} , glycosylated hemoglobin; FPG, fasting plasma glucose; SD, standard deviation; IQR, interquartile range; CHD, coronary heart disease; ACS, acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; ACE, angiotensin-converting enzyme.			

The proportion of increased FPG but normal HbA_{1c} group was higher in patients with age over 65 years, hemoglobin less than 120 g/L, eGFR less than 60 ml min⁻¹ (1.73 m)⁻², Killip class III or IV, STEMI, and were treated with oral glucose-lowering drugs or insulin (Fig. 1, Additional file 1: Table S2).

3.2 Types of discrepancy and in-hospital outcomes

The comparison of in-hospital outcomes between increased HbA_{1c} but normal FPG group and increased FPG but normal HbA_{1c} group were shown in Fig. 2. The rates of all the in-hospital outcomes were higher in increased FPG but normal HbA_{1c} group than in increased HbA_{1c} but normal FPG group. Logistic regression model was performed in order to explore the relationship between the types of discrepancy and in-hospital outcomes, except for the death from any cause because of the small event number. In univariate logistic regression analysis, a significantly higher risk of all the in-hospital outcomes was observed in patients of increased FPG but normal HbA_{1c} group (Table 2). After adjusting for confounders by multivariate logistic regression model, patients in increased FPG but normal HbA_{1c} group had a significantly 1.6-fold increased risk of heart failure (OR, 1.62; 95% CI, 1.08–2.44), a 1.6-fold increased risk of composite of cardiovascular death and heart failure (OR, 1.63; 95% CI, 1.09–2.43), and a 1.6-fold increased risk of composite of MACCE and heart failure (OR, 1.56; 95% CI, 1.08–2.24) (Table 2). The effect on MACCE was not significant (OR, 1.49; 95% CI, 0.85–2.63) (Table 2).

Table 2

Logistic regression analysis for in-hospital outcomes in increased FPG group compared with increased HbA_{1c} group.

	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
MACCE	1.94(1.13–3.34)	0.016	1.49(0.85–2.63)	0.165
Heart failure	2.09(1.42–3.07)	< 0.001	1.62(1.08–2.44)	0.020
Cardiovascular death or heart failure	2.11(1.44–3.07)	< 0.001	1.63(1.09–2.43)	0.018
MACCE or heart failure	1.98(1.41–2.79)	< 0.001	1.56(1.08–2.24)	0.018
* ORs were adjusted for age, gender, systolic blood pressure, heart rate, current smoker, hypertension, hemoglobin at admission, eGFR at admission, Killip class, type of acute coronary syndrome, and glucose-lowering drug use.				
FPG, fasting plasma glucose; HbA _{1c} , glycosylated hemoglobin; MACCE, major adverse cardiovascular and cerebrovascular event.				

Subgroup analysis was performed based on age, gender, medical history, Killip class, hemoglobin, eGFR, type of ACS, and glucose-lowering drug use before hospitalization. Higher risk of all the in-hospital outcomes was observed in patients of increased FPG but normal HbA_{1c} group, which was consistent in all subgroups (all P for interaction > 0.05), except for the eGFR subgroup for MACCE (Fig. 3). which shown

that increased FPG but normal HbA_{1c} group increased the risk of MACCE more clearly in patients with eGFR ≥ 60 ml min⁻¹ (1.73 m)⁻².

4. Discussion

In this study, we investigated the types of discrepancy between HbA_{1c} and FPG in patients with ACS and diabetes. We found that nearly one third of patients had a discrepancy between HbA_{1c} and FPG. Of these patients with discrepancy, the patients with increased FPG had higher risk of in-hospital cardiovascular adverse outcomes than those with increased HbA_{1c}.

Discrepancy between HbA_{1c} and FPG was reported by some studies. A study about the risk of hypertension in patients with prediabetes demonstrated the discrepancy between HbA_{1c} and FPG [20]. A study using data from residents of Yunnan Province, China, showed that the discrepancy between HbA_{1c} and FPG occurred in about 30% of participants [21]. In our study, the discrepancy between HbA_{1c} and FPG can be also found in patients with ACS and diabetes. We found that discrepancy group, which included 77.5% of patients in increased HbA_{1c} but normal FPG group and 22.5% of patients in increased FPG but normal HbA_{1c} group, accounted for 29% of total study population. Patients often experience hyperglycemia in the acute phase of many diseases, such as ACS, which is called stress hyperglycemia. HbA_{1c} reflects average glycemia over approximately 3 months, so an increase in HbA_{1c} usually indicates chronic hyperglycemia. We found that patients in increased FPG but normal HbA_{1c} group were more likely to have lower eGFR and be treated with glucose-lowering agents. Higher proportion of glucose-lowering agents use may be related to the well-controlled blood glucose and lower HbA_{1c}. Furthermore, changes in the metabolism of glucose-lowering drugs, insulin clearance, and the uremic environment in patients with renal function insufficient may also lower HbA_{1c} value [22]. From our study, not only can the discrepancy between HbA_{1c} and FPG be found in patients with chronic kidney disease (CKD), but also the proportion of increased FPG group was significantly higher than that of increased HbA_{1c} group.

There is a strong association between cardiovascular disease, diabetes and CKD. People with diabetes and CKD have a greatly increased risk of all-cause mortality, cardiovascular mortality, and kidney failure [23,24]. Furthermore, we analyzed the relationship between the types of discrepancy and in-hospital outcomes. We have known that HbA_{1c} and FPG were both closely related to the in-hospital outcomes. Most previous studies have shown that increased HbA_{1c} or FPG was significantly associated with poor in-hospital outcomes in patients with ACS and diabetes. An observational study included 250 patients with ACS, which found that coronary atherosclerosis was more advanced in patients with HbA_{1c} $\geq 5.7\%$ than those with HbA_{1c} $< 5.7\%$ [17]. Goyal, et al [25] conducted a post hoc analysis including two randomized controlled trials of acute myocardial infarction with ST-segment elevation, involved 30,536 subjects with diabetes history, which showed that patients with in-hospital glucose ≥ 144 mg/dL had a very high risk of death. However, in clinical practice, some conditions such as acute stress, renal dysfunction, and anemia can cause uncertainty in the measured values of FPG and HbA_{1c}, such as discrepancy between FPG and

HbA_{1c}. Until now, it is not so clear about the association of in-hospital outcomes with the discrepancy between HbA_{1c} and FPG in patients with ACS and diabetes. There are few studies focusing on this issue. From our study, we can draw a conclusion that patients in increased FPG group, who were more likely to have higher heart rate, poorer heart function, higher incidence of STEMI as well as hypertension, had higher risk of in-hospital cardiovascular adverse outcomes than those with increased HbA_{1c}. Stress hyperglycemia, which is a reflection of high free fatty acids, insulin resistance, and steroid hormones, affects the course of the disease in the worst way [26]. From other study, we have learned that the level of stress hyperglycemia often correlates with the severity of disease and predict mortality [27]. In our study we also found that the patients with severe clinical condition, such as the higher heart rate and the poorer heart function, were more likely to have an increase in FPG. As a result, stress hyperglycemia may have greater adverse effect on patients with ACS and diabetes than chronic hyperglycemia.

The findings of this study may have some important implications for clinical practice. The HbA_{1c} test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications [28]. Chronic hyperglycemia is an important risk factor for cardiovascular disease and mortality [24], although the variability of HbA_{1c} in patients with renal insufficiency should be concerned. However, in patients with ACS and diabetes, increased FPG may be associated with the higher risk of adverse in-hospital outcomes, even though the HbA_{1c} is well controlled. These patients, especially including those with renal insufficiency, should be given more attention and closer monitoring in clinical practice.

The major strength of our study is that it is based on a nationally representative registry and aimed at investigating the discrepancy between HbA_{1c} and FPG and the influence on the in-hospital outcomes of patients with ACS and diabetes, which was rarely reported till now. Our study also has certain limitations. Firstly, all-cause mortality was not included in the logistic regression analysis because of very limited events. Secondly, we cannot collect all information affected glucose metabolism from this real-world research for ACS patients based on medical records, thus contributing to some residual confounding from unmeasured confounders. Lastly, fasting statue, blood sample collection and testing methods were difficult to unify, as this was a real-world multicenter study.

5. Conclusion

In summary, our study showed that the discrepancy between HbA_{1c} and FPG accounts for nearly 30% in patients with ACS and diabetes. Patients with an increased level of FPG had a higher risk of in-hospital cardiovascular adverse outcomes than those with an increased level of HbA_{1c}. This result may indicate that when HbA_{1c} and FPG are inconsistent in patients with ACS and diabetes, the increased FPG that may be caused by stress hyperglycemia may have greater adverse effect than those with increased HbA_{1c} that may be caused by chronic hyperglycemia. These high-risk patients, especially including those with renal insufficiency, should be given more attention and closer monitoring in clinical practice.

Declarations

Abbreviations

ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; CCC-ACS, Improving Care for Cardiovascular Disease in China - acute coronary syndrome; CHD, coronary heart disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA_{1c}, glycosylated hemoglobin; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; MACCE, major adverse cardiovascular and cerebrovascular event; NSTEMI-ACS, Non-ST-segment elevation acute coronary syndrome; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.

Ethics approval and consent to participate

Institutional review board approval was granted for the aggregate data set for research and quality improvement by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. No informed consent was required.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the principal investigator of CCC-ACS on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HC, NY, DZ, CSM and JL designed the study; NY, LJY, GQW, WJB, FBX, YCH, JL and NY cleaned the data; NY and LJY analyzed the data; NY and HC wrote the manuscript. All authors reviewed and edited the manuscript. All authors read and approved the final manuscript.

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References

1. Zhao D, Liu J, Wang M, Zhang X, Zhou M. Epidemiology of cardiovascular disease in China: current features and implications. *Nat Rev Cardiol*. 2019;16:203-12.
2. Lenzen M, Ryden L, Ohrvik J, Bartnik M, Malmberg K, Scholte Op Reimer W, et al. Diabetes known or newly detected, but not impaired glucose regulation, has a negative influence on 1-year outcome in patients with coronary artery disease: a report from the Euro Heart Survey on diabetes and the heart. *Eur Heart J*. 2006;27:2969-74.
3. Figueiredo VN, Godoi FC, Martins NS, Quinaglia e Silva JC, Nadruz W, Jr., Coelho OR, et al. Diabetes mellitus unawareness is a strong determinant of mortality in patients manifesting myocardial infarction. *Curr Med Res Opin*. 2013;29:1423-7.
4. Aggarwal B, Shah GK, Randhawa M, Ellis SG, Lincoff AM, Menon V. Utility of Glycated Hemoglobin for Assessment of Glucose Metabolism in Patients With ST-Segment Elevation Myocardial Infarction. *Am J Cardiol*. 2016;117:749-53.
5. Rawshani A, Rawshani A, Franzen S, Sattar N, Eliasson B, Svensson AM, et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med*. 2018;379:633-44.
6. Zhou M, Liu J, Hao Y, Liu J, Huo Y, Smith SC, Jr., et al. Prevalence and in-hospital outcomes of diabetes among patients with acute coronary syndrome in China: findings from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Project. *Cardiovasc Diabetol*. 2018;17:147.
7. Bjarnason TA, Hafthorsson SO, Kristinsdottir LB, Oskarsdottir ES, Johnsen A, Andersen K. The prognostic effect of known and newly detected type 2 diabetes in patients with acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care*. 2019:2048872619849925.
8. Nystrom T, Sartipy U, Contardi A, Lind M, Bellocco R, Eliasson B, et al. Glycated Hemoglobin A1c Levels in Type 1 Diabetes Mellitus and Outcomes After Myocardial Infarction. *Circulation*. 2019;139:2380-2.
9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2013;36 S67-74.
10. Dziewierz A, Giszterowicz D, Siudak Z, Rakowski T, Dubiel JS, Dudek D. Admission glucose level and in-hospital outcomes in diabetic and non-diabetic patients with acute myocardial infarction. *Clin Res Cardiol*. 2010;99:715-21.
11. Li DB, Hua Q, Guo J, Li HW, Chen H, Zhao SM. Admission glucose level and in-hospital outcomes in diabetic and non-diabetic patients with ST-elevation acute myocardial infarction. *Intern Med*. 2011;50:2471-5.
12. Sanjuán R, Núñez J, Luisa Blasco M, Miñana G, Martínez-Maicas H, Carbonell N, et al. Prognostic Implications of Stress Hyperglycemia in Acute ST Elevation Myocardial Infarction. Prospective Observational Study. *Revista Española de Cardiología (English Edition)*. 2011;64:201-7.

13. Tsai JP, Tian J, Wang WY, Ng AC. Glycated hemoglobin vs fasting plasma glucose as a predictor of left ventricular dysfunction after ST-elevation myocardial infarction. *Can J Cardiol*. 2015;31:44-9.
14. Liang H, Guo YC, Chen LM, Li M, Han WZ, Zhang X, et al. Relationship between fasting glucose levels and in-hospital mortality in Chinese patients with acute myocardial infarction and diabetes mellitus: a retrospective cohort study. *BMC Cardiovasc Disord*. 2016;16:156.
15. Farhan S, Clare RM, Jarai R, Giugliano RP, Lokhnygina Y, Harrington RA, et al. Fasting glucose, NT-proBNP, treatment with eptifibatide, and outcomes in non-ST-segment elevation acute coronary syndromes: An analysis from EARLY ACS. *Int J Cardiol*. 2017;232:264-70.
16. Zhao S, Murugiah K, Li N, Li X, Xu ZH, Li J, et al. Admission Glucose and In-hospital Mortality after Acute Myocardial Infarction in Patients with or without Diabetes: A Cross-sectional Study. *Chin Med J (Engl)*. 2017;130:767-75.
17. Acar B, Ozeke O, Karakurt M, Ozen Y, Ozbay MB, Unal S, et al. Association of Prediabetes With Higher Coronary Atherosclerotic Burden Among Patients With First Diagnosed Acute Coronary Syndrome. *Angiology*. 2019;70:174-80.
18. Hao Y, Liu J, Liu J, Smith SC, Jr., Huo Y, Fonarow GC, et al. Rationale and design of the Improving Care for Cardiovascular Disease in China (CCC) project: A national effort to prompt quality enhancement for acute coronary syndrome. *Am Heart J*. 2016;179:107-15.
19. Levey AS SL, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A New Equation to Estimate Glomerular Filtration Rate. *Ann Intern Med*. 2009;150:604-12.
20. Geva M, Shlomai G, Berkovich A, Maor E, Leibowitz A, Tenenbaum A, et al. The association between fasting plasma glucose and glycated hemoglobin in the prediabetes range and future development of hypertension. *Cardiovasc Diabetol*. 2019;18:53.
21. Feng L, Nian S, Zhao Y, Bai X, Luo F, Luo X, et al. Higher HbA1c and/or glucose levels alter the association patterns between glycated hemoglobin and fasting glucose levels. *Diabetes Res Clin Pract*. 2018;142:353-62.
22. Kuo IC, Lin HY, Niu SW, Hwang DY, Lee JJ, Tsai JC, et al. Glycated Hemoglobin and Outcomes in Patients with Advanced Diabetic Chronic Kidney Disease. *Sci Rep*. 2016;6:20028.
23. Fox CS, Matsushita K, Woodward M, Bilo HJG, Chalmers J, Heerspink HJL, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *The Lancet*. 2012;380:1662-73.
24. American Diabetes Association. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2020. *Diabetes Care*. 2020;43:S111-134.
25. Goyal A, Mehta SR, Gerstein HC, Diaz R, Afzal R, Xavier D, et al. Glucose levels compared with diabetes history in the risk assessment of patients with acute myocardial infarction. *Am Heart J*. 2009;157:763-70.
26. Görmeli Kurt N. Relation of Stress Hyperglycemia to Mortality in Acute Myocardial Infarction Patients. *Eurasian Journal of Medicine and Oncology*. 2018;2:138-41.

27. Cheung NW, Wong KYC, Kovoor P, McLean M. Stress hyperglycemia: A prospective study examining the relationship between glucose, cortisol and diabetes in myocardial infarction. J Diabetes Complications. 2019;33:329-34.
28. American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020;43:S66-76.

Supplementary Files Legend

Additional file

Additional file 1.pdf: Table S1. Variables with missing value and missing rates for total population in CCC - ACS project (N = 92509). Table S2. Prevalence of discrepancy in different population. Table S3. Investigators of CCC-ACS project. Figure S1. Flow chart of patients considered for inclusion. Figure S2. Association between discrepancy and renal function.

Figures

Figure 1

Prevalence of discrepancy in different population. HbA1c, glycosylated hemoglobin; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; NSTEMI, non-ST-segment elevation acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction.

Figure 2

In-hospital outcomes in patients with discrepancy between HbA1c and FPG. HbA1c, glycosylated hemoglobin; FPG, fasting plasma glucose; MACCE, major adverse cardiovascular and cerebrovascular event.

Figure 3

Subgroup analysis for association between the type of discrepancy and in-hospital outcomes. Panel a shows the effect of increased FPG group on MACCE compared with increased HbA1c group. Panel b shows the effect of increased FPG group on heart failure compared with increased HbA1c group. Panel c shows the effect of increased FPG group on the composite of cardiovascular death and heart failure compared with increased HbA1c group. Panel d shows the effect of increased FPG group on the composite of MACCE and heart failure compared with increased HbA1c group. eGFR, estimated glomerular filtration rate; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; FPG, fasting plasma glucose; MACCE, major adverse cardiovascular and cerebrovascular event; HbA1c, glycosylated hemoglobin.

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