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Effect of Glucose-6-Phosphate Dehydrogenase Deficiency on the Severity and Prognosis of Coronary Atherosclerosis in Patients with Acute Coronary Syndrome

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Jing Bai and Qianying Chen: Conception and design of the work, supervision, statistical analysis, drafting the manuscript. Jing Bai, Qianying Chen and Xinjing Zhong: Data collection, analysis and interpretation of the data, critical revision of the manuscript, approval of the final manuscript.

Key words
Glucose-6-phosphate dehydrogenase, Acute coronary syndrome, Coronary atherosclerosis, Gensini score

ABSTRACT

This study aimed to investigate the impact of glucose-6-phosphate dehydrogenase (G6PD) deficiency on the severity and prognosis of coronary atherosclerosis in patients with acute coronary syndrome (ACS). Patients diagnosed with ACS accompanied by G6PD deficiency between July 2021 and June 2023 at The First People's Hospital of Yulin were selected as the study group, while patients with ACS and normal G6PD levels during the same period were enrolled as the control group. The severity of coronary atherosclerosis was assessed using the Gensini score. The impact of G6PD activity and other factors on the Gensini score was analysed, and a 12-month follow-up was conducted to observe and document the occurrence of postoperative major adverse cardiovascular events (MACE). We found that after 12 months of follow-up period following percutaneous coronary intervention, the study group showed a significant increase in left ventricular ejection fraction (LVEF) and fractional shortening (FS) and a decrease in left ventricular end-diastolic diameter (LVED) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) compared with the baseline, and the differences were statistically significant (all $p < 0.05$). The improvement in LVEF was more pronounced in the study group than in the control group, and significant decreases in LVED and NT-proBNP and a significant increase in FS were observed in the study group compared with the control group ($p < 0.05$). After 12 months of treatment, the overall cumulative incidence of MACE was 6.94% in the study group, significantly lower than the 16.56% in the control group ($\chi^2 = 7.032$, $p < 0.05$). After clinical intervention, both groups showed an improvement in cardiac function parameters, and the improvement was more pronounced in the G6PD-deficient group. This result suggests that G6PD enzyme activity is a protective factor against MACE in patients with ACS.

INTRODUCTION

Acute coronary syndrome (ACS) encompasses a range of conditions resulting from acute myocardial ischemia due to coronary artery obstruction, such as unstable angina, non-ST-segment elevation myocardial infarction and ST-segment elevation myocardial infarction (Amsterdam *et al*., 2014). ACS is a major cause of morbidity and mortality worldwide, affecting approximately 1.5 million people annually in the United States alone (Benjamin *et al*., 2019). The main risk factors for ACS include age, gender, smoking, hypertension, dyslipidaemia, diabetes, obesity, physical inactivity and family history of coronary heart disease (CHD) (Piepoli *et al*., 2016). The standard treatment for ACS consists of pharmacological therapy, such as antiplatelet agents, anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitors and statins and revascularisation procedures, such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (Ibanez *et al*., 2018).

Glucose-6-phosphate dehydrogenase (G6PD) is a crucial enzyme in the catalysis of the pentose phosphate

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pathway, which generates nicotinamide adenine dinucleotide phosphate (NADPH) and glutathione, two important antioxidants that protect cells from oxidative stress (Meng *et al*., 2022). Deficiency in G6PD is a common X-linked hereditary enzyme defect, affecting over 400 million people worldwide, particularly in malaria-endemic regions (Dean and Kane, 2020; Tao *et al*., 2019). It can cause haemolytic anaemia, neonatal jaundice and increased susceptibility to infections in response to certain drugs, foods or infections (Belfield and Tichy, 2018). However, the impact of G6PD deficiency on the cardiovascular system, particularly coronary atherosclerosis, remains controversial. Some studies have suggested that G6PD deficiency may have a protective effect against CHD and cardiovascular mortality by reducing the oxidative modification of low-density lipoprotein cholesterol (LDL-C) and the expression of vascular cell adhesion molecules (Meloni *et al*., 2008; Cocco *et al*., 1998; Long *et al*., 1967), whereas others have reported no association or even a detrimental effect of G6PD deficiency on coronary artery disease and its complications by impairing the endothelial function and the availability of nitric oxide (Sanna *et al*., 2021; Pes *et al*., 2019; Leopold *et al*., 2001). To date, there is no clear conclusion regarding the impact of G6PD deficiency on coronary atherosclerosis. In this study, patients who were diagnosed with ACS and were also confirmed to have G6PD deficiency at our hospital were included as the study participants to investigate the impact of G6PD deficiency on the severity and short-term prognostic outcomes of coronary atherosclerosis in patients with ACS.

MATERIALS AND METHODS

Subjects

A total of 389 patients diagnosed with ACS and G6PD deficiency at the hospital between July 2021 and June 2023 were selected as the study group, while 326 patients with ACS and normal G6PD levels undergoing treatment at the hospital during the same period were recruited as the control group. Both groups of patients underwent coronary arteriography and PCI. The patients (18-70 years) meeting the diagnostic criteria for ACS set forth by the American College of Cardiology (ACC)/American Heart Association in 2019 (January *et al*., 2019), with complete clinical and laboratory data, these on which the onset of chest pain was within 4 h prior to their admission to the hospital, had no history of allergy to the contrast agents used in this study and underwent coronary arteriography and PCI were included in this study. Those with recent (within the last 3 months) acute myocardial infarction, with coexistence of other myocardial diseases (e.g. dilated or hypertrophic cardiomyopathy) or severe valve diseases, those with history of recent (within the last 6 months) cerebrovascular accidents or gastrointestinal bleeding, with severe heart failure (New York Heart Association functional class >2) or cardiogenic shock, and those with presence of malignancy, autoimmune diseases, coagulation disorders, other severe haematological diseases, infectious diseases or severe liver and kidney dysfunction were excluded.

Coronary arteriography and percutaneous coronary intervention

The procedure for coronary arteries group was performed by two radiologists with >5 years of experience, and all patients and the radiologists were blinded to the grouping information. Percutaneous coronary intervention (PCI) was performed by experts according to the Chinese Guidelines for Percutaneous Coronary Intervention (2016) (Emergency Medicine Society of Chinese Medical Association, 2019).

Glucose-6-phosphate dehydrogenase activity assay

The ratio of G6PD to 6-phosphogluconate dehydrogenase (6GPD) in red blood cells was determined by biochemical detection to quantitatively measure G6PD activity within 24 h of admission for all patients. A ratio ≥1.0 was considered normal, whereas a ratio <0.80 was defined as G6PD-deficient (Sanna *et al*., 2021). Furthermore, a ratio <0.10 was classified as severely G6PD-deficient.

Gensini score

The Gensini score (Han *et al*., 2019) was employed to assess the extent and severity of coronary artery lesions. The scoring system is as follows: (1) scoring based on the degree of coronary artery stenosis: 1– stenosis ≤25%, 2– stenosis 26%–50%, 4– stenosis 51%–75%, 8– stenosis 76%–90%, 16– stenosis 91%–99%, 32– stenosis 100%; (2) scoring based on the location of coronary artery lesions (weighted score): 5.0– left main coronary artery lesion, 2.5/1.5/1.0– proximal/medial/distal anterior descending artery lesion, 1.0– the first diagonal branch artery lesion, 0.5– the second diagonal branch artery lesion, 2.5/1.0– left proximal/distal circumflex artery lesion, 1.0 – obtuse marginal artery lesion, 1.0– posterior descending artery lesion. The Gensini score for each patient is calculated by summing the products of the stenosis scores and the corresponding weights for different coronary artery segments. A higher score indicates more severe coronary artery lesions.

Clinical data collection

Upon admission, clinical data, including age, gender,

height, weight, body mass index, glomerular filtration rate (GFR), tobacco use and cardiac function parameters, were recorded by medical personnel. Cardiac colour Doppler ultrasound parameters included left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVED), left ventricular end-diastolic volume, left ventricular end-systolic volume and fractional shortening (FS). Serology tests were conducted upon admission (pre-PCI) and on days 3, 7 and 14 post-PCI. Fasting venous blood samples (5 mL) were collected and centrifuged at 3,000 rpm for 10 min. The supernatant was harvested and transferred to Eppendorf tubes and stored at −70°C. The following parameters were measured using an automated biochemical analyser: total triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol, LDL-C, haemoglobin (HGB), blood platelet count, white blood cell count, homocysteine and N-terminal pro-B-type natriuretic peptide (NT-proBNP).

Prognostic outcomes

The prognosis began on the day after PCI, with a follow-up period of 12 months. The occurrence, timing, symptoms and treatment of major adverse cardiovascular events (MACE) were documented.

Statistical analysis

Data analysis was performed using the software SPSS 26.0. Normally distributed quantitative data were presented as mean ± standard deviation, and comparisons between two groups were analysed using the *t*-test. Non-normally distributed quantitative data were expressed as median (quartiles) and examined using non-parametric tests. Qualitative data were presented as counts (percentages) and between-group comparisons were assessed using the chi-squared test. The Kaplan–Meier survival curve was employed to evaluate the clinical prognosis of the two groups over the 12-month follow-up period, and multivariate Cox regression analysis was conducted to identify predictors of coronary atherosclerosis severity in patients with ACS. A value of $p < 0.05$ was considered statistically significant.

RESULTS

A total of 389 patients were enrolled in the study group, while 326 patients were recruited as the control group. The study group comprised 73 men (18.77%) with an average age of 63.72±11.139 years, while the control group had 94 men (28.83%) with an average age of 65.21 ± 9.795 years (Table I). The two groups showed significant differences in HGB, TC, LDL, GFR, Gensini score and the G6PD/6GPD ratio (all $p< 0.05$). No statistically significant differences were observed in other clinical data (all $p > 0.05$).

Table I. Comparison of clinical data.

Item	Study group (n = 389)	Control group (n = 326)	t/χ^2	p
Age (years)	63.72±11.139	65.21±9.795	1.903	0.057
Male [n(%)]	73 (18.77)	94(28.83)	0.311	0.577
BMI (kg/m^2)	24.09±6.02	23.89±3.38	1.903	0.651
HGB (g/L)	126.07±22.88	131.81±18.89	3.657	0.000
BPC (×10^9/L)	257.70±67.267	249.72±67.33	-1.573	0.116
WBC (×10^9/L)	10.08±14.67	9.51±10.76	-0.592	0.554
Smoking history [n(%)]	107 (27.51)	133 (40.80)	0.149	0.700
NT-proBNP (ng/L)	666.57 (286.20, 1096.00)	547.00 (246.25, 1004.00)	0.788	0.389
LVEF (%)	49.73±6.090	49.63±6.08	0.353	0.737
LVEDD (mm)	52.18±2.33	51.92±2.58	0.563	0.563
LVEDV (mL)	106.52±10.70	104.63±11.44	1.362	0.183
LVESV (mL)	47.47±8.37	48.47±7.94	1.462	0.168
FS (%)	29.68±1.39	29.37±1.49	1.845	0.071
TC (mmol/L)	4.35±1.21	4.91±3.94	-0.266	0.014
TG (mmol/L)	1.77±1.10	1.73±1.68	-0.266	0.790
HDL-C(mmol/L)	1.09±0.40	1.11±0.63	0.503	0.615
LDL-C(mmol/L)	2.84±1.02	3.28±3.70	2.052	0.041
Hcy (umol/L)	14.47±6.99	14.22±0.71	-0.387	0.699
GFR (ml/min)	77.39±28.40	73.16±26.91	-2.018	0.044
Gensini score	28.92±2.14	32.34±3.12	16.672	0.037
G6PD/6GPD ratio	0.57±0.21	1.21±0.19	0.473	0.002

BMI, body mass index; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; FS, fractional shortening; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein; HGB, hemoglobin; BPC, blood platelets count; WBC count, white blood cell count; Hcy, homocysteine; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table II shows cardiae function parameters of the control and study group. After 12 months of treatment, the study group exhibited a significant increase in LVEF and FS and a significant decrease in LVED and NT-proBNP compared with the pre-treatment levels ($p< 0.05$). Similarly, the control group experienced a significant increase in LVEF and FS and a significant decrease in

Table II. Comparison of cardiac function parameters before and after treatment.

Item	Study group (n = 389)		Control group (n = 326)	
	Preoperative	At 12 months postoperative	Preoperative	At 12 months postoperative
LVEF(%)	49.45±6.21	53.34±5.37*	49.72±5.31	51.34±5.50*
LVEDD (mm)	52.32±2.53	48.53±2.98*	51.67±2.43	49.72±2.84*
FS(%)	29.37±1.47	33.07±1.48*	29.45±1.46	31.75±1.45*
NT-proBNP (ng/L)	666.54 (286.23, 1095.00)	288.27 (189.00, 421.84)*	542.00 (246.25, 1007.00)	347.00 (187.75, 625.25)*

For abbreviations see, Table I. *P < 0. 05 compared to preoperative levels.

LVED and NT-proBNP after 12 months of treatment (p < 0.05). The improvement in LVEF, LVED and NT-proBNP was more pronounced in the study group after 12 months of treatment, compared with the control group (p < 0.05). Additionally, FS in the study group was significantly elevated compared with the control group (p < 0.01). These results suggest that after clinical intervention, both groups showed varying degrees of improvement in the cardiac function parameters. Notably, the improvement was more pronounced in the study group compared with the control group.

Table III. Comparison of MACE incidence at 12 months postoperative [n(%)].

Item	Study group (n = 389)	Control group (n = 326)	χ^2	p
MACE	27(6.94)	54(16.56)	7.032	0.037
All-cause death	9(2.31)	14(4.29)	1.732	0.124
Nonlethal myocardial infarction	7(1.80)	16(4.91)	2.012	0.219
Repeat PCI	8(2.06)	19(5.83)	1.783	1.782
Cerebrovascular accidents	3(0.77)	5(1.53)	1.121	0.211

MACE, major adverse cardiovascular events.

Table III shows incidence of postoperative major adverse cardiovascular events. After 12 months of treatment, the overall cumulative incidence of MACE in the study group was significantly lower than in the control group (6.94% vs 16.56%) (χ^2 = 7.032, p < 0.05). However, there were no statistically significant differences in the individual incidence of all-cause death, nonlethal myocardial infarction, repeat PCI or cerebrovascular accidents (all p > 0.05). Figure 1 shows the Kaplan–Meier survival curve, which indicates that the study group had a higher survival rate and a lower cumulative incidence of MACE than the control group over the 12-month follow-up period (log-rank test, p < 0.05).

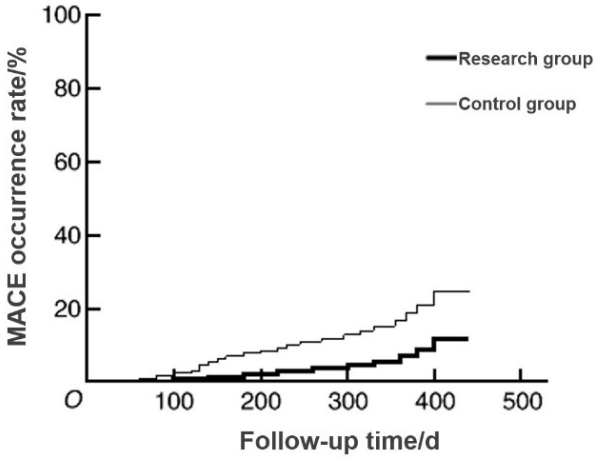

Fig. 1. The Kaplan-Meier survival curve.
MACE, major adverse cardiovascular events.

Table IV shows multivariate Cox regression analysis of major adverse cardiovascular events occurrence. Using the occurrence of MACE during the 12-month follow-up period as the dependent variable (occurred= 1, not occurred = 0), indicators with p < 0.05 in Table I were included in the analysis. The Cox regression analysis was performed using HGB, TC, LDL, GFR, the Gensini score and the G6PD/6GPD ratio as independent variables. The results revealed that GFR (odds ratio [OR] = 1.629, 95% CI: 1.252–1.943, p = 0.029) and Gensini score (OR = 1.423, 95% CI: 1.046–1.619, p = 0.017) were risk factors for MACE occurrence, whereas the G6PD/6GPD ratio was a protective factor against MACE occurrence (OR = 0.622, 95% CI: 0.371, 1.058, p = 0.043).

DISCUSSION

Glucose-6-phosphate dehydrogenase, with its antioxidant properties, plays a crucial role in maintaining redox homeostasis and vascular reactivity within the blood vessels. On the vascular endothelium, patients with G6PD deficiency experience an increase in oxidative

Table IV. Multivariate Cox regression analysis of MACE-related factors.

Factor	Regression coefficient	Standard error	Wald χ2 value	p	OR value	95% CI
HGB	0.232	0.183	1.575	0.221	1.210	(0.885, 1.751)
TC	0.658	0.242	8.252	0.056	1.341	(1.243, 1.922)
LDL-C	-0.557	0.295	1.179	0.073	0.646	(0.361, 1.225)
GFR	0.349	0.238	1.521	0.029	1.629	(1.252~1.943)
Gensini score	0.490	1.237	9.219	0.017	1.423	(1.046~1.619)
G6PD/6GPD ratio	0.252	0.319	1.078	0.043	0.622	(0.371, 1.058)

TC, total cholesterol; LDL-C, low density lipoprotein; HGB, hemoglobin.

damage accompanied by reduced utilisation of nitric oxide (Thompson *et al*., 2013). The impact of G6PD deficiency on the cardiovascular system, particularly coronary artery disease, remains a subject of controversy. Previous studies primarily attributed the atherogenic effect of G6PD deficiency to the depletion of NADPH (Pes *et al*., 2019), which can lead to reduced availability of nitric oxide and glutathione, increasing the susceptibility of LDL to oxidation. Additionally, individuals with G6PD deficiency show an increase in vascular cell adhesion molecules and a decrease in leukocyte interleukin-10 (Leopold *et al*., 2001). However, considering that atherosclerosis is a multifactorial process resulting from complex interactions between genetic and environmental factors, these mechanisms may only weakly correlate or not correlate at all with clinical observations.

This study investigated the impact of G6PD activity on the severity and short-term prognostic outcomes of coronary atherosclerosis in patients with ACS. The results showed that at the end of the 12-month post-PCI follow-up, patients in the study group showed an increase in LVEF and FS and a decrease in LVED and NT-proBNP compared to the pre-PCI levels. Moreover, the improvement in LVEF, as well as the significant decreases in LVED and NT-proBNP, were more pronounced in the study group compared to the control group. Notably, a significant increase in FS was observed in the study group compared to the control group. In addition, the overall cumulative incidence of MACE in the study group was lower than in the control group. Further, the Cox regression analysis revealed that GFR and the Gensini score were two risk factors for MACE, while the G6PD/6GPD ratio was a protective factor against MACE. This might be explained by the use of the SYNTAX score in the assessment of arterial stenosis without considering the role of plaque composition and volume. Additionally, the scoring system used for assessing the severity of coronary atherosclerosis may also have certain limitations.

In endothelial cells with G6PD deficiency, the reduced storage of NADPH and increased accumulation of reactive oxygen species can enhance oxidative stress, leading to impaired endothelial function and the induction of atherosclerosis (Brewer *et al*., 2013). Furthermore, NADPH oxidase can induce an increase in superoxide anions in monocytes, contributing to vascular hardening. Additionally, the elevated G6PD level in adipocytes and the overexpression of NADPH oxidase in phagocytes are both associated with oxidative damage. From this perspective, patients with G6PD deficiency may have a reduced risk of atherosclerosis, as there is a decrease in the risk of developing atheromatous plaques. In response to a series of oxidative stimuli, including those induced by heart failure, G6PD activity increases, often considered an indication of enhanced defensive capabilities in the body. In both human and animal experimental models, G6PD activity is elevated in surviving myocardium and in the myocardium undergoing failure after myocardial infarction (Hecker *et al*., 2012). This may represent a compensatory mechanism by which failing myocardium resists oxidative damage. In the study by Long *et al*. (1967) comparing several cardiovascular parameters in 1,473 patients with G6PD deficiency and healthy controls, the results suggested a higher incidence of hypertension and idiopathic cardiomyopathy in G6PD-deficient patients but a lower incidence of CHD. Two subsequent studies with a similar design also indicated that G6PD deficiency could lower the risk of CHD and the mortality rate from cardiovascular diseases (Meloni *et al*., 2008; Cocco *et al*., 1998).

Consistent with our findings, the study by Meloni *et al*. (2008) indicated a noticeable protective effect of G6PD deficiency on cardiovascular diseases in a large cohort of Sardinian men. They found that G6PD-deficient men had a lower prevalence of CHD and a lower mortality rate from cardiovascular causes than G6PD-normal men, after adjusting for age and other confounding factors. They attributed this effect to the reduced susceptibility of LDL-C to oxidation and the decreased expression of vascular cell adhesion molecules in G6PD-deficient individuals. However, the study by Sanna *et al*. (2021)

suggested no impact of G6PD deficiency on the extent and complexity of coronary atherosclerosis in patients with ACS. They used the SYNTAX score, a comprehensive angiographic tool that quantifies the number, location and severity of coronary artery lesions, to assess the coronary atherosclerosis burden in 105 G6PD-deficient and 210 G6PD-normal patients with ACS. They found no significant difference in the SYNTAX score between the two groups and no association between G6PD activity and the SYNTAX score in the whole population. They argued that the SYNTAX score may be a more reliable indicator of coronary atherosclerosis than the Gensini score, which we used in our study, as it considers not only the degree of stenosis but also the functional significance of each lesion.

However, our study has some limitations. Due to time and budget constraints, the current study has a modest sample size, and the results may be subject to bias. Moreover, future studies should also consider the genetic heterogeneity of G6PD deficiency, as different mutations may have different effects on enzyme activity and stability and thus on cardiovascular outcomes. Therefore, a more comprehensive and precise characterisation of the G6PD genotypes and phenotypes in different populations may help to elucidate the role of G6PD deficiency in cardiovascular diseases.

CONCLUSION

After the clinical intervention, both groups of patients showed an improvement in cardiac function parameters, with a more pronounced improvement in the group with G6PD deficiency. The GFR and the Gensini score appear to be two risk factors for MACE, whereas G6PD activity serves as a protective factor against MACE.

DECLARATIONS

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IRB approval

Ethics Committee of The First People's Hospital of Yulin approved the study (YLSY-IRB-SR-2022033).

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of The First People's Hospital of Yulin. Informed consent was obtained from all patients or their local guardians. This study was approved by the hospital's ethical committee, and informed consent was obtained from all patients or their local guardians.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Amsterdam, E.A., Wenger, N.K., Brindis, R.G., Casey, D.E., Jr, Ganiats, T.G., Holmes, D.R., Jr, Jaffe, A.S., Jneid, H., Kelly, R.F., Kontos, M.C., Levine, G.N., Liebson, P.R., Mukherjee, D., Peterson, E.D., Sabatine, M.S., Smalling, R.W. and Zieman, S.J., 2014. 2014 AHA/ACC guideline for the management of patients with non-st-elevation acute coronary syndromes: A report of the American College of Cardiology/American heart association task force on practice guidelines. *J. Am. Coll. Cardiol*., **64**: e139–e228. https://doi.org/10.1016/j.jacc.2014.09.017

Belfield, K.D. and Tichy, E.M., 2018. Review and drug therapy implications of glucose-6-phosphate dehydrogenase deficiency. *Am. J. Hlth. Syst. Pharm*., **75**: 97-104. https://doi.org/10.2146/ajhp160961

Benjamin, E.J., Muntner, P., Alonso, A., Bittencourt, M.S., Callaway, C.W., Carson, A.P., Chamberlain, A.M., Chang, A.R., Cheng, S., Das, S.R., Delling, F.N., Djousse, L., Elkind, M.S.V., Ferguson, J.F., Fornage, M., Jordan, L.C., Khan, S.S., Kissela, B.M., Knutson, K.L., Kwan, T.W. and American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee, 2019. Heart disease and stroke statistics-2019 update: A report from the American heart association. *Circulation*, **139**: e56–e528. https://doi.org/10.1161/CIR.0000000000000659

Brewer, A.C., Mustafi, S.B., Murray, T.V., Rajasekaran, N.S. and Benjamin, I.J., 2013. Reductive stress linked to small HSPs, G6PD, and Nrf2 pathways in heart disease. *Antioxid. Redox Signal*., **18**: 1114-1127. https://doi.org/10.1089/ars.2012.4914

Cocco, P., Todde, P., Fornera, S., Manca, M.B., Manca, P. and Sias, A.R., 1998. Mortality in a cohort of men expressing the glucose-6-phosphate dehydrogenase deficiency. *Blood*, **91**: 706-709. https://doi.org/10.1182/blood.V91.2.706.706_706_709

Dean, L. and Kane, M., 2020. *Pegloticase therapy*

and G6PD *genotype*. In: *Medical genetics summaries [Internet]*. Bethesda (MD): National Center for Biotechnology Information (US) (eds. V.M. Pratt, S.A. Scott, M. Pirmohamed, B. Esquivel, B.L. Kattman and A.J. Malheiro); 2012. PMID: 33001605.

Emergency Medicine Society of Chinese Medical Association, Committee of Experts on Emergency Medicine of National Health Commission Capacity Building and Continuing Education Center, Emergency and First Aid Branch of China International Exchanges and Promotion Association for Medical and Healthcare, 2019. Guidelines for quick diagnosis and treatment of acute coronary syndrome (2019). *Chinese J. Emerg. Med*., **28**: 421-428.

Han, K., Lu, Q., Zhu, W.J., Wang, T.Z., Du, Y. and Bai, L., 2019. Correlations of degree of coronary artery stenosis with blood lipid, CRP, Hcy, GGT, SCD36 and fibrinogen levels in elderly patients with coronary heart disease. *Eur. Rev. Med. Pharmacol. Sci*., **23**: 9582-9589.

Hecker, P.A., Galvao, T.F., O'Shea, K.M., Brown, B.H., Henderson, R., Riggle, H., Gupte, S.A., Stanley, W.C., 2012. High-sugar intake does not exacerbate metabolic abnormalities or cardiac dysfunction in genetic cardiomyopathy. *Nutrition*, **28**: 520-526. https://doi.org/10.1016/j.nut.2011.09.017

Ibanez, B., James, S., Agewall, S., Antunes, M.J., Bucciarelli-Ducci, C., Bueno, H., Caforio, A.L.P., Crea, F., Goudevenos, J.A., Halvorsen, S., Hindricks, G., Kastrati, A., Lenzen, M.J., Prescott, E., Roffi, M., Valgimigli, M., Varenhorst, C., Vranckx, P., Widimský, P. and ESC Scientific Document Group, 2018. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur. Heart J*., **39**: 119-177. https://doi.org/10.5603/KP.2018.0041

January, C.T., Wann, L.S., Calkins, H., Chen, L.Y., Cigarroa, J.E., Cleveland Jr, J.C., Ellinor, P.T., Ezekowitz, M.D., Field, M.E., Furie, K.L., Heidenreich, P.A., Murray, K.T., Shea, J.B., Tracy, C.M. and Yancy, C.W., 2019. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society in collaboration with the society of thoracic surgeons. *Circulation*, **140**: e125-e151. https://doi.org/10.1161/CIR.0000000000000665

Leopold, J.A., Cap, A., Scribner, A.W., Stanton, R.C. and Loscalzo, J., 2001. Glucose-6-phosphate dehydrogenase deficiency promotes endothelial oxidant stress and decreases endothelial nitric oxide bioavailability. *FASEB J*., **15**: 1771-1773. https://doi.org/10.1096/fj.00-0893fje

Long, W.K., Wilson, S.W. and Frenkel, E.P., 1967. Associations between red cell glucose-6-phosphate dehydrogenase variants and vascular diseases. *Am. J. Hum. Genet*., **19**: 35-53.

Meloni, L., Manca, M.R., Loddo, I., Cioglia, G., Cocco, P., Schwartz, A., Muntoni, S. and Muntoni, S., 2008. Glucose-6-phosphate dehydrogenase deficiency protects against coronary heart disease. *J. Inherit. Metab. Dis*., **31**: 412-417. https://doi.org/10.1007/s10545-008-0704-5

Meng, Q., Zhang, Y., Hao, S., Sun, H., Liu, B., Zhou, H., Wang, Y. and Xu, Z.X., 2022. Recent findings in the regulation of G6PD and its role in diseases. *Front. Pharmacol*., **13**: 932154. https://doi.org/10.3389/fphar.2022.932154

Pes, G.M., Parodi, G. and Dore, M.P., 2019. Glucose-6-phosphate dehydrogenase deficiency and risk of cardiovascular disease: A propensity score-matched study. *Atherosclerosis,* **282**: 148-153. https://doi.org/10.1016/j.atherosclerosis.2019.01.027

Piepoli, M.F., Hoes, A.W., Agewall, S., Albus, C., Brotons, C., Catapano, A.L., Cooney, M.T., Corrà, U., Cosyns, B., Deaton, C., Graham, I., Hall, M.S., Hobbs, F.D.R., Løchen, M.L., Löllgen, H., Marques-Vidal, P., Perk, J., Prescott, E., Redon, J., Richter, D.J. and ESC Scientific Document Group, 2016. 2016 European guidelines on cardiovascular disease prevention in clinical practice: The sixth joint task force of the European society of cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention and Rehabilitation (EACPR). *Eur. Heart J*., **37**: 2315–2381. https://doi.org/10.1093/eurheartj/ehw106

Sanna, G.D., Canonico, M.E., Siciliano, R., Guarino, S., Montereggi, F., Ponti, E., Corda, G., Talanas, G. and Parodi, G., 2021. Impact of glucose-6-phosphate dehydrogenase deficiency on the severity of coronary atherosclerosis in patients with acute coronary syndromes. *J. Cardiovasc.*

Med. (Hagerstown), **22**: 813-817. https://doi.org/10.2459/JCM.0000000000001227

Sanna, G.D., Deriu, S., Uras, M., Murgia, A., Talanas, G., Moccia, E., Corda, G., Mura, E., Saba, P.S., Parodi, G., 2021. Aspirin adherence in subjects with glucose-6-phosphate-dehydrogenase deficiency having an acute coronary syndrome. *Eur. Heart J. Cardiovasc. Pharmacother*., **7**: e41-w44. https://doi.org/10.1093/ehjcvp/pvaa060

Tao, Z.X., Zhu, A.N. and Yang, F., 2019. Research progress in glucose-6-phosphate dehydrogenase deficiency. *Chinese J. Prenat. Diagn.* (*Electron. Ver.*), **11**: 49–53.

Thompson, P.A., Chew, E. and Szer, J., 2013. Deep vein thrombosis in association with acute intravascular haemolysis in glucose-6-phosphate dehydrogenase deficiency: A unique case. *Intern. med. J.*, **43**: 1164-1165. https://doi.org/10.1111/imj.12268