Preoperative Fasting Blood Glucose Levels and the Risk of Contrast-induced Nephropathy in Patients With Diabetes and Pre-diabetes Receiving Coronary Arteriography or Percutaneous Coronary Intervention: a Cross-sectional Study

Peng Zhang

Tianjin Chest Hospital

Han Fu

Tianjin Medical University

Shicheng Yang

Tianjin Chest Hospital

Zhigang Guo

Tianjin Chest Hospital

Naikuan Fu (✉ cdrfnk@163.com)

Tianjin Chest Hospital <https://orcid.org/0000-0003-2039-9373>

Original investigation

Keywords: diabetes mellitus, preoperative fasting blood glucose, percutaneous coronary intervention, contrast-induced nephropathy, risk factors

Posted Date: July 19th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-700134/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Diabetes mellitus is an independent risk factor for contrast-induced nephropathy in patients undergoing coronary arteriography /percutaneous coronary intervention. In this study, we evaluated whether preoperative fasting blood glucose levels in diabetic and prediabetic patients who received CAG/PCI impacted the occurrence of postoperative CIN.

Methods: We reviewed the incidence of preoperative FBG and postoperative CIN in 3437 patients with CAG/PCI from January 1, 2019, to May 28, 2021 in Tianjin Chest Hospital. Patients were divided into 5 groups based on their preoperative FBG levels. Blood samples were collected at admission and at 48 h and 72 h after operation to determine the serum creatinine levels of patients. P for trend was used to analyze the trend between preoperative FBG levels and the increased risk of CIN. Univariable and multivariable logistic regression analysis were used to exclude the influence of the confounding factors, and some high-risk confounders were selected for subgroup analysis.

Results: We found that patients with elevated preoperative FBG levels had higher body mass index (BMI), received PCI more often, and had higher basal SCr levels. The incidence of CIN in the 5 groups of patients was 6.7%, 10.5%, 17.5%, 18.4%, and 23.2%. The trend test was used to determine the odds ratio (OR) (1.000, 1.425, 2.489, 2.704, 3.234). Multivariate logistic regression analysis confirmed that in the main high-risk subgroups including BMI, PCI, hypertension, and age>65, patients with elevated preoperative FBG levels (≥ 150 mg/dL) had a higher risk of CIN. There was a significant relationship between higher preoperative FBG levels and greater risk for CIN in patients with HbA1c 6.5%-8.0% ($P=0.007$) and HbA1c 8.0%-9.5% ($P=0.011$).

Conclusions: Results of our cross-sectional study shows that elevated preoperative FBG levels are independently associated with the risk of CIN in diabetic and prediabetic patients undergoing CAG/PCI, and that the incidence of CIN gradually increases with an increase in preoperative FBG levels. Therefore, patients with elevated preoperative FBG at admission should be carefully monitored and more active measures should be taken to prevent CIN.

Background

Improvements in percutaneous coronary intervention (PCI)-related technology have led to an increase in the number of surgeries annually and the increasing use of contrast media (CM). (1) Contrast-induced nephropathy is a reversible acute renal failure observed after the administration of iodinated CM during angiographic or other medical procedures. It is defined as an increase in serum creatinine (Scr) levels of 25% or more or an absolute increase of 0.5 mg/dL (44.2 mmol/L) or more from baseline value after 48–72 h following the exposure to CM.(1) The exact mechanism of contrast-induced nephropathy (CIN) is unclear; however, it may be related to hemodynamic effects, the formation of reactive oxygen species, and renal tubular cytotoxicity.(4, 5)The incidence of CIN in patients with normal renal function is not high, but factors such as advanced age, diabetes, and high-dose CM can increase the incidence of CIN.

(6)Diabetic nephropathy, especially, has been identified as a strong and independent risk factor for CIN. (6)Long-term hyperglycemia not only accelerates coronary atherosclerosis, but also threatens the prognosis of CAG. (9)To date, studies have confirmed that elevated preoperative fasting blood glucose (FBG) levels are associated with a greater risk of CI- acute kidney injury (AKI) in patients without known diabetes who undergo coronary arteriography (CAG) in the setting of an acute myocardial infarction.(9) Glycemic exposure, i.e., the degree and duration of hyperglycemia, is a major risk factor for diabetic microvascular complications.(11, 12) Hyperglycemia results in many pathophysiological changes, such as endothelial and microvascular dysfunction, increased production of vascular inflammatory markers and reactive oxygen species (ROS), and impaired immune responses.(13) Both diabetes and the use of iodinated radio CM are associated with marked alterations in renal physiology, including changes in the eGFR and renal hemodynamics, enhanced tubular transport activity and oxygen expenditure, intensification of medullary hypoxia, and ROS generation.(14) With the increasing popularity of coronary angiography and the growing number of diabetic patients resorting to this intervention, there are only limited data to confirm whether preoperative FBG levels in diabetic and prediabetic patients affect the occurrence of CIN. In this study, we determined whether preoperative FBG levels in diabetic and prediabetic patients undergoing CAG/PCI due to unstable angina or non-ST segment myocardial infarction were related to the risk of CIN, and compared our findings with those from previous clinical trials. The current study was in accordance with the STROBE reporting guidelines.

Methods

Study population

In this cross-sectional study, we screened patients with diabetes and prediabetes who underwent CAG in the Department of Cardiology, Tianjin Chest Hospital, from January 1, 2019, to May 28, 2021. This study was approved by the ethics committee of Tianjin Chest Hospital. All patients provided written informed consent prior to enrolment. First, patients were classified based on their preoperative FBG levels. Next, the treatment method (oral drugs, stent placement, or coronary artery bypass) was determined based on the degree of coronary artery disease during the operation. Lastly, the incidence of CIN in each group of patients was compared.

Glucose assessment and diabetes definition

We initially assessed 4019 patients who underwent CAG/PCI. Inclusion criteria were as follows: Patients who meet the diagnostic criteria for diabetes and pre-diabetes. [The American Diabetes Association (ADA) defines criteria for the diagnosis of diabetes: (1)FBG > 126 mg/dL (7.0 mmol/L); (2)2h plasma glucose (PG) > 200 mg/dL (11.1 mmol/L) during oral glucose tolerance test (OGTT); (3) glycated-haemoglobin (HbA1c) > 6.5% (48 mmol/mol); (4)In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose > 200 mg/dL (11.1 mmol/L)].(14) The diagnosis of pre-diabetes: (1) FBG between 100–125 mg/dL (5.6–6.9 mmol/L); (2)2h PG between 140–199 mg/dL (7.8–11.0 mmol/L) during OGTT; (3) HbA1c > 5.7–6.4% (39–47 mmol/mol);(16) Exclusion criteria were acute ST-segment elevation myocardial infarction (STEMI) receiving emergency PCI, receiving CM 14 days

before PCI, using any renal toxicity drugs during the perioperative period, severe renal insufficiency (creatinine clearance < 30 mL/min) or severe cardiac insufficiency (LVEF < 30%), cardiogenic shock and heart failure, hypersensitivity to CM, severe liver damage, autoimmune diseases, malignant tumor, infectious diseases or fever. (Fig. 1)

Study protocol

We finally evaluated 3437 diabetic and pre-diabetic patients undergoing CAG/PCI. All patients were given a diabetic diet after admission, and hypoglycemic drugs and insulin were applied according to the individual situation. All patients received loading doses of aspirin and clopidogrel (300 mg each) before operation. Clinicians can decide whether to use the following medicines based on clinical requirements or guidelines, including β -antagonist, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics, and statin. FBG is between 100–125 mg/dl as the diagnostic criteria for pre-diabetes. (Group 1) Patients were grouped according to the quartile of baseline fasting glucose: [Group 2: 126 to 150 mg/dl(n = 806); Group 3: 150 to 175 mg/dl(n = 1027); Group 4: 175 to 200 mg/dl(n = 735); Group 5: > 200 mg/dl(n = 349).] There was no significant difference in the average of the time between the operation time and the blood glucose measurement of the five groups of patients. Because related studies have proved that hydration in the perioperative period is effective in preventing the occurrence of CIN,⁽¹⁷⁾ all patients received isotonic saline (0.9% sodium chloride) 12 hours before and after surgery and supplemented with standard hydration solution (at least 1,000 mL) at a rate of 1 mL/kg/h. Hydration rate was reduced to 0.5 mL/kg/h for patients with LVEF $\leq$ 45%. All patients were treated with iodoprolamide contrast agent during the operation. (18)

The sample size was determined by the number of cases treated in the cardiology department of Tianjin Chest Hospital during the study period. Blood samples were collected at admission, 48h and 72h after operation to measure the Scr value of patients. The laboratory staff handling the serum samples are isolated from the treatment tasks, and the samples are only affixed with coded tags. Doctors doing the CAG/PCI therapy were remained under cover to treatment assignment. All basic patient information, blood biochemical examination and CAG/PCI data were collected in a special database in advance.

Study endpoints

The primary study endpoint was CIN, which was determined based on elevated Scr levels after exposure to CM for 48 and 72 h. Hypertension, BMI, and PCI were considered potential confounding factors for statistical analysis. Factors that were considered potential effect modifiers included health management compliance and the coronary artery condition of patients. The other clinical endpoints included adverse events such as all-cause mortality, hypotension, acute heart failure, coronary artery bypass, and cerebrovascular events, during hospitalization and after a 14-day follow-up.

Statistical analysis

Prior to the statistical analysis, patients with severe data gaps were excluded, and other missing data used missing at random (MAR) assumptions. Because only few patients lost, and follow-up results had little impact on study results, patients who missed follow-up were treat to have no major adverse events. Results are expressed as numbers (%) or mean $\pm$ SD. Compare the number of cases or means between five groups: categorical variables were compared using a chi-square test, and continuous variables were compared using an analysis of variance. Fisher's exact test was used to compare the percentages when the expected frequency was less than five. Univariable and multivariable logistic regression analysis was used to exclude the influence of confounding factors, and some high-risk confounders were selected for subgroup analysis. P for trend was used to analyze the trend between preoperative FBG levels and the increased risk of CIN. All statistical data were analyzed by SPSS software 22.0 (Inc. Chicago, IL, USA).

Results

Of the 4019 patients initially enrolled in the study, 12 received emergency PCI, 148 were administered CM before the operation, 70 were allergic to CM, 58 had severe renal insufficiency, 66 had severe cardiac insufficiency, 13 had malignant tumors, and 47 had recently used drugs leading to renal toxicity. The data of 68 patients were incomplete (Group 1: n = 11; Group 2: n = 16; Group 3: n = 20; Group 15: n=; Group 5: n = 8). The main reason for the missing data in most patients was attributed to their early discharge, which resulted in imperfect Scr levels. A total of 3437 patients were included in the study and 3185 were followed up; statistical analysis was performed based on the data of 3437 patients. There were no significant differences in the rate of major adverse events among the groups comprising the 3185 patients who were followed up.

Baseline clinical characteristics

There were no significant differences in the baseline characteristics among the 5 groups (age, male sex, smoking, left-ventricular ejection fraction (LVEF) < 45%, hypertension, contrast volume; TG, TC, HDL-C, and LDL-C levels; hydration levels; the use of beta-blockers, ACEI/ARB, CCBs, hypoglycemic agents, and insulin) before operation. Patients with elevated preoperative FBG levels were found to have higher BMI (p = 0.001) HbA1c (P < 0.0001) and Scr (P = 0.038). In addition, patients with higher blood glucose levels were found to have undergone PCI more often (P = 0.002). (Table 1)

Table 1. Comparisons of baseline characteristics between the five groups.

Variables	FBG 100 to 125 mg/dl (n=520)	FBG 126 to 150 mg/dl (n=806)	FBG 150 to 175 mg/dl (n=1027)	FBG 175 to 200 mg/dl (n=735)	FBG >200 mg/dl (n=349)	P
Age (years)	67.43±6.32	67.75±6.19	68.45±6.81	69.29±5.42	69.44±6.43	0.060
Male (%)	16(55.2)	40(47.6)	91(55.8)	86(48.0)	40(51.9)	0.605
Smoking (%)	60(57.7)	97(60.3)	131(63.9)	93(63.3)	50(71.4)	0.328
LVEF <45% (%)	3(2.9)	5(3.1)	8(3.9)	6(4.1)	2(2.9)	0.969
Hypertension (%)	64(61.5)	100(62.1)	125(61.0)	83(56.5)	42(60.0)	0.874
BMI (kg/m ²)	23.62±1.65	24.34±2.14	24.50±2.24	24.48±2.24	24.90±2.16	0.001*
Contrast volume (mL)	157.74±37.87	154.50±49.96	154.10±52.79	151.28±34.36	155.16±42.27	0.886
TG (mmol/L)	1.71±0.97	1.75±0.91	1.86±1.07	1.91±0.74	1.77±0.70	0.358
TC (mmol/L)	4.54±0.40	4.51±0.41	4.57±0.56	4.41±0.84	4.56±0.87	0.179
HDL-C (mmol/L)	1.27±0.35	1.25±0.33	1.27±0.34	1.27±0.42	1.28±0.48	0.972
LDL-C (mmol/L)	2.54±0.61	2.49±0.59	2.49±0.56	2.56±0.77	2.36±0.72	0.471
Hydration amount (mL)	1205.0±291.08	1228.4±241.17	1245.5±266.76	1218.0±203.26	1213.9±192.00	0.664
β-antagonist (%)	89(85.6)	129(80.1)	160(78.0)	120(81.6)	58(82.9)	0.587
ACEI/ARB (%)	67(64.4)	104(64.6)	137(66.3)	99(67.4)	52(74.3)	0.663
CCB (%)	13(12.5)	20(12.4)	38(18.5)	20(13.6)	9(12.9)	0.432
Hypoglycemic agents (%)	74(71.2)	112(69.6)	142(69.3)	99(70.2)	49(70.0)	0.343
Insulin (%)	19(18.3)	32(19.9)	43(21.0)	27(18.4)	15(21.4)	0.958
PCI (%)	39(37.5)	76(47.2)	109(53.2)	88(59.9)	41(58.6)	0.002*
HbA1c (%)	5.98±0.43	7.60±1.09	8.07±1.20	8.44±1.36	9.77±1.44	<0.0001*
Basal Scr (mmol/L)	80.21±14.05	82.78±14.45	83.55±12.04	84.02±15.99	86.74±11.84	0.038*
48h Scr(mmol/L)	91.43±15.74	94.69±17.65	97.46±16.17	99.26±17.84	101.49±17.84	<0.0001*
72h Scr (mmol/L)	87.07±14.93	89.15±17.03	93.89±15.69	93.60±17.74	96.88±17.22	<0.0001*
$\frac{48h\ Scr - basal\ Scr}{basal\ Scr}$	0.15±0.11	0.15±0.12	0.17±0.16	0.20±0.20	0.17±0.12	0.025*
$\frac{72h\ Scr - basal\ Scr}{basal\ Scr}$	0.09±0.10	0.08±0.12	0.13±0.18	0.13±0.18	0.12±0.12	0.006*

Table 1. Data are expressed as mean ± SD or n (%). FBG: Fasting Blood Glucose; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; CCB: calcium channel blockers; PCI: Percutaneous Coronary Intervention; HbA1c: glycosylated hemoglobin.

Comparison of Scr levels and CIN incidence among groups

Patients with elevated preoperative FBG had higher basal Scr (p = 0.038) and higher Scr levels at 48 h and 72 h after CAG/PCI. We also compared the percent change in mean Scr compared with the baseline creatinine levels at 48 and 72 h in the 5 groups and found that the difference was statistically significant (p < 0.0001). The incidence of CIN in the 5 groups of patients was 6.7%, 10.5%, 17.5%, 18.4%, and 23.2%. Univariable logistic regression analysis was used to analyze the factors affecting CIN. CIN was chosen as the dependent variable, and factors that could affect CIN development (male gender, age, LVEF < 45%,

contrast volume, hydration amount, basal Scr, BMI, hypertension, HbA1c, ACEI/ARB, CCB, PCI, and preoperative FBG) were considered as independent variables. The significant influencing factors from univariate analysis were selected for multivariate logistic regression analysis [odds ratio (OR) = 1.008 (1.001–1.016), $p = 0.028$]. (Table 2)

Table 2. Univariable and multivariable logistic regression analyses analysis for certain confounding factors of CIN.

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age (years)	1.017(0.984-1.052)	0.317		
Male	0.805(0.529-1.224)	0.310		
LVEF<45%	1.171(0.483-2.840)	0.727		
Hypertension	3.220(1.925-5.386)	<0.0001*	3.006(1.773-5.097)	<0.0001*
BMI (kg/m ²)	1.191(1.076-1.318)	0.001*	1.165(1.046-1.297)	0.005*
Basal Scr (mmol/L)	0.997(0.982-1.013)	0.729		
Contrast volume (mL)	1.004(0.999-1.008)	0.085		
PCI	2.998(1.888-4.763)	<0.0001*	2.562(1.591-4.126)	<0.0001*
HbA1c	1.152(1.013-1.310)	0.028*	0.995(0.841-1.178)	0.957
Hydration amount (mL)	1.000(0.999-1.001)	0.785		
ACEI/ARB	0.788(0.499-1.246)	0.308		
CCB	1.523(0.784-2.960)	0.214		
preoperative FBG	1.009(1.003-1.015)	0.002*	1.008(1.001-1.016)	0.028*

Table 2. BMI: body mass index; LVEF: left ventricular ejection fraction; PCI: Percutaneous Coronary Intervention; HbA1c: glycosylated hemoglobin; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blockers. FBG: Fasting Blood Glucose.

The trend test was used to further demonstrate the relationship between preoperative FBG levels and the incidence of CIN. It can be seen from the changes in OR (1.000, 1.425, 2.489, 2.704, 3.234) that the incidence of CIN increased significantly ($p < 0.0001$) with an increase in the preoperative FBG levels. (Table 3)

Table 3. The logistic regression analysis and the trend test

preoperative FBG	Participants, n	CIN, n	Odd Ratio		
			Model 1	Model 2	Model 3
FBG 100 to 125 mg/dl	520	35	1.000(Reference)	1.000(Reference)	1.000(Reference)
FBG 126 to 150 mg/dl	806	85	1.636(0.645-4.093)	1.661(0.662-4.167)	1.425(0.553-3.673)
FBG 150 to 175 mg/dl	1027	182	2.952(1.265-6.887)	2.975(1.271-6.964)	2.489(1.034-5.998)
FBG 175 to 200 mg/dl	735	135	3.261(1.365-7.787)	3.299(1.376-7.908)	2.704(1.094-6.684)
FBG >200 mg/dl	349	81	4.106(1.590-10.600)	4.082(1.575-10.580)	3.234(1.199-8.723)
P for trend	--	--	<0.0001*	<0.0001*	<0.0001*

Table 3. Model 1 was not adjusted. Model 2 was adjusted for age, male, hydration amount, CM. Model 3 additionally was adjusted for PCI, BMI, HbA1c and hypertension.

subgroup analysis

Multivariate analysis was used to confirm the association between preoperative FBG levels and the risk of CIN after adjusting for the baseline confounding factors. Our results showed that patients with elevated preoperative FBG levels (above the median value 150 mg/dL) in the main high-risk subgroups, such as BMI ($> 23.9 \text{ kg/m}^2$: adjusted OR = 2.835 (1.533–5.242), $p = 0.001$), age (≥ 65 : adjusted OR = 2.075 (1.187–3.629), $p = 0.010$), hypertension (hypertension: adjusted OR = 2.294 (1.337–3.936), $p = 0.003$), and PCI (PCI: adjusted OR = 2.298 (1.241–4.253), $p = 0.008$) had a higher risk of CIN. (Fig. 2)

Previous research shows that in diabetic patients undergoing CAG/PCI, elevated HbA1c is independently associated with the risk of CIN, and when HbA1c $> 9.5\%$, the incidence of CIN trends increase.(19) Based on previous research, we further studied the relationship between preoperative FBG levels and CIN in the HbA1c subgroup. There was a significant relationship between higher preoperative FBG levels and greater risk for CIN in patients with HbA1c 6.5%-8.0% ($P = 0.007$) and HbA1c 8.0%-9.5% ($P = 0.011$). However, the relationship between preoperative FBG and CIN was not significant among patients HbA1c 9.5%-11.0% ($P = 0.735$) and HbA1c $> 11.0\%$ ($P = 0.867$). (Fig. 3)

Discussion

In this cross-sectional study, we evaluated the relationship between preoperative FBG levels and the incidence of CIN in patients undergoing CAG/PCI. The findings of our controlled trial showed that elevated preoperative FBG levels were independently associated with the risk of CIN in diabetic and pre-diabetic patients undergoing CAG/PCI, and that the incidence of CIN gradually increased with an increase in preoperative FBG levels.

Patients who develop CIN have a greater risk for nonrenal complications including cardiac, vascular, and systemic problems. In patients who develop CIN, treatment is limited to supportive measures until renal impairment resolves. It is important to determine and control the blood glucose levels of patients before surgery to prevent postoperative CIN.(20) In addition, no single drug has been found to have a preventive

effect comparable to hydration. Therefore, identifying patients at a high risk for CIN and ensuring appropriate preventive measures is key in reducing the incidence of CIN. (21)

Type 2 diabetes mellitus is a major risk factor leading to coronary artery disease. Despite significant advances in the treatment of cardiovascular disease over the past 20 years, this condition remains the leading cause of morbidity and mortality in patients with type 2 diabetes mellitus. (22, 23) High glucose levels are associated with the increased levels of markers responsible for vascular inflammation and endothelial dysfunction. Moreover, high blood glucose levels have been associated with high levels of free fatty acids, insulin resistance, and impaired myocardial glucose utilization, which lead to increased oxygen consumption and the worsening of ischemia. Diabetes is an important predisposing factor for CIN, particularly in patients who are renally impaired. Both diabetes and contrast agents enhance ROS formation and hamper renal oxygenation, either directly or through increased ROS generation. (24) An *in vivo* study shows that CM-induced changes in diabetic rats led to significantly impaired renal function, oxidative stress, vascular dysfunction, and apoptosis compared with non-diabetic rats. (25)

Barbieri et al. have reported that elevated HbA1c is independently associated with the risk of CIN among patients without diabetes undergoing CAG/PCI. (26) Other studies included both diabetic and non-diabetic patients and were, therefore, not targeted. Thus, it is unclear whether preoperative FBG levels affect the occurrence of CIN in diabetic patients. Accordingly, we further studied whether preoperative FBG levels had an impact on the occurrence of CIN in diabetic patients, and obtained favorable results. However, the subsequent subgroup analysis of HbA1c produced interesting results. We found that for patients with known diabetes, when the HbA1c level is greater than 9.5%, the incidence of postoperative CIN is still high despite the ideal preoperative FBG control before operation. This latest result supports the latest guidelines of the European Society of Cardiology on diabetes, pre-diabetes and cardiovascular disease, suggesting that diabetes screening for cardiovascular disease patients should start with preoperative FBG and HbA1c. (27, 28) Glycemic variability is associated with intraday fluctuations in blood glucose, which may ultimately be reflected in HbA1c levels above the normal range. (29) Our findings are clinically significant because CIN is a frequent complication following intravascular administration of CM. Additionally, it is the third most common cause of AKI in hospitalized patients and second only to ischemic and drug-induced injuries. (30) In future studies, we intend to further explore whether preoperative intervention on preoperative FBG levels can reduce the incidence of CIN. The findings will likely be of great significance for diabetic patients undergoing selective PCI. Further studies on the pathogenesis of CIN and preventive measures to completely prevent this condition are also needed.

Limitations

Our study has a few limitations. We excluded patients with severe renal insufficiency and those receiving CM 14 days before the operation, as well as patients with severe cardiac insufficiency, heart failure, malignant tumors, fever, and emergency PCI. Moreover, the mechanism by which elevated blood glucose

levels cause CIN is unclear. Additionally, it is possible that stress and recent diet played a role in affecting blood glucose levels in patients.

Conclusions

In this study, we found that elevated preoperative FBG was independently associated with the risk of CIN in diabetic and prediabetic patients undergoing CAG/PCI. Meanwhile, we found that the incidence of CIN gradually increased with an increase in preoperative FBG levels. A higher risk of CIN was confirmed in patients with elevated preoperative FBG levels (> 150 mg/dL) and in major high-risk subgroups, including advanced age (> 65 years), BMI > 23.9 kg/m², hypertension, and PCI. Furthermore, patients with higher HbA1c levels (HbA1c $> 9.5\%$) still have a higher incidence of CIN regardless of whether preoperative FBG level. Therefore, patients with elevated preoperative FBG at admission should be closely monitored and active measures should be taken to prevent CIN.

Abbreviations

FBG: fasting blood glucose

CIN: Contrast-induced nephropathy

CAG: Coronary arteriography

PCI: percutaneous coronary intervention

Scr: serum creatinine

ACEI: angiotensin-converting enzyme inhibitor;

ARB: angiotensin receptor blocker

BMI: body mass index

TC: total cholesterol

TG: triglyceride

HDL-C: high-density lipoprotein cholesterol

LDL-C: low-density lipoprotein cholesterol

LVEF: left ventricular ejection fraction

CCB: calcium channel blockers

HbA1c: Glycosylated Hemoglobin

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Acknowledgements

We thank all the participants and enrolled patients of Tianjin Medical University in Tianjin of China for their cooperation.

Authors' contributions

ZP completed the collection and sorting of data and conducted the writing guidance of the article. FH was mainly responsible for writing the article and completed the related literature search; YS analyzes and interprets the data, and was responsible for the collection and analysis of blood samples for all patients. All authors took responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Funding

This study was funded by a Grant from the Tianjin Municipal Health and Family Planning Commission (Grant number: 14KG124).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflicts of interest concerning this study.

References

1. Bhatt DL. Percutaneous Coronary Intervention in 2018. JAMA. [Journal Article; Review]. 2018 2018-05-22;319(20):2127-8.
2. Mamoulakis C, Tsarouhas K, Fragkiadoulaki I, Heretis I, Wilks MF, Spandidos DA, et al. Contrast-induced nephropathy: Basic concepts, pathophysiological implications and prevention strategies.

- PHARMACOL THERAPEUT. 2017;180:99-112.
3. Mehran R, Nikolsky E. Contrast-induced nephropathy: Definition, epidemiology, and patients at risk. KIDNEY INT. 2006 2006-01-01;69:S11-5.
 4. Seeliger E, Sendeski M, Rihal CS, Persson PB. Contrast-induced kidney injury: mechanisms, risk factors, and prevention. EUR HEART J. [Journal Article; Review]. 2012 2012-08-01;33(16):2007-15.
 5. Geenen RWF, Kingma HJ, van der Molen AJ. Contrast-induced nephropathy: pharmacology, pathophysiology and prevention. Insights into Imaging. 2013;4(6):811-20.
 6. Zhang F, Lu Z, Wang F. Advances in the pathogenesis and prevention of contrast-induced nephropathy. LIFE SCI. [Journal Article; Review]. 2020 2020-10-15;259:118379.
 7. Chen Y, Fu N, Xu J, Yang S, Li S, Liu Y, et al. A simple preprocedural score for risk of contrast-induced acute kidney injury after percutaneous coronary intervention. CATHETER CARDIO INTE. 2014 2014-01-01;83(1):E8-16.
 8. Toprak O, Cirit M, Yesil M, Bayata S, Tanrisev M, Varol U, et al. Impact of diabetic and pre-diabetic state on development of contrast-induced nephropathy in patients with chronic kidney disease. NEPHROL DIAL TRANSPL. 2007 2007-01-05;22(3):819-26.
 9. Aronson D, Rayfield EJ. How hyperglycemia promotes atherosclerosis: molecular mechanisms. CARDIOVASC DIABETOL. [Journal Article]. 2002 2002-04-08;1:1.
 10. Stolker JM, McCullough PA, Rao S, Inzucchi SE, Spertus JA, Maddox TM, et al. Pre-Procedural Glucose Levels and the Risk for Contrast-Induced Acute Kidney Injury in Patients Undergoing Coronary Angiography. J AM COLL CARDIOL. 2010;55(14):1433-40.
 11. The absence of a glycemic threshold for the development of long-term complications: the perspective of the Diabetes Control and Complications Trial. DIABETES. [Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, U.S. Gov't, P.H.S.]. 1996 1996-10-01;45(10):1289-98.
 12. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. [Journal Article; Research Support, Non-U.S. Gov't]. 2000 2000-08-12;321(7258):405-12.
 13. Heyman SN, Rosenberger C, Rosen S, Khamaisi M. Why Is Diabetes Mellitus a Risk Factor for Contrast-Induced Nephropathy? BIOMED RES INT. 2013;2013:1-8.
 14. Deedwania P, Kosiborod M, Barrett E, Ceriello A, Isley W, Mazzone T, et al. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. CIRCULATION. [Journal Article]. 2008 2008-03-25;117(12):1610-9.
 15. Das SR, Everett BM, Birtcher KK, Brown JM, Januzzi JL, Kalyani RR, et al. 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes. J AM COLL CARDIOL. 2020;76(9):1117-45.

16. Standards of Medical Care in Diabetes—2020 Abridged for Primary Care Providers. *Clinical Diabetes*. 2020;38(1):10-38.
17. Nijssen EC, Rennenberg RJ, Nelemans PJ, Essers BA, Janssen MM, Vermeeren MA, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *LANCET*. [Clinical Trial, Phase III; Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. 2017 2017-04-01;389(10076):1312-22.
18. Subramaniam RM, Suarez-Cuervo C, Wilson RF, Turban S, Zhang A, Sherrod C, et al. Effectiveness of Prevention Strategies for Contrast-Induced Nephropathy: A Systematic Review and Meta-analysis. *ANN INTERN MED*. [Journal Article; Meta-Analysis; Research Support, U.S. Gov't, P.H.S.; Review; Systematic Review]. 2016 2016-03-15;164(6):406-16.
19. Zhang H, Fu H, Fu X, Zhang J, Zhang P, Yang S, et al. Glycosylated hemoglobin levels and the risk for contrast-induced nephropathy in diabetic patients undergoing coronary arteriography/percutaneous coronary intervention. *BMC NEPHROL*. [Journal Article]. 2021 2021-06-02;22(1):206.
20. Finn WF. The clinical and renal consequences of contrast-induced nephropathy. *NEPHROL DIAL TRANSPL*. 2006 2006-06-01;21(suppl_1):i2-10.
21. Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. *CMAJ*. [Journal Article; Review]. 2005 2005-05-24;172(11):1461-71.
22. Naito R, Miyauchi K. Coronary Artery Disease and Type 2 Diabetes Mellitus. *INT HEART J*. [Journal Article; Review]. 2017 2017-08-03;58(4):475-80.
23. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. *DIABETES CARE*. [Consensus Development Conference; Journal Article; Review]. 2003 2003-11-01;26(11):3160-7.
24. Andreucci M, Faga T, Pisani A, Sabbatini M, Michael A. Acute Kidney Injury by Radiographic Contrast Media: Pathogenesis and Prevention. *BIOMED RES INT*. 2014;2014:1-21.
25. Hussien NI, Sorour SM, El-kerdasy HI, Abdelrahman BA. The glucagon-like peptide-1 receptor agonist Exendin-4, ameliorates contrast-induced nephropathy through suppression of oxidative stress, vascular dysfunction and apoptosis independent of glycaemia. *CLIN EXP PHARMACOL P*. 2018;45(8):808-18.
26. Barbieri L, Verdoia M, Schaffer A, Cassetti E, Di Giovine G, Marino P, et al. Pre-diabetes and the risk of contrast induced nephropathy in patients undergoing coronary angiography or percutaneous intervention. *DIABETES RES CLIN PR*. 2014;106(3):458-64.
27. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *EUR HEART J*. [Journal Article; Review]. 2020 2020-01-07;41(2):255-323.
28. Karayiannides S, Djupsjö C, Kuhl J, Hofman-Bang C, Norhammar A, Holzmann MJ, et al. Long-term prognosis in patients with acute myocardial infarction and newly detected glucose abnormalities:

predictive value of oral glucose tolerance test and HbA1c. CARDIOVASC DIABETOL. [Journal Article]. 2021 2021-06-14;20(1):122.

29. Penno G, Solini A, Zoppini G, Orsi E, Fondelli C, Zerbini G, et al. Hemoglobin A1c variability as an independent correlate of cardiovascular disease in patients with type 2 diabetes: a cross-sectional analysis of the renal insufficiency and cardiovascular events (RIACE) Italian multicenter study. CARDIOVASC DIABETOL. [Journal Article]. 2013 2013-07-05;12:98.
30. Waikar SS, Liu KD, Chertow GM. Diagnosis, Epidemiology and Outcomes of Acute Kidney Injury. CLIN J AM SOC NEPHRO. 2008 2008-01-01;3(3):844-61.

Figures

Figure 1

Patient flowchart. CM: contrast media; CAG: Coronary arteriography PCI; percutaneous coronary intervention; Scr: serum creatinine; CIN: contrast-induced nephropathy

Figure 2

The association between preoperative FBG and CIN risk after adjusting for baseline confounding factors. The definition of elderly is greater than 65 years of age. Chinese standard BMI value: normal :18.5-23.9 kg/m². 150 mg/dl is the median elevated preoperative FBG levels. BMI: body mass index; PCI: Percutaneous Coronary Intervention.

Figure 3

The association between preoperative FBG levels and CIN across subgroups of HbA1c. FBG: Fasting Blood Glucose; CIN: contrast-induced nephropathy; HbA1c: glycosylated hemoglobin.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Proofofpolish.png](#)