Original Research

Analysis of the risk factors for contrast-induced nephropathy in over-aged patients receiving coronary intervention

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Impact statement

In this work, we evaluated the risk factors for contrast-induced nephropathy (CIN) in over-aged patients receiving coronary angiography (CAG) and percutaneous coronary intervention (PCI). We found that hypertension grade, emergency/selective operation, degree of coronary artery stenosis, eGFR, and urine microalbumin were the risk factors for CIN in over-aged patients receiving CAG and PCI. This study provides guidance for the clinical prevention of CIN in over-aged patients undergoing coronary intervention, highlighting that a perioperative comprehensive management strategy is needed to improve the prognosis.

Abstract

Contrast-induced nephropathy has been the common cause of hospital-acquired acute kidney injury in the elderly patients. This study aimed to analyze the risk factors for contrast-induced nephropathy in over-aged patients undergoing coronary angiography or percutaneous coronary intervention. A total of 470 over-aged patients ($\geq$80 years old) were judged as the contrast-induced nephropathy group ($n = 46$) and non-contrast-induced nephropathy group ($n = 424$) according to the postoperative 48-h serum creatinine levels. The patients' clinical information such as hypertension grade, number and degree of coronary artery stenosis, and death rate was compared. The risk factors for contrast-induced nephropathy were also analyzed. The hypertension grade in the contrast-induced nephropathy group was significantly higher than that in the non-contrast-induced nephropathy group ($P = 0.004$). The degree of coronary artery stenosis was significantly more in the contrast-induced nephropathy group compared with the non-contrast-induced nephropathy group ($P = 0.003$). The death rate of the contrast-induced nephropathy group (15.8%) was significantly higher than that of the non-contrast-induced nephropathy group (0.6%; $P = 0.000$). The percentage of patients with abnormal urine microalbumin was significantly bigger in the contrast-induced nephropathy group (62.5%) when comparing to the non-contrast-induced nephropathy group (23.6%; $P = 0.00$). Besides, there was also significant difference in the emergency/selective operation between the contrast-induced nephropathy group and non-contrast-induced nephropathy group ($P = 0.001$). Further, hypertension grade ($P = 0.019$), emergency/selective operation ($P = 0.025$), degree of coronary artery stenosis ($P = 0.038$), eGFR ($P = 0.034$), and urine microalbumin ($P = 0.005$) were the risk factors for contrast-induced nephropathy. Hypertension grade, emergency/selective operation, degree of coronary artery stenosis, eGFR, and urine microalbumin were the risk factors for contrast-induced nephropathy in over-aged patients receiving coronary angiography and percutaneous coronary intervention, providing guidance for the clinical prevention of contrast-induced nephropathy.

Keywords: Contrast-induced nephropathy, over-aged patients, coronary angiography, percutaneous coronary intervention, risk factors

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Introduction

With the extension of average life expectancy, the number of elderly patients receiving coronary angiography (CAG) and percutaneous coronary intervention (PCI) has also increased.[1–6] Currently, contrast-induced nephropathy (CIN) has been the common cause of hospital-acquired acute kidney injury in the elderly patients.[7] The elderly patients are often complicated with multiple diseases, remarkably increasing the clinical risk.[8,9] Once CIN occurs, the complications such as renal insufficiency, diabetes, heart failure, and hypertension would significantly increase the incidence and mortality of renal and

cardiovascular adverse events, severely affecting the survival and prognosis of elderly patients.[7,10] Studies have shown that the incidence of CIN in elderly patients with coronary heart disease receiving PCI was as high as 19.51%.[11,12]

No effective method has been established in the treatment of CIN, therefore the prevention of CIN was of clinical significance. In this study, we retrospectively reviewed a total of 470 over-aged patients undergoing CAG and PCI to examine the incidence and risk factors of CIN, providing a scientific basis for the establishment of a perioperative comprehensive management strategy for the interventional diagnosis and treatment of over-aged patients with coronary heart disease.

Materials and methods

Subjects

This retrospective study was approved by the Shanghai Tong Ren Hospital. Written informed consent was obtained from all patients. A total of 470 over-aged patients (more than 80 years old) who had previously received CAG and PCI at the Cardiology Department of Shanghai Tong Ren Hospital from June 2015 to December 2017 were enrolled, including 270 females and 200 males.

Exclusion criteria. Patients with one of the following situations were excluded: patients who are allergic to contrast agent, patients receiving coronary artery bypass grafting (CABG), patients with malignant tumors, patients undergoing PCI one week before surgery, patients with kidney transplantation or end-stage renal disease requiring dialysis, patients with severe infection and liver function damage, patients with hematonosis, patients with systemic immune system or connective tissue disease, and patients who had used the nonsteroidal anti-inflammatory drugs or nephrotoxic drugs (such as dimethylamine) in the perioperative period.

Methods

Selective CAG was performed using the Judkins' method.[13] With more than 50% coronary artery stenosis was diagnosed as coronary heart disease. More than 50% stenosis in the left main coronary artery; and more than 70% stenosis in left anterior descending coronary artery, left circumflex coronary artery or right coronary artery were set as the standards for stent placement.

Perioperative drug preparations for selective patients. The patients with a normal preoperative creatinine level (female $\leq$84 pM, male $\leq$106 pM) were treated with conventional nonionic contrast agent (Iodohexanol; Beijing North Road Pharmaceutical Co. Ltd).

The patients with a mildly or moderately abnormal preoperative creatinine level (female $\leq$84–120 pM, male $\leq$106–120 pM) were also treated with iodohexanol. Besides, these patients were hydrated with 0.9% NaCl solution (1 mL/kg.h) within postoperative 6–12 h. For the patients with left ventricular ejection fraction (LVEF) $<$50%, and Fillip cardiac functional grading 11 or New York Heart Association (NYHA) Functional Classification I, IV, the hydration rate was adjusted to 0.5 mL/kg h.

The patients with a severely abnormal preoperative creatinine level ($>$120 pM) were treated with iso-osmolar contrast agent (Iodixanol; GE Healthcare Ireland) as well as preoperative and postoperative hydration.

All patients were administrated with a preoperative 300 mg of aspirin and 300 mg of clopidogrel. At least one-year treatment of 100 mg/d of aspirin and 75 mg/d of clopidogrel was required after PCI. If no contraindications occurred, all the patients in this study routinely received β blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin 11 receptor antagonists (ARBs), and statins.

Examinations and grouping. The patients' basic data including age, gender, weight, dosage of contrast agent, medical history, type of coronary heart disease, preoperative renal function, albumin, creatine kinase (CK) and troponin I (TnI), fasting blood glucose, LVEF, the renal function, urine routine, urine microalbumin were recorded. Moreover, the estimated glomerular filtration rate (eGFR) before surgery and at 24 h, 48 h and seven days after surgery were also recorded. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) Study equation,[14,15] and eGFR less than 60 mL/(min·m^2) was defined as renal insufficiency.[16]

According to the postoperative 48-h serum creatinine, the patients were divided into the CIN group ($n = 46$) and non-CIN group ($n = 424$), and the above indicators were comparatively analyzed.

Diagnostic criteria of CIN: the serum creatinine levels were increased by $>$25% compared with normal creatinine levels or the absolute value of serum creatinine $>$ 44.2 umol/L 48 h after the use of contrast agent, according to the 2011 ACCF/AHA/SCAI Guideline for PCI.[17]

Definitions and criteria. The criteria of hypertension grade and degree of coronary artery stenosis are shown in Table 1. Table 2 displays the criteria of other clinical indicators

Table 1. Criteria of hypertension grade and severity of coronary heart disease.

Definitions	Grades	Indexes
Hypertension grade	0	Normal blood pressure
	1	140 < SBP < 159 mmHg or 90 < DBP < 99 mmHg
	2	160 < SBP < 179 mmHg or 100 < DBP < 109 mmHg
	3	SBP≥180 mmHg or DBP≥110 mmHg
Degree of coronary artery stenosis	0	Normal
	1	Mild (stenosis less than 50%)
	2	Moderate (stenosis between 50–70%)
	3	Severe (stenosis more than 70%)
	4	Chronic and total occlusion (100% stenosis)

SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2. Criteria of other clinical indicators.

Indexes	Normal range	Abnormal range
Albumin (g/L)	35–55	<35
Creatine kinase (CK, U/L)	30–135	>135
Fasting blood glucose (mmol/L)	3.5–6.1	–
Troponin I (TnI, ng/mL)	0–0.5	>0.5
brain natriuretic peptide (BNP, pg/mL)	0–100	>100
LVEF (%)	>55%	–
Uric acid (μmol/L)	155–357	>357
Urea (mmol/L)	2.9–8.2	>8.2
Creatinine (mmol/L)	45–84	>84
Urine microalbumin (mg/L)	0–19	>19
eGFR	–	$\leq$60 mL/(min · 1.73 m^2)

eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction.

including the level or value of albumin, CK, fasting blood glucose, TnI, BNP, LVEF, uric acid, urea, creatinine, urine microalbumin, and eGFR.

Statistical analysis

The statistical analysis was performed using SPSS16.0 software. The measurement data were shown as mean ± SD, and the enumeration data were shown as *n* (%). The one sample Kolmogorov–Smirnov test was conducted for all statistical variables. The comparison between groups was performed using the Mann–Whitney U test and Wilcoxon test (variables not in accordance with normal distribution). Multiple stepwise regression analysis was used to analyze the risk factors for CIN using the CIN as the dependent variable and other indexes as the independent variables. *P*-value less than 0.05 was considered as statistically significant.

Results

Comparison of patients' basic information between the control and treatment groups

Among the 470 cases of over-aged patients, 46 cases (9.8%) of patients suffered from CIN and were defined as the CIN group, including 18 males and 28 females (9/14). There were 424 cases (90.2%) of patients in the non-CIN group, including 182 males and 242 females (91/121). Their basic and clinical data are compared and displayed in Table 3.

The hypertension grade in the CIN group was significantly higher than that in the non-CIN group ($P = 0.004$). The degree of coronary artery stenosis was significantly more in the CIN group compared with the non-CIN group ($P = 0.003$). The death rate of the CIN group was significantly higher than that of the non-CIN group ($P = 0.000$). The percentage of patients with abnormal urine microalbumin was significantly bigger in the CIN group when comparing to the non-CIN group ($P = 0.000$). Besides, there was also significant difference in the emergency/selective operation between the CIN group and non-CIN group ($P = 0.001$). No significant difference was found in the other parameters (Table 3)

Table 3. The basic clinical data of over-aged patients in CIN group and non-CIN group.

Groups	CIN group ($n = 46$)	Non-CIN group ($n = 424$)	*P*
Male/female	18/28	182/242	0.612
Age (years)	84.68 ± 4.16	83.19 ± 3.25	0.071
Hypertension grade	2.48 ± 0.79	2.08 ± 1.36	0.004
Mortality	15.8	0.6	0.000
Operation timing			0.001
Emergency (%)	20.1	4.8	
Selective operation (%)	81.2	96.1	
Surgery type			0.678
CAG (%)	70.6	69.4	
CAG+PCI (%)	30.5	33.4	
Number of stenosed coronary vessels	3.12 ± 2.24	2.29 ± 2.30	0.016
Degree of coronary artery stenosis	2.69 ± 0.81	2.40 ± 1.19	0.003
Perioperative drugs			0.623
Iodohexanol (%)	69.2	73.4	
Iodixanol (%)	20.4	16.3	
Abnormal albumin (%)	16.7	8.6	0.142
Abnormal CK (%)	50.1	25.2	0.061
Abnormal blood glucose (%)	36.4	32.7	0.725
Abnormal TnI (%)	17.0	13.4	0.633
Abnormal BNp (%)	69.2	55.1	0.132
Abnormal LVEF (%)	5.9	4.8	0.586
Abnormal uric acid (%)	20.6	16.9	0.863
Abnormal urine microalbumin (%)	62.5	24.6	0.000
Abnormal urea (%)	46.3	41.9	0.762
Abnormal creatinine (%)	36.1	31.2	0.469

CIN: contrast-induced nephropathy; LVEF: left ventricular ejection fraction.

Table 4. Analysis of the risk factors for CIN in over-aged patients.

Indexes	Coefficient	*P*
Hypertension grade	0.589	0.019
Emergency/selective operation	−3.540	0.025
Degree of coronary artery stenosis	0.598	0.038
eGFR	−1.116	0.034
Urine microalbumin	1.513	0.005

eGFR: estimated glomerular filtration rate; CIN: contrast-induced nephropathy.

Analysis of the risk factors for CIN in over-aged patients

As mentioned above, multiple stepwise regression analysis was used to analyze the risk factors for CIN using the CIN as the dependent variable and other indexes as the independent variables. As shown in Table 4, hypertension grade ($P = 0.019$), emergency/selective operation ($P = 0.025$), degree of coronary artery stenosis ($P = 0.038$), eGFR ($P = 0.034$), and urine microalbumin ($P = 0.005$) were the risk factors for CIN in over-aged patients receiving CAG and PCI.

Analysis of eGFR in over-aged patients with or without CIN

The eGFR before surgery and at 24 h, 48 h and seven days after surgery in the CIN group and non-CIN group were

Table 5. eGFR detected at different stages in CIN group and non-CIN group (mL/[min · 1.73 m^2]).

Stages	CIN group ($n = 46$)	Non-CIN group ($n = 424$)	*P*
Before surgery	72.07 ± 21.35	73.68 ± 32.54	0.826
24 h after surgery	67.19 ± 26.78	69.28 ± 30.65	0.935
48 h after surgery	72.36 ± 28.43	73.58 ± 29.65	0.768
7 days after surgery	78.2 ± 28.66	77.94 ± 30.21	0.854

CIN: contrast-induced nephropathy; eGFR: estimated glomerular filtration rate.

comparatively analyzed. It indicated that no significant difference was observed between the two groups in eGFR before surgery and at 24 h, 48 h and seven days after surgery (Table 5). Among the 46 cases of patients with CIN, there were 2 cases (4.3%) with the eGFR < 30 mL/(min·m^2), 16 cases (34.8%) with the eGFR between 30 and 60 mL/(min·m^2), 17 cases (37%) with the eGFR between 60 and 90 mL/(min·m^2), and 11 cases (23.9%) with the eGFR ≥90 mL/(min·m^2).

Discussion

With the rapid development of the diagnosis and treatment technologies of coronary artery, more and more patients with coronary heart disease have been treated actively, especially for the elderly patients. However, hypertension and arteriosclerosis in the elderly patients can lead to the ischemia of renal tissue, loss of functional nephrons, decreased effective nephrons, and reduced glomerular filtration rate.[18] Therefore, the elderly patients themselves are at high risk for CIN. Studies have shown that the incidence of CIN in elderly patients with coronary heart disease receiving PCI was as high as 19.51%.[11,12] A meta-analysis of randomized, controlled trials revealed that the incidence of CIN was markedly reduced after the renal protective measures were taken.[19] Animal studies demonstrated that the renal vessels were firstly expanded briefly and then subjected to a sustained contraction of ~3 h after the injection of contrast agent.[20] However, in previous study, the human renal blood flow was reduced by 50% about 4 h after the use of contrast agent.[21,22] After the injection of contrast medium, renal vascular endothelial cells would increase the release of various vasoconstriction factor and decrease the release of vasodilatation factors, and this imbalance could result in renal hypoxia and aggravated injury. There has been no effective method in the treatment of CIN, and therefore the prevention of CIN was of clinical significance.

Full hydration and the use of nonionic isotonic contrast agent have been recognized as the most effective way to prevent CIN. They could accelerate the removal of contrast agent, increase the effective circulating blood volume, and prevent the renal vascular obstruction, thereby reducing the nephrotoxicity of contrast agent, relieving the renal ischemia and hypoxia, and reducing the degree of kidney damage. In this study, a different contrast agent was used in the two groups. However, no obvious difference between the two groups was found, which might be due to the limited samples and preoperative strict selection of the contrast agent and hydration method according to the renal function.

The conditions of over-aged patients with acute myocardial infarction undergoing emergency surgery were always severe, with obvious vascular calcification and circuity, more stenosed left main coronary artery and branches, difficult interventional operation, and increased contrast agent dose, leading to a higher incidence of complications and mortality rate.[23–25] In this study, we found that there was significant difference in the emergency/selective operation between the CIN group and non-CIN group, and emergency/selective operation was the risk factor for CIN in over-aged patients receiving CAG and PCI, consistent with previous studies. Therefore, caution should be taken for the over-aged patients with coronary heart disease undergoing emergency surgery.

Hypertension is also an important risk factor for CIN, and this clinical risk is associated with preoperative renal function.[26] Previous studies showed that the long-term increase of arterial blood pressure could damage the self-regulating function of renal vessel,[27] and induce arteriosclerosis as well as renal arteriole thickening, resulting in the hypertension and high filtration of glomerular capillary, and eventually causing the ischemia and sclerosis of glomerulus.[28] Hypertension-induced kidney injury increased with the time and grade levels of hypertension.[29,30] Consistent with these studies, in the present study, the hypertension grade in the CIN group was significantly higher than that in the non-CIN group. Moreover, classification of hypertension was the risk factor for CIN in over-aged patients receiving CAG and PCI.

In the early stage of renal injury, the blood creatinine was normal and the eGFR was negative, but the urine microalbumin could be detected and widely observed in patients with hypertension and diabetes.[31,32] Hypertension and diabetes are the most important risk factors for coronary heart disease.[33] The probability of patients with abnormal urine microalbumin receiving CGA was significantly higher than that of general population; therefore, urine microalbumin could be used as a sensitive marker to indicate early kidney disease and injury before the interventional diagnosis and treatment of coronary heart disease.[34] Abnormal urine microalbumin was not only associated with multiple cardiovascular risk factors or diseases, but also was closely related to cardiac death and total death.[35] In this study, we found that the percentage of patients with abnormal urine microalbumin was significantly bigger in the CIN group when comparing to the non-CIN group, and urine microalbumin was the risk factor for CIN in over-aged patients receiving CAG and PCI. These results suggested that the preoperative measurement of urine microalbumin was beneficial to the early detection of the risk factors and timely prevention for CIN. In addition, care manager is also considered as a significant factor for CIN in the health care system, as suggested by Ciccone.[36]

In conclusion, classification of hypertension, emergency/selective operation, the degree of coronary artery stenosis, eGFR, and urine microalbumin were the risk factors for CIN in over-aged patients receiving CAG

and PCI. Our study provides a scientific basis for developing a perioperative comprehensive management strategy for the interventional diagnosis and treatment of over-aged patients with coronary heart disease, aiming to improve the prognosis.

Authors' contributions: Hui-Chao Pan conceived and designed the study and drafted the manuscript. Xian-Hao Wu collected the data and Qian-Li Wan contributed to the statistical analysis. Bao-Hong Liu interpreted the data. Xu-Sheng Wu put forward the concept of the study and reviewed the manuscript. All authors read and approved the final manuscript.

DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ETHICS APPROVAL

The study was approved by ethics committee of Shanghai Tong Ren Hospital.

CONSENT FOR PUBLICATION

The study was undertaken with the patient's consent.

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