International Journal of Gerontology 12 (2018) 196–199

Contents lists available at ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Original Article

Clinical Features of CINin ChineseVery Elderly Patients Undergoing Coronary Angiography Procedure With Hydration Treatment: A Three-Center, Prospective Study

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ARTICLE INFO

Article history:
Received 27 June 2017
Received in revised form
28 February 2018
Accepted 29 May 2018
Available online 19 July 2018

Keywords:
Contrast induced nephropathy,
hydration treatment,
morbidity,
risk factors,
very elderly patient

SUMMARY

Background: To assess the morbidity and risk factors of contrast induced nephropathy (CIN) in Chinese very elderly patients.

Methods: The very elderly patients whose age ≥75 year-old, from North Huashan Hospital, South Renji Hospital and Tongren Hospital, underwent coronary angiography or percutaneous coronary intervention, were included in this study. All of these patients were treated by hydration, those who developed contrast-induced nephropathy were divided into CIN group and the others were divided into non-CIN group. The baseline information was evaluated and serum creatinine was measured prior to the coronary angiography and 24 h, 48 h after procedure. The data was analyzed by the software SPSS17.0.

Results: 163 very elderly patients were included in this study. The occurrence of CIN in very elderly patients was approximately 8.6%. In CIN group, serum creatinine concentration was statistical significance between prior data and 24 h/48 h after procedure data, but there's no statistically significant differences between 24 h data and 48 data after procedure. Multivariable analysis showed that patient's age (p value 0.026, OR 1.171, 95% CI 1.019–1.347), and complicated lesion (p value 0.025, OR 3.91, 95% CI 1.185–12.896) were correlation with CIN.

Conclusion: The incidence of CIN with hydration treatment is similar to that of average patients. Very elderly patient with older age, higher dosage of contrast media and complicated lesion is vulnerable to develop CIN.

1. Introduction

Contrast induced nephropathy (CIN) is the 3rd major reason of acute renal failure in patients admitted in hospital, which happened about 5% in relatively healthy patients. In general, according to definition of contrast induced acute kidney injury (AKI) from the European Society of Urogenital Radiology, CIN is diagnosed when serum creatinine (Scr) levels increased by 25% or 0.5 mg/dl after use of contrast.[1,2] Previous study demonstrated that older age is one of the most important risk factors of CIN in general population.[3] Besides, diabetes, chronic renal dysfunction, overuse of contrast were also proved to be the risk factors which contributes to CIN development and the prevention procedure includes hydration treatment, special medication.[4–8]

In 2010, the average life expectancy of China was officially[9] estimated at 72.5 year-old in male and 76.8 year-old in female, compared with earlier data, which indicates that the elderly population has increased significantly these years in China contributes to the economic development and the living standards' improvement. Based on an estimation by the United Nation,[10] in China, the population of 75 year-old or even older will reach to 103 million in 2050 which will become a great burden to Chinese healthcare system. Elderly population are prone to have more cardiovascular problems combined with hypertension and diabetes, accompanied with renal function impairment, who need coronary angiography (CAG) or percutaneous coronary intervention (PCI) for diagnosis and treatment. More contrast agents will be used in these elderly patients.

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https://doi.org/10.1016/j.ijge.2018.05.010

By this reason, it is important for Chinese doctors to understand whether very elderly patients, whose age ≥75 year-old, are more vulnerable to contrast agents or not, and what other factors combined with elderly age would lead more possibility to develop CIN. In this study, we prospectively analyzed renal function change of elderly patients receiving contrast agents for CAG/PCI procedure and undergoing the treatment of hydration. We compared incidence of CIN in very elderly patients receiving CAG or PCI treatment with average patient in other studies and analyzed the risk factors combined with elderly age that may help lead to CIN in this population.

2. Materials and methods

2.1. Study population

A total of 163 patients whose age ≥75 year-old undergoing CAG with or without PCI were enrolled in succession in this study from February 2012 to March 2013 in three centers in Shanghai, including North Huashan Hospital, South Renji Hospital and Tongren Hospital, which represents the population of north, southeast and middle part of Shanghai. Patients were enrolled for CAG if they complained of angina at rest or after exercise and possessed cardiovascular risk factors and excluded if: (1) they received contrast agents within one week prior to this study; (2) patients with allergy to contrast agents and/or anesthetic agents; (3) patients receiving hemodialysis treatment or e GFR < 30 ml/min/1.73 m^2 at the same time. After confirmed stenosis of coronary greater than 75%, patients diagnosed ACS or angina will be treated by PCI. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Fudan University. Written informed consent was obtained from all participants.

2.2. Study protocol

Patients' baseline clinical data, such as age, gender, weight, history of hypertension, diabetes, heart failure, contrast volume and multiple vessel disease were recorded if enrolled into study. Serum creatinine were sampled prior to the operation, 24 h and 48 h after procedure and according to serum creatinine concentration, eGFR was calculated by MDRD formula[11,12] in every patient. CIN was diagnosed when serum creatinine levels increased by 25% or 0.5 mg/dl after the use of contrasts. Hypertension is defined as previous diagnosis treated with anti-hypertension drug or blood pressure over 140/90 mmHg twice admitted in hospital. Diabetes is defined as previous diagnosis treated with hypoglycemic agent or fasting blood glucose over 7.0 mmol/L or OGTT glucose over 11.0 mmol/L admitted in hospital. Heart failure is defined as systolic or diastolic dysfunction of left ventricular measured by echo admitted in hospital.

Patients were divided into two subgroups according to eGFR: normal group (eGFR≥60 mL/min/1.73 m^2) and abnormal group (eGFR<60 mL/min/1.73 m^2). All patients were given hydration treatment (treated by 0.5% saline given intravenously at a rate of 1 ml/kg/h starting the same day of CAG and from about 3 h before scheduled time for CAG) because of their very elderly age to prevent them from renal dysfunction in a certain extent.

2.3. Contrast agents use

Combined with hydration, non-ionic contrast agent, iopamidol, produced by Bracco Xinyi Pharmaceutical Co Ltd, Shanghai, was used for patients in this study. Generally, specific formula [5 (ml) × patient's body weight (kg)/serum creatinine (mg/dl)] was used to calculate the maximum recommended dose of contrast agent prior to the operation and the maximum dose of contrast could not exceed 300 mL in every patient.

2.4. Statistical analysis

SPSS17.0 software was used for statistical analysis. Pearsonchi-square test was used for comparison of data rate between groups. The t-test was used for analysis of measurement data as mean ± standard deviation between groups for normal distribution of measurement data. For not normal distribution of measurement data between the two groups, Wilcox on test was used. Multivariable analysis was used to detect the risk factors. $P < 0.05$ was considered statistically difference.

3. Results

A total of 163 subjects were enrolled from North Huashan Hospital, South Renji Hospital and Tongren Hospital during February 2012 to March 2013, which included 96 patients with simple coronary angiography and 67 patients with coronary angiography treatment by PCI. In 163 patients, 111 patients were divided into normal group (eGFR ≥60 mL/min/1.73 m^2) and 52 patients into abnormal group (eGFR <60 mL/min/1.73 m^2). All of these patients in both groups were treated by hydration and 14 (8.6%) patients (7.2% in normal group lower than 11.5% in abnormal group, $P < 0.05$) were diagnosed CIN according to CIN definition. According to the incidence of CIN, we classified all subjects into 4 groups, CIN with CAG group (5 patients), CIN with PCI group (9 patients), non-CIN with CAG group (91 patients) and non-CIN with PCI group (58 patients) (Table 1).

The patients' age was average at 81.3 year-old and 40.5% of them were male. Baseline database was recorded, which indicated 93% patients in CIN group and 63% in non-CIN group had hypertension, 29% in CIN group and 17% in non-CIN group had diabetes, 14% in CIN group and 6% in non-CIN group had chronic heart failure. Baseline serum, BUN and hemoglobin were also recorded (Table 2).

The absolute changes or relative changes compared with baseline serum creatinine concentration was the basic steps to the judgment of CIN. So we analyzed that the creatinine values in the CIN and non-CIN group before operation, 24-h after operation and 48-h after operation (Table 3). There was obvious difference between pre-operation and 24 h post-operation in CIN group, P value was 0.016; the result was the same between preoperative and 48 h postoperative data in CIN group, P value was 0.027. Furthermore, there was no significant statistics difference between 24 h postoperative data and 48 h postoperative data (P value was 0.70) in CIN group. On the other hand, no obvious statistics difference was discovered between preoperative, 24 h postoperative and 48 h postoperative data in non-CIN group.

Compared with patients in both groups, age, gender, volume of contrast and complex lesion showed statistical significance in single factor regression analysis. Then multivariable analysis showed

Table 1
The incidence of CIN in both groups.

	Normal group			Abnormal group		
	CIN group	Non-CIN group	Total	CIN group	Non-CIN group	Total
CAG	3	66	69	2	25	27
PCI	5	37	42	4	21	25
Total	8 (7.2%)	103	111	6 (11.5%)	46	52

Note: CAG, coronary angiography; PCI, percutaneous coronary intervention; CIN, contrast induced nephropathy; non-CIN, non-contrast induced nephropathy.

Table 2
Baseline clinical characteristics of all patients.

	CIN group			Non-CIN group		
	Total (N = 14)	CAG (N = 5)	PCI (N = 9)	Total (N = 149)	CAG (N = 91)	PCI (N = 58)
Age (year)	84.4 ± 4.8**	82.8 ± 3.8	85.3 ± 5.2	81.0 ± 3.7	81.1 ± 3.8	80.8 ± 3.5
Gender (male%)	34	20	49	38	37	39
Weight (kg)	63 ± 4	62 ± 5	63 ± 2	63 ± 2	62 ± 5	63 ± 6
BMI	22.31 ± 1.47	22.67 ± 2.20	22.18 ± 1.50	22.58 ± 2.03	22.60 ± 2.39	21.98 ± 1.79
Hypertension (%)	93**	100	89	63	60	62
Diabetes (%)	29**	20*	33	17	21*	10
Heart failure (%)	14**	0*	22	6	8	3
Scr (umol/L)	81.7 ± 23.1	73.2 ± 25.6*	86.4 ± 21.6	84.2 ± 26.5	82.6 ± 25.5	86.8 ± 28.1
BUN(mmol/L)	7.13 ± 2.23	6.86 ± 2.34*	7.18 ± 2.30	6.99 ± 2.44	6.87 ± 2.31*	7.18 ± 2.63
Hemoglobin (g/L)	118.9 ± 14.94**	121.8 ± 9.91	117.2 ± 17.46	122.62 ± 13.81	122.36 ± 13.43	123.03 ± 14.5
e-GFR	72.2 ± 23.6	82.9 ± 28.1*	66.2 ± 19.9	71.3 ± 21.2	72.5 ± 19.7	69.5 ± 23.5
Contrast volume (ml)	127.1 ± 53.8**	68.0 ± 17.9*	160.0 ± 33.9	94.0 ± 50.7	60.3 ± 10.5*	146.9 ± 42.8
MVD (%)	50**	60*	44	14	14	14

Note: **P < 0.05, compared with parameters in patients with Non-CIN group. *P < 0.05, compared with parameters in patients between CAG group AND PCI group. CAG, coronary angiography; PCI, percutaneous coronary intervention; CIN, contrast induced nephropathy; non-CIN, non-contrast induced nephropathy; MVD, multiple vessel disease.

Table 3
Serum creatinine concentration in CIN and non-CIN group of preoperative and postoperative.

	CIN group			non-CIN group		
	CAG	CAG + PCI	Total	CAG	CAG + PCI	Total
Preoperation	73.2 ± 25.6	86.4 ± 21.6	81.7 ± 23.1	82.6 ± 25.5	86.8 ± 28.1	84.2 ± 26.5
24 h	98.2 ± 34.1	127.8 ± 50.6	117.2 ± 46.4*	83.2 ± 24.5	82.2 ± 23.8	82.8 ± 24.2
48 h	89.2 ± 26.6	122.8 ± 42.7	110.8 ± 40.2#	81.5 ± 24.1	81.9 ± 23.0	81.7 ± 23.6

Note: preoperation: serum creatinine before operation; 24 h: serum creatinine after 24 h of procedure; 48 h: serum creatinine after 48 h of procedure; CIN, contrast induced nephropathy; non-CIN, non-contrast induced nephropathy. *P = 0.016 difference between pre-operation and 24 h post-operation data in CIN group, #P = 0.027 difference between preoperative and 48 h post-operative data in CIN group.

that age (value 0.026, OR 1.171, 95% CI 1.019–1.347) and multiple vessel disease (MVD) values (p value 0.025, OR 3.91, 95% CI 1.185–12.896) were correlated with CIN within these 4 factors (Table 4).

4. Discussion

In general, with the coronary angiography becoming more popular, the studies of safety in CAG/PCI have getting more focused in these decades. Although CIN is one of the most concerned disease, the morbidity of contrast nephropathy in very elderly patients still remained uncovered in the situation of accelerated aging process on a global scale. But the studies of contrast nephropathy in very elderly patients are still limited. Although this study included low case number, but all these patients came from three parts of Shanghai and they followed a succession protocol to be included in this study. Contrast induced nephropathy not only causes renal impairment, but also increases the incidence of cardiac complications in patients after percutaneous coronary intervention. Therefore, specific risk assessments are important before coronary interventions in these very elderly patients. Our study used a 75 year-old as a cut-off point based on the current life span of expectation in metropolitan area of China like Shanghai to estimate the CIN incidence in very elderly patients receiving CAG with/without PCI in order to discover the real statistic of CIN in Chinese advanced aged patients.

Table 4
Logistic regression model.

	P value	Exp (β)	95% CI for Exp (β)	
			Lower	Upper
Gender	0.305	0.504	0.144	1.813
Age	0.026*	1.171	1.019	1.347
Volume of contrast	0.344	1.005	0.994	1.016
Complicated lesion	0.025*	3.91	1.185	12.896

*P < 0.05.

Although there were several approaches to prevent from renal dysfunction, we chose the most ordinary and safe one: hydration. Our hydration procedure was done on the same day of CAG and 3–6 h before planned CAG time. Some articles have proved hydration a prevention method to avoid CIN and the recommended protocol is similar to ours.[12]

Firstly, we found that approximately 8.6%, which consists of about 7.2% in normal group and 11.5% in abnormal group of these patients developed CIN, even they were treated by hydration. In Chinese population, Jin et al.[13] reported their results in a randomized, controlled trial, the incidence of CIN in elderly patients with hydration therapy was 7.4%, which is similar to our results. In Chen et al. study,[14] about 6.67% of 330 patients received hydration with normal renal function developed CIN, which incidence was lower than our data. Key et al.[15] concluded about 4% in 100 patients developed CIN with protective methods; otherwise, 14.8% of CIN among 196 patients under PCI without any prevention treatment was reported in Peng et al. study.[16] Our result was similar to some studies in Chinese elderly patients with hydration and the incidence was higher than some trials in average aged population with prevention treatment, which in some way demonstrated that elderly patients are prone to developing CIN. Compared with Peng's results, our data showed that the incidence of CIN in elderly population with protection treatment was lower than those average aged patients without any protection methods, such as hydration or acetylcysteine taken. These previous studies of Chinese population combined with our data indicates that higher incidence of CIN in Chinese very elderly population and hydration treatment may protect them from developing CIN. Contrast-induced nephropathy

appears to be a reduction in renal blood flow and direct tubular epithelial toxicity. Hydration helps renal perfusion and which may counteract various pathological mechanisms underlying CIN. Additionally, hydration may release inflammation, reduce oxidative stress reactions, and protect the kidney from injury due to contrast injection.[17–21]

Secondly, the serum creatinine concentration of patients in CIN group increased rapidly after procedure both in 24 h data and 48 h data and there's no statistically significance between these two data groups. On the other hand, in non-CIN group, the serum creatinine concentration had no statistically rising in either groups. The potential renal function in very elderly patients was lower than average aged patients so that they had poor recovery ability from contrast injection injury. In order to diagnose CIN, our results remind doctors could rely on the first 24 h postoperative data after CAG/PCI, which means that the first 24 h outcomes of serum creatinine could definitely diagnose CIN and additional test can be avoided in elderly patients only for diagnosis. Besides, long-term serum creatinine observation in very elderly patients should be recommended firmly in order to discover the persistent impaired renal function and give the proper and seasonable prescription for these patients.

Thirdly, multivariable analysis showed patients with three risk factors, elderly age, higher contrast volume and multiple vessel diseases, are more vulnerable to develop CIN. In addition to other two factors, age may be one of the most important factors, which causes CIN developing. We speculated from this result that, very elderly patients had more inclinations to undergo PCI treatment than receive CAG alone. In other word, these patients were prone to boasting complex multiple vessel disease and which may lead to increased contrast volume use during PCI treatment. In many former studies, pre-exist CKD, dehydration, hypotension before surgery, diabetes mellitus, advanced age, co-administration of nephrotoxic drug, increased volume of contrast were proved as risk factors of CIN occurrence.[22–25] In our studies, we estimated patients' renal function carefully by eGFR using MDRD formula in order to take more attention to serum creatinine change. Besides, we avoided using nephrotoxic drugs in patients with abnormal renal function and utilized hydration to prevent very aged patients from dehydration and protect renal function from decreased blood flow and direct tubular epithelial toxicity in advance. Even by hydration methods, approximately 11.5% in abnormal group had diagnosed CIN. In conclusion, we suggest that necessary steps should be taken to mitigate risks for aged patients very carefully, especially for patients undergoing PCI with increased dose of contrast agents use. Furthermore, the maximum dose of contrast agent needs to be carefully estimated and more prevention methods addition to hydration, should be used in very elderly patients.

5. Limitation

The present study had several limitations. First of all, the samples were small, probably with less power in reaching the definite conclusions. Another limitation is the protection method of hydration has no matched group because of sample amount. At last, most patients can be safely discharge, long-term renal function observation should be paid more attention.

6. Conclusion

We will make further research on pathogenesis, prevention and treatment of contrast-induced nephropathy in very elderly patient, and bring more benefit to the elderly undergoing coronary interventions treatment and reduce the incidence of CIN to some extent.

Conflicts of interest

The authors declare no conflict of interest.

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