Low free triiodothyronine is associated with contrast-induced acute kidney injury and long-term outcome in elderly patients who underwent percutaneous coronary intervention

Chunjin Lin#, Kaiyang Lin#, [1], Yansong Guo#, [1], Zhebin You, Weiping Zheng, Fan Lin, Tailin Guo, Pengli Zhu

Department of Geriatric Medicine, Fujian Provincial Hospital, Fujian Key Laboratory of Geriatrics, Fujian Provincial Center for Geriatrics, Fujian Medical University; Fuzhou-*China*
[1]Department of Cardiology, Fujian Provincial Hospital, Fujian Medical University, Fujian Cardiovascular Institute; Fuzhou-*China*

Abstract

Objective: Low free triiodothyronine (fT_3) is common in elderly patients with cardiovascular disease. The purpose of this study was to evaluate the relationship between low fT_3 and contrast-induced acute kidney injury (CI-AKI), including the long-term outcomes, in elderly patients after a percutaneous coronary intervention (PCI).
Methods: A total of 350 patients aged ≥75 years who underwent PCI between January 2012 and December 2015 were consecutively enrolled. The perioperative thyroid function, including fT_3, was measured before PCI. A low fT_3 was defined as fT_3 <3.1 pmol/L with normal thyrotropin and free thyroxine. CI-AKI was defined as an absolute serum creatinine (SCr) increase ≥0.30 mg/dL or a relative increase in SCr ≥50% from the baseline value within 48 hours after contrast media exposure. A multivariate logistic regression analysis was applied to analyze whether low fT_3 was an independent risk factor for CI-AKI. The Cox regression analysis was used to evaluate the relationship between low fT_3 and long-term prognosis.
Results: A total of 46 (13.1%) patients developed CI-AKI. The incidence of CI-AKI was significantly higher in the low fT_3 group than in the normal group (26.5% vs. 9.9%, p<0.01). A multivariable logistic analysis demonstrated that a low fT_3 level was significantly related to CI-AKI [odds ratio (OR)=2.41; 95% confidence interval (CI), 1.11–5.27; p=0.027]. The Cox regression analysis showed that a low fT_3 was associated with long-term mortality [adjusted hazard ratio (HR)=2.00; 95% CI, 1.04–3.83; p=0.037] during the follow-up of mean 1.67 years.
Conclusion: A low fT_3 concentration was independently associated with CI-AKI and poor prognosis in elderly patients who had undergone PCI.
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Keywords: percutaneous coronary intervention, free triiodothyronine, contrast-induced acute kidney injury, long-term prognosis, elderly

Introduction

Percutaneous coronary intervention (PCI) is one of the most effective strategies in treating coronary artery diseases. Advanced health care has increased the life expectancy among elderly patients, thereby providing the opportunity to undergo angiography and PCI. Although significant achievements have been made in the treatment in recent years, contrast-induced acute kidney injury (CI-AKI) remains a frequent and severe complication following PCI, especially among elderly patients older than 75 years (1, 2). CI-AKI is usually irreversible and associated with short-term and long-term adverse effects (3, 4); therefore, identifying high-risk patients and providing early prophylactic measures are critical in the elderly.

Alterations in plasma concentrations of thyroid hormones during acute and chronic illnesses have been long recognized (5, 6). Non-thyroidal illness syndrome (NTIS) has been used to describe the patients who had alterations in the concentration of the thyroid hormone without being previously diagnosed with intrinsic thyroid disease (5, 7). A decrease in total serum triiodothyronine (T_3) and free triiodothyronine (fT_3) with normal levels of thyroxine (T_4) and thyrotropin (TSH), known as low T_3 syndrome, is the most common form of NTIS (5). The thyroid hormone has a great impact on the cardiovascular system, and low T_3 is common in patients with cardiac disease and may lead to a poor long-term prognosis (8-10). The interaction between thyroid and kidney functions has been well established for many years. Thyroid hormone levels may affect the renal blood flow (RBF),

#C.L., K.L. and Y.G. have contributed equally to this work.

Address for correspondence: Pengli Zhu, MD, Department of Geriatric Medicine, Fujian Provincial Hospital, Fujian Key Laboratory of Geriatrics, Fujian Provincial Center for Geriatrics, Fujian Medical University, 134 Dongjie Street, Fuzhou, 350001-*China*
Phone: +86-13675069988 Fax: +86-591-87557768 E-mail: zpl7755@sina.com
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glomerular filtration rate, tubular function, and electrolyte homeostasis (11). Low T_3 syndrome has been common in patients with chronic kidney disease (CKD) and has been confirmed to be a strong predictor of adverse clinical outcomes in the elderly (12, 13). Although the number of elderly patients after PCI who are at high risk for CI-AKI is growing, few studies have analyzed the correlation between a low fT_3 state and CI-AKI. Therefore, the current study focuses on the relationship between low circulating fT_3 and CI-AKI in patients 75 years or older who had undergone PCI, and it discusses the impact of low fT_3 on the short- and long-term prognosis.

Methods

Study population

This study was performed between January 2012 and December 2015, and it retrospectively evaluated consecutive 746 elderly patients aged 75 years and older, with coronary artery disease undergoing PCI. Patients with malignant tumors (n=31), patients with a thyroid dysfunction defined as TSH<0.27 mIU/L (n=50) or TSH>4.20 mIU/L (n=6), or talking L-thyroxine (n=0), patients without pre-procedural or post-procedural serum creatinine (SCr) (n=67) or the fT_3 level (n=242) data were excluded from the study. Finally, a total of 350 patients were evaluated in the analysis.

Study protocol

This was a retrospective cohort study. Demographic data and clinical history including age, gender, height, weight, diabetes mellitus, hypertension, smoking, prior myocardial infarction (MI), etc., were collected. The blood pressure was measured at admission. Serum concentrations of fT_3, free thyroxine (fT_4), and TSH were measured before or 24 hours within PCI by electrochemiluminescence (Roche, COBAS E601). The SCr was measured at admission and for 2 consecutive days after the contrast medium exposure. Other laboratory data including the lipid profile, hemoglobin level, uric acid, and other standard clinical parameters were measured in the morning of the first or next day after admission. Left ventricular ejection fraction (LVEF) was also measured by echocardiography during hospitalization. PCI was performed by qualified interventional cardiologists in accordance to a standard clinical procedure. Nephrotoxic drugs such as metformin and aminoglycoside were suspended before PCI according to the guidelines (14). All patients received nonionic, low-osmolar contrast media (either Iopamiron or Ultravist, 370 mgI/mL). In addition, all patients received intravenous isotonic saline (0.9%) at a rate of 1 mL/kg/h for 12 hours before and continued for 24 hours after the procedure (or 0.5 mL/kg/h for 12 hours if patients were in overt heart failure) according to the guidelines (14). The usage of medications such as antiplatelet agents (aspirin or clopidogrel), statins, angiotensin receptor blocker, and angiotensin-converting enzyme inhibitors were based on interventional guidelines.

Definition and follow-up

The primary end point was CI-AKI, which was defined as an absolute SCr increase ≥0.30 mg/dL or a relative increase in SCr ≥50% from the baseline value within 48 hours after the contrast media administration (15, 16). The additional end point were short-term outcomes, including in-hospital mortality and required renal replacement therapy, long-term outcomes including all-cause mortality, and major adverse clinical events (MACEs) including mortality, stent restenosis, non-fatal MI, and target vessel revascularization. The normal reference ranges of thyroid hormones in our laboratory were as follows: fT_3, 3.1–6.8 pmol/L; fT_4, 12.0–22.0 pmol/L; TSH, 0.27–4.20 mIU/L; low fT_3 was defined as fT_3<3.1 pmol/L with normal TSH and fT_4 levels. Anemia was defined as hematocrit <0.39 (male) or <0.36 (female). Heart failure at admission was defined as a New York Heart Association class >2 or Killip class >1 at hospital admission (1). Perioperative hypotension was described as systolic blood pressure <80 mm Hg lasting at least 1 hour and requiring inotropic support with medications or intra-aortic balloon pump 24 hours peri-procedure (1).

The participants were followed up by outpatient clinical visits or by telephone after discharge by trained medical workers. The mean follow-up duration after discharge was 1.67 years.

Statistical analysis

The Statistical Program for Social Sciences (SPSS) software 22.0 (SPSS, Inc., Chicago, Illinois, USA) was used for statistical analysis. Continuous variables were expressed as the mean±standard deviation. Categorical variables were described as absolute values (percentages). The continuous variables were evaluated by Student's t-test or the Wilcoxon rank-sum test, and categorical variables by chi-squared or Fisher's exact test. A p-value<0.05 indicated statistical significance. The baseline characteristics were compared between the patients with and without CI-AKI. Univariate logistic regression was adopted to identify the variables associated with the development of CI-AKI. Variables found in the univariate analysis with significance and other variables that were confirmed to be significant in previous studies will be included in the multivariate logistic regression analysis. The association of low fT_3 level with long-term mortality was investigated by the Cox regression analysis. The Kaplan–Meier curve was used to compare the survival time between the CI-AKI and non-CI-AKI groups, and also between the two groups divided by the lower reference limit of fT_3.

Results

This study involved a total of 350 consecutive elderly patients who underwent PCI. The mean age was 79.23±3.65 years, 93 (26.6%) patients were female, 144 (41.1%) had diabetes mellitus, and 271 (77.4%) had hypertension. Sixty-eight (19.4%) patients had a low fT_3, and 133 (38.0%) patients were diagnosed

Table 1. Baseline clinical features in patients with or without CI-AKI

Variables	Total (n=350)	CI-AKI (+) (n=46)	CI-AKI (–) (n=304)	*P*
Demographics				
Age, years	79.23±3.65	79.85±4.38	79.13±3.53	0.22
Females, n, %	93 (26.6)	14 (30.4)	79 (26.0)	0.52
BMI, kg/m^2	23.54±3.26	23.84±4.15	23.51±3.16	0.64
Heart failure at admission, n, %	102 (29.1)	25 (54.3)	77 (25.4)	<0.001
MI, n, %	133 (38.0)	33 (71.7)	100 (32.9)	<0.001
Medical history				
Hypertension, n, %	271 (77.4)	36 (78.3)	235 (77.3)	0.88
Diabetes mellitus, n, %	144 (41.1)	22 (47.8)	122 (40.1)	0.32
Smoking, n, %	133 (38.0)	19 (41.3)	114 (38.1)	0.69
Prior MI, n, %	63 (18.0)	10 (21.7)	53 (17.4)	0.48
Prior PCI, n, %	84 (24.0)	7 (15.2)	77 (25.4)	0.13
Prior CABG, n, %	2 (0.6)	0 (0)	2 (0.7)	0.58
Laboratory parameters				
SCr, mg/dL	1.00±0.33	0.96±0.32	1.01±0.33	0.32
SCr>1.5 mg/dL, n, %	25 (7.1)	3 (6.5)	22 (7.2)	1.0
Baseline RBC, 10^{12}/L	4.17±0.57	4.2±0.69	4.17±0.55	0.78
Hemoglobin, g/L	127.79±16.98	125.61±22.3	128.12±16.04	0.35
Anemia, n, %	179 (51.1)	24 (52.2)	155 (51.0)	0.88
LDL, mmol/L	2.58±0.94	2.59±0.82	2.59±0.96	1.00
TC, mmol/L	4.10±1.09	4.01±0.92	4.11±1.11	0.55
TG, mmol/L	1.39±0.99	1.32±0.67	1.41±1.03	0.57
HDL, mmol/L	1.09±0.32	1.03±0.33	1.1±0.32	0.18
Uric acid, μmol/L	369.17±112.17	395.3±107.66	365.16±112.48	0.09
LVEF, %	56.42±7.71	49.83±9.41	57.5±6.84	<.001
fT_3, pmol/L	3.84±0.93	3.39±0.96	3.91±0.9	<.001
fT_4, pmol/L	16.76±3.44	17.12±3.31	16.7±3.46	0.45
S-TSH, mIU/L	1.90±0.87	1.65±0.95	1.93±0.86	0.09
Low fT_3, n, %	68 (19.4)	18 (39.1)	50 (16.4)	<0.001
Perioperative medications				
Antiplatelet, n, %	342 (97.7)	45 (97.8)	297 (97.7)	0.72
ACEI/ARB, n, %	282 (80.6)	33 (71.7)	249 (81.9)	0.10
Statin, n, %	342 (97.7)	45 (97.8)	297 (97.7)	0.96
Procedural characteristics				
Number of diseased vessels, n	2.42±0.82	2.63±0.64	2.39±0.84	0.06
LM, n, %	38 (10.8)	5 (10.9)	33 (10.8)	1.00
LAD, n, %	267 (76.3)	28 (93.3)	239 (89.2)	0.75
LCX, n, %	196 (56.0)	22 (73.3)	174 (64.9)	0.36
RCA, n, %	213 (60.8)	24 (80.0)	189 (70.5)	0.28
Stent length, mm	40.10±23.82	43.42±22.48	39.57±24.02	0.31
Number of stents, n	1.53±0.79	1.64±0.77	1.52±0.79	0.32

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Table 1. Cont.

Variables	Total (n=350)	CI-AKI (+) (n=46)	CI-AKI (–) (n=304)	*P*
Perioperative hypotension, n, %	24 (6.9)	11 (23.9)	13 (4.3)	<0.001
Contrast volume, mL	215.37±58.96	214.09±59.19	215.57±59.03	0.88
Contrast volume>150 mL, n, %	309 (88.3)	40 (86.9)	269 (88.5)	0.76

Data are presented as the mean±standard deviations or as numbers and percentages.
CI-AKI - contrast-induced acute kidney injury; BMI - body mass index; MI - myocardial infarction; PCI - percutaneous coronary intervention; CABG - coronary artery bypass grafting; SCr - serum creatinine; RBC - red blood cell; LDL - low-density lipoprotein; TC - total cholesterol; TG - triglyceride; HDL - high-density lipoprotein; LVEF - left ventricular ejection fraction; fT_3 - free triiodothyronine; fT_4 - free thyroxine; S-TSH - sensitive thyroid-stimulating hormone; ACEI/ARB - angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; LM - left main; LAD - left anterior descending branch; LCX - left circumflex branch; RCA - right coronary artery

Table 2. Multivariate logistic analysis of CI-AKI risk indicators

Risk factors	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.05	0.97-1.14	0.219	1.02	0.93-1.11	0.688
Low fT_3	3.27	1.68-6.35	<0.001	2.41	1.11-5.27	0.027
Heart failure in admission	3.49	1.85-6.60	<0.001	1.47	0.66-3.25	0.348
Anemia	1.05	0.56-1.95	0.881	0.63	0.30-1.32	0.634
Perioperative hypotension	7.04	2.93-16.90	<0.001	3.32	1.25-8.83	0.016
Myocardial infarction	5.18	2.61-10.27	<0.001	3.56	1.54-8.24	0.003
Diabetes mellitus	1.37	0.73-2.55	0.324	1.30	0.64-2.61	0.468
SCr>1.5 mg/dL	0.89	0.26-3.12	0.894	0.44	0.11-1.79	0.255
Contrast volume>150 mL	0.82	0.29-2.50	0.724	1.33	0.39-4.48	0.647

CI-AKI - contrast-induced acute kidney injury; OR - odds ratio; CI - confidence interval; fT_3 - free triiodothyronine; SCr - serum creatinine

with acute MI (AMI). Overall, 46 (13.1%) patients developed CI-AKI. The demographical, medical history, laboratory parameters, perioperative medications, and procedural characteristics are shown in Table 1. Patients who developed CI-AKI had a higher prevalence of heart failure at admission, AMI, perioperative hypotension, and low fT_3 (all, p<0.05). However, the LVEF was significantly lower among patients with CI-AKI. The age, baseline SCr, contrast volume, and the incidence of anemia were similar between the two groups (all, p>0.05).

Compared to patients with a normal fT_3 concentration, the low fT_3 group was more likely to develop CI-AKI (26.5% vs. 9.9%, p<0.001), had a higher rate of in-hospital mortality (11.8% vs. 2.1%, p=0.002), and required renal replacement therapy (7.4% vs. 0.0%, p<0.001) (Fig. 1). A univariate logistic regression analysis showed that low fT_3 was significantly associated with CI-AKI (OR=3.27; 95% CI, 1.70–6.35; p<0.001). The odd ratios of heart failure on admission (OR=3.49; 95% CI, 1.85–6.60; p<0.001), perioperative hypotension (OR=7.04, 95% CI, 2.93–16.90, p<0.001), and MI (OR=5.18; 95% CI, 2.61–10.27; p<0.001) are also statistically significant. All of the above variables, as well as other variables that were confirmed to be significant in previous studies such

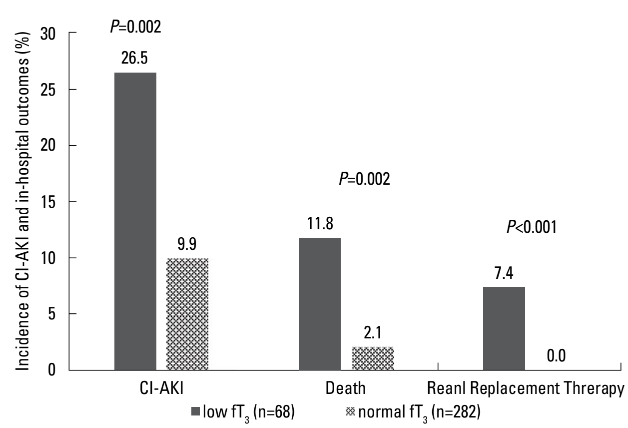


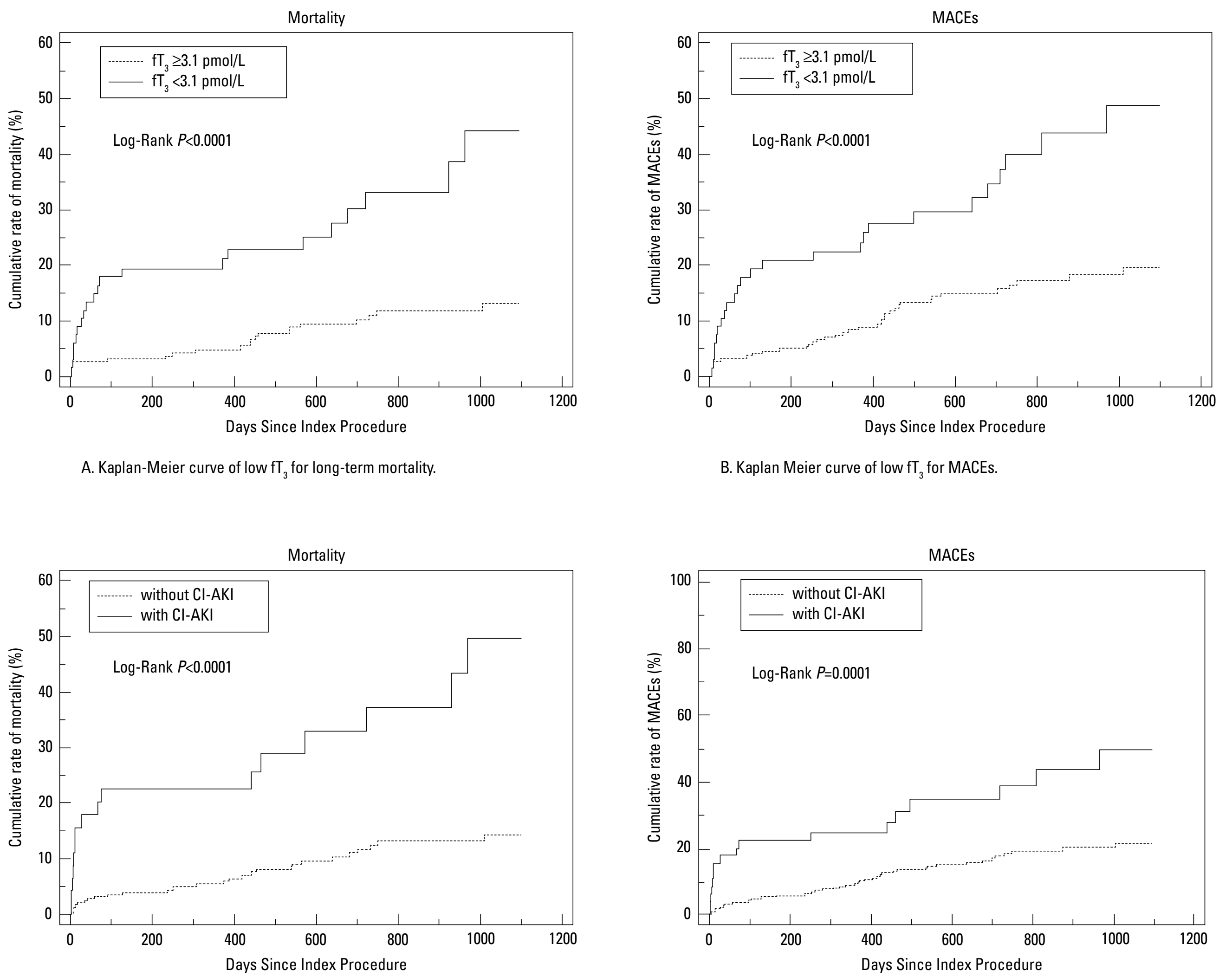
Figure 1. Incidence of CI-AKI, in-hospital death, and renal replacement therapy between a low fT_3 and normal fT_3.
fT_3 - free triiodothyronine; CI-AKI - contrast-induced acute kidney injury

as age, anemia, diabetes mellitus, SCr >1.5 mg/dL, and contrast volume >150 mL, were conducted in a multivariate analysis. And we found that after adjusting for age, SCr, anemia, diabetes mellitus, contrast >150 mL, and heart failure on admission, low fT_3

Table 3. Cox regression analysis for independent risk factors of long-term mortality

Risk factors	Univariate			Multivariate		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.10	1.02-1.18	0.012	1.05	0.98-1.13	0.153
SCr>1.5 mg/dL	2.60	1.16-5.81	0.02	1.29	0.53-3.11	0.578
Heart failure at admission	3.79	2.11-6.82	<0.001	1.97	0.96-4.04	0.065
Anemia	3.69	1.78-7.64	<0.001	2.58	1.22-5.48	0.014
Perioperative hypotension	4.13	1.99-8.56	<0.001	1.69	0.75-3.84	0.208
Myocardial infarction	3.46	1.88-6.34	<0.001	1.52	0.72-3.19	0.268
Low fT_3	3.73	2.09-6.67	<0.001	2.00	1.04-3.83	0.037

HR - hazard ratio; CI - confidence interval; SCr - serum creatinine; fT_3 - free triiodothyronine



A. Kaplan-Meier curve of low fT_3 for long-term mortality.

B. Kaplan Meier curve of low fT_3 for MACEs.

C. Kaplan-Meier curve of long-term mortality between patients with or without CI-AKI

D. Kaplan Meier curve of MACEs between patients with or without CI-AKI.

Figure 2. Kaplan–Meier curve of long-term outcomes

fT_3 - free triiodothyronine; MACEs - major adverse clinical events, which include all-cause mortality, stent restenosis, non-fatal myocardial infarction, and target vessel revascularization; CI-AKI - contrast-induced acute kidney injury

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(OR=2.41; 95% CI, 1.11–5.27; p=0.027), perioperative hypotension (OR=3.40; 95% CI, 1.29–8.99; p=0.013), and MI (OR=3.60; 95% CI, 1.56–8.34; p=0.003) remained significant predictors of the development of CI-AKI in elderly patients after PCI (Table 2).

The mean follow-up duration was 1.67 years. After adjusting for variables that were found in univariate analysis with statistical significance such as age, heart failure at admission, anemia, SCr >1.5 mg/dL, perioperative hypotension, and MI, low fT_3 remained an independent risk factor for long-term mortality in elderly patients undergoing PCI (HR=2.00; 95% CI, 1.04–3.83; p=0.037; Table 3).

The Kaplan–Meier curve indicated that low fT_3 concentration had a higher all-cause mortality and MACEs as compared to normal fT_3 (p<0.001), and patients who developed CI-AKI displayed a higher rate of all-cause mortality and MACEs as compared to those without CI-AKI (p<0.001) (Fig. 2).

Discussion

This is the first study, to the best of our knowledge, to demonstrate that a low serum fT_3 concentration is positively associated with an increased risk of CI-AKI and is negatively correlated with short- and long-term outcomes in elderly patients, 75 years or older, who underwent PCI.

CI-AKI is an important complication of the intravascular administration of contrast media, which is compulsory in many diagnostic and therapeutic procedures and is strongly correlated with prolonged hospitalization, late renal and cardiovascular adverse events, mortality, and higher costs (3, 16, 17). As the number of catheterizations in patients with coronary disease increases, the incidence of CI-AKI will continually increase as well. Previous studies have identified several patient-related risk factors for CI-AKI, including pre-existing CKD, diabetes mellitus, old age, reduced left ventricular systolic function, simultaneous use of nephrotoxic drugs, anemia, and hemodynamic instability (1, 18, 19). An advanced age is considered to be an important risk factor for CI-AKI. A meta-analysis by Song et al. (20) showed that the estimated incidence of patients older than 75 years is 16.5%, which is higher than the previously reported incidence in a nonsegregated population (21). Then, we focused on the very old patients (≥75 years) and found that the incidence of CI-AKI in our study was 13.1%, which is similar to the previous studies. There are no effective therapies to cure CI-AKI (15), so timely preventive measures are crucial for the patients who are at high risk for CI-AKI. Therefore, identifying the potential risk factors for CI-AKI prior to contrast exposure and adopting preventive measures for elderly patients with risk factors is important.

Low T_3 syndrome is common in patients with acute and chronic heart disease, especially among elderly patients. The reduction in the T_3 level during illness has been generally considered to be a diminution in the hepatic/renal type I iodothyronine deiodinase activity and an increase in hepatic type III iodothyronine deiodinase activity, resulting in the reduction of T4 to T_3 and an increase in the rT_3 level (22). Its pathophysiological role is not well understood, and the prevailing view is that it is an adaptive mechanism to conserve energy (23, 24). Numerous studies have shown that serum fT_3 levels are related to cardiovascular risk factors or events. Wang et al. (25) showed that fT_3 was significantly and negatively correlated with Ig-CKMB and Ig-TnI, indicating that a lower fT_3 level is correlated with a more severe cardiac injury in the ST segment elevation MI (STEMI) patients. In another study, Jankauskienė et al. (26) demonstrated that low fT_3 levels were significantly associated with worse left ventricular (LV) mechanics and important for the prediction of the LV structure and function after MI. Furthermore, low T_3 is known to affect the short-term and long-term prognosis of patients with cardiovascular disease, including STEMI (27), heart failure (28), and coronary artery bypass grafting (29). On the other hand, low fT_3 is also associated with renal disease. A retrospective study of 2284 cases with a normal TSH level showed that low T_3 syndrome was highly prevalent in CKD and was a remarkable finding in early CKD, and serum T_3 levels were associated with CKD severity (30). Low T_3 is not only closely associated with CKD, but also significantly increases the risk of cardiovascular events and all-cause mortality in CKD patients (31). However, to the best of our knowledge, the relationship between low fT_3 and CI-AKI in patients who underwent PCI has not been reported previously. Therefore, we examined fT_3 as a variable to explore whether a low fT_3 is a CI-AKI risk factor. The present study demonstrated that the incidence of CI-AKI in elderly patients with a low fT_3 who underwent PCI was significantly higher than those with a normal fT_3, after adjusting for other confounding variables, such as anemia, diabetes mellitus, SCr >1.5 mg/dL, and contrast volume >150 mL, low fT_3 remained an independent risk factor of CI-AKI. Meanwhile, we found that perioperative hypotension and MI were also the independent predictors of CI-AKI.

The exact pathophysiological mechanism of CI-AKI is unclear and is considered to be complex and multifactorial. The potential mechanisms underlying the relationship between a low fT_3 and CI-AKI may include the following. First, a low fT_3 may affect the RBF. The medullary hypoxia due to medullary vasoconstriction was an important pathophysiological mechanism of CI-AKI. In an animal experiment conducted by Sendeski et al. (32), single specimens of descending vasa recta was isolated from rats and perfused with a buffered solution containing iodixanol, the authors found that the contrast medium reduced bioavailability of nitric oxide (NO) and intensified angiotensin II-induced vasoconstriction. In another study, 24 rats were divided into 3 groups, sham operated control group (n=8), 5/6 nephrectomized group (Nx, n=8), and 5/6 nephrectomized group treated with T_3 for 2 weeks (T_3-Nx, n=8), the author showed that the endothelial NO synthase expression was increased in the remnant kidney of the T_3-Nx group, and the serum levels of urea and creatinine were significantly decreased compared to the Nx group (33). Therefore, a low fT_3 might enhance the effect of vasoconstriction by contrast media and reduce RBF, resulting in the development of CI-AKI, which was probably a mechanism that linked low fT_3 and CI-AKI. Second, both renal endothelial cells and proximal tubular epithelial cells damaged by a contrast medium produced cytokines and chemokines that result in inflammation, which may be another important mechanism that contributes to CI-AKI (34, 35), the association between a low T_3 and different inflammatory markers has been well established. Fan et al. (13) showed that serum T_3 was negatively related to interleukin-6 (IL-6) and C-reactive protein (CRP), which reflect the inşammatory status in non-dialysis patients with CKD. Zoccali et al. (36) demonstrated a strong and inverse associations between fT_3 and IL-6, CRP, intercellular adhesion molecule-1 (ICAM-1), and vascular cellular adhesion molecule-1 (VCAM-1). Meanwhile, a low fT_3 might represent an active inflammation and lead to an increased risk of CI-AKI. Third, a low T_3 is associated with the traditional risk factors for CI-AKI, such as CKD, advanced age, atherosclerotic disease, and myocardial injury, which may indirectly increase the risk of CI-AKI. Another mechanism underlying the inverse link between a low fT_3 and CI-AKI may be anemia and malnutrition. Fan et al. (13) found that the serum T_3 was positively correlated to protein metabolism (serum total protein, albumin) and anemia indicators (hemoglobin and red blood cells), while lower serum albumin and anemia were associated with a higher CI-AKI risk (37, 38).

Furthermore, this study showed that a low fT_3 was not only related to the occurrence of CI-AKI, but also to adverse events during hospitalization and long-term adverse outcomes after discharge. Therefore, a low fT_3 may be a prognostic indicator and should be closely monitored by clinicians.

Study limitations

The results of the current study should be evaluated keeping in mind some limitations. 1) We only analyzed fT_3 without analyzing T_3, T_4, and rT_3, because these indexes were not regularly checked in our routine practice. 2) We did not follow up the post-operative fT_3 and renal function, so we could not further clarify the relationship between a low fT_3 and CI-AKI. 3) This is an observational study that was conducted at a single center, and it only included a small population. 4) Numerous patients were excluded because of the lack of data on thyroid function, which may lead to selection confounding. 5) As the deregulation of fT_3 often occurs in patients with AMI, including patients with MI seems to complicate the analysis. However, our sample size was too small to conduct a subgroup analysis. In our future studies, we may expand the sample size and focus on the elective and stable ischemic heart disease patients. 6) Measurements of the peak SCr levels might have been missed due to the variations in the measurement times. Consequently, it caused an underestimation of the true incidence of CI-AKI in this population. Future multi-center studies with larger sample sizes are needed to confirm these findings.

Conclusion

This study demonstrated that a low serum fT_3 concentration may be associated with the development of CI-AKI and poor prognosis in patients older than 75 years who are undergoing PCI. Therefore, given the importance of fT_3 and its cost-effective measurement, it should be routinely measured before PCI.

Ethical approval: This study was approved by the Ethics Committee of the Fujian Provincial Hospital, China (ethics approval number: K2012-001-01). All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study.

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