Effect of Oral Hydration on Contrast-Induced Acute Kidney Injury among Patients after Primary Percutaneous Coronary Intervention

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Keywords

Oral hydration · ST-elevation myocardial infarction · Contrast-induced acute kidney injury

Abstract

Objectives: The purpose of this study was to evaluate the protective effect of oral hydration volume to weight ratio (OHV/W) on contrast-induced acute kidney injury (CI-AKI) among patients with ST-elevation myocardial infarction (STEMI) following percutaneous coronary intervention (PCI). **Methods:** A total of 754 patients with STEMI undergoing PCI were selected. Each patient was encouraged to drink as much water as possible 24 h after PCI. Total volume intake was recorded for all patients. The ratio of OHV/W was calculated. The occurrence of CI-AKI was defined as ≥ 0.5 mg/dL absolute or $\geq 25\%$ relative increase in serum creatinine within 48–72 h following PCI. Logistic regression analysis and generalized additive model were performed to evaluate the relationship between OHV/W and CI-AKI. **Results:** There was a nonlinear relationship between OHV/W and CI-AKI with an inflection point of 15.69 mL/kg. On the right side of the inflection point (OHV/W ≥ 15.69 mL/kg), a negative relationship was detected between OHV/W and CI-AKI (HR = 0.90, 95% CI: 0.82–0.98, $p = 0.0126$). However, no relationship was

observed between OHV/W and CI-AKI on the left of inflection point (HR = 1.19, 95% CI: 0.95–1.49, $p = 0.1302$). Subgroup analysis showed that significant interactions were observed only for gender difference (p for interaction = 0.0155), male patients had a significantly lower risk of CI-AKI (HR = 0.84, 95% CI: 0.75–0.93, $p = 0.0012$). **Conclusion:** OHV/W ≥ 15.6 mL/kg for 24 h post-procedure may be an effective preventive strategy of CI-AKI. In addition, male patients may particularly benefit from OHV to prevent CI-AKI.

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Introduction

Contrast-induced acute kidney injury (CI-AKI) is one of the common causes of hospital-acquired acute renal insufficiency, which is caused by intravascular injection of contrast media (CM) [1, 2]. The risk of CI-AKI is associated with the increase of CM volume [3] and contributes toward poorer clinical outcomes [4, 5]. At the same time, with the increasing frequency of primary percutaneous coronary intervention (PCI), the incidence of CI-AKI gradually increases, ranging from 2% of patients with adequate renal function at baseline to 20–30% of pa-

Fig. 1. Flowchart of patient selection. CI-AKI, contrast-induced acute kidney injury; PCI, percutaneous coronary intervention.

tients with chronic kidney disease [6]. Today, the strategies to prevent CI-AKI include fluid expansion, application of a hypotonic or isotonic contrast agents, and minimization of CM dose. Fluid expansion includes intravascular volume expansion and oral volume expansion [7–10], and intravascular volume expansion has been accepted as the cornerstone to prevent CI-AKI [10]. However, there is limited information on oral volume expansion for the prevention of CI-AKI risk in patients with ST-elevation myocardial infarction (STEMI). Compared with selective PCI [11], patients with STEMI treated by primary PCI have a higher risk of CI-AKI due to the use of large amounts of contrast agent, and patients with STEMI have an urgent need for surgery and lack of effective preventive measures [12–14]. In the present study, we aimed to explore the value of post-procedural oral hydration in preventing CI-AKI risk in STEMI patients flowing PCI.

Methods

Research Subjects

This was a single-center, retrospective, observational study. A total of 754 consecutive patients aged ≥ 18 years with STEMI undergoing PCI from January 2013 to January 2019 were selected from Guangdong Province Hospital of Integrated Traditional Chinese and Western Medicine. The diagnosis of STEMI was in accordance with STEMI diagnostic criteria [15]: (1) Sustained

chest pain >30 min; (2) ST-segment elevation in ≥ 2 contiguous leads or new left bundle-branch block; (3) elevated cardiac troponin T within 24 h of symptoms onset. Exclusion criteria included: (1) a history of dialysis; (2) patients who died within 24 h of admission; (3) use of nephrotoxic drugs in the last 7 days; (4) AKI of alternative etiology; (5) active decompensated heart failure; (6) malignancy; (7) missing data (Fig. 1). The study was approved by the Ethics Committee of Guangdong Province Hospital of Integrated Traditional Chinese and Western Medicine. This was a retrospective study, so informed consent from patients was not required.

Measurement

The blood pressure was measured after at least 15 min of rest. Body weight and standing height were measured. Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared). Venous blood samples were collected on the day of admission and every 48–72 h after the procedure and at hospital discharge. Serum creatinine (Scr), blood urea nitrogen, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and uric acid levels were measured using Olympus AU-640 autoanalyzer (Olympus, Shinjuku-ku, Japan). Cardiac function was determined by ultrasonography with ACUSON X700 ultrasound system (Siemens, Shinagawa-ku, Japan).

Interventions

All eligible patients were treated with routine regimens of perioperative intravenous hydration including continuous intravenous infusion of $\leq 1,000$ mL of isotonic saline within 12 h. Other perioperative interventions include: fluids mixed with medications and normal glucose or saline injections. In addition, each patient was encouraged to drink as much water as possible 24 h

after PCI. For patients with systolic dysfunction or chronic heart function, hydration dosage was set at 1.5–2 L/day and 0.5 mL/kg/h in order to prevent decompensation of patients. The total oral hydration intake was recorded for all patients and the ratios of OHV/W were calculated. During the period of oral hydration, the patients' responses were observed and inquired, and the clinical assessment of cardiac function and hemodynamic data were performed in real time. The use of diuretics by monitoring body fluids was based on a clinical assessment of cardiac function determined by cardiologists.

Diagnostic Standards and Outcomes

The occurrence of CI-AKI was defined as ≥ 0.5 mg/dL absolute or $\geq 25\%$ relative increase in Scr within 48–72 h following PCI. The primary outcome was the effect of oral hydration vol/wt on CI-AKI. The secondary outcomes were a composite of death and need for dialysis during hospitalization.

Statistical Analysis

Continuous variables were expressed as means $\pm$ standard deviation or as the median (quartile) according to distribution. Categorical variables were expressed in frequency or as a percentage. These continuous variables were compared using Student's *t* test or Wilcoxon rank-sum test according to distribution, and categorical variables were compared using the χ^2 test, Fisher's exact test. Univariate and multivariate logistic regression models were used to evaluate the correlation between variables and CI-AKI. In addition, we further applied a multivariate piecewise linear regression model to examine the threshold effect of the OHV/W on CI-AKI by smooth curve fitting. Stratified logistic regression models were used for subgroup analysis. The interaction and modification between the subgroups were examined by likelihood ratio test. Data were analyzed with the use of statistical packages R (The R Foundation; <http://www.r-project.org>; version 3.4.3 2018-02-18) and EmpowerStats (www.empowerstats.com; X&Y Solutions Inc., Boston, MA, USA).

Results

The Demographic and Laboratory Data of the Participants

Overall, 754 participants were included in the analysis. The demographic and laboratory data were listed in Table 1. 616 were male and 138 were female. The mean age of the subjects was 59.91 ± 11.84 years in patients without CI-AKI, and 62.65 ± 14.09 years in patients with CI-AKI. The total incidence of CI-AKI was 15.65% (118/754). The participants were divided into 2 groups: No CI-AKI group and CI-AKI group. Differences were found in terms of age, OHV/W, intravenous hydration volume (IVHV), number of stents and diabetes mellitus (DM). However, there were no differences in terms of gender, systolic pressure (SBP), diastolic pressure (DBP), BMI, left ventricular ejection fraction (LVEF), high blood pres-

Table 1. Baseline characteristics of participants

Risk factors	No CI-AKI	CI-AKI	<i>p</i> value
<i>N</i>	636	118	–
Age, years	59.91 $\pm$ 11.84	62.65 $\pm$ 14.09	0.022
Gender male, <i>n</i> (%)	526 (82.70)	90 (76.27)	0.097
BMI, kg/m ²	24.62 $\pm$ 3.71	24.71 $\pm$ 3.52	0.817
BUN, mmol/L	4.76 $\pm$ 1.03	4.84 $\pm$ 1.00	0.435
UA, μ mol/L	440.62 $\pm$ 91.23	452.44 $\pm$ 86.29	0.193
TC, mmol/L	5.65 $\pm$ 1.18	5.78 $\pm$ 1.00	0.271
HDL, mmol/L	1.31 $\pm$ 0.25	1.28 $\pm$ 0.22	0.223
LDL, mmol/L	3.45 $\pm$ 0.82	3.47 $\pm$ 0.89	0.844
TG, mmol/L	2.71 $\pm$ 2.24	3.09 $\pm$ 3.35	0.116
GLU, mmol/L	5.77 $\pm$ 1.76	5.77 $\pm$ 1.52	0.984
SBP, mm Hg	125.79 $\pm$ 12.12	126.15 $\pm$ 11.62	0.763
DBP, mm Hg	78.11 $\pm$ 8.29	78.59 $\pm$ 8.85	0.565
LVEF, %	52.76 $\pm$ 11.78	50.63 $\pm$ 11.33	0.083
Scr, mmol/L	80.03 $\pm$ 15.68	78.18 $\pm$ 15.96	0.240
OHV/W, mL/kg	19.89 $\pm$ 9.37	16.94 $\pm$ 6.62	0.001
IVHV, mL/24 h	750 (500–1,000)	767 (511–1,160)	0.005
DM, <i>n</i> (%)	178 (27.90)	44 (37.29)	0.040
HBP, <i>n</i> (%)	258 (40.44)	46 (38.98)	0.767
CCB, <i>n</i> (%)	174 (27.27)	26 (22.03)	0.236
ACEI/ARB, <i>n</i> (%)	268 (42.01)	56 (47.46)	0.272
β -Blocker, <i>n</i> (%)	195 (30.66)	36 (30.51)	0.974
Diuretics, <i>n</i> (%)	54 (8.491)	8 (6.780)	0.715
Insulin, <i>n</i> (%)	54 (8.491)	10 (8.475)	0.995
OAD, <i>n</i> (%)	134 (21.069)	34 (28.814)	0.063
Contrast agent, <i>n</i> (%)			
≤ 100 mL	456 (71.7)	86 (72.88)	0.793
> 100 mL	180 (28.3)	32 (27.12)	
No. of stents, <i>n</i> (%)			
≤ 1	521 (81.92)	106 (89.83)	0.035
> 1	115 (18.08)	12 (10.17)	
Diuretics, <i>n</i> (%)	54 (8.49)	8 (6.78)	0.715

BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetes mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs; CI-AKI, contrast-induced acute kidney injury.

sure, lipidemia, blood glucose (GLU), baseline Scr, contrast agent, medications such as β -blocker, calcium channel blocker (CCB), angiotensin receptor blocker/angiotensin-converting enzyme inhibitor (ARB/ACEI), oral antidiabetic drugs (OAD), insulin, and diuretics. During hospitalization, no patient died or received renal replacement therapy.

Table 2. Correlations between exposure factors and CI-AKI

Exposure	Statistic	OR (95% CI)	<i>p</i> value
Age, years	60.34±12.25	1.02 (1.00, 1.04)	0.026
BMI, kg/m ²	24.63±3.68	1.01 (0.95, 1.06)	0.817
BUN, mmol/L	4.78±1.03	1.08 (0.83, 1.41)	0.563
UA, μmol/L	442.64±90.53	1.00 (1.00, 1.00)	0.365
TC, mmol/L	5.67±1.16	1.09 (0.87, 1.37)	0.435
HDL, mmol/L	1.28±0.26	2.16 (0.76, 6.15)	0.151
LDL, mmol/L	3.45±0.83	1.03 (0.74, 1.43)	0.873
TG, mmol/L	2.77±2.45	1.06 (0.96, 1.16)	0.281
GLU, mmol/L	5.77±1.73	1.00 (0.85, 1.18)	0.979
SBP, mm Hg	125.84±12.03	1.00 (0.98, 1.03)	0.829
DBP, mm Hg	78.17±8.39	1.01 (0.97, 1.04)	0.671
IVHV, mL/24 h	750 (500~1,000)	1.000 (1.000, 1.001)	0.153
LVEF, %	52.41±11.78	0.98 (0.96, 1.01)	0.228
Scr, mmol/L	9.02±1.78	0.99 (0.98, 1.01)	0.392
Gender, <i>n</i> (%)			
Male	616 (81.70)	1.0	0.099
Female	138 (18.30)	1.49 (0.93, 2.38)	
No. of stents, <i>n</i> (%)			
≤1	627 (83.16)	1.0	0.038
>1	127 (16.84)	0.51 (0.27, 0.96)	
DM, <i>n</i> (%)			
No	532 (70.56)	1.0	0.043
Yes	222 (29.44)	1.53 (1.01, 2.31)	
HBP, <i>n</i> (%)			
No	450 (59.68)	1.0	0.748
Yes	304 (40.32)	0.94 (0.63, 1.40)	
CCB, <i>n</i> (%)			
No	554 (73.47)	1.0	0.230
Yes	200 (26.53)	0.75 (0.47, 1.20)	
ACEI/ARB, <i>n</i> (%)			
No	430 (57.03)	1.0	0.284
Yes	324 (42.97)	1.24 (0.84, 1.84)	
β-Blocker, <i>n</i> (%)			
No	523 (69.36)	1.0	0.974
Yes	231 (30.64)	0.99 (0.65, 1.52)	
OHV/W, mL/kg	19.43±9.07	0.96 (0.93, 0.99)	0.023
Diuretics, <i>n</i> (%)			
No	692 (91.78)	1.0	0.535
Yes	62 (8.22)	0.78 (0.36, 1.69)	
Insulin, <i>n</i> (%)			
No	690 (91.51)	1.0	0.995
Yes	64 (8.49)	1.00 (0.49, 2.02)	
OAD, <i>n</i> (%)			
No	586 (77.72)	1.0	0.065
Yes	168 (22.28)	1.52 (0.97, 2.36)	
Contrast agent, <i>n</i> (%)			
≤100 mL	542 (71.9)	1.0	0.943
>100 mL	212 (28.1)	0.943 (0.61, 1.47)	

BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetic mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs; CI-AKI, contrast-induced acute kidney injury.

Table 3. Relationship between OHV/W and CI-AKI in different models

Variable	Model 1 OR (95% CI)	<i>p</i> value	Model 2 OR (95% CI)	<i>p</i> value	Model 3 OR (95% CI)	<i>p</i> value
OHV/W, mL/kg	0.96 (0.93, 0.99)	0.0225	0.96 (0.93, 1.00)	0.0297	0.96 (0.92, 1.00)	0.0503
OHV/W (trisection), mL/kg						
<12	1.0		1.0		1.0	1.0
12~24	1.01 (0.51, 1.99)	0.9861	1.04 (0.52, 2.08)	0.9037	0.91 (0.34, 2.43)	0.8492
>24	0.53 (0.22, 1.27)	0.1531	0.55 (0.23, 1.31)	0.1774	0.49 (0.16, 1.51)	0.2158

Model 1 was adjusted for: none. Model 2 was adjusted for: gender and age. Model 3 was adjusted for: gender, age, BMI, BUN, UA, TC, HDL, LDL, TG, GLU, SBP, DBP, LVEF, Scr, IVHV, DM, HBP, CCB, ACEI/ARB, No. of stents, diuretics; OAD and insulin. BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetes mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs; CI-AKI, contrast-induced acute kidney injury.

Fig. 2. The relationship between OHV/W and CI-AKI by smooth curve fitting. A nonlinear relationship between them was detected after adjusting for gender, age, BMI, BUN, UA, TC, HDL, LDL, TG, GLU, SBP, DBP, LVEF, Scr, IVHV, DM, HBP, CCB, ACEI/ARB, No. of stents, diuretics, OAD and insulin. CI-AKI, contrast-induced acute kidney injury; OHV/W, oral hydration volume to weight ratio; BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetes mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs.

Univariate Analysis

We used univariate analysis model to evaluate the associations between exposure factors and CI-AKI, and the results showed that the factors related to CI-AKI were OHV/W (OR = 0.96, 95% CI: 0.93~0.99, $p = 0.023$), age (OR = 1.02, 95% CI: 1.00~1.04, $p = 0.026$), No. of stents (OR = 0.51, 95% CI: 0.27~0.96, $p = 0.038$), DM (OR = 1.53, 95% CI: 1.01~2.31, $p = 0.043$). However, BMI, SBP, DBP, LVEF, IVHV, lipidemia, GLU, Scr, number of stents, contrast agent, and medications such as β -blocker, ACEI/ARB, CCB, OAD, insulin, and diuretics were not associated with CI-AKI (All $p > 0.05$) (Table 2).

The Effect Analysis of OHV/W on CI-AKI Using Multiple Logistic Regression

Multiple logistic regression model was performed to investigate the correlation between OHV/W and CI-AKI. Unadjusted and adjusted models were shown in the Table 3. In model 1 (unadjusted model), result showed a negative association with CI-AKI (OR = 0.96, 95% CI: 0.93~0.99, $p = 0.0225$). In addition, the negative association was also observed in model 2 (adjusted for age and gender) between OHV/W and CI-AKI (OR = 0.96, 95% CI: 0.93~1.00, $p = 0.0297$). However, in the model 3 (fully adjusted model), there was no correlation between OHV/W and CI-AKI (OR = 0.96, 95% CI: 0.92~1.00, $p = 0.0503$). For further sensitivity analysis, we also treated OHV/W as a categorical variable, and found nonassociation between OHV/W and CI-AKI in model 1 to model 3 (all $p > 0.05$).

Table 4. The independent correlation between OHV/W and CI-AKI by multivariate piecewise linear regression

Infection point of OHV/W, mL/kg	Effect size (HR)	95% CI		<i>p</i> value
		lower	upper	
<15.69	1.19	0.95	1.49	0.1302
≥15.69	0.90	0.82	0.98	0.0126

Adjusting for gender, age, BMI, BUN, UA, TC, HDL, LDL, TG, GLU, SBP, DBP, LVEF, Scr, IVHV, DM, HBP, CCB, ACEI/ARB, No. of stents, diuretics; OAD and insulin. BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetes mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs; CI-AKI, contrast-induced acute kidney injury.

The Effect Analysis of OHV/W on CI-AKI Using Piecewise Linear Regression

Since OHV/W was continuous variable, it was necessary to use nonlinear regression analysis. In the present study (Fig. 2), nonlinear relationship was detected between OHV/W and CI-AKI (adjusted for age, BMI, gender, blood urea nitrogen, uric acid, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, GLU, SBP, DBP, LVEF, Scr, IVHV, DM, high blood pressure, CCB, ACEI/ARB, diuretics, OAD and insulin). By 2-piecewise linear regression model, the inflection point was 15.69 mL/kg. On the right side of the inflection point (OHV/W ≥15.69 mL/kg), a negative relationship was detected between OHV/W and CI-AKI (HR = 0.90, 95% CI: 0.82~0.98, *p* = 0.0126). However, the relationship between OHV/W and CI-AKI on the left of inflection point was not observed (HR = 1.19, 95% CI: 0.95~1.49, *p* = 0.1302) (Table 4).

The Effect of OHV/W on CI-AKI with Subgroup Analyses

To further explore the relationship between OHV/W and CI-AKI, we analyzed the subgroup (Table 5). Stratified analyses were performed by age (<60, ≥60 years), gender, BMI (<25, ≥25 kg/m²), drugs including CCB, ARB/ACEI, diuretics, β-blocker, OAD, and insulin (yes/no). Subgroup analysis showed that significant interactions were observed only for gender difference (*p* for interaction = 0.0155), male patients had a significantly low-

er risk of CI-AKI (HR = 0.84, 95% CI: 0.75~0.93, *p* = 0.0012). However, the test for interactions were not statistically significant for age, BMI and drugs including CCB, ARB/ACEI, diuretics, β-blocker and OAD (*p* for all interactions >0.05).

Discussion

The present study was to examine the protection effect of OHV/W on CI-AKI among patients with STEMI treated with PCI. As shown in multiple logistic regression model (fully adjusted), OHV/W was not correlation with CI-AKI. However, we further found that there was a nonlinear relationship between OHV/W and CI-AKI. The different correlations of OHV/W and CI-AKI were found on the left and right sides of inflection point (OHV/W = 15.69 mL/kg). On the right side of the inflection point (OHV/W ≥15.69 mL/kg), a negative relationship was detected between OHV/W and CI-AKI (HR = 0.90, 95% CI: 0.82~0.98, *p* = 0.0126). However, the relationship between OHV/W and CI-AKI on the left of inflection point was not observed (HR = 1.19, 95% CI: 0.95~1.49, *p* = 0.1302). Subgroup analysis showed that male patients had a significantly lower risk of CI-AKI.

CI-AKI was a complication of angiographical procedures [16]. Severe CI-AKI not only prolonged hospitalization, increased the cost of medical treatment, but also increased the mortality of patients [3, 17, 18]. 2018 ESC/EACTS Guidelines recommend that adequate hydration remains the chief measure to prevent CI-AKI [19]. However, there was limited research on CI-AKI caused by PCI in emergency [20]. Taylor et al. [21] reported that for patients with mild to moderate renal dysfunction undergoing elective cardiac catheterization, the efficacy of oral hydration was similar to that of intravenous hydration in the prevention of CI-AKI. In 2006, Dussol et al. [22] conducted a small sample, randomized controlled trial, which proved that oral saline hydration and intravenous saline hydration were equally effective in preventing CI-AKI in patients with chronic kidney disease. Recently, Cho et al. [23] compared 2 methods of oral hydration and intravenous hydration, and the results showed that the incidence of CI-AKI, hospital stay, mortality, and other complications were similar. Wrobel et al. [24] compared 102 patients with diabetes undergoing coronary angiography and showed that oral mineral water was as efficient as intravenous hydration. Likewise, another study showed

Table 5. Subgroup analysis of the associations between OHV/W and CI-AKI

Characteristic	Effect size (HR)	95% CI		<i>p</i> value	<i>p</i> for interaction
		lower	upper		
Age					
<60 years	0.96	0.91	1.01	0.0871	0.5252
≥60 years	0.94	0.90	0.98	0.0028	
Gender					
Male	0.84	0.75	0.93	0.0012	0.0155
Female	0.95	0.91	0.99	0.0125	
BMI					
<25	0.92	0.87	0.96	0.0005	0.0541
≥25	0.99	0.93	1.05	0.6834	
CCB					
No	0.96	0.92	0.99	0.0198	0.3275
Yes	0.91	0.83	1.00	0.0548	
ARB/ACEI					
No	0.90	0.85	0.96	0.022	0.2610
Yes	0.95	0.90	1.00	0.035	
Diuretics					
No	0.96	0.922	1.003	0.0667	0.6919
Yes	0.94	0.819	1.069	0.3299	
β-Blocker					
No	0.97	0.94	1.00	0.0785	0.0718
Yes	0.92	0.86	0.97	0.0051	
OAD					
No	0.97	0.93	1.01	0.0938	0.0728
Yes	0.89	0.82	0.97	0.0100	
Insulin					
No	0.96	0.92	0.99	0.084	0.0520
Yes	0.82	0.69	0.97	0.0207	

Above model adjusted for gender, age, BMI, BUN, UA, TC, HDL, LDL, TG, GLU, SBP, DBP, LVEF, Scr, IVHV, DM, HBP, CCB, ACEI/ARB, No. of stents, diuretics; OAD and insulin. In each case, the model is not adjusted for the stratification variable. BMI, body mass index; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, total cholesterol; GLU, blood glucose; SBP, systolic pressure; DBP, diastole pressure; LVEF, left ventricular ejection fraction; Scr, serum creatinine; OHV/W, oral hydration vol/wt; IVHV, intravenous hydration volume; DM, diabetes mellitus; HBP, high blood pressure; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; OAD, oral antidiabetic drugs; CI-AKI, contrast-induced acute kidney injury.

that oral hydration may be as effective as intravenous hydration in the prevention of contrast-induced nephropathy [25]. However, these studies [20–25] were only aimed at patients with nonemergency coronary angiography or PCI, and the hydration scheme was variable, which had insufficient significance for clinical practice. Moreover, little was known about oral hydration strategy on prevention of a high-risk population such as STEMI patients following PCI.

The ratio of CM/estimated glomerular filtration rate is one of the most commonly used indexes to predict CI-AKI in patients with STEMI undergoing PCI. Studies

have shown that the cutoff value of the CM/estimated glomerular filtration rate was 3.7, which is a strong independent predictor of CI-AKI [26, 27]. However, no literature on the cutoff value of the protective effect of oral hydration on CI-AKI was conducted. Song et al. [28] examined the protective effect of the OHV/W on CI-AKI among patients with STEMI after PCI. They found that OHV/W ratio ≥12 mL/kg was an independent protective factor associated with CI-AKI (OR = 0.349, 95% CI: 0.147~0.828, *p* = 0.017). The value of oral hydration in the study was set as 12 mL/kg artificially, and logistic analysis was used to analyze the effect of oral hydration

volume (12 mL/kg) on CI-AKI. However, in our study, in addition to using logistic model, we also used generalized additive model (GAM) to evaluate the nonlinear relationship between OHV/W and CI-AKI. The results showed that OHV/W was nonlinear correlated with CI-AKI. GAM has obvious advantages over logistic model in dealing with nonlinear relations. It can automatically estimate the function (curve) relations of each prediction term by using data [29]. Obviously, the use of GAM will help us better discover the real relationship between OHV/W and CI-AKI.

Although the previous study showed a linear association between OHV/W and CI-AKI, our study did not find this relationship after adjusting for age, gender, intravenous hydration volume, number of stents, medications, and other potential confounders. In view of the nonlinear relationship between OHV/W and CI-AKI, further subgroup analysis was needed. The results of subgroup analysis showed that there was a significant interactive effect of OHV/W and gender difference (p for interaction = 0.0155), male patients had a significantly lower risk of CI-AKI (HR = 0.84, 95% CI: 0.75~0.93, p = 0.0012). Our findings suggested that male patients may particularly benefit from OHV to prevent CI-AKI.

Our research showed that OHV/W ≥ 15.6 mL/kg for 24 h post-procedure may be an effective preventive strategy of CI-AKI. However, overload of oral hydration capacity should be avoided, especially in patients with systolic dysfunction or chronic heart function. Our strategy was that hydration dosage was set at 0.5 mL/kg/h in order to prevent decompensation of patients. Our results showed that there was no heart failure or renal replacement therapy and no patient died during the hospitalization period, suggesting the safety of oral hydration.

There were some limitations of the study: (1) the present study was conducted retrospectively in a single-center, even though we adjusted potential confounding factors with the GAM model. Some selection bias must be noted; (2) data regarding concomitant use of statins were not present for participants, and their impact on the development of CI-AKI cannot be assessed; (3) variations in the times at which the measurements were undertaken may have missed the post-procedural peak creatinine levels; (4) all participants received routine intravenous hydration. Hemodilution can reduce Scr, and cumulative daily fluid balance directly affects the concentration of Scr, and may finally affect the conclusion.

Conclusion

Our study showed a nonlinear relationship between OHV/W and CI-AKI in patients with STEMI after adjusting for potential confounding factors. This finding suggests that OHV/W ≥ 15.69 mL/kg for 24 h post-procedure may be an effective preventive strategy of CI-AKI. In addition, male patients may particularly benefit from OHV to prevent CI-AKI.

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Statement of Ethics

The study was approved by the Ethics Committee of Guangdong Province Hospital of Integrated Traditional Chinese and Western Medicine. This was a retrospective study that did not need informed consent.

Conflict of Interest Statement

The authors declare no potential conflict of interests.

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Author Contributions

Weining Xie contributed to acquisition, analysis, and interpretation of data and took responsibility for the construction of the whole of the manuscript. Yuge Zhou contributed to acquisition and analysis of data, drafting the manuscript, and literature review. Zhishan Liao contributed to acquisition, analysis, and interpretation of data. Biying Lin designed the work, constructed an idea for the research, supervised the course of the project, and reviewed the article.

Data Availability Statement

The data used to support the findings of the study can be made available upon request to the corresponding author.

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