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Simplified rapid hydration and contrast-associated acute kidney injury among CKD patients stratified by Mehran score: sub-analysis from the TIME Trial

Yanyan Zhang[1], Yaokun Liu[1], Bin Zhang[1], Fan Yang[1], Yanjun Gong[1], Bo Zheng[1*] and Yong Huo[1]

Abstract

Simplified rapid hydration has been proven to be non-inferior to standard hydration in preventing contrast-associated acute kidney injury among chronic kidney disease patients undergoing coronary angiography. The current investigation aimed to further confirm the feasibility and safety of the newly proposed hydration method-simplified rapid hydration (SH) in each risk stratification by Mehran risk score (MRS). Eligible patients ($n=954$) randomized to the SH group and standard hydration group were allocated into 2 groups based on MRS: low to moderate-risk and high to very high-risk groups. Primary endpoints were the incidence of contrast-associated acute kidney injury (CA-AKI) and acute heart failure (AHF) (SH vs standard hydration). Secondary endpoints included serum creatinine (Scr), blood urea nitrogen (BUN), cystatin-C (Cys-C), and C-reactive protein (CRP) at 24 h, 48 h, and 72 h after PCI procedure, and the incidence of major adverse cardiac events (MACE). MRS was associated with a higher incidence of CA-AKI (OR = 1.101, 95%CI 1.049–1.156, $P<0.001$). In the low to moderate-risk and high to very-high-risk groups, the incidence of CA-AKI in the SH and standard hydration group was 3.3% versus 4.9% ($P=0.5342$), 10% versus 12% ($P=0.6392$), respectively. Meanwhile, there might be subtle differences in renal function indexes and inflammatory indicators between SH and the control group at different time points. The preventive effect of SH in CA-AKI was similar to standard hydration regardless of MRS-guided risk stratification.

Keywords Chronic kidney disease, Contrast-associated acute kidney injury, Mehran risk score, Risk stratification, Simplified rapid hydration

Introduction

Patients with chronic kidney disease (CKD) exhibited an increasing demand for coronary revascularization driven by an elevated occurrence of conventional coronary artery disease (CAD) risk elements like diabetes and hypertension, alongside nontraditional implications related to uremia, such as inflammation, oxidative stress, and disordered metabolism of calcium and phosphorus (Sarnak et al. 2019). Contrast-associated acute kidney injury (CA-AKI) was inevitable during coronary angiography (CAG) involving contrast medium and associated angiographic procedures (such as hemodynamic disturbances and anemia) (Li and Pan 2022). CA-AKI was associated with mortality, major adverse cardiac events (MACE), prolonged hospitalization, and higher economic burden, exacerbating clinical outcomes and diminishing life quality (James et al. 2013; Pistolesi et al. 2018).

*Correspondence:
Bo Zheng
zhengbopatrick@163.com
[1] Department of Cardiology, Peking University First Hospital, Beijing 100034, China

Currently, there is no established therapy for CA-AKI, underscoring the crucial importance of risk prediction and preventive strategies. The Mehran risk score (MRS), a risk assessment tool for CA-AKI has been widely recognized in clinical practice (Mehran et al. 2004; Abellás-Sequeiros et al. 2016). The estimated risks for CA-AKI in groups classified by MRS as very high-level (>15), high-level (11–15), moderate-level (6–10), and low-level (≤5) were 7.5%, 14%, 26%, and 57%, respectively (Abellás-Sequeiros et al. 2016). In populations susceptible to CA-AKI, effective prevention of AKI occurrence has been demonstrated through appropriate use of contrast medium, personalized hydration, remote ischemic preconditioning, and prophylactic drugs such as trimetazidine and alprostadil (Zhang et al. 2021; Liu et al. 2022). According to 2023 ESC guidelines, periprocedural hydration remained the cornerstone of the prevention of CA-AKI (Byrne et al. 2023). However, the debate surrounding standard hydration, defined as a 12-h period before and a 24-h period after the procedure (Andreucci et al. 2014) has intensified in recent years due to escalating risks of phlebitis, pulmonary edema, heart failure, arrhythmias, and short-term mortality, particularly in vulnerable patients (Nijssen et al. 2019, 2020). No consensus was reached regarding the optimal hydration approach.

The TIME Trial introduced a simplified rapid hydration (SH) method (saline at the rate of 3 mL/kg/h from 1 h before to 4 h after contrast media; 1.5 mL/kg/h for patients with LVEF < 45% or cardiac function class > II) with a shorter hydration duration and proved that it was non-inferior to standard hydration (saline at the rate of 1 mL/kg/h initiating 12 h before to 12 h after contrast media; 0.5 mL/kg/h for patients with LVEF < 45% or cardiac function class > II) in preventing CA-AKI (Liu et al. 2023). However, the optimal method for a specific risk stratification population remained unclear. Our research was to further compare the effectiveness of SH and standard hydration in preventing CA-AKI among patients with varying MRS levels.

Materials and methods

The present study sub-analyzed the data derived from a multicenter, open-label, randomized controlled trial (the TIME trial, NCT 02232997) carried out in 21 teaching hospitals across China from October 2014 to December 2021, which compared the efficacy of SH versus standard hydration for preventing CA-AKI among CKD patients scheduled for CAG or PCI in different MRS categories. A total of 1002 patients were randomly assigned to the simplified rapid hydration method (SH group, $n = 501$) or the standard hydration method (control group, $n = 501$). All patients provided a signed informed consent, and ethics approvals were obtained from all institutions. The trial conformed to the principles outlined in the Declaration of Helsinki.

Enrolled patients were ≥18 years and with at least 1 risk factor (age > 75 years, medical history of diabetes or hypertension, congestive heart failure [CHF] [New York Heart Association functional class > II or LVEF ≤ 35%], or a history of acute pulmonary edema) (Mehran et al. 2004). CKD was defined as an eGFR of 15 to 60 mL/min/1.73 m^2 (Levey et al. 1999). In our study, these patients were stratified into 2 subgroups based on MRS level: low to moderate-risk group ($n = 508$) and high- to very high-risk group ($n = 446$). Specific counting criteria included hypotension (systolic blood pressure < 80 mmHg for at least 1 h, 5 points), use of intra-aortic balloon pump (5 points), congestive heart failure (New York Heart Association classification III/IV or pulmonary edema, 5 points), age (> 75 years, 4 points), anemia (hematocrit: men < 39%, women < 36%, 3 points), diabetes mellitus (3 points), contrast media volume (1 point per 100 mL), and estimated glomerular filtration rate (eGFR, in mL/min per 1.73 m^2; 60 to 40, 2 points, 40 to 20, 4 points, < 20, 6 points).

In concordant with the main trial, the primary endpoint was the occurrence of CA-AKIa, which referred to a ≥25% or 0.5 mg/dL absolute increase in Scr from baseline during the first 48 to 72 h following the operation(Windecker et al. 2014). The safety endpoint was still postprocedural acute heart failure (AHF) during hospitalization and MACE prespecified in the TIME trial. In the present study, the focus was on differences among MRS-dependent groups. As exploratory endpoints, we also analyzed changes in serum creatinine (Scr), blood urea nitrogen (BUN), cystatin-C (Cys-C), and C-reactive protein (CRP) at baseline and within 24 h, 48 h, and 72 h after exposure to contrast media.

For statistical analysis, continuous variables were presented as the mean ± SD or median (IQR) if applicable. Categoric variables were described as counts and percentages in each category. Secondly, continuous variables were compared using an unpaired *t* test or analysis of variance (ANOVA), while categorical variables were examined with a $\chi 2$ test; the Fisher exact test was conducted to compare the percentages. Then, multivariate logistic regression was employed to identify independent variables associated with endpoints. Next, the time-to-event analysis was performed by Kaplan–Meier between 2 groups. $P < 0.05$ was considered significant (2-sided). All data were analyzed through R software (Version 4.3.0, R Core Team).

Results

Baseline characteristics

The trial initially enrolled 1002 CKD patients prepared for CAG. After selection, 48 patients were excluded due to missing data and 954 patients were eligible for the trial. Subsequently, patients were grouped in line with MRS: the low-risk group ($n=151$), the moderate-risk group ($n=357$), the high-risk group ($n=290$), and the very high-risk group ($n=156$). Since the incidence of pre-specified events in the low-risk group was scarce, the low-risk group and moderate-risk group were merged into the "low to moderate-risk group" for the convenience of the following analysis. The high-risk group and very high-risk group were treated as a whole for the same reason. Finally, two subgroups were established: the low- to moderate-risk group ($n=508$; SH group $n=261$; control group $n=247$), and the high- to very-high-risk group ($n=446$; SH group $n=221$; control group $n=225$) (Fig. 1).

Most variables including age, gender, history of diseases, renal function, and perioperative items were similar between the SH group and control group in the two risk groups. In the low- to moderate-risk group, BUN was notably higher in the SH group (8.0 mmol/L) than in the control group (7.5 mmol/L) ($P=0.0191$). Also, the non-PCI operation of the SH group was more frequent compared with the control group (57.1%, 44.9%; $P=0.0081$) (Table 1).

Main outcomes

Above all, MRS counted as a continuous variable was associated with a higher incidence of CA-AKI (OR = 1.101, 95%CI 1.049–1.156, $P<0.001$). Then as a categorical variable, no significant difference between the SH group and control group was present for each MRS subgroup. In the low- to moderate-risk group, the occurrence of CA-AKI in the SH group and control group was 3.3% and 4.9% ($P=0.5342$). In high- to very high-risk groups, the incidence of CA-AKI in two groups was 10% and 12% ($P=0.6392$) (Fig. 2).

According to the multivariate logistic regression result, a predictive factor of CA-AKI in low- to moderate-risk populations stratified by MRS was DM (OR = 3.696, $P=0.036$). On the contrary, a higher baseline LVEF acted as a protective factor of CA-AKI in the high- to very high-risk population (OR = 0.974, $P=0.04$) (Table 2).

For safety endpoints, postprocedural AHF was similar between the SH group and the control group. In the low- to moderate-risk group, 3 patients of both the SH group (1.1%) and control group (1.2%) developed AHF. In the high- to very high-risk group, AHF happened in 12 patients (5.4%) of the SH group and 13 patients (5.8%) of the control group (all $P>0.05$) (Fig. 2). Likewise, there

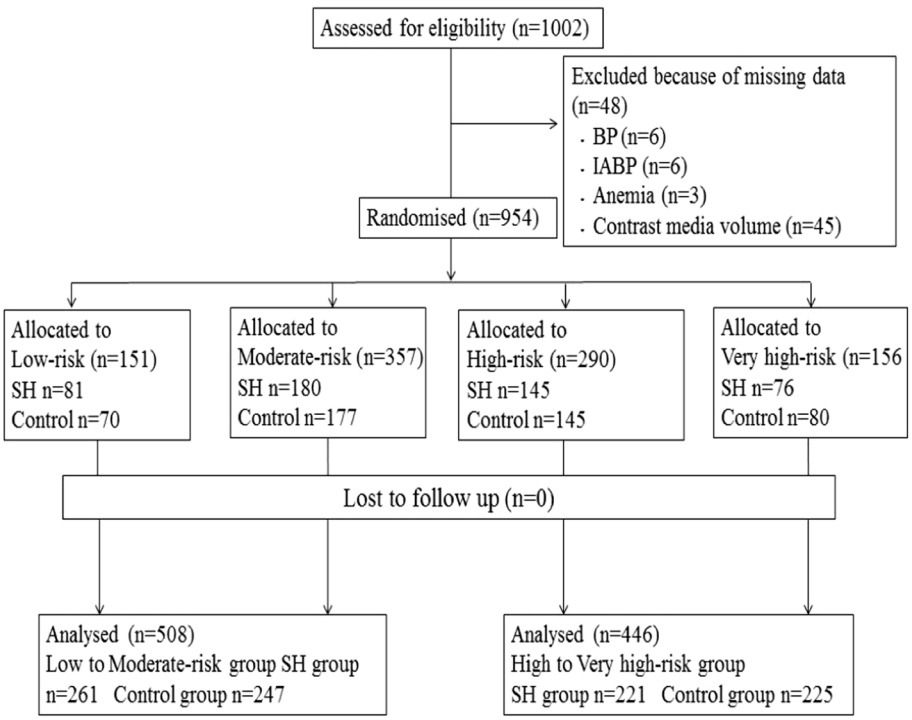

Fig. 1 Flow chart

Table 1 Comparisons of baseline characteristics between the SH group and control group in the low- to moderate-risk ($n=508$), and high- to very high-risk ($n=446$) MRS group, respectively

Variables	Low- to moderate-risk group ($n=508$)			High- to very high-risk group ($n=446$)		
	SH group ($n=261$)	Control group ($n=247$)	*P*	SH group ($n=221$)	Control group ($n=225$)	*P*
Age, years	67.9 (8.8)	66.9 (9.3)	0.2072[a]	71.3 (10.5)	70.6 (10.1)	0.4604[a]
Male, %	68 (26.1)	61 (24.7)	0.8031[b]	54 (24.4)	58 (25.8)	0.8275[b]
DM, *n* (%)	77 (29.5)	76 (30.8)	0.8302[b]	129 (58.4)	133 (59.1)	0.9501[b]
CHF, *n* (%)	21 (8.0)	17 (6.9)	0.7418[b]	108 (48.9)	102 (45.3)	0.5137[b]
CAD, *n* (%)	237 (90.8)	220 (89.1)	0.6150[b]	209 (94.6)	210 (93.3)	0.7271[b]
AMI, *n* (%)	36 (13.8)	32 (13.0)	0.8833[b]	38 (17.2)	46 (20.4)	0.4493[b]
Hypertension, *n* (%)	230 (88.1)	217 (87.9)	1.0000[b]	193 (87.3)	182 (80.9)	0.0837[b]
Scr, mg/dL	1.4 (0.2)	1.4 (0.2)	0.6103[a]	1.8 (0.5)	1.8 (0.5)	0.7444[a]
eGFR, mL/min/1.73 m^2	51.1 (6.5)	51.2 (7.3)	0.9605[a]	40.0 (10.6)	40.0 (14.9)	0.9782[a]
BUN, mmol/L	8.0 (2.5)	7.5 (2.1)	0.0191[a]	10.6 (4.4)	10.5 (4.2)	0.8155[a]
CysC, mg/L	1.4 (0.4)	1.4 (0.4)	0.9416[a]	1.8 (0.5)	1.9 (0.6)	0.6082[a]
CRP, mg/L	16.6 (25.0)	27.6 (61.5)	0.3102[a]	17.1 (21.9)	24.7 (37.4)	0.2438[a]
BNP, pg/ml	264.2 (442.1)	261.8 (428.2)	0.9856[a]	399.2 (554.1)	478.4 (613.8)	0.5935[a]
LVEF, %	58.5 (9.8)	58.8 (11.6)	0.8181[a]	55.6 (12.5)	53.8 (13.1)	0.1731[a]
Anemia, *n* (%)	97 (37.2)	78 (31.6)	0.2184[b]	154 (69.7)	155 (68.9)	0.9369[b]
IABP, *n* (%)	0 (0.0)	0 (0.0)	NA	2 (0.9)	5 (2.2)	0.4605[b]
Non-PCI, %	149 (57.1)	111 (44.9)	0.0081[b]	111 (50.2)	105 (46.7)	0.5110[b]
CMV, mL	102.9 (67.3)	113.6 (65.1)	0.0706[b]	126.2 (81.5)	122.7 (68.6)	0.6219[b]
Periprocedural intravenous hydration volume, mL	1200.4 (619.1)	1601.7 (776.7)	< 0.0001[a]	1072.4 (569.0)	1412.5 (674.1)	< 0.0001[a]
Periprocedural urine volume, mL	1763.4 (1148.5)	1991.4 (1155.6)	0.0965[a]	1584.4 (962.9)	2135.0 (3803.5)	0.1021[a]

Abbreviations: *MRS* Mehran risk score, *DM* diabetes mellitus, *CHF* congestive heart failure, *CAD* coronary artery disease, *AMI* acute myocardial infarction, *Scr* serum creatinine, *eGFR* estimate glomerular filtration rate, *IABP* intra-aortic balloon pump, *CMV* contrast media volume, *PCI* percutaneous coronary intervention, *SH group* simplified rapid hydration group, *Control group*, standard hydration group

Values are mean ± SD, *n* (%), or median (IQR)

[a] Independent *t*-test

[b] The $\chi 2$ test

was no obvious discrepancy in MACE at 1, 3, 6, and 12 months of these two risk groups in line with MRS (Fig. 3).

Other laboratory index

Based on available data, renal function indexes Scr, BUN, Cys-C, and inflammatory indicators CRP in the SH group and control group were compared in the overall population and two risk categories respectively (Table 3).

Baseline values of Scr, BUN, Cys-C, and CRP were basically the same among each group before contrast agent exposure ($P>0.05$). In the low- to moderate-risk group, renal function parameters Scr and CysC 72 h after operation were distinctly lower in the SH group (all $P<0.05$). In the high- to very high-risk group, the CRP value 48 h after the operation of the control group was significantly higher than that of the SH group ($P=0.0394$) and the same was true in the general population ($P=0.0232$). No obvious difference was observed in BUN between the two groups 24–72 h after intervention (all $P>0.05$).

Discussion

Our research demonstrated that SH was similar to standard hydration in preventing CA-AKI among CKD patients of different MRS levels undergoing CAG, which aligned with the previous conclusion in the TIME Trial (Liu et al. 2023). Meanwhile, AHF occurred with hydration in both MRS categories and was also comparable with the overall population. Therefore, it further confirmed the feasibility and safety of the newly proposed hydration method-SH, even in the CA-AKI susceptible population stratified by MRS.

With CA-AKI being the third most common reason for AKI among hospitalized individuals, it was proven to cause clinical adverse effects such as CKD progression, cardiovascular events, and mortality (Do 2017). In the overall population, the estimated incidence of CA-AKI

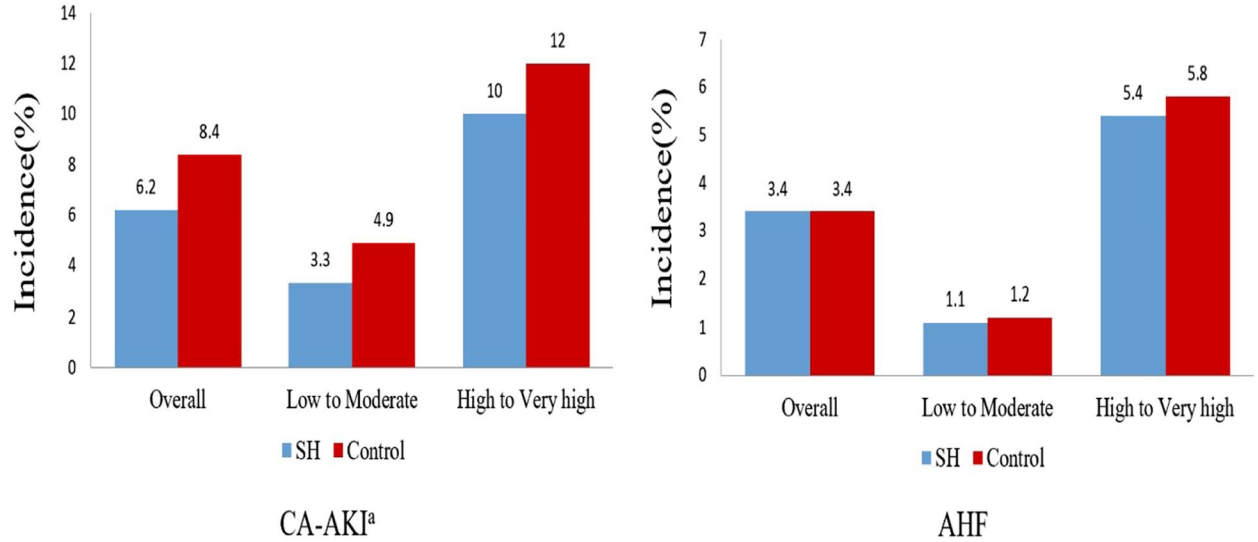

Fig. 2 Incidence of CA-AKI[a] and postprocedural acute heart failure (AHF) in the SH group and control group in the low- to moderate-risk and high to very high-risk MRS group, respectively. CA-AKI[a] indicates a ≥ 25% or 0.5 mg/dL absolute increase in Scr from baseline during the first 48 to 72 h after the procedure. SH group, simplified rapid hydration group; control group, standard hydration group

Table 2 Multivariable logistic regression analyses for predictors of CA-AKI in low to moderate ($n=508$) and high- to very high-risk ($n=446$) population stratified by MRS

Variables	Overall ($n=954$)		Low to moderate ($n=508$)		High to very high ($n=446$)	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1.008 (0.979,1.038)	0.613	1.045 (0.967,1.139)	0.286	0.99 (0.96,1.023)	0.55
Male	1.479 (0.76,2.797)	0.237	1.742 (0.393,7.006)	0.445	1.198 (0.528,2.579)	0.652
DM, *n*(%)	1.644 (0.915,3.006)	0.100	3.696 (1.11,13.433)	0.036	1.046 (0.523,2.147)	0.901
Anemia, *n*(%)	1.564 (0.86,2.918)	0.149	2.249 (0.708,7.52)	0.171	1.037 (0.515,2.19)	0.922
AMI, *n*(%)	0.995 (0.45,2.018)	0.990	0.483 (0.025,2.715)	0.5	1.071 (0.447,2.358)	0.871
Baseline Scr	1.654 (0.947,2.767)	0.064	1.35 (0.024,21.545)	0.866	1.181 (0.607,2.168)	0.605
Baseline LVEF	0.975 (0.954,0.998)	0.028	1.01 (0.959,1.073)	0.733	0.974 (0.949,0.999)	0.04
PCI, *n* (%)	0.892 (0.463,1.688)	0.729	0.344 (0.074,1.341)	0.143	1.175 (0.554,2.462)	0.671
Contrast volume, mL	1.003 (0.998,1.007)	0.241	0.997 (0.985,1.007)	0.614	1.003 (0.998,1.008)	0.199

Abbreviations: *CA-AKI* contrast-associated acute kidney injury, *MRS* Mehran risk score, *OR* odds ratio

ranged from 1 to 6%. According to a recent meta-analysis by Wu et al. incidence of CA-AKI rose to 9% in patients receiving angiography (Wu et al. 2022). Currently, the main mechanisms involve direct tubular cell injury by osmotic stress and reactive oxygen species or free radicals, along with hemodynamic changes (Katzberg 2005; Katzberg and Haller 2006). Considering these theories, it is plausible that pre-existent risk factors such as advanced age, heart failure, CKD, and diabetes, could decrease renal blood flow, alter vasoactive mediators, and increase oxidative stress, further exacerbating these pathophysiologic processes to CA-AKI (Vemireddy and Bansal 2023). Our research observed that MRS, a comprehensive risk assessment tool comprising hemodynamic conditions and the aforementioned comorbidities, was significantly correlated with CA-AKI occurrence. In accordance with previous studies, it strongly validated the applicability of MRS in the prediction of CA-AKI and optimization of prophylactic therapy (Abellás-Sequeiros et al. 2016).

Current guidelines from the American College of Cardiology recommended prophylaxis hydration in clinical practice and it was supported by numerous trials (Solomon 2023). Whether various hydration strategies have different degrees of effects on CA-AKI is still under investigation. Firstly, selective hydration targeting different populations was required. Building upon the findings

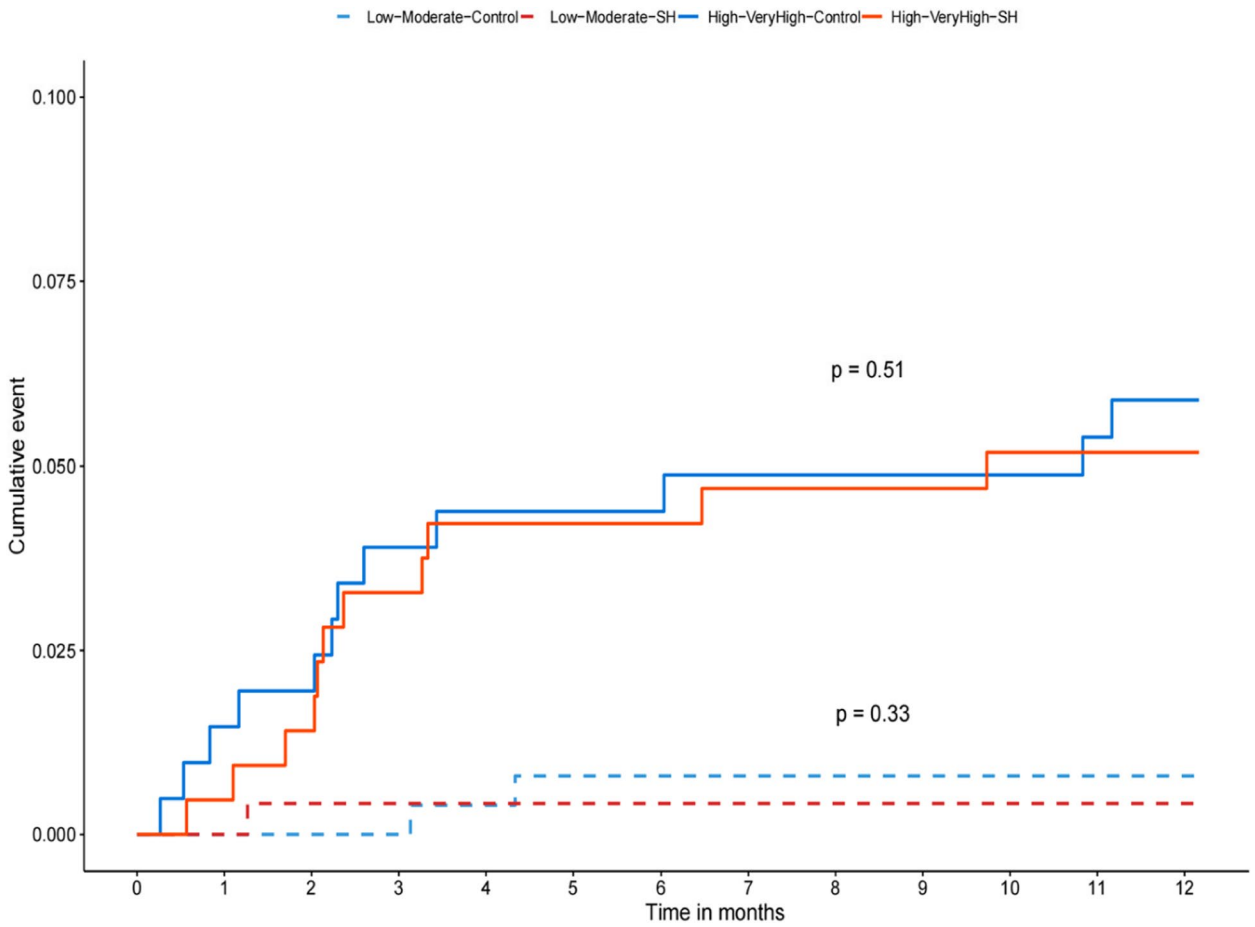

Fig. 3 Incidence of MACE in the SH group and control group in the low- to moderate-risk and high to very high-risk MRS group, respectively. The time-to-event analysis was conducted using the Kaplan–Meier method among 2 groups. $P < 0.05$ was considered significant (2-sided). MACE, major adverse cardiac events; MRS, Mehran risk score

of the TIME Trial, which established the equivalence of SH with standard hydration in the general population, our analysis further validated the efficacy and safety of SH among patients in each risk category. Different from SH, drugs like alprostadil and trimetazidine exerted protective effects to varying degrees dependent on risk stratification and demonstrated a preference for moderate- and high-risk populations according to MRS (Zhang et al. 2021; Liu et al. 2022). In the second place, explorations into various aspects of hydration, including timing, method, and dosage were persistently in progress. Recently Chen et al. demonstrated that the preventive effect of postprocedural hydration was equal to preoperative hydration in terms of CA-AKI for patients with CAD after elective PCI (Chen et al. 2023). According to an observational study by Mariana et al. outpatient oral hydration appeared to be as effective as intravenous hydration for renal protection in elective coronary interventions (Pioli et al. 2023). Taking both timing and method into consideration, Kong et al. proved that oral or intravenous hydration, administered both pre- and post-procedural was similar in efficacy to oral hydration alone after the procedures in preventing CA-AKI (Kong et al. 2012). For dosage, the association between post-procedural oral hydration and CA-AKI among STEMI patients was studied by Song et al. and adequate oral hydration ($\geq$12 mL/kg) was regarded as an independent protective factor (Song et al. 2019). Besides, hydration in combination with all kinds of oral drugs such as alprostadil, febuxostat, and N-acetylcysteine was becoming prevalent. Apparently, more large-scale trials were needed to explore hydration from all aspects.

Although the occurrence of CA-AKI in these two hydration methods was similar, distinctions in renal function indexes and inflammatory indicators were found in our research. Except for patients with a high to very high risk of CA-AKI, both Scr and CysC at 72 h after PCI were lower in the SH group than those in the standard hydration group, implying a potential advantage of SH to some extent. The inflammatory markers CRP

Table 3 Changes in, Scr, BUN, CysC, and CRP at 24 h, 48 h, and 72 h after PCI

Variables	Overall			Low- to moderate-risk group			High- to very high-risk group		
	SH group (*n* = 230)	Control group (*n* = 267)	*P*	SH group (*n* = 112)	Control group (*n* = 136)	*P*	SH group (*n* = 71)	Control group (*n* = 73)	*P*
Scr (mg/dL)									
Baseline	1.6 (0.5)	1.6 (0.5)	0.5748[a]	1.4 (0.3)	1.4 (0.2)	0.7960[a]	1.8 (0.5)	1.9 (0.5)	0.2561[a]
24 h	1.5 (0.5)	1.5 (0.5)	0.4638[a]	1.3 (0.3)	1.3 (0.3)	0.9835[a]	1.7 (0.5)	1.8 (0.6)	0.1417[a]
48 h	1.6 (0.6)	1.6 (0.6)	0.6000[a]	1.4 (0.3)	1.4 (0.3)	0.2742[a]	1.9 (0.7)	1.9 (0.7)	0.8752[a]
72 h	1.5 (0.5)	1.8 (0.7)	*0.0114[a]	1.3 (0.3)	1.5 (0.4)	*0.0448[a]	1.8 (0.5)	2.0 (0.8)	0.2210[a]
ANOVA			0.6100[b]			0.5000[b]			*0.0030[b]
BUN (mmol/L)									
Baseline	8.7 (3.4)	9.1 (3.9)	0.3438[a]	7.6 (2.6)	7.7 (2.2)	0.6747[a]	9.8 (3.7)	10.7 (4.7)	0.0919[a]
24 h	7.6 (2.9)	7.6 (3.6)	0.8377[a]	6.3 (2.0)	6.2 (1.7)	0.5178[a]	8.7 (3.1)	9.3 (4.5)	0.3173[a]
48 h	7.9 (3.0)	8.0 (3.9)	0.7632[a]	6.6 (1.8)	6.8 (2.0)	0.4396[a]	9.3 (3.3)	9.2 (4.9)	0.8607[a]
72 h	8.1 (2.5)	9.6 (5.1)	0.0584[a]	7.6 (2.1)	7.6 (2.1)	0.9375[a]	8.8 (2.8)	11.0 (6.1)	0.1143[a]
ANOVA			0.1610[b]			*0.0010[b]			0.3880[b]
CysC (mg/L)									
Baseline	1.7 (0.5)	1.7 (0.5)	0.8498[a]	1.4 (0.3)	1.5 (0.3)	0.9126[a]	1.9 (0.5)	1.9 (0.6)	0.7044[a]
24 h	1.6 (0.4)	1.6 (0.6)	0.2846[a]	1.4 (0.3)	1.4 (0.4)	0.7441[a]	1.8 (0.5)	1.9 (0.7)	0.3003[a]
48 h	1.6 (0.5)	1.7 (0.6)	0.1465[a]	1.4 (0.3)	1.4 (0.4)	0.3343[a]	1.9 (0.6)	2.0 (0.7)	0.3213[a]
72 h	1.6 (0.4)	2.3 (1.8)	*0.0288[a]	1.3 (0.3)	1.6 (0.4)	*0.0045[a]	1.8 (0.3)	2.2 (0.9)	*0.0479[a]
ANOVA			0.5500[b]			0.9120[b]			0.6790[b]
CRP (mg/L)									
Baseline	20.7 (25.5)	23.8 (33.2)	0.6238[a]	26.5 (32.3)	18.5 (26.1)	0.3882[a]	16.6 (18.9)	29.0 (39.1)	0.1558[a]
24 h	22.6 (36.1)	24.4 (31.4)	0.8431[a]	26.5 (38.7)	29.4 (45.0)	0.8657[a]	17.5 (33.4)	20.0 (22.8)	0.8032[a]
48 h	20.2 (20.2)	39.7 (33.1)	*0.0232[a]	18.3 (17.5)	31.3 (39.9)	0.3947[a]	21.5 (22.4)	43.6 (30.2)	*0.0394[a]
72 h	15.8 (17.5)	47.8 (62.2)	0.2063[a]	16.2 (18.7)	33.1 (45.5)	0.5776[a]	15.4 (19.5)	56.3 (72.0)	0.3053[a]
ANOVA			0.7480[b]			0.9150[b]			0.5120[b]

Changes of Scr, BUN, CysC, and CRP in the overall population (*n* = 497, SH group *n* = 230, control group *n* = 267), low- to moderate-risk group (*n* = 248, SH group *n* = 112, control group *n* = 136), high- to very high-risk group (*n* = 144, SH group *n* = 71, control group *n* = 73)

[*] Means *P* value < 0.05

[a] The independent *t* test

[b] Analysis of covariance (ANOVA)

were closely linked to the pathogenesis of CA-AKI and the predictive value of CRP was even proved to be similar to the MRS (Guo et al. 2017; Liu et al. 2012). In our study, CRP levels at 48 h after PCI were lower in the SH group than those in the standard hydration group in both overall and high- to very high-risk populations. It was likely that the anti-inflammatory phenomenon was related to renal protective effect and the speculation was expected to be verified in studies with larger samples.

Certainly, the limitations of our study cannot be neglected. Firstly, due to a limited number of patients, we did not separate the low-risk from the moderate-risk group and took them as a whole. High-risk and very high-risk groups were combined in the same way. However, we did compare the occurrence of CA-AKI in each group and the conclusion still applied. Secondly, though renal function indexes and inflammatory indicators seemed to function in hydration, the absence of certain related data restricted a more in-depth analysis of the corresponding mechanism.

Conclusions

In conclusion, our findings support the consideration of SH as a preventive measure against the occurrence of CA-AKI in CKD patients after CAG or PCI, irrespective of risk stratification guided by the MRS. However, further exploration is warranted to investigate any undiscovered advantages or disadvantages of SH compared to standard hydration.

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Authors' contributions
Yanyan Zhang: interpretation of data and manuscript revision and the initial draft of the manuscript; Yaokun Liu: data analysis and validation of the manuscript; Bin Zhang: data analysis, manuscript review; Fan Yang: methodology, formal analysis, and manuscript revision; Yanjun Gong: study conceptualization and manuscript review; Bo Zheng: study conceptualization, methodology, and manuscript review; Yong Huo: study conceptualization, methodology, and manuscript review. All authors contributed to the article and approved the submitted version.

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Data availability
Data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Institutional review board statement
The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board.

Competing interests
The authors declare no competing interests.

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