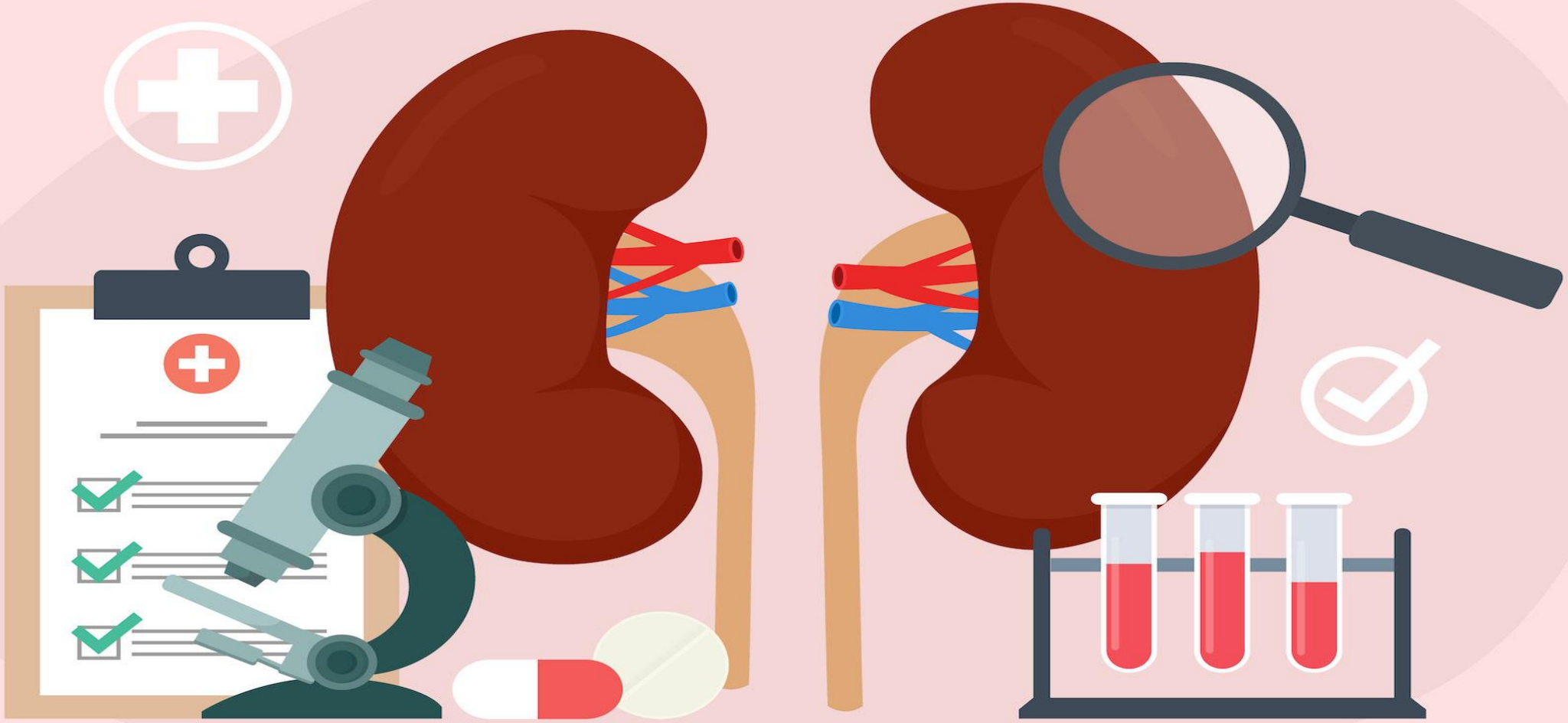
Contrast-induced nephropathy



A SUMMERY OF INTRODUCTION AND PATHOPHYSIOLOGY

DEFINITION

ACR suggested contrast-associated acute kidney injury (**CA-AKI**), formerly called post-contrast acute kidney injury (PC-AKI), as a **general term** to describe a *decline in kidney function that occurs within 48 h after the intravascular administration of iodinated CM.*

CA-AKI is a correlative diagnosis, regardless of the exact etiology of AKI.

They suggested the term **contrast-induced acute kidney injury** (**CI-AKI**), **formerly known as CIN**, as a **causative diagnosis** describing AKI due to CM.

DEFINITION

It is difficult to identify the definite cause of AKI in patients receive CM, because **various patient- and procedure-related factors can influence kidney function**, such as **hemodynamic instability** or **atheroembolism** caused by catheter manipulation.

DEFINITION

It is difficult to differentiate CI-AKI from CA-AKI in most studies, mainly due to the lack of a suitable control group.

The incidence of CI-AKI might have included cases of CA-AKI, although CI-AKI is a subgroup of CA-AKI.

DIAGNOSIS

Kidney dysfunction in CIN is usually **reversible**

Decline in kidney function occurs ***2–3 days*** *after exposure* to CM and *returns to the baseline level within* ***1–2 weeks***

DIAGNOSIS

KDIGO initiative diagnoses CIN if one of the following occurs within 48 h after intravascular administration of CM

- Absolute increase in Scr ≥ 0.3 mg/dL (≥26.4 μmol/L)
- Relative increase in sCr ≥ 50% (≥1.5 times baseline)
- Urinary volume <0.5 mL/kg/h for ≥6 h, which is now adopted as the standard for both CA-AKI and CI-AKI

DIAGNOSIS

Diverse definitions of CIN in clinical studies	***Absolute*** increase in ***sCr ≥0.3–0.5 mg/dL***
	Relative increase in ***sCr ≥ 25–50%*** from baseline values

*Relative increase ≥25% is the most sensitive indicator, and an absolute increase ≥0.5 mg/dL is the least sensitive.

*Therefore, the incidence of CIN reported in clinical studies should be interpreted carefully in light of the definition used

DIAGNOSIS

The elevated **sCr** might **not be a sensitive** marker for assessing changes in GFR:

- SCr increases **slowly** after a reduction in GFR and is **affected** by **multiple factors** such as *muscle mass, age, sex, and hydration* status

Because of the low sensitivity and specificity of sCr, ***various new biomarkers*** have been studied to detect kidney injury more precisely.

DIAGNOSIS

Biomarkers of CIN can be divided them into two categories

- **Functional** biomarkers that can detect a decrease in kidney function with more sensitivity than creatinine, including **cystatin C**
- **Structural** biomarkers such as ***neutrophil gelatinase associated lipocalin, liver-type fatty acid-binding protein, and kidney injury molecule-1*** (KIM-1).

DIAGNOSIS

Some biomarkers can detect early kidney injury even ***before functional change develops***, and some can ***predict*** the occurrence or prognosis of CIN.

In a recent sub-study of the PRESERVE trial that evaluated plasma and urine biomarkers, only plasma **KIM-1** was significantly associated with CIN.

However, for general application of biomarkers as a routine procedure in clinical practice, further studies are needed to evaluate and validate the clinical significance and cutoff values for each one.

MANAGEMENT

At present, prevention is the best management strategy for CIN and can be divided into patient-, procedure-, and pathophysiology-related methods.

All patients receiving intravascular CM should be evaluated for the risk of CIN, and clinicians should adopt interventions for modifiable risk factors such as dehydration and consider discontinuing nephrotoxic medications before CM administration.

Table 2. Strategies to reduce the development of contrast-induced nephropathy. Preventive strategies against contrast-induced nephropathy (CIN) are presented, taking into account patient- and procedure-related risk factors and CIN pathophysiology. * Hydration is a patient-, procedure-, and pathophysiology-related preventive strategy against CIN.

Patient-related	Risk stratification of individual patients Evaluate and correct patient's volume status Correct modifiable factors including cessation of nephrotoxic drugs
Procedure-related	Use low-osmolar or iso-osmolar contrast media Minimize the volume of contrast media - limit maximum contrast volume - consider the interval of contrast administration
Pathophysiology-related	Hydration * Pharmaceutical agents targeting pathogenic process including oxidative stress

PREVENTION

Mehran risk scoring system involves eight clinical and procedural variables, to predict CIN after PCI

ACEF (age, creatinine, and ejection fraction) score was developed to assess the **mortality risk** in **patients undergoing elective cardiac operations**

ACEF has subsequently been validated in other clinical conditions, including CIN after CAG or PCI.

It is now the **basis for comparison**, *along with Mehran's* score system, **for new CIN risk scoring systems**

PREVENTION

Zeng et al. proposed a risk score based on four variables:

- Age > 75 years,
- Acute myocardial infarction,
- scr > 1.5 mg/dl
- Use of an IABP

Ni et al. suggested a pre-procedure risk score that considers five factors:

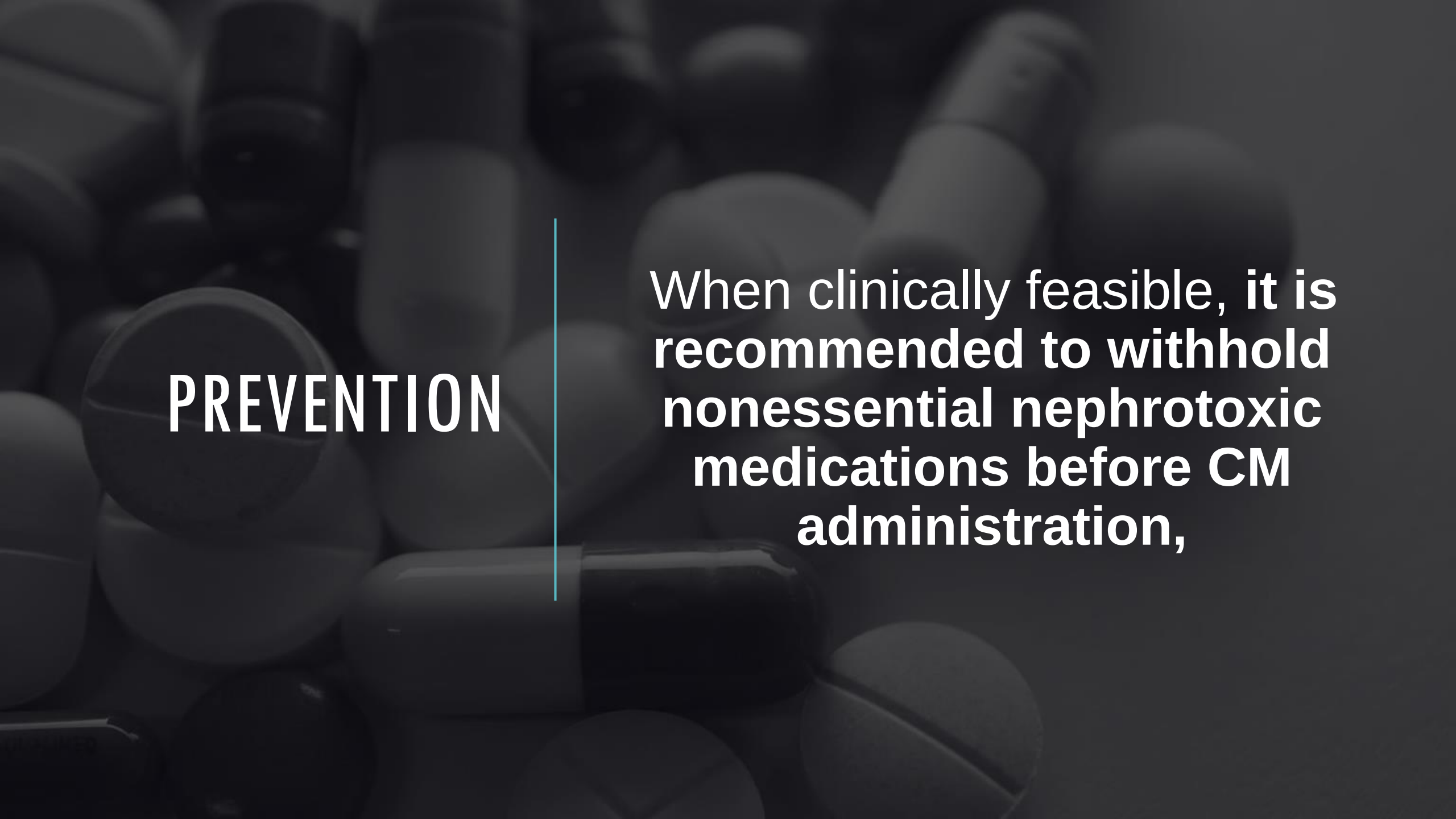
- Age > 75 years
- Hypotension
- Acute myocardial infarction
- scr ≥ 1.5 mg/dl
- Congestive heart failure

PREVENTION

Those risk scoring systems have been evaluated for their ability to predict CIN, procedure-related mortality, and major adverse clinical events in patients undergoing CAG or PCI.

However, those systems are not yet relevant for IV administration of CM or patients receiving non-coronary angiography.

External validation of those models and the development of a novel risk scoring system that can be generally applied to all cases of CM use are required.



PREVENTION

When clinically feasible, **it is recommended to withhold nonessential nephrotoxic medications before CM administration,**

Table 1. Risk factors predisposing the development of contrast-induced nephropathy. Risk factors for contrast-induced nephropathy (CIN) can be divided into patient-related and procedure-related risk factors. Some patient-related risk factors such as volume depletion and using nephrotoxic medications are modifiable. With regard to procedure-related risk factors, the risk of CIN varies according to type, volume, and route of CM administration. Atheroembolism related to catheter manipulation and repeated CM administration also poses an increased risk of CIN. CM, contrast media.

Patient-Related	Impaired renal function Diabetes mellitus Effective intravascular volume depletion: dehydration, blood loss, congestive heart failure, liver cirrhosis, nephrosis Advanced age Female gender Cardiovascular disease including hypertension Malignancy Inflammation Anemia Hyperuricemia Nephrotoxic medications: diuretics, nonsteroidal antiinflammatory drugs, aminoglycosides, amphotericin B, antiviral drugs such as acyclovir, cyclosporine A, cisplatin
Procedure-Related	Route of CM administration: intra-arterial vs. intravenous administration Type of procedure: catheter-based procedure Type of CM Volume of CM Repeated CM administration within 24–72 h

PREVENTION

Because RAAS blockade can change **renal hemodynamics and induce AKI**

A **meta-analysis** with 14 studies composed of 15,447 patients (7288 treated with ACEI or ARB and 8159 in the control group) undergoing **CAG**.

The overall estimate demonstrated significantly **increased risk of CIN in the ACEI/ARB** group compared to the control group ***(OR 1.50, 95% CI 1.03–2.18, p = 0.03),*** but the **association was not observed in the seven RCTs (OR 0.88, 95% CI 0.41–1.90, *p* = 0.74).**

PREVENTION

A **meta-analysis** included 12 studies with 14 trials, containing 4864 patients (2484 treated with RAAS blockers and 2380 in the control group), the pooled **relative risk of CIN incidence in the RAAS blocker group was *1.22 (95% CI 0.81–1.84).***

Increased risk of CIN in the RAAS blocker group was observed among **older people *(RR 2.02, 95% CI 1.21–3.36)***, **non-Asians *(RR 2.30, 95% CI 1.41–3.76),* chronic users *(RR 1.69, 95% CI 1.10–2.59),*** and **studies with larger sample sizes *(population ≥ 200, RR 1.83, 95% CI 1.28–2.63)***

PREVENTION

Only a few RCTs directly investigated the effects of withholding ACEI/ARB on the incidence of CIN:

1. Discontinuing captopril 36 h before PCI did not change the incidence of CIN in patients with sCr ≤ 1.5 mg/dL or GFR ≥ 60 mL/min.
2. Withholding ACEI/ARB 24 h before CAG did not appear to influence the incidence of CIN in patients with CKD stages 3–4.

PREVENTION

A **retrospective** study and analyzed changes in renal function during ***one-month*** post **CAG** in ***CKD stages 2–5 patients who take ACEI/ARB and are not on dialysis***. Continuation of ACEI/ARB was not associated with significant renal injury after CAG.

PREVENTION

Post-hoc analysis of an **RCT** showed that the **continuation of ACEI/ARB** was **associated with** a ***significant decrease in baseline, eGFR < 60 mL/min compared to the discontinuation group***, *there was no significant difference in changes of renal function between the two groups in patients with eGFR ≥ 60 mL/min*.

In patients with **moderate renal insufficiency,** withholding ACEI/ARB resulted in a *non-significant reduction in CIN* and a ***significant reduction in the post-procedural increase in Cr.***

It remains inconclusive whether ACEI/ARBs increase or decrease the
incidence of CIN

currently, withholding RAAS blockers before CM administration is
not recommended in guidelines

PREVENTION

Metformin is mainly excreted by the kidneys and **confers an increased risk of lactic acidosis when CIN occurs**, although **it does not increase the risk of CIN**.

However, as the reported *incidence* of **metformin-associated *lactic acidosis*** has been *very low* (<10 cases per 100,000 patient-years), guidelines have become less strict.

PREVENTION

Many guidelines recommend to **stop taking metformin at the time of CM administration in**:

1. Patients with egfr < 30 ml/min/1.73 m2 receiving IV CM or IA CM with second pass renal exposure
2. Patients receiving IA CM with first pass renal exposure
3. Patients with AKI

*They also recommend to *measure eGFR within 48 h and restart metformin if renal function has not changed significantly*

PREVENTION

Minimizing the total volume of CM and using the least nephrotoxic CM should be applied in all cases.

There have been efforts to reduce the contrast volume (iodine dose) as low as reasonably achievable during both CAG and CECT.

Consider the interval of CM administration when repeated procedures are needed because multiple doses of CM within a short period of time (24–72 h) increase the risk of CIN

PREVENTION

Intravenous fluid hydration is the mainstay of CIN preventive strategies:

1. Hydration is theoretically reasonable because it can correct or improve the patient's volume status, dilute CM concentration, and increase kidney blood flow and tubular urine flow, which can subsequently reduce CM retention and toxic effects in the tubular lumen.

PREVENTION

Intravenous fluid hydration is the mainstay of CIN preventive strategies

- Hydration can correct or **improve volume status**, **dilute CM concentration**, and **increase kidney blood flow** and **tubular urine flow**, which can subsequently **reduce CM retention and toxic effects in the tubular lumen.**

PREVENTION

There is **no consensus on the optimal hydration regime.**

Two tailored hydration regimens have been widely investigated:

- left ventricular end-diastolic pressure (LVEDP)-guided hydration and
- urine flow rate (UFR)-guided hydration using the RenalGuard system

PREVENTION

The POSEIDON trial compared LVEDP-guided hydration with standard hydration in 396 patients undergoing **cardiac catheterization**.

All patients received a bolus infusion of normal saline (3 mL/kg) for 1 h prior to the procedure. During and for 4 h after the procedure

LVEDP-guided group received normal saline at a rate of 1.5 to 5 mL/kg/h, depending on the LVEDP,

Control group received 1.5 mL/kg/h of normal saline.

PREVENTION

Total hydration volume was higher in the LVEDP-guided group (*mean volume, 1727 mL vs. 812 mL, p < 0.001)*, and significantly fewer cases of CIN occurred in that group *(6.7% vs. 16.3%, p = 0.005).*

***The odds of CIN* decreased by 9% for every additional 100 mL of normal saline** administered *(OR 0.91, 95% CI 0.89–0.94, p = 0.01)*.

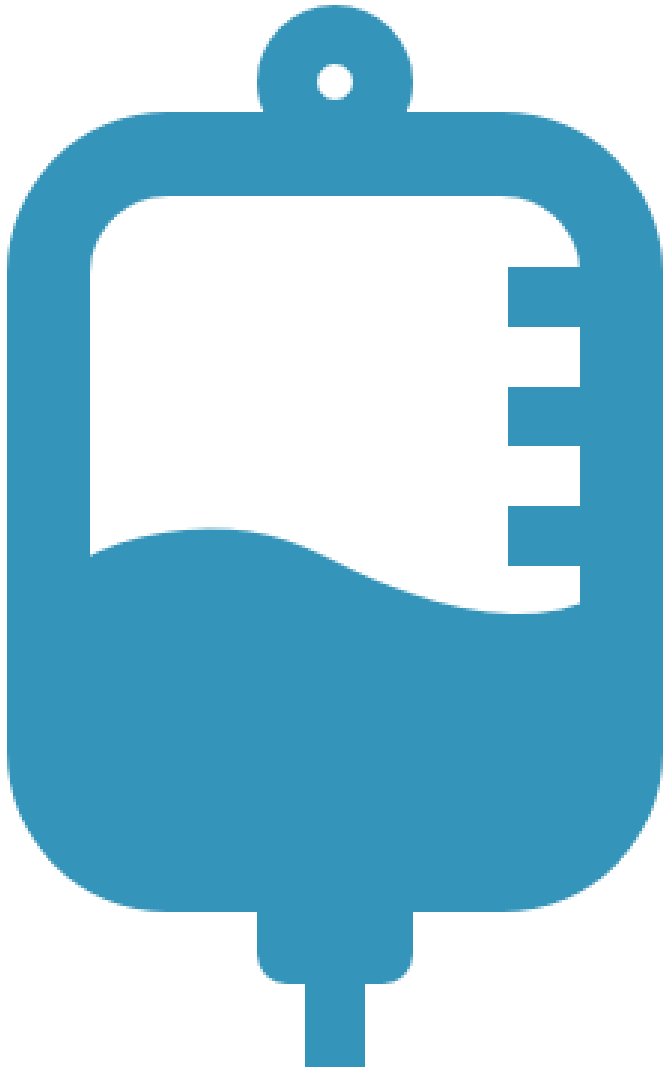
The rate of shortness of breath was *1.5% and similar in the two groups*.

6-month composite outcome that considered *all-cause mortality, myocardial infarction, and renal replacement therapy*

PREVENTION

Increasing the **UFR above 150 mL/h** was reported to reduce CIN in another study.

High UFR will rapidly remove CM from the kidney, reducing its toxicity within the nephron.



PREVENTION

For UFR-guided hydration, a bolus of normal saline hydration plus IV furosemide (0.25 mg/kg) was initially administered to achieve UFR ≥300 mL/h, followed by urine output-matched hydration using the RenalGuard system.

With the RenalGuard system, no significant electrolyte imbalance or pulmonary edema was documented.

Also, In a meta-analysis of six RCTs, the RenalGuard system was demonstrated to reduce CIN significantly in patients undergoing PCI

PREVENTION

Briguori et al. compared these two tailored hydration regimens in an RCT with708 patients scheduled for coronary or peripheral angiography or angioplasty

Total hydration volume was significantly higher in the UFR-guided group than in the LVEDP-guided group

UFR-guided hydration was superior to LVEDP-guided hydration in **preventing CIN and 1-month major adverse events**.

Acute pulmonary edema developed less often in the UFR-guided group than the LVEDP-guided group, although that difference was not significant.

Hypokalemia developed more often with UFR-guided hydration than LVEDP-guided hydration (6.2% vs. 2.3%, $p = 0.013$)

PREVENTION

Recently, non-invasive methods to guide hydration have been reported. The HYDRA study by evaluated the effect of bioimpedance vector analysis (BIVA) to determine IV infusion volumes

303 patients with low body fluid levels as assessed by BIVA and scheduled for CAG were divided into
two groups:

- The standard volume saline group (1 mL/kg/h for 12 h before and after the procedure) and the double volume saline group (2 mL/kg/h).

Significantly more patients in the double volume saline group achieved the optimal BIVA before the angiographic procedure (50.0% vs. 27.7%, $p = 0.0001$), and showed a significantly lower incidence of CIN (11.5% vs. 22.3%, $p = 0.015$) than the standard volume saline group.

The occurrence of CIN was lower (9.4%, 66 of 704) in patients with an optimal BIVA level on admission who were included in a registry group and received standard volume saline.

PREVENTION

Yan et al. used inferior vena cava ultrasonography (**IVCU**) to guide hydration in chronic heart failure patients with New York Heart Association functional classification ≥2 and left ventricular ejection fraction <50%.

207 patients receiving **CAG or PCI** were divided into two groups:

Control group (isotonic saline at a rate of 0.5 mL/kg/h for 6 h before and 12 h after the procedure) and the **IVCU-guided hydration group** (isotonic saline at a rate of 0.5, 1.0, or 1.5 mL/kg/h when their IVC diameter was >25, 20–25, or <20 mm, respectively, for the same time period).

The **hydration volume** was significantly higher in the IVCU-guided group than the control group

Incidence of CIN was significantly lower *(12.5% vs. 29.1%, p = 0.004).*

PREVENTION

As a non-invasive and cost-effective hydration method, **oral hydration** has been compared with IV hydration.

Oral hydration can **suppress the release of vasopressin** and lead to rapid diuresis.

It has been shown to be **non-inferior to IV hydration** in preventing CIN.

PREVENTION

A recently published NICIR study comparing oral hydration with IV hydration in patients with CKD stage IIIb who underwent elective CECT.

The oral hydration was 500 mL of water 2 h before and 2000 mL in the following 24 h after CECT

IV hydration used sodium bicarbonate (166 mmol/L) at 3 mL/kg/h starting 1 h before the procedure and 1 mL/kg/h during the hour after CECT.

Oral hydration was shown to be non-inferior to IV hydration regarding the incidence of CIN, but baseline eGFR was significantly higher in the oral hydration group (39.0 vs. 36.0 mL/min/1.73 m2, $p = 0.002$) due to non-stratified randomization

PREVENTION

Few studies have compared the incidence of CIN with and without hydration.

The ***AMACING trial*** investigated the prophylactic value of hydration in 660 high-risk patients undergoing an elective procedure requiring CM administration.

The incidence of CIN was 2.6% (8 of 307) in the non-hydrated patients and 2.7% (8 of 296) in the hydrated patients, which was inconclusive evidence for the effectiveness of IV hydration.

PREVENTION

A meta-analysis by Jiang et al. of six RCTs with different hydration regimens reported that patients who received prophylactic hydration had a lower risk of CIN than those who did not.

In a subgroup analysis, they found that hydration offered no benefit to patients with a baseline eGFR of 30–60 mL/min/1.73 m2, which possibly reflected patients' baseline hydration status.

PREVENTION

A more recent meta-analysis by Michel et al. analyzed 37 RCTs with 12,166 patients to assess IV volume expansion strategies and IV volume expansion was associated with a lower risk of CIN compared with no fluid administration or oral fluid intake.

Intensive IV volume expansion with an average absolute volume of 1.6 L over a 17 h peri-contrast exposure was associated with a reduced risk of CIN compared with standard volume expansion strategies.

*In the **AMACING trial**, a minimum volume of pre-warmed (37 ◦C) iopromide (300 mg iodine per mL) was used in all patients, with mean CM volumes of 92 and 89 mL in the hydration and no hydration groups, respectively. That might have contributed to the low incidence of CIN and explain the finding of no efficacy for hydration in high-risk patients. It also stresses the importance of minimizing contrast volume.*

PREVENTION

Cai et al. reviewed **hydration strategies** in 60 **RCTs** and performed a network **meta-analysis** to find an optimal strategy

They reported that the RenalGuard system was best, followed by hemodynamic guidance monitoring for hydration. The latter reflected only three RCTs using central venous pressure, LVEDP, and bioimpedance.

PREVENTION

About the type of hydration, normal saline (0.9% sodium chloride) is recommended in the guidelines as the primary choice.

Another type of fluid, apart from sodium bicarbonate, was investigated recently.

Park et al. conducted a multicenter RCT to determine the efficacy of a **balanced salt solution versus normal saline** in high-risk patients undergoing scheduled CECT.

That study failed to meet its target enrollment and reported no significant differences between the two fluid groups containing a total of 493 patients.

No optimal hydration strategy has been established as a preventive measure for CIN.

PREVENTION

Due to concerns about CIN furthering renal damage, particularly in **patients with advanced CKD who are not on maintenance dialysis**, prophylactic hemodialysis or hemofiltration has been applied to remove CM.

A **meta-analysis** that included 9 RCTs and two non-RCTs with 1010 patients (eight studies using hemodialysis and three using hemofiltration or hemodiafiltration) demonstrated **no benefit of periprocedural RRT compared to standard medical therapy** *(RR 1.02, 95% CI 0.54–1.93)*, and **hemodialysis appeared to increase the incidence of CIN** *(RR 1.61, 95% CI 1.13–2.28)*

PREVENTION

With no favorable evidence of preventive RRT, current guidelines do not recommend using prophylactic hemodialysis or hemofiltration for the purpose of CIN prevention, regardless of renal function

For patients on maintenance dialysis, extra hemodialysis or changes in hemodialysis schedule in relation to CM administration are not recommended, unless there is the **risk of volume overload**

Patients on maintenance dialysis who have residual renal function (urine > 100 mL/day) should be treated as patients with advanced CKD who are not undergoing dialysis

PREVENTION

Studies on **prophylactic hemofiltration against CIN** have been conducted.

Two **meta-analysis studies**, showed that periprocedural hemofiltration decreased the incidence of CIN in CKD patients undergoing coronary interventions compared to saline hydration

A study by Choi et al. in 2014 compared periprocedural versus simultaneous hemofiltration in CKD patients undergoing CAG and demonstrated **better late-stage (days 5–30) renal outcome in the simultaneous hemofiltration group compared to the periprocedural hemofiltration group**

PREVENTION

A **pilot study** in 2020 investigated the protective effect of **high flow-volume intermittent hemodiafiltration** against CIN compared to **saline hydration**.

This novel technique with **increased CM removal efficiency** was **applied just before and for 2.5 h after CM-using interventions** in patients with **advanced CKD** (stage 3b or 4) and ***reduced the incidence of CIN both at day 2–3 and 1 month*** compared to saline hydration.

PREVENTION

Due to the invasiveness, bleeding risk, and costs, further studies are essential to provide sufficient evidence and to find a specific population who can benefit the most.

At present, a careful risk–benefit assessment is needed in patients with advanced CKD who are not on maintenance dialysis.

It is also important that vital diagnostic and interventional procedures requiring CM administration should not be withheld or postponed solely due to the risk of CIN in those patients.

PREVENTION

Scavenging of the ROS produced during CM administration was suggested, and **IV sodium bicarbonate** and **oral NAC** have been widely tried for that purpose

In the **RENO** study, 111 ACS patients undergoing emergency PCI were randomized

The **active prophylactic treatment group** received **5 mL/kg/h of sodium bicarbonate** solution plus **2400 mg of NAC** in the **same solution during 1 h preceding CM** administration, and **the fluid without NAC** was continued at a rate of **1.5 mL/kg/h for 12 h after PCI**

The **control group** received **1 mL/kg/h of isotonic saline for 12 h after PCI**. **Two 600 mg doses of oral NAC** were administered the next day in both groups

Baseline characteristics, including **kidney and heart function, were comparable in the two groups**, but the occ*urrence of CIN was significantly*

PREVENTION

The PRESERVE trial showed different results.

It was a large RCT using a 2- by-2 factorial design and involved 5177 high-risk patients, scheduled for angiography, whose eGFR was 15–44.9 mL/min/1.73 m2 or 45–59.9 mL/min/1.73 m2 with diabetes.

They received either IV 1.26% sodium bicarbonate or IV normal saline and either 5 days of 1200 mg NAC orally or an oral placebo.

The trial demonstrated **no benefit of IV sodium bicarbonate** or **oral NAC *on the incidence of CIN and the 90-day composite outcome of death, need for dialysis, or persistent decline in kidney function***.

PREVENTION

The **PRIMARY** trial is a single center **RCT** of **382 CKD stage III–IV** patients undergoing elective CAG to evaluate the 5-year outcomes of patients with CIN and to assess the long-term effects of hydration with sodium bicarbonate

Patients who developed CIN had significantly higher 5-year mortality than those without CIN, but IV sodium bicarbonate showed no benefit over normal saline on the incidence of CIN, mortality, RRT, or major adverse kidney and cardiovascular events.

PREVENTION

Another large RCT of **2308** patients that **added 1200 mg of oral NAC to hydration (ACT trial)** also showed that ***NAC offered no benefit in reducing the risk of CIN***

No concrete evidence or consensus supports the routine use of either sodium bicarbonate or NAC

The conflicting result of the ***RENO*** study might be attributable to the *dose and route of administration of the agents or factors related to the patients and procedures.*

Contrast volume used in the RENO study was much higher (mean volume of 290 and 279 mL in each group) than that in the PRESERVE trial (median volume of 85 mL in both groups) or PRIMARY trial (mean volume of 156 and 160 mL in each group)

PREVENTION

Various pharmacologic strategies for preventing CIN have been evaluated, but the results have often conflicted with one another. Su et al. reviewed 150 RCTs that evaluated pharmaceutical agents in combination with hydration and classified the agents into 12 categories based on drug species or dose as follows:

- Natriuretic peptides: atrial natriuretic peptide, B-type natriuretic peptide, and carperitide
- Vitamins and analogues: ascorbic acid, tocopherol, and α-lipoic acid
- high-dose statins: simvastatin (40–80 mg), rosuvastatin (20–40 mg), and atorvastatin (40–80 mg)
- low-dose statins: simvastatin (10–20 mg), rosuvastatin (10 mg), and atorvastatin (10–20 mg)
- prostaglandins: iloprost, alprostadil, misoprostol, and prostaglandin E1
- theophylline (aminophylline)
- NAC
  fenoldopam
- sodium bicarbonate
- sodium bicarbonate plus NAC
- highdose statins plus NAC
- Hydration

*They assessed those 12 interventions using a Bayesian network meta-analysis and found that the use of high-dose statins plus NAC and high-dose statins on their own, both in combination with hydration, were the best and the second-best strategies for reducing CIN, respectively.

PREVENTION

A meta-analysis by Ma et al. of 107 studies with 21,450 patients also demonstrated that the use of statins plus NAC plus saline hydration was the most effective strategy for preventing CIN in patients undergoing CAG

PREVENTION

Statins have pleiotropic effects, including causing improvements in vascular tone by increasing endothelial NO production and antiinflammatory and antioxidant effects that can contribute to renoprotection in CIN

A meta-analysis by Zhou et al. of seven RCTs with 4256 patients demonstrated that short-term moderate or high-dose statin pretreatment reduced the occurrence of CIN

PREVENTION

Of note, the **subgroup analysis** in that study revealed that *statin pretreatment exhibited a preventive effect in patients with both CKD and diabetes, but it did not reduce the risk of CIN in non-diabetic patients with CKD.*

Both **atorvastatin and rosuvastatin** *showed protective effects against CIN in patients with CKD, but one study using a high dose of simvastatin showed no preventive effect on CIN*

PREVENTION

Most of the patients included in the studies using statins received CAG or cardiac catheterization, and, in those patients, statins might reduce the incidence of CIN via their beneficial effects on underlying vascular disease, including coronary artery disease.

For statins to be generally recommended as a preventive measure for CIN, further studies of patients with different underlying diseases and procedures are needed

PREVENTION

In summary, both the ESUR and KDIGO guidelines currently recommend IV volume expansion with either saline or sodium bicarbonate solutions in patients at risk of CIN, although no benefit of IV sodium bicarbonate has been demonstrated over normal saline, and IV saline hydration is preferred. Neither guideline recommends oral hydration as the sole preventive method

In addition, they make no recommendations for pharmacological prophylaxis because the preventive effect of pharmaceutical agents has not been consistently and fully validated, although the KDIGO guideline does suggest using oral NAC with IV hydration in patients at risk of CIN with a very low grade of evidence (2D)

TREATMENT

Treatment of CIN is mainly **supportive,** consisting mainly of **careful fluid and electrolyte management,** although **dialysis** may be required in some cases. *The available treatment option makes prevention the corner stone of management.*

CONCLUSION

SUMMARY OF FEW RELATED STUDIES

Impact of pretreatment with carnitine and tadalafil on contrast-induced nephropathy in CKD patients

Armaly et al.

The present study assesses whether phosphodiesterase type 5 (PDE-5) inhibitor or carnitine exert nephroprotective effects against clinical contrast-induced nephropathy

Intervention Groups: Treated with N-acetyl-L-cysteine at a dose of 600 mg twice daily, a day before, on the day of, and 1 day after the contrast administration contrast agent

The carnitine group: Infused with 20 mg/kg carnitine over 10 min 2 h prior to the radiocontrast administration and 24 h post CT.

The PDE-5 inhibitor group were given 20 mg tablets of tadalafil 2 h prior to the administration of the radiocontrast and in the subsequent day.

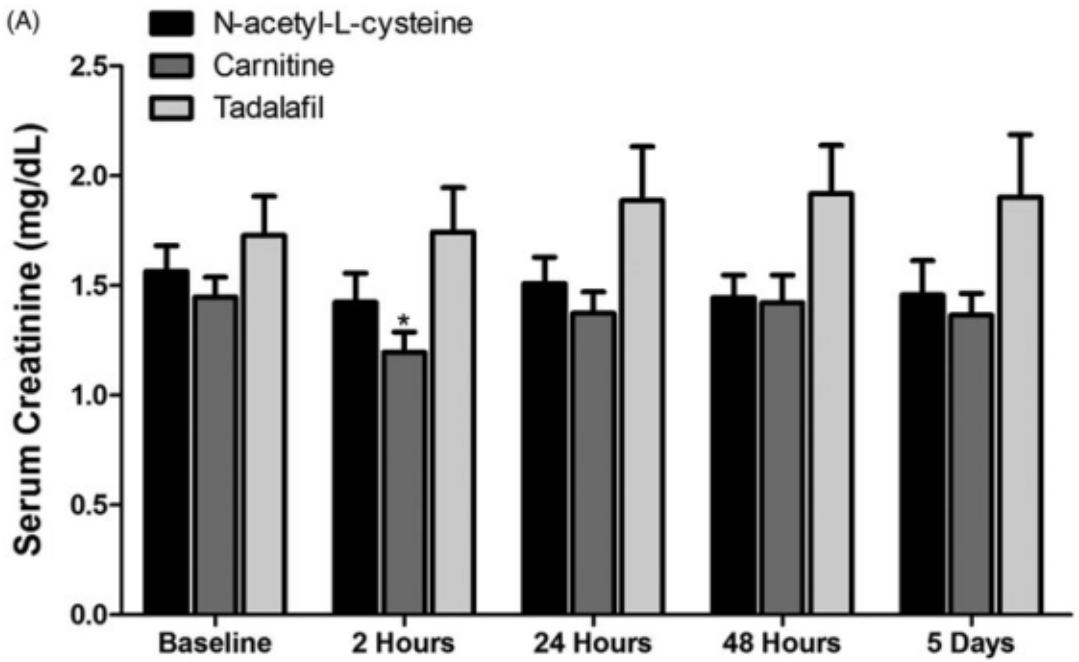
***All three arms received saline**

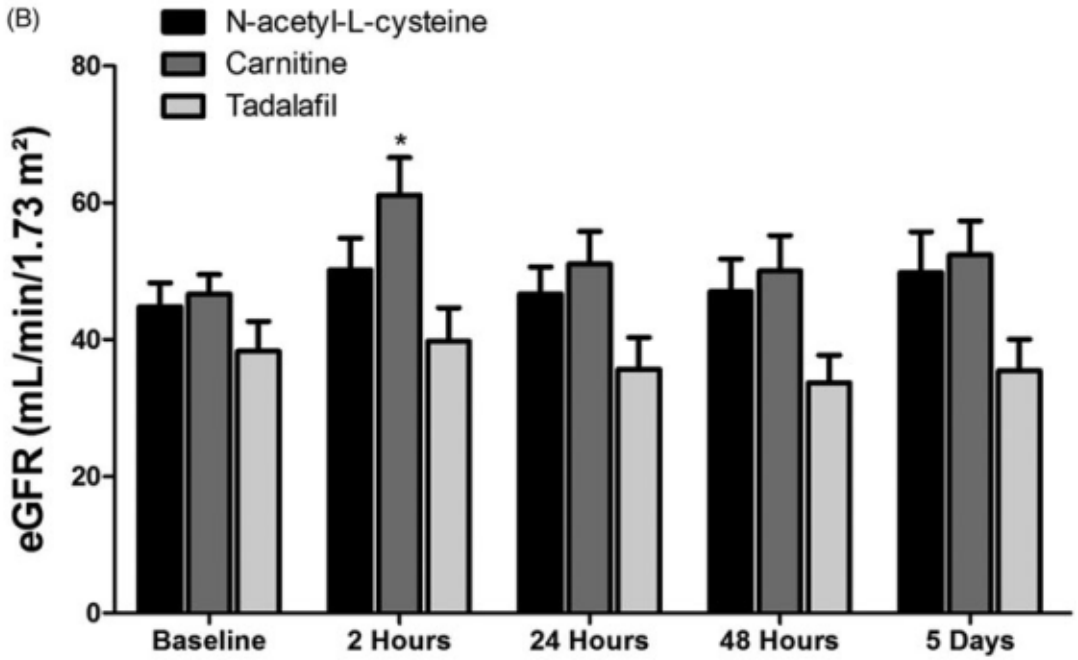
Outcome Assessment: Urine and blood samples were collected before and at the following time sequence: 2, 6, 12, 24, 48, and 120 h after the contrast administration, for creatinine and NGAL determination.

Armaly et al.

Results:

- Pretreated with N-acetyl-L-cysteine prior to administration of contrast media (CM) to CKD patients caused a significant increase in urinary but not of plasma neutrophil gelatinase-associated lipocalin (NGAL) and serum creatinine (SCr).
- In contrast, pretreatment with carnitine prevented the increase in urinary NGAL and reduced SCr below basal levels. Similarly, tadalafil administration diminished the elevation of CM-induced urinary NGAL.


(A)
N-acetyl-L-cysteine
Carnitine
Tadalafil
Serum Creatinine (mg/dL)
2.5
2.0
1.5
1.0
0.5
0.0
*
Baseline
2 Hours
24 Hours
48 Hours
5 Days


(B)
N-acetyl-L-cysteine
Carnitine
Tadalafil
eGFR (mL/min/1.73 m²)
80
60
40
20
0
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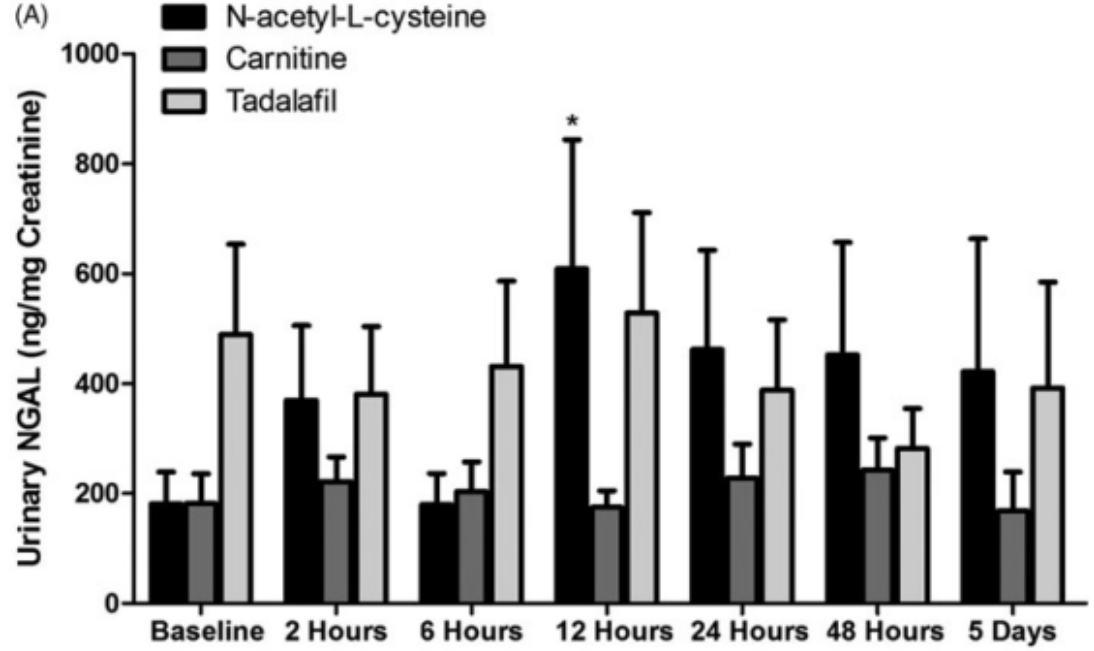
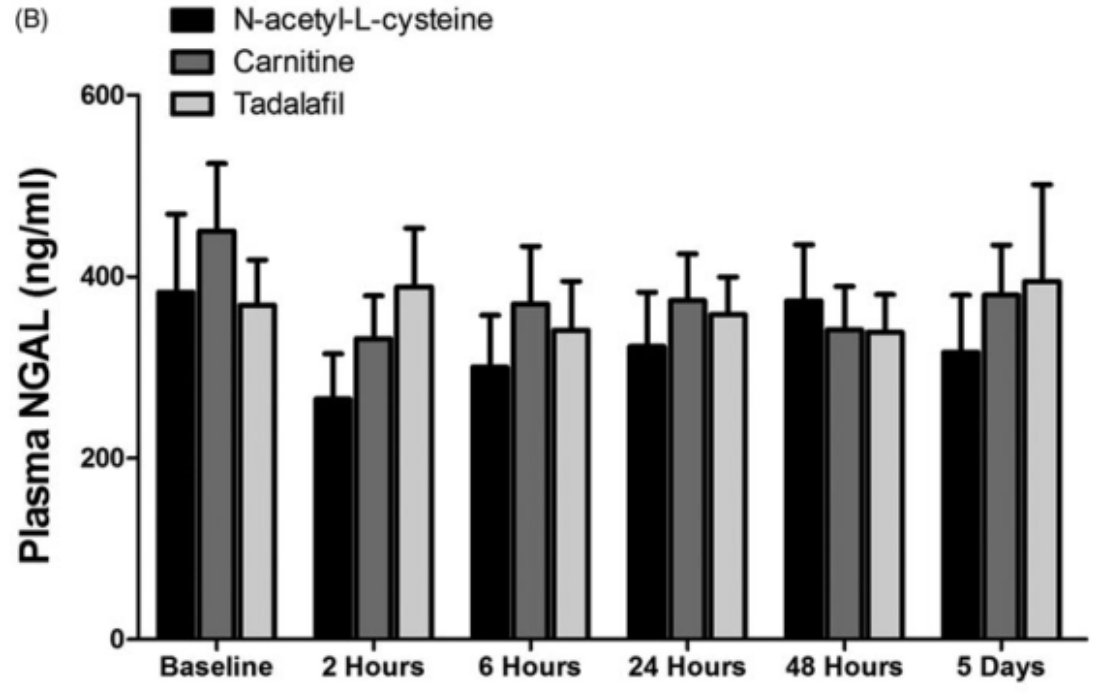
Baseline
2 Hours
24 Hours
48 Hours
5 Days


(A)
N-acetyl-L-cysteine
Carnitine
Tadalafil
Urinary NGAL (ng/mg Creatinine)
1000
800
600
400
200
0
*
Baseline
2 Hours
6 Hours
12 Hours
24 Hours
48 Hours
5 Days


(B)
N-acetyl-L-cysteine
Carnitine
Tadalafil
Plasma NGAL (ng/ml)
600
400
200
0
Baseline
2 Hours
6 Hours
24 Hours
48 Hours
5 Days

Prevention of contrast-induced nephropathy by adequate hydration combined with isosorbide dinitrate for patients with renal insufficiency and congestive heart failure
Geng qian et al.

Background: Adequate hydration remains the mainstay of contrast-induced nephropathy prevention, and nitrates could reduce cardiac preload.

Hypothesis: This study aimed to explore the adequate hydration with nitrates for patients with chronic kidney disease (CKD) and congestive heart failure (CHF) to reduce the risk of contrast-induced nephropathy (CIN) and at the same time avoid the acute heart failure.

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The **control group** (N=198) received a continuous intravenous infusion of isotonic saline at a rate of 0.5 mL/kg/h 6 hours before and 12 hours after the operation. The **experiment group** (N=196) received continuous intravenous infusion of isosorbide dinitrate at a rate of 2 mg/h combined with intravenous infusion of isotonic saline at a rate of 1 mL/kg/h 6 hours before and 12 hours after the operation.

The definition of CIN was a 25% or 0.5 mg/dL rise in serum creatinine over baseline.

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Results

Baseline characteristics were well-matched between the two groups. CIN occurred less frequently in adequate hydration group than the control group (12.8% vs 21.2%; $P = 0.018$).

The **incidence of acute heart failure** did not differ between the two groups (8 [4.08%] vs 6[3.03%]; $P = 0.599$).

Cumulative major adverse events (death, myocardial infarction, stoke, hospitalization for acute heart failure) during the 90-day follow-up were lower in the adequate hydration with nitrates group ($P = 0.002$).

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The **main finding** of this study is that in patients with CKD and CHF undergoing coronary angiography, a prophylactic nitrates with matched adequate hydration is an effective and safe strategy for the prevention of CIN in this patients.

TABLE 2 Incidence of CIAKI and AHF

Definition of CIAKI	Adequate hydration group (*n* = 196)	Control group (*n* = 198)	*P* value
SCr >50% ↑ *n* (%)	9(4.6%)	15(4.4%)	0.152
SCr >25% ↑ *n* (%)	21(10.7%)	37(18.7%)	0.018
SCr >0.5 mg/dL ↑ *n* (%)	20(10.2%)	35(17.8%)	0.023
SCr >0.3 mg/dL ↑ *n* (%)	31 (15.8%)	54(27.3%)	0.004
Incidence of CIAKI *n* (%)	25(12.8%)	42(21.2%)	0.018
Incidence of AHF *n* (%)	8(4.08%)	6(3.03%)	0.599

Abbreviations: AHF, acute heart failure; CIAKI, contrast-induced acute kidney injury; SCr, serum creatinine.

[a] Fisher's Exact.

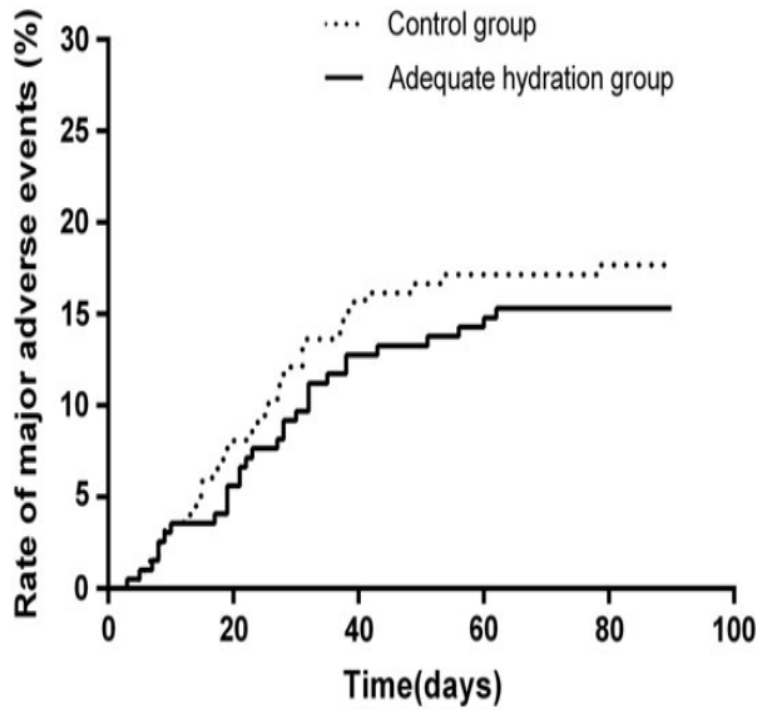


FIGURE 3 Cumulative major adverse events at 90 days for the adequate hydration groups and control group

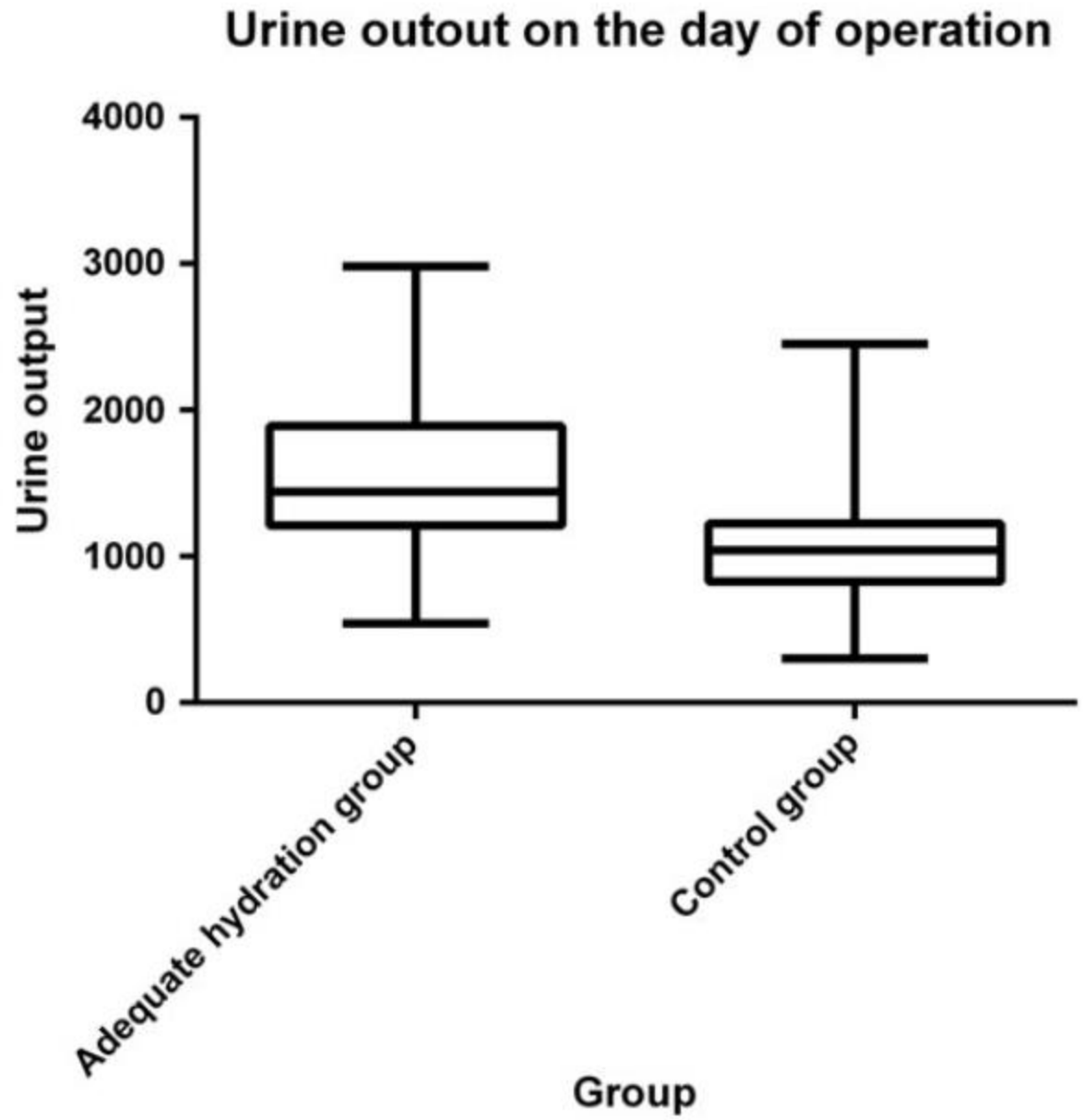
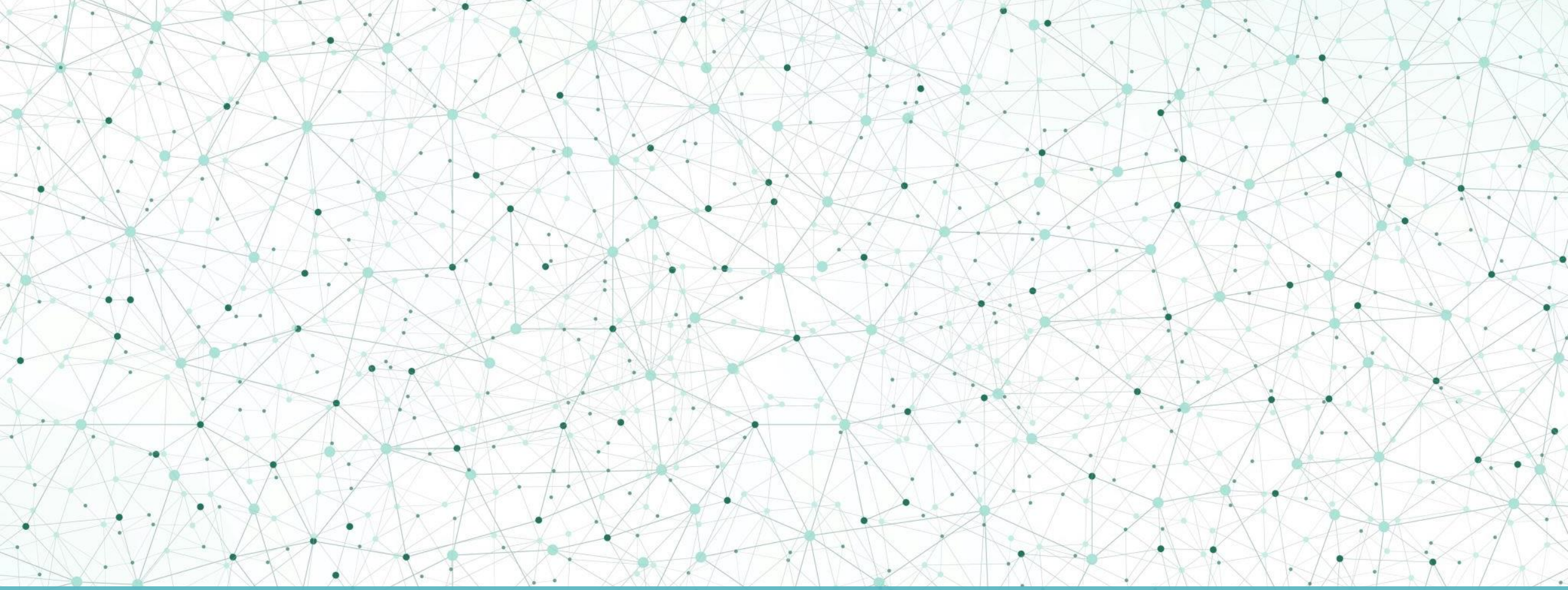


FIGURE 2 Urine output in study patients during the operation day



THANKS FOR YOUR ATTENTION