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Prevention of post procedural acute kidney injury in the catheterization laboratory in a real-world population

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ABSTRACT

Background: Radiologists and cardiologists have a remarkably different approach to the clinical importance and to the need for prophylactic treatment of contrast-induced acute kidney injury (CI-AKI).
Objectives: To evaluate the efficacy of forced diuresis with matched controlled hydration (FMH) in a real-world, high risk population.
Methods: This is an investigator-driven, single-center, retrospective analysis of prospectively collected data. A total of 150 consecutive patients undergoing coronary angiography, angioplasty or TAVR who were treated with FMH were compared to a matched historical control cohort.
Results: In the FMH treated patients, eGFR improved following the procedure from 37 ml/min per 1.73 m^2 at baseline to 39 ml/min per 1.73 m^2 ($p < 0.001$); the net creatinine decreased from 1.85 mg/dl to 1.78 mg/dl ($p < 0.001$). Among the matched control group, eGFR deteriorated from a baseline value of 36.7 ml/min per 1.73 m^2 to 33.2 ml/min per 1.73 m^2 post procedurally ($p < 0.001$); the net creatinine increased from 1.88 mg/dl to 2.14 mg/dl ($p < 0.001$). The incidence of post procedural AKI was substantially lower in the FMH treated group (2.7%) compared to the control group (26.7%). By multivariable analysis FMH treatment was independently correlated with reduced incidence of post procedural AKI compared with the control group (OR 0.06, $p < 0.001$). Contrast volume did not correlate with AKI in neither univariate nor multivariate analyses.
Conclusions: In patients undergoing coronary angiography, angioplasty or TAVR, who are considered high risk to develop post procedural AKI, forced diuresis with matched controlled hydration resulted in a significant net creatinine decrease, eGFR increase and a decrease in the incidence of AKI.
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1. Introduction

The perception of the clinical importance of contrast-induced acute kidney injury (CI-AKI) is diverse between different disciplines (cardiology, radiology, nephrology and general medicine) [1–6]. The position of the American College of Radiology (ACR) committee on drugs and contrast media is that CI-AKI is a rare entity [7]. Four large studies released in 2013 and 2014 (each with >10,000 patients) of patients undergoing CT scans demonstrated that in patients with a stable baseline estimated glomerular filtration rate (eGFR) ≥45 ml/min/1.73 m^2, intravenous (IV) iodinated contrast media is not an independent risk factor for the development of AKI [6,8–10], and in patients with a stable baseline eGFR 30–44 ml/min/1.73 m^2, IV iodinated contrast media is either not an independent risk factor or rarely so [6,8–10]. In contrast to the radiologists, many interventional cardiologists continue to consider all intravascular iodinated contrast material, regardless of whether it is administered intra-arterial or IV, to be harmful, especially in patients with moderate or severe renal dysfunction. In the cardiology literature, CI-AKI has been reported to be the third most common cause of hospital acquired renal failure [11] with 4–5 fold increase in short and long term morality [12]. It has been associated with increased contrast media volume delivered, and with reduced renal function [13], ranging from 2% in patients with normal baseline renal function to as high as 20–30% in patients with a baseline serum creatinine >2.0 mg/dl [14].

As no treatment specifically targets post procedural AKI once it develops the main goal for clinicians remains prevention. The most effective prophylactic strategy is volume expansion with isotonic IV fluid

Abbreviations: AKI, Acute kidney injury; CI-AKI, Contrast-induced acute kidney injury; CKD, Chronic kidney disease; CHF, Congestive heart failure; Cr, Creatinine; DM, Diabetes mellitus; eGFR, Estimated glomerular filtration rate; FMH, Furosemide-induced diuresis with matched intravenous hydration; IHD, Ischemic heart disease; PCI, Percutaneous coronary intervention; TAVR, Transcatheter aortic valve replacement; UFR, Urine flow rate.

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[13]; however, the fear of over hydration limits the use of this strategy, especially in patients with chronic kidney disease (CKD), severe aortic stenosis (AS) and congestive heart failure (CHF). Given the ever increasing proportion of patients with more advanced CKD undergoing PCI, there is an urgent need for safer approaches for these high-risk patients [15].

The RenalGuard system (PLC Medical Systems, Inc., Franklin, MA) was designed to reduce the incidence of CI-AKI by induction of forced high urinary flow rate and matching it with controlled intravenous delivery of isotonic fluids. This therapy is based on the theory that maintaining high urine output through the kidneys allows the body to rapidly eliminate contrast, reducing its toxic effects. Scarce previous studies aiming to evaluate the efficacy of this system in patients exposed to contrast media at the catheterization laboratories showed promising results [16,17].

In the present study we evaluated the efficacy of forced diuresis with controlled matched hydration using the RenalGuard system to prevent AKI in a real-world patient population undergoing coronary angiography, angioplasty or transcatheter aortic valve replacement (TAVR), who were considered high risk to develop post procedural AKI. We also evaluated the correlation between AKI rates and contrast media volume delivered.

2. Methods

2.1. Study design and patient selection

This is a single-center, observational study assessing the effectiveness of controlled intravenous delivery of isotonic fluids which matches urinary output in patients at high risk to develop post procedural AKI.

This is a retrospective analysis of a prospectively collected data from the Tel Aviv Prospective Angiographic Survey (TAPAS). TAPAS is a prospective, single-center registry that enrolls all patients undergoing cardiac catheterization and TAVR at the Tel Aviv Medical Center [18]. The current study cohort consists of consecutive patients referred for coronary angiography, angioplasty or TAVR in our institution who were considered at high risk to develop post procedural AKI and therefore were treated with the RenalGuard system. The decision to use the RenalGuard system was made by the treating interventional cardiologist according to laboratory data and his clinical judgment. Excluded from the analysis were patients lacking either pre- or post-procedural serum creatinine levels, patients who underwent multiple PCIs during a single hospitalization, and patients on dialysis. All participants provided written informed consent for participation in the TAPAS registry, which is approved by the institutional ethics committee in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.2. Treatment protocol

All patients were treated with the RenalGuard system (PLC Medical Systems, Inc., Franklin, MA) as previously reported [16,17]. Briefly, following placement of a Foley catheter and an antecubital vein line, the system administered an initial IV bolus of 250 ml of normal saline (NS) over 30 min (pre procedural phase). After the priming, furosemide (0.25–0.5 mg/kg) was administered intravenously to achieve the recommended urine flow rate (UFR) ≥300 ml/h. As soon as the UFR reached the target value, the patient was transferred into the catheterization laboratory and the procedure was started (procedural phase). Controlled hydration by the RenalGuard system continued during the procedure and for 4 h after the procedure (post procedural phase). Urine flow rate was monitored and maintained at the target value throughout the procedure and during the following 6 h. Additional furosemide doses (in increments of 0.25 mg/kg every 30 min) were allowed in cases in which the target UFR was not achieved either in the pre or in the post-procedural phases. At the end of the therapy, intravenous saline infusion (0.5–1 ml/kg/h according to the hemodynamic conditions) was continued in order to complete 12 h of infusion after contrast administration, unless contraindicated by the clinical status. Iodixanol contrast media (Visipaque, GE [290 mOsm/kg mOsm per kilogram of water]) was used in all procedures. Iodixanol is a nonionic, iso-osmolar contrast media that is associated with less nephrotoxicity compared to high-osmolar contrast media commonly in use [6].

2.3. Matched historical control group

For the historical control cohort patients were selected from the TAPAS registry. Each patient in the study cohort was matched for age, gender, type of procedure (angiography, angioplasty or TAVR), diabetes status and renal function indices to a suitable patient from the TAPAS registry who was not treated with the RenalGuard therapy. Excluded from the control cohort were patients without known serum creatinine during both baseline and at 24–72 h post contrast administration. All the participants in the control cohort provided written informed consent for participation in the TAPAS registry. Patients in the control group were treated with intravenous volume expansion by isotonic saline prior the procedure according to their hemodynamic condition. At the end of the therapy, intravenous saline infusion was continued in order to complete 12 h of infusion after contrast administration, unless contraindicated by the patient's clinical status.

2.4. Biomarkers of kidney function and study outcome

Estimated GFR values were calculated according to age, gender and serum creatinine values using the CKD-EPI equation [19]. The post-procedural creatinine value was defined as the highest value within 72 h after the index procedure.

AKI was defined as an increase in serum creatinine by 25% or 0.5 mg/dl measured 24–72 h after the procedure [20].

2.5. Statistical analysis

Differences between participants and controls and between pre-procedural and post-procedural values were compared using a pair-wise Student *t*-test. Differences in contrast media amounts between different groups were calculated either using a student *t*-test (for comparison of two groups) or a one-way ANOVA (for comparison of more than two groups). Comparisons of incidences of AKI were done using a Fisher exact test. To reduce the effect of covariates, a binary logistic regression model was built using RenalGuard treatment, the procedure performed, gender, concurrent diabetes, age, contrast media volume and baseline creatinine as variables with AKI as the dependent factor. To determine the power of the logistic regression to detect significance of contrast media amount between groups a-priori power estimation for logistic regression was used. All calculations were done using SPSS v15.0 by IBM and MedCalc V14.8 by MedCalc software, and power analysis was performed using "A-priori Sample Size Calculator for Multiple Regression" Software by Soper, D.S.

3. Results

3.1. Study population

A total of 272 patients who were treated with the RenalGuard system were identified during the period of January 2013 to February 2016. 122 patients (45%) were excluded according to the exclusion criteria. The study group consisted of 150 patients who underwent coronary angiography (16%), angioplasty (51.3%) or TAVR (32.7%) all of whom were treated with peri-procedural FMH using the RenalGuard system. Baseline clinical profile and prevalence of comorbidities are listed in Table 1. Baseline mean creatinine was 1.85 ± 0.73 mg/dl and

Table 1
Renal guard treated patient characteristics ($n = 150$).

Characteristics	Frequency
Age (years ± SD)	76.91 ± 10.26
Male gender (%)	68.7
Baseline serum creatinine (mg/dl ± SD)	1.85 ± 0.73
Baseline eGFR (ml/min ± SD)	37.12 ± 15.95
BMI (kg/m^2 ± SD)	27.26 ± 4.52
Current smoking (%)	14.0
HTN (%)	90.7
AF (%)	23.1
PVD (%)	19.0
DM type 2 (%)	56.1
Dyslipidemia (%)	67.1
IHD (%)	74.0
HF (%)	41.3
Severe AS (%)	41.5
Procedure related data	
Procedure angiography (%)	16.0
Procedure PCI (%)	51.3
Procedure TAVR (%)	32.7
RenalGuard treatment characteristics	
Total treatment time, hh:mm (mean ± SD)	06:07 ± 02:28
Total furosemide dose, mg (mean ± SD)	47 ± 35
Urine rate at first contrast, ml/h (mean ± SD)	390 ± 224
Total urine out-put, ml (mean ± SD)	2366 ± 1407
Total IV normal saline in-put, ml (mean ± SD)	2609 ± 1426
Total fluid balance, ml (mean ± SD)	242 ± 204

Abbreviations: HTN — hypertension, AF — atrial fibrillation, PVD — peripheral vascular disease, DM — diabetes mellitus, IHD — ischemic heart disease, HF — heart failure, AS — aortic stenosis, PCI — percutaneous coronary intervention, TAVR — transcatheter aortic valve replacement.

the baseline mean eGFR was 37 ± 15 ml/min per 1.73 m^2. The study cohort was characterized by male predominance (68.7%), elderly patients (mean age 76.9 ± 10.2 years) with high prevalence of hypertension, DM, dyslipidemia, history of smoking and IHD. The 150 matched control patients and the matched parameters are presented in Table 2. Baseline creatinine and contrast media volume were borderline higher in the control group ($0.10 > p > 0.05$), yet with a difference which is non-significant clinically (0.03 mg/dl for creatinine, 7.88 ml for contrast media amount).

In the subgroup of patients who underwent coronary angioplasty, patients treated with the RenalGuard system were exposed to a higher volume of iodinated contrast medium compared with the control group (Table 3).

3.2. Serum creatinine and eGFR kinetic

Serum creatinine and eGFR kinetics in the two groups are presented in Table 4 and Fig. 1. In the FMH treated patients, eGFR improved following the procedure from 37.12 ± 15 ml/min per 1.73 m^2 at baseline to 39.38 ± 17 ml/min per 1.73 m^2 ($p < 0.001$). Among the matched control group, eGFR deteriorated from a baseline value of 36.77 ± 16 ml/min per 1.73 m^2 to 33.26 ± 16 ml/min per 1.73 m^2 post procedurally ($p < 0.001$). Control patients had a net creatinine increase from 1.88 mg/dl to 2.14 mg/dl ($p < 0.001$) and eGFR decrease while FMH treated patients had a net creatinine decrease from 1.85 mg/dl to 1.78 mg/dl ($p < 0.001$) and eGFR increase; these differences were statistically significant. The change in eGFR was most prominent in the TAVR subgroup (Fig. 2).

3.3. Post procedural acute kidney injury

The incidence of CI-AKI was significantly and substantially lower in the RenalGuard treated group (2.7%) in comparison to the control group (26.7%) with a NNT of 4.17 (Table 5 and Fig. 3). In subgroup analysis according to procedure type this finding remained significant for both TAVR and angioplasty procedures. Furthermore, in the multivariable binary logistic model, RenalGuard treatment was independently correlated with reduced incidence of CI-AKI compared with the matched control group of patients (odds ratio 0.06, 95% confidence interval 0.02–0.21, $p < 0.001$), as was procedure type (TAVR vs. Angiography) and baseline creatinine (Table 6). Contrast volume was not significantly correlated with CI-AKI in neither a univariate nor a multivariate analysis, although our study was only moderately powered to detect significant differences in CI-AKI incidence with regard to contrast media used in a univariate analysis (1-β = 70%) and weakly powered in a multivariate analysis (1-β = 38%).

4. Discussion

In this study, we evaluated the efficacy of forced diuresis with matched IV delivery of normal saline using the RenalGuard system in a real-world population of patients undergoing coronary angiography, angioplasty or TAVR who were at high risk to develop post procedural AKI. The main findings of the present analysis are: 1. RenalGuard treated patients had a net decrease of creatinine level and an increase of eGFR following the interventional cath-lab procedure while the matched control group of patients had a net creatinine level increase and eGFR decrease. 2. The incidence of post procedural AKI was significantly lower among RenalGuard treated patients. 3. RenalGuard treatment and baseline creatinine were significantly correlated with the incidence of post procedural AKI. 4. The volume of contrast delivered did not correlate with post procedural AKI.

4.1. Which is the proper terminology: contrast-induced AKI or post procedural AKI?

For many years the causative association between contrast media and post procedural deterioration in renal function was taken for granted, naming this entity CI-AKI. In the present study, we found that contrast volume did not correlate with the incidence of AKI following interventional cardiology procedures. Accordingly, several recent radiological studies raised doubts regarding the role of contrast media in the pathophysiology of AKI, and presented evidence that contrast media has only minimal impact on the development of AKI following IV contrast media administration [3,4]. Currently, it is the position of the American College of Radiology Committee on Drugs and Contrast Media that CI-AKI is a rare entity therefore prophylactic strategy is not necessary [7]. Nevertheless, AKI following exposure to contrast material is a common entity in hospitalized patients [21,22], and it is often difficult to isolate the effect of contrast material per se from other potential coexisting factors [3–4,21,23–24].

4.2. Prophylactic strategy to mitigate post procedural AKI

Numerous approaches to prevent post-procedural AKI have been studied, including various contrast agents which are less nephrotoxic, renal protective drugs, and hydration regimens [25]. Almost all have failed to show effectiveness in large RCTs with the exception of simply limiting contrast dose and ensuring adequate pre-procedural hydration [26]. The RenalGuard system causes renal flushing by carefully matching IV infusion of isotonic saline solution to furosemide-forced diuresis. The current study demonstrated a lower incidence of post procedural AKI as assessed by decreases in serum creatinine.

While interpreting these results, it should be kept in mind that there is an ongoing controversy regarding the possible difference in nephrotoxicity between IV and intra-arterial (specifically, intracoronary and suprarenal) iodinated contrast material administration [27,28]. This difference has been posited to help explain the disparity in AKI rates between patients undergoing CT scans and patients undergoing coronary angiography. In interventional cardiology procedures, the contrast medium may have greater impact on the incidence of AKI, as contrast media is administered intra-arterially, the injection requires a catheter that can dislodge atheroemboli, potentially leading to kidney embolism and the amount of contrast media is often larger than in CT

Table 2
Baseline characteristics of study groups.

Characteristics	Study ($n = 150$)	Control ($n = 150$)	Study-control difference	*p*-Value
Male gender (%)	68.7	68.7	Matched	–
DM type 2 (%)	56.1	56.1	Matched	–
Procedure angiography (%)	16.0	16.0	Matched	–
Procedure PCI (%)	51.3	51.3	Matched	–
Procedure TAVR (%)	32.7	32.7	Matched	–
Age (years ± SD)	76.91 ± 10.96	77.49 ± 10.5	−0.57	0.488
Baseline creatinine (mg/dl ± SD)	1.85 ± 0.73	1.88 ± 0.81	−0.03	0.099
Estimated baseline GFR (ml/min ± SD)	37.12 ± 15.95	36.77 ± 16.07	0.34	0.146
Contrast volume (ml ± SD)	95.84 ± 43.52	90.42 ± 39.53	7.88	0.087

Abbreviations: DM — diabetes mellitus, PCI — percutaneous coronary intervention, TAVR — transcatheter aortic valve replacement.

Table 3
Contrast media volume injected according to procedure.

Procedure	Contrast media volume (ml ± SD) All patients	Contrast media volume (ml ± SD) Treated patients	Contrast media volume (ml ± SD) Control patients	*p*-Value(between treated and control)
Angiography only	65.47 ± 30.00	66.20 ± 35.62	64.55 ± 21.88	0.857
PCI	85.64 ± 35.86	91.04 ± 38.42	78.46 ± 31.15	0.039*
TAVR	117.20 ± 42.27	118.41 ± 44.00	115.94 ± 40.82	0.776
p-value	<0.001	<0.001	<0.001	–

Abbreviations: PCI — percutaneous coronary intervention, TAVR — transcatheter aortic valve replacement.
* $p < 0.05$.

Table 4
Post procedure results — pair wise comparison.

Characteristics	Study	Control	Study-control difference	*p*-Value
Post procedure creatinine (mg/dl ± SD)	1.78 ± 0.77	2.14 ± 1.12	−0.35	<0.001*
Post procedure eGFR (ml/min ± SD)	39.38 ± 17.10	33.26 ± 16.33	6.12	<0.001*
Serum creatinine change (ml/min ± SD)	−0.06 ± 0.30	0.25 ± 0.54	−0.32	<0.001*
eGFR change (ml/min ± SD)	−2.27 ± 7.03	3.51 ± 9.7	5.77	<0.001*
eGFR change from baseline GFR (% ± SD)	−0.72 ± 0.20	8.82 ± 24.87	8.90	<0.001*

* $p < 0.05$.

scans. Moreover, the patient population undergoing coronary angiography may be different and at higher risk of developing AKI than patients undergoing CT imaging.

4.3. Previous reports

The efficacy and safety of forced diuresis with matched isotonic intravenous hydration (FMH) using the RenalGuard system were first established in two randomized controlled trials. The REMEDIAL II trial [16] that included patients at very high risk to develop CI-AKI (eGFR < 30 ml/min/1.73 m^2 and/or a Mehran risk score ≥ 11) demonstrated that FMH therapy was superior to sodium bicarbonate and *N*-acetylcysteine administration in preventing CI-AKI. It showed reduction in AKI rates from 20.5% in the control group to 11% in the RenalGuard group. The MYTHOS trial [17] that included both elective and acute patients with eGFR < 60 ml/min/1.73 m^2, similarly demonstrated a significant reduction of CI-AKI rates from 18% in the control group to 4.6% in the FMH treatment group. The efficacy of FMH treatment was even more pronounced in patients undergoing urgent angiography with CI-AKI rate reductions from 30% to 5%. A recent observational registry from the REMEDIAL II investigators group [29], has further investigated the efficacy of RenalGuard treatment and confirmed the importance of achieving high urinary flow rate. This study has demonstrated that urinary flow rate was significantly lower in the 8.5% of patients developing CI-AKI under RenalGuard treatment and suggested a higher intraprocedural urinary flow rate ≥450 ml/h as an optimal target for CI-AKI prevention.

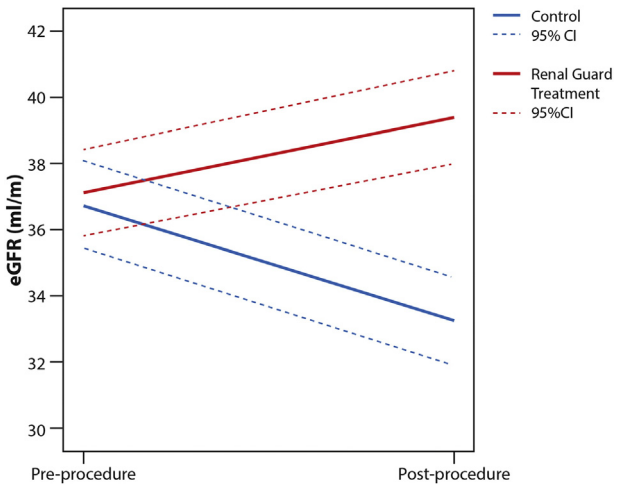

Fig. 1. eGFR change in pre and post procedure according to study group.

4.4. Pathophysiology of contrast induced AKI

The pathophysiology of contrast induced AKI is only partially understood and currently explained by two main mechanisms: a direct cytotoxic effect of contrast media causing tubular injury, and renal medullary hypoxia secondary to hypoperfusion due to vasoconstriction and increased blood viscosity [12]. Hydration is the cornerstone of CI-AKI prevention as it directly counteracts these pathophysiological processes. It produces expansion of plasma volume with concomitant suppression of the renin-angiotensin-aldosterone axis, down-regulation of tubule-glomerular feedback, and dilution of contrast media, thus, preventing renal vasoconstriction and tubular obstruction [17,30]. Unfortunately, hydration is limited in certain high risk populations due to the risk of pulmonary congestion, especially in patients with chronic kidney disease, congestive heart failure, and severe aortic stenosis which represent a significant portion of patients requiring intervention in the cardiac catheterization laboratory. Induction of

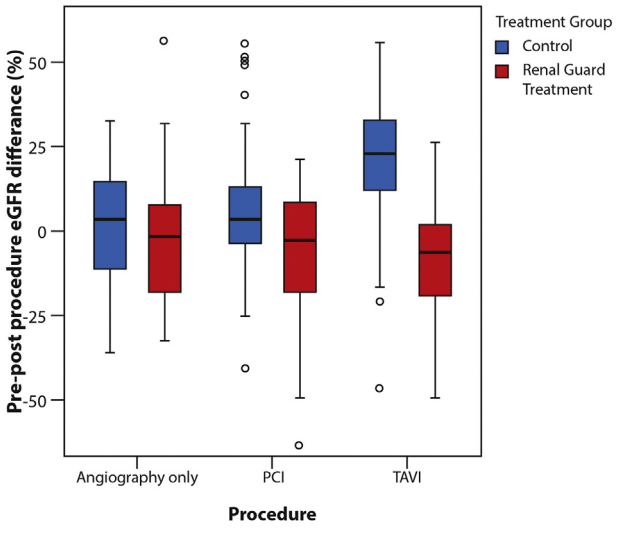

Fig. 2. Change in eGFR in treated versus control patients according to the performed procedure.

Table 5
AKI incidence depending on treatment group and procedure type.

Procedure	Incidence among treated patients (% [n])	Incidence among control patients (% [n])	RR [95% CI]	NNT	*p*-Value
All procedures	2.7% [4]	26.7% [40]	0.10 [0.04–0.27]	4.17	<0.001*
TAVR	2.0% [1]	49% [24]	0.04 [0.01–0.30]	2.13	<0.001*
PCI	1.3% [1]	14.5% [11]	0.09[0.01–0.69]	7.60	0.005*
Angiography only	8.0% [2]	20.0% [5]	0.40[0.09–1.87]	8.33	0.417

Abbreviations: AKI — acute kidney injury, PCI — percutaneous coronary intervention, TAVR — transcatheter aortic valve replacement.
* $p < 0.05$.

high urine flow rate is another preventive tool to reduce the incidence of CI-AKI, as was shown in the PRINCE study, where increased urine flow rate (>150 ml/h) reduced the toxic effect of contrast media [31]. The renal protective aspects of high urine rate are accomplished via several effects including a more rapid transit of contrast media through the kidneys, diluted concentration of the contrast media in the kidneys, and maintenance of flow in the renal tubules which reduces slugging and precipitation of contrast media in tubular cells [16]. However, previous clinical studies utilizing forced diuresis as a tool to reduce CI-AKI failed, and moreover, the net effect was an increased CI-AKI rate [31]. The major reasons for this failure were lack of adequate matching between hydration and urine flow [17] and the high diuretic dose used. These two factors caused a net negative fluid balance with a reduction in the effective circulating volume causing concomitant activation of the renin-angiotensin-aldosterone axis and vasoconstriction, with consequent reduction in renal blood flow and GFR [16,17]. This fluid imbalance can be prevented by the use of the RenalGuard system, with its matched fluid replacement capability, enabling the physician to safely achieve high urine output with a relatively low furosemide dose, continuously maintaining adequate intravascular effective volume, thus preventing hypovolemia and, at the same time, fluid overload [16].

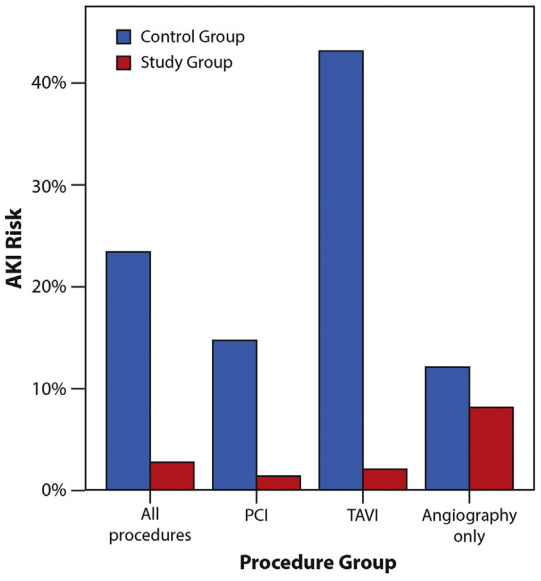

Fig. 3. AKI incidence depending on treatment group and procedure type.

Table 6
Univariate and multivariate analysis of AKI incidence.

Characteristic	OR [95%CI]	*p*-Value
Univariate analysis		
RenalGuard treatment	0.08 [0.03–0.22]	<0.001*
Procedure PCI (compared to angiography)	0.53 [0.20–1.42]	0.205
Procedure TAVI (compared to angiography)	2.10 [0.84–5.27]	0.113
Female gender	1.16 [0.59–2.28]	0.671
Diabetes	0.70 [0.37–1.33]	0.274
Age (for 10 year increment)	1.20 [0.87–1.67]	0.263
Contrast volume (for 10 ml increment)	1.02 [0.95–1.11]	0.567
Baseline creatinine (for 0.1 mg/dl increment)	1.03 [0.99–1.06]	0.167
Baseline estimated GFR (for 10 ml increment)	1.006[0.82–1.23]	0.955
Multivariate analysis		
RenalGuard treatment	0.05 [0.02–0.17]	<0.001*
Procedure PCI (compared to angiography)	0.58 [0.16–2.1]	0.403
Procedure TAVI (compared to angiography)	5.15 [1.29–20.5]	0.02*
Female gender	0.94 [0.40–2.21]	0.569
Diabetes	0.75 [0.33–1.73]	0.499
Age (for 10 year increment)	0.84 [0.52–1.36]	0.476
Contrast volume (for 10 ml increment)	0.97 [0.87–1.08]	0.588
Baseline creatinine (for 0.1 mg/dl increment)	1.07 [1.02–1.12]	0.001*

Abbreviations: AKI — acute kidney injury, PCI — percutaneous coronary intervention, TAVR — transcatheter aortic valve replacement.
* $p < 0.05$.

4.5. Limitations

Our study has several limitations. Although our data was collected from a prospective registry, the analysis was performed retrospectively on a non-pre-specified group; therefore, our results may be subjected to possible confounders and bias by the nature of this design. For technical reasons some of our patients didn't have adequate laboratory follow up and therefore were excluded from our analysis. Our study was not randomized and for the comparative analysis we used a matched historical control group from our own facility registry. Although we matched these historical controls by many important variables this type of control group may introduce bias to our analysis. Finally, we do not have data regarding long term sequelae and complications.

5. Conclusions and therapeutic implications

The results of the current study support the use of forced diuresis with matched intravenous hydration with normal saline in patients undergoing coronary angiography, angioplasty or TAVR, who are considered at high risk to develop post procedural AKI. RenalGuard therapy seems to be safe and effective for the prevention of post procedural AKI, however it should be evaluated in larger multicenter randomized trials enrolling patients at moderate to high risk of post-procedural AKI.

Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

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None.

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