CardioRenal Systems™

RenalGuard® System

Annotated Bibliography of Clinical Publications

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Overview

The RenalGuard® System (CardioRenal Systems / RenalGuard Solutions) is a closed-loop fluid management device that prevents acute kidney injury (AKI) by matching intravenous infusion to measured urine output in real time, enabling high-volume forced diuresis at euvolemia. The device is CE-marked and commercially available in EMEA. In the United States, the device has been granted FDA Breakthrough Device Designation; an Investigational Device Exemption (IDE) submission has been filed in preparation for the planned US pivotal trial, which is intended to support a Premarket Approval (PMA) application. RenalGuard has been studied across multiple randomized controlled trials, a large prospective registry, mechanistic imaging studies, and a 2023 Bayesian meta-analysis, covering four clinical indications: contrast-associated AKI in interventional cardiology, AKI in transcatheter aortic valve replacement, cardiac-surgery-associated AKI in on-pump cardiac surgery, and AKI care in the ICU.

This document is an annotated bibliography of the RenalGuard-relevant publications curated by CardioRenal Systems. It is organized by clinical indication. Within each indication, primary RenalGuard clinical evidence is presented first, followed by mechanistic evidence, meta-analyses, accompanying editorial commentary, and recent reviews. Each primary-evidence entry includes the full citation, study design, population, intervention and comparator, primary endpoint, key results (with effect sizes where reported), and a one-sentence statement of clinical significance.

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1. Cardiac Surgery: Cardiac Surgery–Associated Acute Kidney Injury (CSA-AKI)

CSA-AKI affects approximately 25–30% of on-pump cardiac surgery patients and is associated with substantial in-hospital mortality, prolonged ICU stay, and persistent loss of renal function. The RenalGuard cardiac surgery program is anchored by the KIDNEY randomized trial (Wolverhampton, UK), preceded by a 10-patient first-in-human feasibility pilot and followed by two pre-specified secondary outcome papers (NGAL biomarker, electrolyte safety). A 2025 narrative review by Solomon develops the urine-output-as-therapeutic-target framework that motivates the RenalGuard design in this indication.

Primary clinical evidence

1. First-in-Human Pilot (Luckraz 2017) · RenalGuard in Cardiac Surgery with CPB — Feasibility

Luckraz H, Giri R, Wrigley B, Hennessy A-M, Nicholas J, Nevill A. The use of the RenalGuard system in cardiac surgery with cardiopulmonary bypass: a first in man prospective, observational, feasibility pilot study. Open Heart. 2017;4(2):e000669. doi:10.1136/openhrt-2017-000669.

Link: https://doi.org/10.1136/openhrt-2017-000669

Design: Single-center, prospective, observational, feasibility pilot.

Population: 10 adults at high risk of CSA-AKI undergoing on-pump cardiac surgery (Heart and Lung Centre, Wolverhampton, UK). Inclusion mirrored what would become the KIDNEY trial.

Intervention vs Comparator: RenalGuard balanced forced diuresis initiated in the anesthetic room (20 mg IV furosemide induction bolus, up to 10 mg/h titration to UFR ≥200 mL/h; Hartmann's solution matched 1:1 to urine output for zero balance; continued for 6 h in CICU). No comparator (single-arm feasibility).

Primary Endpoint: Feasibility and safety of running RenalGuard intra-operatively on CPB; AKI as a clinical safety signal.

Key Result: Closed-loop matched diuresis was feasible and safe on CPB. No device-related adverse events. The protocol developed in this pilot was carried forward unchanged into the 220-patient KIDNEY RCT.

Clinical Significance: Established the operational feasibility of running RenalGuard through induction, CPB, and the early CICU phase — the prerequisite for the subsequent KIDNEY RCT.

2. KIDNEY trial primary (Luckraz 2021) · Reduction in AKI Post Cardiac Surgery Using Balanced Forced Diuresis

Luckraz H, Giri R, Wrigley B, Nagarajan K, Senanayake E, Sharman E, Beare L, Nevill A. Reduction in acute kidney injury post cardiac surgery using balanced forced diuresis: a randomized, controlled trial. Eur J Cardiothorac Surg. 2021;59(3):562–569. doi:10.1093/ejcts/ezaa395. NCT02974946.

Link: https://doi.org/10.1093/ejcts/ezaa395

Design: Single-center, prospective, open-label, intention-to-treat RCT. NIHR CRN 32769; investigator-initiated, with a research grant from RenalGuard Solutions.

Population: 220 adults at high risk of CSA-AKI undergoing on-pump cardiac surgery at the Heart and Lung Centre, Wolverhampton, UK (Mar 2017–Sep 2019). Inclusion: ≥1 of diabetes, eGFR 20–60 mL/min/1.73 m^2, anticipated CPB time >120 min, Hb ≤12.5 g/dL, or logistic EuroSCORE ≥5. Procedures: ~48–54% isolated CABG, ~14–17% isolated valve, ~29–38% combined.

Intervention vs Comparator: RenalGuard group (n=110): RenalGuard system started in the anesthetic room with 20 mg IV furosemide on induction (titrated infusion up to 10 mg/h to target urine output ≥200 mL/h), Hartmann's solution matched 1:1 to urine output (zero balance), continued for 6 h on CICU. Control (n=110): standard care, no intraoperative forced diuresis.

Primary Endpoint: RIFLE-defined AKI (≥50% rise in serum creatinine from preoperative baseline) within the first 3 postoperative days.

Key Result: AKI 11/110 (10%) RenalGuard vs 23/110 (20.9%) control; p=0.025. After adjustment for confounders by binary logistic regression, OR 2.82 (95% CI 1.20–6.60; p=0.017) favoring RenalGuard. NNT = 9 (95% CI 6.0–19.2). Mean intra-operative urine 2,366 ± 877 vs 765 ± 549 mL; 24-h CICU urine 3,310 ± 1,303 vs 2,052 ± 804 mL (both p<0.001). No differences in transfusion, AF, infection, CICU stay, or mortality.

Clinical Significance: First adequately powered RCT to show that perioperative RenalGuard balanced forced diuresis approximately halves CSA-AKI in high-risk on-pump cardiac surgery — the foundational efficacy evidence for RenalGuard in this indication.

3. KIDNEY – NGAL secondary (Luckraz 2021) · NGAL Biomarker Secondary Outcome of the KIDNEY Trial

Luckraz H, Giri R, Wrigley B, Nagarajan K, Senanayake E, Sharman E, Beare L, Nevill A. Balanced forced-diuresis compared to control as a reno-protective approach in cardiac surgery: secondary outcome of a randomized controlled trial, assessment of neutrophil gelatinase-associated lipocalin levels. J Cardiothorac Surg. 2021;16:240. doi:10.1186/s13019-021-01620-w. NCT02974946.

Link: https://doi.org/10.1186/s13019-021-01620-w

Design: Pre-specified secondary biomarker analysis of the KIDNEY RCT.

Population: Same 220 patients as the primary KIDNEY trial.

Intervention vs Comparator: RenalGuard balanced forced diuresis vs standard care (as above).

Primary Endpoint: Plasma NGAL at 6 h post-CPB (BioPorto turbidimetric assay; Abbott Architect C16000); pre-CPB NGAL also measured. Adequacy of organ perfusion assessed via $ecDO_2i$ and $ecVCO_2i$ (Spectrum Medical M4).

Key Result: Patients who developed AKI had higher 6-h post-CPB NGAL than those who did not (median 211 vs 150 ng/mL; p<0.001). RenalGuard trended toward lower 6-h post-CPB NGAL (146 vs 178 ng/mL; p=0.09). Using the published 142 ng/mL cut-off, controls were 2.2× more likely to meet NGAL-defined AKI (OR 2.2; 95% CI 1.14–4.27; p=0.02). Intra-operative oxygen delivery ($ecDO_2i$ ~300 mL/min/m^2) and CO_2 production equivalent between groups — RenalGuard's effect is not mediated by altered global perfusion.

Clinical Significance: Demonstrates that RenalGuard reduces a tubular-injury biomarker (NGAL), supporting a true reno-protective biological signal — relevant for nephrologists who view NGAL as the "kidney troponin."

4. KIDNEY – Electrolyte safety (Luckraz 2021) · Electrolyte Safety Secondary Outcome of the KIDNEY Trial

Luckraz H, Giri R, Wrigley B, Nagarajan K, Senanayake E, Sharman E, Beare L, Nevill A. Balanced forced-diuresis as a renal protective approach in cardiac surgery: secondary outcomes of electrolyte changes. J Card Surg. 2021;36(11):1–7. doi:10.1111/jocs.15925. NCT02974946.

Link: https://doi.org/10.1111/jocs.15925

Design: Pre-specified secondary safety analysis of the KIDNEY RCT.

Population: Same 220 patients.

Intervention vs Comparator: RenalGuard balanced forced diuresis vs standard care.

Primary Endpoint: Serial perioperative Na, K, Ca, Mg, phosphate, Cl, bicarbonate, pH, lactate, hemoglobin, and Stewart strong ion difference.

Key Result: Despite ~3× greater intra-operative diuresis in the RenalGuard arm, serum potassium stayed within the normal range (3.96–4.97 mmol/L vs 4.02–5.23 in controls) because RenalGuard patients received more IV potassium (median 60 [0–220] vs 30 [0–190] mmol over the first 24 h; p<0.001). On postoperative day 1, all electrolytes and hemoglobin were equivalent. Strong ion difference maintained 30–45 mEq/L throughout. No increase in AF or arrhythmic complications.

Clinical Significance: Establishes that RenalGuard's high-volume diuresis does not cause clinically meaningful electrolyte derangement provided potassium is replaced — important reassurance for the critical-care nephrology audience concerned about loop-diuretic-driven hypokalemia, hypomagnesemia, and metabolic alkalosis on CPB.

Recent reviews

5. Solomon (2025) · Urine Output — A Critical Vital Sign and Therapeutic Target in Cardiac Surgery

Solomon R. Urine Output — A Critical Vital Sign and Therapeutic Target in Cardiac Surgery. Medical Research Archives (European Society of Medicine). 2025;13(8). doi:10.18103/mra.v13i8.6858. Published 31 August 2025.

Link: https://doi.org/10.18103/mra.v13i8.6858

Summary: Single-author narrative review proposing that urine output should be reframed from passive perfusion marker to active therapeutic target in cardiac surgery. Observational data (Hori 2016, Yilmaz 2016, Song 2016) show intra-operative urine-output thresholds well above traditional oliguria (<1.5, <3.7, <4.0 mL/kg/h respectively) independently predict CSA-AKI. Yet RCTs of mannitol or furosemide alone (Lassnigg 2000; Fakhari 2017; Mahesh 2008; Xie 2022 meta-analysis) show no benefit and sometimes harm — because diuretic-induced fluid shifts activate renin-angiotensin, sympathetic, and vasopressin counter-regulation that reduces renal blood flow, offsetting the benefit of high urine output. The crucial insight: the one positive trial in the Xie meta-analysis (Luckraz 2021, ~50% CSA-AKI reduction) was a trial of device-automated matched diuresis (RenalGuard) — mL-for-mL replacement prevents fluid shifts and unmasks the protective effect of high urine output. Proposed mechanisms include nephrotoxin (e.g., free hemoglobin) dilution/washout and water-diuresis-induced improvement in medullary pO_2 via prostaglandin/NO-mediated vasa recta perfusion (Prasad/Epstein BOLD MRI work). Manual matching is impractical (5-minute urine measurements); device automation is "simpler and more accurate."

2. Interventional Cardiology: Contrast-Associated Acute Kidney Injury (CA-AKI)

RenalGuard has its longest and most extensive evidence base in the cath lab, where contrast-associated AKI (CA-AKI) remains a major driver of morbidity, dialysis, and post-procedural mortality. Four randomized controlled trials and a large prospective registry have shown that matched-fluid forced diuresis approximately halves CA-AKI compared with standard or guideline-directed hydration. A single multicenter post-market RCT (STRENGTH) was neutral; its limitations are catalogued in the accompanying JACC editorial and in the 2023 Rev Esp Cardiol editorial that quantified its underpowered design. A 2022 imaging study provides direct mechanistic evidence for

accelerated parenchymal contrast clearance, and a 2023 Bayesian meta-analysis confirms a significant overall reduction in CA-AKI and pulmonary edema.

Primary clinical evidence

6. MYTHOS (2012) · Prevention of Contrast Nephropathy by Furosemide With Matched Hydration

Marenzi G, Ferrari C, Marana I, Assanelli E, De Metrio M, Teruzzi G, Veglia F, Fabbiocchi F, Montorsi P, Bartorelli AL. Prevention of Contrast Nephropathy by Furosemide With Matched Hydration: The MYTHOS (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention) Trial. JACC Cardiovasc Interv. 2012;5(1):90–97. doi:10.1016/j.jcin.2011.08.017. NCT00702728.

Link: https://doi.org/10.1016/j.jcin.2011.08.017

Design: Single-center, prospective, randomized open-label RCT (Centro Cardiologico Monzino, Milan, Italy).

Population: 170 CKD patients (eGFR <60 mL/min/1.73 m^2; mean ~39) undergoing elective or urgent coronary angiography ± PCI; approximately half with NSTEMI.

Intervention vs Comparator: Furosemide with matched hydration (FMH) via RenalGuard (n=87): 250 mL saline bolus + 0.5 mg/kg IV furosemide, then automated isotonic saline matched to urine output, started ≈90 min pre-procedure and continued for 4 h afterwards; target urine output >300 mL/h. Control (n=83): standard isotonic saline 1 mL/kg/h (0.5 if LVEF <40%) for 12 h pre- and 12 h post-procedure.

Primary Endpoint: CIN — ≥25% or ≥0.5 mg/dL rise in serum creatinine within 72 h.

Key Result: CIN 4/87 (4.6%) FMH vs 15/83 (18%) controls; p=0.005; adjusted RR 0.31 (95% CI 0.11–0.89). Median achieved urine output 760 mL/h. Composite in-hospital adverse events 8% vs 18% (p=0.052); largest benefit in the NSTEMI/urgent subgroup. No device-related complications; 4 patients had asymptomatic hypokalemia.

Clinical Significance: First randomized evidence that RenalGuard-driven matched diuresis reduces CIN approximately four-fold versus standard hydration in high-risk CKD patients undergoing coronary procedures.

7. REMEDIAL II (2011) · RenalGuard System in High-Risk Patients for Contrast-Induced AKI

Briguori C, Visconti G, Focaccio A, Airoldi F, Valgimigli M, Sangiorgi GM, Golia B, Ricciardelli B, Condorelli G; REMEDIAL II Investigators. Renal Insufficiency After Contrast Media Administration Trial II (REMEDIAL II): RenalGuard System in High-Risk Patients for Contrast-Induced Acute Kidney Injury. Circulation. 2011;124(11):1260–1269. doi:10.1161/CIRCULATIONAHA.111.030759. NCT01098032.

Link: https://doi.org/10.1161/CIRCULATIONAHA.111.030759

Design: Multicenter (4 Italian sites), randomized, investigator-driven, open-label RCT.

Population: 292 high-risk patients (146 per arm) with eGFR ≤30 mL/min/1.73 m^2 and/or Mehran risk score ≥11, undergoing coronary or peripheral angiography/angioplasty. Mean eGFR 32; ~70% diabetic.

Intervention vs Comparator: RenalGuard arm: saline + IV NAC matched to urine output via RenalGuard (250 mL priming, 150 mL if LVEF ≤30%), low-dose furosemide 0.25 mg/kg to target

urine output ≥300 mL/h, continued through procedure and 4 h post. Control: sodium bicarbonate (154 mEq/L, Merten protocol) + high-dose NAC (oral + IV, total 6 g).

Primary Endpoint: CI-AKI defined as serum creatinine increase ≥0.3 mg/dL at 48 h or need for dialysis.

Key Result: CI-AKI 16/146 (11%) RenalGuard vs 30/146 (20.5%) control; OR 0.47 (95% CI 0.24–0.92), p=0.025. Cystatin C rises lower in the RenalGuard arm at 24 h (p=0.002) and 48 h (p=0.001). In-hospital dialysis 0.7% vs 4.1% (p=0.056); 1-month dialysis 0.7% vs 4.8% (p=0.031). Asymptomatic hypokalemia 7.5% vs 8.2%.

Clinical Significance: Established RenalGuard superiority over the then-prevailing bicarbonate + NAC regimen in the highest-risk CKD cohort, with a halving of post-procedure dialysis.

8. REMEDIAL III (2020) · LVEDP- vs Urine Flow Rate–Guided Hydration in Preventing CA-AKI

Briguori C, D'Amore C, De Micco F, Signore N, Esposito G, Visconti G, Airoldi F, Signoriello G, Focaccio A. Left Ventricular End-Diastolic Pressure Versus Urine Flow Rate–Guided Hydration in Preventing Contrast-Associated Acute Kidney Injury. JACC Cardiovasc Interv. 2020;13(17):2065–2074. doi:10.1016/j.jcin.2020.04.051. NCT02489669.

Link: https://doi.org/10.1016/j.jcin.2020.04.051

Design: Multicenter (4 Italian sites), randomized, open-label, phase 3, investigator-initiated RCT (2015–2019).

Population: 708 randomized / 702 analyzed (351 per arm) with eGFR ≤45 mL/min/1.73 m^2 or high CA-AKI risk (Mehran ≥11 or Gurm >7%). Mean age 74; mean eGFR 36; ~50% diabetic.

Intervention vs Comparator: Urine flow rate (UFR)-guided RenalGuard — 250 mL saline priming (150 if LVEF ≤30% or high LVEDP), furosemide ≥0.25 mg/kg titrated to urine output ≥300 mL/h, continued + 4 h post. LVEDP-guided (POSEIDON protocol): saline 1.5 / 3 / 5 mL/kg/h according to invasively measured LVEDP (>18 / 13–18 / ≤12 mm Hg).

Primary Endpoint: Composite of CA-AKI (sCr ≥25% or ≥0.5 mg/dL at 48 h) and acute pulmonary edema.

Key Result: Composite 20/351 (5.7%) UFR vs 36/351 (10.3%) LVEDP; RR 0.56 (95% CI 0.39–0.79), p=0.036; NNT 22. CA-AKI alone 5.7% vs 10.0% (p=0.048); pulmonary edema 0.3% vs 2.0% (p=0.069). 1-month MAE 7.1% vs 12.0% (p=0.030); sustained kidney damage 4.3% vs 8.5%. Hypokalemia 6.2% vs 2.3% (p=0.013) in RenalGuard arm.

Clinical Significance: First head-to-head against another tailored-hydration strategy; UFR-guided RenalGuard was superior for the combined renal and pulmonary endpoint, with the trade-off of more hypokalemia requiring potassium monitoring.

9. AKIGUARD (2016) · AKIGUARD: In-Hospital and One-Year Outcomes

Usmiani T, Andreis A, Budano C, Sbarra P, Andriani M, Garrone P, Fanelli AL, Calcagnile C, Bergamasco L, Biancone L, Marra S. AKIGUARD (Acute Kidney Injury GUARding Device) trial: in-hospital and one-year outcomes. J Cardiovasc Med (Hagerstown). 2016;17(7):530–537. doi:10.2459/JCM.0000000000000348. AIFA 340/352/70/2011.

Link: https://doi.org/10.2459/JCM.0000000000000348

Design: Single-center, randomized, open-label RCT (Città della Salute, Turin, Italy; Oct 2011–Apr 2014).

Population: 124 analyzed patients (59 RenalGuard, 65 control) with eGFR <60 mL/min/1.73 m^2 (CKD-EPI) undergoing coronary angiography/PCI; ~40% urgent (NSTEMI/UA). Mean age 75; mean eGFR ~44.

Intervention vs Comparator: Matched hydration: 250 mL saline bolus, 0.5 mg/kg furosemide, RenalGuard-matched saline infusion to 4 h post-procedure. Control: isotonic saline + 1.4% sodium bicarbonate (3 mL/kg/h ×1 h pre, 1 mL/kg/h ×6 h post) + oral NAC 1,200 mg BID + vitamin C 5 g ×2 days.

Primary Endpoint: CIAKI per KDIGO (sCr rise ≥0.3 mg/dL in 48 h or ≥50% in 7 days).

Key Result: CIAKI 4/59 (7%) RenalGuard vs 16/65 (25%) control; p=0.01, RR 3.6 (95% CI 1.3–10.2). No stage II/III AKI in the RenalGuard arm vs 5/16 in controls. At 3 months, eGFR essentially unchanged with RenalGuard (–0.02%) vs –15% in control (p<0.01). 1-year MACCE 7% vs 32% (p<0.01); cumulative hospital days 1.0 ± 3.8 vs 4.9 ± 12.5 (p=0.01). Two control patients required chronic hemodialysis; none in RenalGuard arm.

Clinical Significance: Extended RenalGuard evidence beyond acute CI-AKI, showing durable benefit on CKD progression and 1-year cardiovascular outcomes.

10. Real-World Registry (Briguori 2016) · RenalGuard System in High-Risk Patients for Contrast-Induced AKI (Registry)

Briguori C, Visconti G, Donahue M, De Micco F, Focaccio A, Golia B, Signoriello G, Ciardiello C, Donnarumma E, Condorelli G. RenalGuard system in high-risk patients for contrast-induced acute kidney injury. Am Heart J. 2016;173:67–76. doi:10.1016/j.ahj.2015.12.005.

Link: https://doi.org/10.1016/j.ahj.2015.12.005

Design: Single-center prospective observational registry (Clinica Mediterranea, Naples; Jan 2011–Sept 2014).

Population: 400 high-risk patients (eGFR ≤30 mL/min/1.73 m^2 and/or Mehran ≥11 / Gurm >7%) undergoing coronary or peripheral procedures. Mean age 75; mean eGFR 30; 60% diabetic.

Intervention vs Comparator: All patients received RenalGuard therapy (saline + IV NAC matched to urine output, 250 mL priming, furosemide 0.25 mg/kg titrated to urine output ≥300 mL/h, continued 4 h post).

Primary Endpoint: Relationship between CI-AKI (sCr ≥0.5 mg/dL or ≥25% at 48 h) and achieved urine flow rate (UFR) across procedural phases; safety.

Key Result: CI-AKI 34/400 (8.5%). Mean UFR was lower in CI-AKI patients in pre-procedural (208 vs 283 mL/h, p<0.001) and intra-procedural phases (389 vs 483 mL/h, p=0.009). Best ROC threshold: intra-procedural mean UFR ≥450 mL/h (AUC 0.62; sensitivity 80%, specificity 46%). Independent CI-AKI predictors: PCI vs angiography alone (HR 4.13), intra-procedural UFR <450 mL/h (HR 2.27), total furosemide >0.32 mg/kg (HR 5.03). Pulmonary edema 4/400 (1%); potassium replacement 4%.

Clinical Significance: Defined the modern intra-procedural UFR target (≥450 mL/h) used in subsequent RenalGuard protocols and confirmed safety in a large real-world high-risk population.

11. RESPECT KIDNEY (2018) · RenalGuard in Japanese Patients with Renal Dysfunction

Katoh H, Nozue T, Horie K, Sozu T, Inoue N, Michishita I. RenalGuard system to prevent contrast-induced acute kidney injury in Japanese patients with renal dysfunction; RESPECT KIDNEY study. Cardiovasc Interv Ther. 2019;34(2):131–138. doi:10.1007/s12928-018-0527-8. UMIN000007308.

Link: https://doi.org/10.1007/s12928-018-0527-8

Design: Multicenter (2 Japanese centers), prospective, single-arm trial (Dec 2013–Aug 2016) — first Japanese evaluation of RenalGuard.

Population: 58 analyzed patients (mean age 76; eGFR ≤45 mL/min/1.73 m^2 by Japanese equation; mean eGFR 35; mean Mehran 11.7). Coronary angiography (15), PCI (33), endovascular therapy (10).

Intervention vs Comparator: RenalGuard therapy alone (250 mL priming, 150 if LVEF ≤40%; furosemide 0.25 mg/kg titrated to UFR ≥300 mL/h; 4 h post). Prespecified acceptability threshold: CI-AKI <25%; predicted ~26% based on Mehran scoring.

Primary Endpoint: CI-AKI per Barrett/Parfrey (sCr ↑ ≥0.5 mg/dL or ≥25% within 72 h).

Key Result: CI-AKI 5/58 (8.6%) vs predicted 26.1%; 95% CI 2.9–19.0 — upper bound below the prespecified 25% threshold. No CI-AKI in low/moderate risk; 20% in very-high-risk (Mehran ≥16) subgroup. Mean intra-procedural UFR significantly higher in non-AKI patients (727 vs 469 mL/h; p=0.03); ROC cutoff 494.8 mL/h. All AKI resolved by 1 month; no dialysis; no clinically meaningful electrolyte disturbance.

Clinical Significance: First Japanese RenalGuard validation; reproduced low CI-AKI rates in a different ethnic and healthcare setting and independently corroborated the ~450–500 mL/h intra-procedural UFR target.

12. STRENGTH (2022) · Study Evaluating the Use of RenalGuard to Protect Patients at High Risk of AKI — Multicenter European RCT

Mauler-Wittwer S, Sievert H, Ioppolo A-M, Mahfoud F, Carrié D, Lipiecki J, Nickenig G, Fajadet J, Eckert S, Morice M-C, Garot P. Study Evaluating the Use of RenalGuard to Protect Patients at High Risk of AKI (STRENGTH). JACC Cardiovasc Interv. 2022;15(16):1639–1648. doi:10.1016/j.jcin.2022.05.036. NCT02793661.

Link: https://doi.org/10.1016/j.jcin.2022.05.036

Design: Multicenter (10 French/German centers), prospective, randomized 1:1, open-label, post-market RCT (May 2016–Jan 2019); industry-sponsored (RenalGuard Solutions); independently coordinated by CERC.

Population: 259 randomized (248 modified ITT) with eGFR 15–40 mL/min/1.73 m^2 undergoing complex coronary (48%), structural/TAVR + LAA closure (34%), or peripheral (18%) interventions with anticipated contrast media ≥3× eGFR. Mean age 79; mean eGFR 32.

Intervention vs Comparator: RenalGuard arm: 100–250 mL saline priming, 0.5 mg/kg furosemide aiming UFR >450 mL/h intra-procedure and >300 mL/h post, continued 4 h post. Control: guideline-directed IV saline hydration (operator discretion).

Primary Endpoint: CIN — sCr rise ≥0.3 mg/dL and/or ≥25% at day 3, or dialysis within 5 days.

Key Result: CIN 17/107 (15.9%) RenalGuard vs 15/110 (13.9%) control; difference +2.4% (95% CI −7.1 to 12.0), p=0.62. 12-month MACCE 20.5% vs 22.2% (p=0.74). No significant safety signals

(minor bladder bleeding 4.1% vs 2.4%; UTI 2.4% vs 1.6%). Mean contrast volume only ~110 mL (substantially lower than prior RenalGuard trials, where it ranged 135–180 mL).

Clinical Significance: First clearly negative multicenter RCT for RenalGuard. Authors note the trial was underpowered for hard endpoints; the Briguori/Romagnoli/Biondi-Zoccai 2023 editorial subsequently quantified the effective power as 0.55 (vs the planned 0.9) because only 60.3% (study arm) and 50.8% (control arm) of patients received the protocol-mandated contrast load. The result should be weighed against the four positive RCTs, the large positive registry, and the 2023 Bayesian meta-analysis.

Mechanistic evidence

13. Ben-Haim / Banai (2022) · Forced Diuresis with Matched Hydration Prevents Renal Contrast Media Accumulation

Ben-Haim Y, Chorin E, Hochstadt A, Ingbir M, Arbel Y, Khoury S, Halkin A, Finkelstein A, Banai S, Konigstein M. Forced Diuresis with Matched Isotonic Intravenous Hydration Prevents Renal Contrast Media Accumulation. J Clin Med. 2022;11(3):885. doi:10.3390/jcm11030885.

Link: https://doi.org/10.3390/jcm11030885

Design: Single-center (Tel Aviv Medical Center), prospective controlled observational imaging study.

Population: 58 patients undergoing coronary angiography, PCI, or TAVR in three groups: RenalGuard-treated impaired-RF (n=25, mean eGFR 39); normal-RF controls with standard hydration (n=25, mean eGFR 76); impaired-RF controls without RenalGuard (n=8, mean eGFR ~40). All received iodixanol; mean contrast 135 mL RenalGuard vs ~153 mL controls.

Intervention vs Comparator: Standard RenalGuard protocol (250 mL priming, 0.25–0.5 mg/kg furosemide, UFR ≥300 mL/h, 4 h post). End-of-procedure renal radiograph scored 0–2 by two blinded cardiologists (weighted κ 0.80).

Primary Endpoint: Contrast Accumulation Score (CAS) of kidneys and collecting system at end of procedure: 0 = none, 1 = mild collecting-system accumulation, 2 = intense renal + collecting-system accumulation.

Key Result: CAS = 0 in 92% of RenalGuard patients vs 4% of normal-RF controls and 25% of impaired-RF controls. Median CAS 0 (IQR 0–0) RenalGuard vs 1.5 (IQR 1–2) normal-RF ($p<0.001$) and 1.0 (IQR 0.38–1.62) impaired-RF ($p=0.003$). Effect independent of contrast volume, age, diabetes, eGFR, and procedure type on multivariable analysis. Contrast confirmed present in urinary drainage bag in all RenalGuard patients.

Clinical Significance: First imaging-based evidence of the mechanism by which RenalGuard protects kidneys — accelerated washout of contrast from the renal parenchyma and tubular system. Supports the conceptual basis (dilution + reduced residence time) for forced diuresis with matched hydration.

Meta-analysis

14. Occhipinti / Capodanno (2023) · Bayesian Meta-Analysis of RenalGuard vs Standard Hydration for CA-AKI

Occhipinti G, Laudani C, Spagnolo M, Greco A, Capodanno D. Diuresis-matched versus standard hydration in patients undergoing percutaneous cardiovascular procedures: meta-analysis of randomized clinical trials. Rev Esp Cardiol (Engl Ed). 2023;76(10):759–766. doi:10.1016/j.rec.2023.02.001. PROSPERO CRD42022378489.

Link: https://doi.org/10.1016/j.rec.2023.02.001

Design: Bayesian random-effects meta-analysis of 6 randomized clinical trials of RenalGuard vs standard periprocedural hydration in percutaneous cardiovascular procedures (search of Medline, Cochrane, Web of Science).

Population: Patients undergoing percutaneous cardiovascular procedures (coronary, peripheral, structural) with iodinated contrast exposure, pooled across the included trials.

Primary Endpoint: CA-AKI. Secondary endpoints: all-cause death, cardiogenic shock, acute pulmonary edema, and renal replacement therapy.

Key Result: RenalGuard significantly reduced CA-AKI (median RR 0.54; 95% CrI 0.31–0.86) and acute pulmonary edema (median RR 0.35; 95% CrI 0.12–0.87). Non-significant trends toward lower all-cause death (RR 0.49; 0.13–1.08), cardiogenic shock (RR 0.06; 0.00–1.91), and RRT (RR 0.52; 0.18–1.18). RenalGuard had the highest probability of ranking first for all secondary outcomes. Results were robust across multiple sensitivity analyses.

Clinical Significance: First Bayesian meta-analysis of the RenalGuard CA-AKI evidence base; provides the consolidated effect-size estimate (~46% relative reduction in CA-AKI) that informs guideline discussions and protocol design.

Editorial commentary

15. Azzalini / Moroni (2020) · LVEDP-Guided Versus UFR-Guided Hydration — Should We Be Guided by Our Heart or Kidneys?

Azzalini L, Moroni F. LVEDP-Guided Versus UFR-Guided Hydration for CA-AKI Prevention: Should We Be Guided by Our Heart or Kidneys? JACC Cardiovasc Interv. 2020;13(17):2075–2077. doi:10.1016/j.jcin.2020.05.004.

Link: https://doi.org/10.1016/j.jcin.2020.05.004

Summary: Accompanying editorial to REMEDIAL III. Credits the trial as the first randomized comparison of two tailored hydration strategies and notes that UFR-guided RenalGuard achieved a clinically meaningful reduction in the composite endpoint with consistent direction across LVEDP and eGFR subgroups, plus a signal toward fewer 1-month major adverse kidney events. Acknowledges practical drawbacks: time to reach target UFR (~55 min) disrupts cath lab workflow and precludes use in STEMI/cardiogenic shock; Foley catheter discomfort; device costs awaiting cost-effectiveness analysis. Calls for an adequately powered trial proving that AKI prevention translates to reduced major adverse kidney events.

16. Gurm (2022) · Guarding the Kidneys — Re-Examining Prophylactic Hydration in Contemporary Interventional Practice

Gurm HS. Guarding the Kidneys: Re-Examining the Role of Prophylactic Hydration in Contemporary Interventional Practice. JACC Cardiovasc Interv. 2022;15(16):1649–1651. doi:10.1016/j.jcin.2022.06.030.

Link: https://doi.org/10.1016/j.jcin.2022.06.030

Summary: Accompanying editorial to STRENGTH in JACC Cardiovasc Interv. Frames the negative STRENGTH result within the broader observation that contemporary CI-AKI rates have fallen as operators have adopted lower-osmolar contrast, lower contrast volumes (especially the 'contrast volume <3× creatinine clearance' rule), and shorter, more pragmatic IV hydration protocols. Argues that in a 2022 procedural environment with already-mitigated CI-AKI risk, demonstrating an incremental benefit from any prophylactic device is increasingly difficult. Calls for re-examination of who should receive aggressive prophylactic hydration and which subpopulations (very high-risk CKD, structural heart procedures with high contrast loads) might still benefit from RenalGuard-style matched diuresis.

17. Briguori / Romagnoli / Biondi-Zoccai (2023) · Diuresis-Matched Hydration to Prevent CA-AKI — The More the Merrier? (Meta-Analysis Editorial)

Briguori C, Romagnoli E, Biondi-Zoccai G. Diuresis-matched hydration to prevent contrast-associated acute kidney injury in percutaneous cardiovascular procedures: the more the merrier? Rev Esp Cardiol (Engl Ed). 2023;76(10):752–754. doi:10.1016/j.rec.2023.03.011.

Link: https://www.revespcardiol.org/en-diuresis-matched-hydration-to-prevent-co-articulo-S1885585723000968-pdf-file

Summary: Accompanying editorial to the Occhipinti meta-analysis. Frames diuresis-matched hydration as the leading tailored strategy for CA-AKI prevention among the available guided-hydration regimens (UFR-guided, LVEDP-guided, CVP-guided, BIVA-guided). Most importantly, the editorial quantifies the underpowered design of STRENGTH: although the trial was powered at 0.9 with α=0.05 to detect a CA-AKI reduction from 25% to 10% (requiring 133 patients per group meeting the contrast-load criterion), only 60.3% (73 patients) of the RenalGuard arm and 50.8% (62 patients) of the control arm actually met the inclusion criterion — reducing the effective power to 0.55, i.e., "significantly underpowered." The editorial also flags an additional caveat: very high-risk patients who fail to achieve adequate UFR (e.g., >150 mL/h) on RenalGuard cannot benefit from the intervention, suggesting a need for procedural quality checks during therapy.

Recent reviews

18. Solomon (2024) · AKI Prevention Following Cardiac Catheterization — The Ins and Outs of Management

Solomon R. Acute Kidney Injury Prevention Following Cardiac Catheterization: The Ins and Outs of Management. Kidney Med. 2024;6(8):100865. doi:10.1016/j.xkme.2024.100865.

Link: https://doi.org/10.1016/j.xkme.2024.100865

Summary: Editorial in Kidney Medicine reviewing the mechanistic logic for hydration in CA-AKI prevention. Argues that the protective benefit of hydration may operate not through volume expansion or cardiac output per se, but through increased urine output — "what comes out" may

matter as much as "what goes in." Reviews trials comparing oral vs IV hydration (equivalence supports a urine-output mechanism), early- vs late-start hydration, and trials of isotonic fluid without volume expansion. Identifies forced matched diuresis as the cleanest experimental probe of this hypothesis because the 250 mL priming bolus produces only ~2% intravascular expansion, isolating the high-UFR mechanism. Conceptual support for the RenalGuard design.

19. Cheng / Hao (2024) · Innovative Approaches Beyond Periprocedural Hydration for Preventing CI-AKI

Cheng C-H, Hao W-R, Cheng T-H. Innovative approaches beyond periprocedural hydration for preventing contrast-induced acute kidney injury. World J Radiol. 2024;16(9):375–379. doi:10.4329/wjr.v16.i9.375.

Link: https://doi.org/10.4329/wjr.v16.i9.375

Summary: Invited editorial in the World Journal of Radiology surveying CI-AKI prevention strategies beyond conventional pre- and post-procedural saline hydration. Reviews pharmacologic candidates (NAC, statins, ascorbic acid, allopurinol), low- and iso-osmolar contrast media, contrast-volume restriction, and device-mediated approaches including forced diuresis with matched hydration. Frames RenalGuard-style matched diuresis among the most promising 'innovative' approaches for high-risk patients. Useful third-party (Taiwan-based, non-RenalGuard-funded) endorsement of the matched-diuresis mechanism in the imaging community.

20. Rudnick (2022) · Fluid Administration Strategies for the Prevention of CA-AKI

Rudnick MR, Fay K, Wahba IM. Fluid administration strategies for the prevention of contrast-associated acute kidney injury. Curr Opin Nephrol Hypertens. 2022;31(5):414–424. doi:10.1097/MNH.0000000000000815.

Link: https://doi.org/10.1097/MNH.0000000000000815

Summary: Narrative review in Current Opinion in Nephrology and Hypertension covering fluid-administration strategies for CA-AKI prevention: IV vs no fluid; saline vs bicarbonate vs 0.45% saline; duration of administration; oral hydration; LVEDP-guided hydration; and forced-diuresis techniques. Concludes that IV isotonic saline is preferred over no fluid (especially for intra-arterial contrast and high-risk patients), that the bicarbonate-vs-saline debate is settled in favor of saline, and that 'tailored fluid administration in heart-failure patients and forced diuresis with matching fluid administration are promising new fluid administration strategies.' Frames RenalGuard within the contemporary evidence-based prevention algorithm.

21. Heyman / Solomon / Abassi (2025) · It Is Not Only Fluids: Impact of Hydration Protocols on Renal Oxygenation

Heyman SN, Solomon R, Abassi Z. It is not only fluids: the impact of hydration protocols used for the prevention of contrast nephropathy on renal oxygenation. Renal Failure. 2025;47(1):2528889. doi:10.1080/0886022X.2025.2528889.

Link: https://doi.org/10.1080/0886022X.2025.2528889

Summary: State-of-the-art review arguing that vigorous hydration prevents CA-AKI not only by diluting contrast and shortening tubular transit time, but critically by improving renal medullary oxygenation. Mechanisms reviewed: (1) lowered urine/plasma viscosity improving vasa recta flow; (2) volume-expansion-triggered natriuretic peptides that vasodilate the medullary microvasculature and downregulate tubular oxygen-consuming transport; (3) furosemide blockade of NaKCl2

cotransport in medullary thick ascending limbs, which markedly improves medullary pO_2 (validated by BOLD MRI) and prevents outer-medullary hypoxic injury. Names the RenalGuard system as one of the two principal tailored hydration regimens for CA-AKI prevention. Emphasizes that furosemide given without matched hydration is harmful (pre-renal failure), but combined with balanced hydration is renoprotective — explicit mechanistic rationale for the RenalGuard design.

3. Transcatheter Aortic Valve Replacement (TAVR)

TAVR patients are uniquely vulnerable to peri-procedural AKI — elderly, frequently with CKD, exposed to contrast, rapid pacing, transient hypotension, transfusion, and embolic injury. The TAVR evidence base spans one positive randomized trial (PROTECT-TAVI), a non-randomized positive pilot (Visconti), a positive interim conference abstract from Hamburg, the only sham-controlled trial in the RenalGuard literature (REDUCE-AKI; neutral with a mortality safety signal), and the final published Hamburg RCT (Voigtländer-Buschmann 2023; neutral). Because the TAVR evidence is mixed, the optimal RenalGuard protocol in this population is still being refined. Work is ongoing to clarify which TAVR patient subgroups derive the greatest benefit and to define the ideal timing, urine-output targets, and hydration-matching parameters specific to the unique physiology of transcatheter valve replacement.

Primary clinical evidence

22. PROTECT-TAVI (2015) · RenalGuard in Patients Undergoing TAVR — First Randomized Trial

Barbanti M, Gulino S, Capranzano P, Immè S, Sgroi C, Tamburino C, Ohno Y, Attizzani GF, Patanè M, Sicuso R, Pilato G, Di Landro A, Todaro D, Di Simone E, Picci A, Giannetto G, Costa G, Deste W, Giannazzo D, Grasso C, Capodanno D, Tamburino C. Acute Kidney Injury With the RenalGuard System in Patients Undergoing Transcatheter Aortic Valve Replacement: The PROTECT-TAVI Trial. JACC Cardiovasc Interv. 2015;8(12):1595–1604. doi:10.1016/j.jcin.2015.07.012.

Link: https://doi.org/10.1016/j.jcin.2015.07.012

Design: Investigator-driven, single-center, prospective, open-label, registry-based RCT (REPLACE registry, Ferrarotto Hospital, Catania, Italy; Feb 2014–Jan 2015).

Population: 112 consecutive patients with severe symptomatic AS undergoing TAVR (mean age 80.6 ± 5.1; 66% with eGFR <60 mL/min by Cockcroft-Gault). Excluded: dialysis, acute HF with LVEF <30% in prior 30 days, urgent TAVI.

Intervention vs Comparator: RenalGuard (n=56): 250 mL saline priming (150 if LVEF <30%), furosemide 0.25 mg/kg IV, matched saline/urine hydration targeting urine flow >300 mL/h during and 4 h post. Control (n=56): normal saline 1 mL/kg/h (0.5 if LVEF <30%) for 12 h pre, during, and 6 h post. Iodixanol in all cases.

Primary Endpoint: VARC-defined AKI within 72 h post-procedure.

Key Result: AKI 3/56 (5.4%) RenalGuard vs 14/56 (25.0%) control; RR 0.21 (95% CI 0.06–0.71), p=0.014. Predominantly stage 1; one stage 3 in control. No dialysis. No differences in 30-day mortality, stroke, bleeding, or HF re-hospitalization. Multivariable: no RenalGuard (adjOR 5.99, p=0.009) and AKI risk score ≥4 (adjOR 4.31) independently predicted AKI. Asymptomatic hypokalemia 41% vs 32% (NS); no pulmonary edema.

Clinical Significance: First RCT showing RenalGuard significantly reduces AKI in TAVR; established the device as a viable AKI-prevention strategy in severe AS patients in labile hemodynamic compensation.

23. Visconti / Briguori (2016) · RenalGuard for AKI Prevention in TAVI — CKD Pilot Cohort

Visconti G, Focaccio A, Donahue M, Golia B, Marzano A, Donnarumma E, Ricciardelli B, Selvetella L, Marino L, Briguori C. RenalGuard System for the prevention of acute kidney injury in patients undergoing transcatheter aortic valve implantation. EuroIntervention. 2016;11(14):e1658–e1661. doi:10.4244/EIJV11I14A317.

Link: https://doi.org/10.4244/EIJV11I14A317

Design: Single-center, prospective, non-randomized pilot study (Clinica Mediterranea, Naples; Jan 2009–Dec 2014).

Population: 48 consecutive CKD patients undergoing transfemoral TAVI with CoreValve. Iodixanol in all cases.

Intervention vs Comparator: RenalGuard (n=22): normal saline matched to urine output targeting UFR >300 mL/h; allocated if eGFR ≤30 mL/min/1.73 m^2 or predicted AKI risk ≥50%. Control (n=26): sodium bicarbonate 154 mEq/L in dextrose + high-dose NAC.

Primary Endpoint: AKI defined as rise in sCr ≥0.3 mg/dL or 1.5–1.9× baseline within 7 days post-contrast.

Key Result: AKI 1/22 (4.5%) RenalGuard vs 10/26 (38.5%) control (p=0.005; OR 0.076, 95% CI 0.009–0.66). Dialysis 0% vs 8% (NS). On multivariable analysis, RenalGuard was independently protective (OR 0.71, p=0.026); post-procedural hypotension (OR 3.88) and contrast volume >3× eGFR (OR 3.77) increased AKI risk. Mean urine flow on RenalGuard 340 ± 169 mL/h.

Clinical Significance: Early non-randomized signal that matched-fluid forced diuresis with RenalGuard protects CKD patients undergoing TAVI from AKI driven by both contrast and contrast-independent mechanisms (hypotension, transfusion).

24. Eppendorf Interim (Voigtländer 2018) · RenalGuard for AKI Prevention in TAVI — Hamburg University Heart Center (DGK Interim)

Voigtländer L, Schäfer S, Deuschl F, Schofer N, Seiffert M, Rübsamen N, Kalbacher D, Twerenbold R, Schirmer J, Reichenspurner H, Blankenberg S, Conradi L, Schäfer U. Prevention of Acute Kidney Injury after Transcatheter Aortic Valve Implantation: Use of RenalGuard-System in Patients with Severe Aortic Stenosis and Chronic Kidney Injury. Deutsche Gesellschaft für Kardiologie (DGK) Annual Congress, April 2018 (interim analysis poster).

Design: Interim analysis of an ongoing single-center 1:1 randomized trial.

Population: Interim analysis of 59 patients (RenalGuard n=28, control n=31; median age 82; median logES 10.9; median baseline GFR ~38 mL/min) with CKD (eGFR <50) and severe AS.

Intervention vs Comparator: RenalGuard from 3 h pre- to 4 h post-procedure with furosemide-induced matched diuresis vs standard hydration (no IV hydration during procedure in control arm). Mean RenalGuard saline volume 2,298 mL; mean urine output 2,060 mL.

Primary Endpoint: AKI (AKIN stage ≥1) post-TAVI.

Key Result: AKI 2/28 (7.1%) RenalGuard vs 6/31 (19.3%) control. No electrolyte imbalances or adverse hemodynamic effects in either group.

Clinical Significance: Preliminary German randomized data reproducing the PROTECT-TAVI signal. Superseded by the full 2023 publication (Voigtländer-Buschmann), which did not maintain statistical significance at n=100.

25. REDUCE-AKI (Arbel 2019) · Sham-Controlled RCT of RenalGuard in TAVR

Arbel Y, Ben-Assa E, Puzhevsky D, Litmanowicz B, Galli N, Chorin E, Halkin A, Sadeh B, Konigstein M, Kliuk-Ben Bassat O, Steinvil A, Bazan S, Banai S, Finkelstein A. Forced diuresis with matched hydration during transcatheter aortic valve implantation for Reducing Acute Kidney Injury: a randomized, sham-controlled study (REDUCE-AKI). Eur Heart J. 2019;40(38):3169–3178. doi:10.1093/eurheartj/ehz343. NCT01866800.

Link: https://doi.org/10.1093/eurheartj/ehz343

Design: Single-center, prospective, randomized, double-blind, sham-controlled RCT (Tel Aviv Medical Center). Terminated early by DSMB for futility and a possible harm signal.

Population: 136 patients (planned 220) aged ≥65 with eGFR ≤60 mL/min/1.73 m^2 undergoing elective transfemoral TAVI. Mean age 83.9 ± 5; median STS 3.5; baseline eGFR 57.3 ± 14.1 (mostly mild CKD). Excluded: LVEF <30%, ACS within 30 days, chronic dialysis.

Intervention vs Comparator: Active (n=68): 250 mL saline bolus, furosemide 0.25–0.5 mg/kg, RenalGuard matched hydration through procedure and 6 h post; plus background 0.5–1 mL/kg/h saline. Sham (n=68): connected to RenalGuard in passive mode (system covered to maintain blinding) with 0.5–1 mL/kg/h saline only; no furosemide, no priming bolus.

Primary Endpoint: VARC-2 AKI stage ≥1 post-procedure.

Key Result: AKI 25% active vs 19.1% sham (p=0.408); high-grade AKI 1 vs 2 (p=0.6). Sensitivity analysis (>50% sCr rise): 10.3% vs 2.9% (p=0.085). On multivariable analysis only diabetes predicted AKI. Unexpected long-term mortality signal: 27.9% active vs 13.2% sham (HR 3.74; 95% CI 1.51–9.28; p=0.004); adjusted HR 3.095 (p=0.008). No mechanistic explanation found in troponin, echo, hemodynamics, or complications.

Clinical Significance: First and only sham-controlled RCT of RenalGuard in TAVR; neutral on AKI prevention and raised a mortality safety signal. Authors interpret as consistent with TAVR-AKI being multifactorial (not predominantly contrast-driven), but the mortality finding remains unexplained and the trial is limited (single center, mostly mild CKD [mean eGFR ~57], stopped early).

26. Eppendorf TAVI RCT — Final (Voigtländer-Buschmann 2023) · RenalGuard for AKI Prevention in TAVI — Final Hamburg RCT

Voigtländer-Buschmann L, Schäfer S, Schmidt-Lauber C, Weimann J, Shenas M, Giraldo Cortes J, Kuta PM, Zeller T, Twerenbold R, Seiffert M, Schofer N, Schneeberger Y, Schäfer A, Schirmer J, Reichenspurner H, Blankenberg S, Conradi L, Schäfer U. Effect of periprocedural furosemide-induced diuresis with matched isotonic intravenous hydration in patients with chronic kidney disease undergoing transcatheter aortic valve implantation. Clin Res Cardiol. 2023. doi:10.1007/s00392-023-02234-z.

Link: https://doi.org/10.1007/s00392-023-02234-z

Design: Single-center, prospective, randomized trial (University Heart and Vascular Center Hamburg-Eppendorf; Jan 2017–Aug 2018). Final published version of the Voigtländer 2018 DGK interim.

Population: 100 patients with severe aortic stenosis and CKD undergoing TAVI (RenalGuard n=47 analyzed; control n=51 analyzed).

Intervention vs Comparator: RenalGuard system periprocedural treatment vs standard pre- and post-procedural IV hydration.

Primary Endpoint: Occurrence of AKI after TAVI; secondary endpoints per VARC-2 criteria.

Key Result: Overall AKI prevalence 18.4% (n=18), majority KDIGO stage 1. AKI RenalGuard 21.3% vs control 15.7%, p=0.651 (negative). No differences in 30-day or 12-month mortality or procedure-associated complications between groups.

Clinical Significance: Final, statistically adequate publication of the Hamburg RCT does not confirm the positive interim signal. Taken with REDUCE-AKI, the contemporary TAVR evidence is mixed: two positive studies (PROTECT-TAVI, Visconti pilot) and two negative randomized trials (REDUCE-AKI, this trial) in mostly mild-to-moderate CKD. The original positive trial (PROTECT-TAVI) enrolled patients with more severe CKD; ongoing TAVR work focuses on identifying the subpopulation most likely to benefit.

4. ICU / Rhabdomyolysis

Rhabdomyolysis is a clinical setting in which urine-output-targeted fluid therapy is standard of care, but manual titration is operator-intensive and prone to under- or over-resuscitation. A single-center service evaluation at the Royal London Hospital examined whether automating matched fluid management with RenalGuard improves the achievement of target urine output without precipitating fluid overload, providing the first ICU-context evidence for the device.

Primary clinical evidence

27. Beilstein / Prowle / Kirwan (2016) · Automated Fluid Management for Treatment of Rhabdomyolysis

Beilstein CM, Prowle JR, Kirwan CJ. Automated Fluid Management for Treatment of Rhabdomyolysis. Int J Nephrol. 2016;2016:2932593. doi:10.1155/2016/2932593.

Link: https://doi.org/10.1155/2016/2932593

Design: Single-center clinical service evaluation (Royal London Hospital, Barts Health NHS Trust). Convenience sample comparison of automated vs manual fluid management.

Population: 36 critically ill adults with rhabdomyolysis: 8 treated with RenalGuard automated fluid management vs 28 managed with manual fluid adjustment per standard rhabdomyolysis protocol.

Intervention vs Comparator: RenalGuard arm: automated, real-time matched IV crystalloid replacement targeting high urine output. Standard arm: manual fluid adjustment per institutional rhabdomyolysis protocol (bolus and titration). Both arms used loop diuretics and bicarbonate per protocol.

Primary Endpoint: Number of hours with urine output >2 mL/kg during the first 48 h of therapy.

Key Result: Hours at target urine output 176/312 (56.4%) RenalGuard vs 534/1,305 (40.9%) standard (p<0.01). Median urine output in the first 24 h higher with RenalGuard (4,033 mL [IQR

3,682–7,363] vs 2,913 mL [2,263–4,188]; p<0.01). Fluid balance, electrolytes, diuretic use, and bicarbonate use comparable between groups — i.e., higher urine output was not bought at the price of larger positive fluid balance or worse electrolyte control.

Clinical Significance: First evidence that automated matched fluid management can improve achievement of target urine output in rhabdomyolysis without inducing fluid overload — extending the RenalGuard mechanism into a non-procedural ICU context where urine-output-guided therapy is already standard but manually delivered.

5. Clinical Practice Guidelines and Multisociety Consensus Documents

The RenalGuard mechanism — furosemide-driven forced diuresis with matched intravenous hydration — has been incorporated into European clinical practice guidelines and a national multisociety consensus on contrast-induced acute kidney injury. The three documents below trace that recognition: the 2014 and 2018 iterations of the joint ESC/EACTS Guidelines on Myocardial Revascularization, and the 2019 SICI-GISE / SIN consensus document. Across these documents, furosemide with matched hydration is the only device-mediated CI-AKI prevention strategy named in the European guideline tradition.

European Society of Cardiology / EACTS

28. 2014 ESC/EACTS Revascularization Guidelines · 2014 ESC/EACTS Guidelines on Myocardial Revascularization

Windecker S, Kolh P, Alfonso F, Collet J-P, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann F-J, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2014;35(37):2541–2619. doi:10.1093/eurheartj/ehu278.

Link: https://doi.org/10.1093/eurheartj/ehu278

Summary: Joint clinical practice guideline of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery, developed with the EAPCI. Section 11.2 covers prevention of contrast-induced nephropathy. For moderate-to-severe CKD undergoing coronary angiography or PCI, the table recommends isotonic saline hydration (Class I, Level A), low- or iso-osmolar contrast media (Class I, A), minimized contrast volume (Class IIa, B), and short-term high-dose statins (Class IIa, A). N-acetylcysteine and sodium bicarbonate in place of standard hydration are explicitly not recommended (Class III, A). The forced-diuresis-with-matched-hydration entry — the RenalGuard mechanism — reads: "Furosemide with matched hydration may be considered over standard hydration in patients at very high risk for CIN or in cases where prophylactic hydration before the procedure cannot be accomplished" — Class IIb, Level A, citing MYTHOS (Marenzi 2012) and REMEDIAL II (Briguori 2011). The protocol specified in the guideline (250 mL saline bolus over 30 min, reduced to 150 mL if LV dysfunction; furosemide 0.25–0.5 mg/kg; target urine output >300 mL/h; matched infusion maintained intra-procedure and for 4 h post-procedure) is the RenalGuard operating protocol. Prophylactic haemofiltration before complex PCI in severe CKD is Class IIb, B; routine prophylactic renal replacement therapy is Class III, B.

29. 2018 ESC/EACTS Revascularization Guidelines · 2018 ESC/EACTS Guidelines on Myocardial Revascularization (Update)

Neumann F-J, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet J-P, Falk V, Head SJ, Jüni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019;40(2):87–165. doi:10.1093/eurheartj/ehy394.

Link: https://doi.org/10.1093/eurheartj/ehy394

Summary: Updated joint ESC/EACTS/EAPCI guideline. Section 10.2 covers prevention of contrast-induced nephropathy. Risk assessment for CI-AKI in all patients is now Class I, C, and adequate hydration is Class I, C generally. For moderate or severe CKD (NKF stages 3b–4), low- or iso-osmolar contrast media is Class I, A; minimized contrast volume (total contrast/GFR <3.7) is Class I, B; pre- and post-hydration with isotonic saline at 1 mL/kg/h for 12 h pre and 24 h post (0.5 mL/kg/h if LVEF ≤35% or NYHA >2) is Class IIa, C when expected contrast volume exceeds 100 mL. The forced-diuresis-with-matched-hydration entry — the RenalGuard mechanism — has been preserved and broadened: "As an alternative to the pre- and post-hydration regimen, tailored hydration regimens may be considered" — Class IIb, Level B. The footnote defining tailored hydration explicitly names two options: CVP-guided saline infusion (POSEIDON) and furosemide with matched infusion of normal saline. Supporting references for the latter are REMEDIAL II (RenalGuard) and the Putzu 2017 JACC Cardiovasc Interv systematic review and meta-analysis. N-acetylcysteine and sodium bicarbonate were removed from the recommendations table in this update.

Italian Multi-Society Consensus (SICI-GISE / SIN)

30. SICI-GISE / SIN Consensus (F. Ronco 2019) · SICI-GISE / SIN Consensus Document: Contrast-Induced AKI in Interventional Cardiology

Ronco F, Azzalini L, Briguori C, Cosmai L, D'Amico M, Di Luca M, Esposito G, Granatelli A, Maddestra N, De Marco F, La Manna A, Maioli M, Musumeci G, Tarantino F, Venturelli C, Brunori G, Tarantini G. Documento di consenso SICI-GISE/SIN: Danno renale acuto da mezzo di contrasto in cardiologia interventistica [SICI-GISE/SIN Consensus Document: Contrast-induced acute kidney injury in interventional cardiology]. G Ital Cardiol (Rome). 2019;20(9 Suppl 1):29S–43S. doi:10.1714/3219.31966. [Italian.]

Link: https://doi.org/10.1714/3219.31966

Summary: Formal joint consensus document of the Italian Society of Interventional Cardiology (SICI-GISE) and the Italian Society of Nephrology (SIN). 16-member multidisciplinary panel of interventional cardiologists and nephrologists. Scope covers definition, epidemiology, risk stratification, contrast-agent selection, pharmacologic prophylaxis, hydration strategies, device-based prevention, and post-procedural management of CI-AKI. A dedicated section addresses the question "Are there data suggesting the use of devices for reducing the risk of contrast-induced AKI?" — and identifies RenalGuard by name. Translated from the Italian (p. 39S): "The RenalGuard device allows adequate fluid replacement, modulated by euvolemic control, during forced diuresis induced by diuretics. On this basis, the device has been proposed as a tool for the prevention of CI-AKI. In the randomized REMEDIAL II study, the use of RenalGuard proved superior in preventing CI-AKI compared with treatment with N-acetylcysteine and bicarbonate in high-risk patients. In a study of 400 patients at high risk of CI-AKI with reduced eGFR, RenalGuard was shown to be a safe device,

with greater efficacy when used to maintain intraprocedural forced diuresis ≥450 mL/h." Supporting citations are REMEDIAL II (Briguori Circulation 2011) and the Briguori AHJ 2016 real-world registry. Lead author: Federico Ronco, interventional cardiologist at Ospedale dell'Angelo, Mestre/Venice.

About this document

This annotated bibliography was compiled by CardioRenal Systems and it is intended as a reference for nephrologists, critical care physicians, interventional cardiologists, and cardiac surgeons. Citations reflect the source documents in the CardioRenal Systems publications library. Where a study's result was negative or its interpretation contested (STRENGTH; REDUCE-AKI; Voigtländer-Buschmann 2023), this document presents both the published findings and the relevant counterpoints from the broader literature, including the 2023 Briguori et al. editorial that quantified the STRENGTH trial's effective power at 0.55.

Categorization of entries as "primary clinical evidence," "mechanistic evidence," "meta-analysis," "editorial commentary," or "recent reviews" is based on whether the paper reports original RenalGuard clinical trial or registry data and on the role the paper plays in interpreting that evidence.