CE Mark

US: Investigational device. Limited by Federal Law to investigational use only.

RenalGuard
Protection from Acute Kidney Injury

RenalGuard®

Learning Objectives

At the end of this presentation, you will understand:

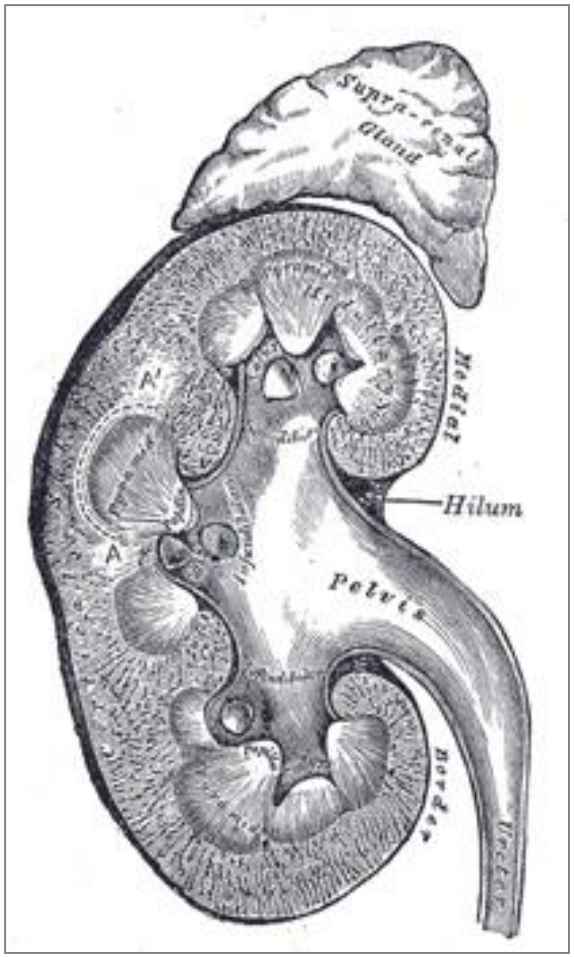
- The Basics of CIN causes and outcomes
- How RenalGuard Therapy was Developed
- The Basics of RenalGuard Therapy
- The impact RenalGuard Therapy has on CIN rates

Kidney Demands Respect

20% of Cardiac Output dedicated to the kidney for good reason.

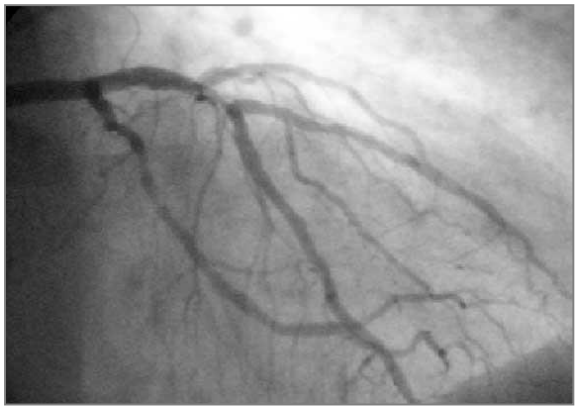
Proper Kidney function required to:

- Clear waste
- Maintain extracellular environment
- Balance water and electrolytes
- Regulate systemic and renal hemodynamics
- Secrete hormones to support other processes, including:
  - EPO to stimulate red blood cell formation
  - Calcitriol to influence bone metabolism



Contrast-Induced Nephropathy (CIN): Short-Term Insult with Long-Term Impact

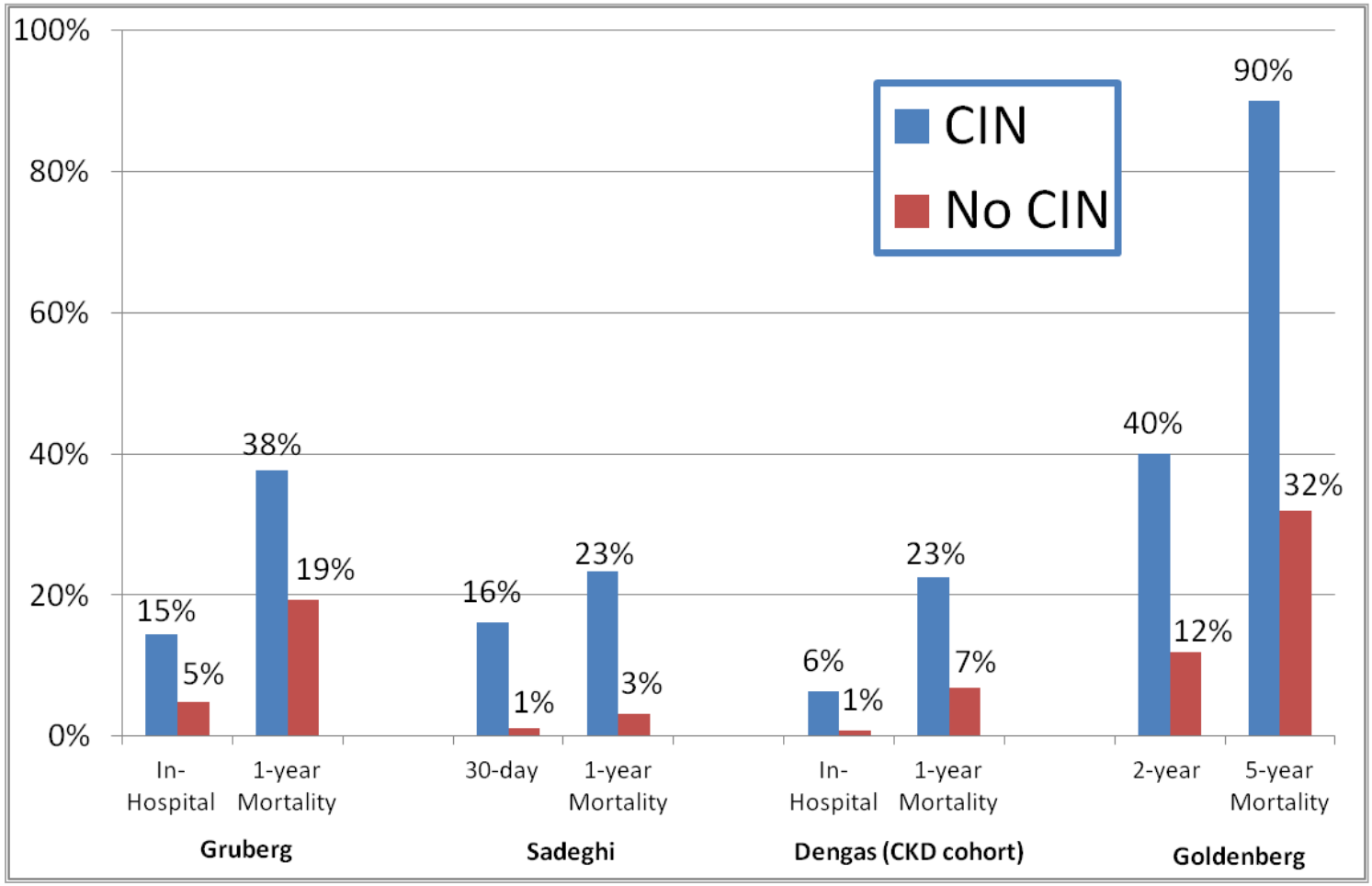
- Contrast toxic to kidney cells- 40% of nephrons put in contrast for 15 minutes did not survive[1]



- Contrast media(CM) begins as a viscous fluid and is further concentrated in the nephron- urine viscosity can be higher than native contrast media further worsening hypoxia[2].
- Combination of Ischemia, hypoxia, increased viscosity and toxicity of contrast creates a vicious cycle, worsening effect of each insult.
- This short term insult can only be diagnosed by measuring a rise in serum creatinine 2-4 days after exposure, so many patients develop CIN without diagnosis.
- Even though most CIN insults do not require dialysis, a spike in serum creatinine, even if it returns to baseline, has been associated with increased morbidity and mortality.

[1]Romano et al. *Eur. Heart J.* 2008.
[2] Persson et al. *Eur. Heart J.* 2012.

CIN's Long Term Impact



Rise in serum creatinine, *even if it returns to baseline*, predicts significant increase in mortality.

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Gruberg et al. *J. Am. Coll. Cardiol.* 2000.
Dangas et al. *Am. J. Cardiol.*
Sadeghi et al. *Circulation*. 2003.
Goldenberg et al. *Am. J. Nephrol.* 2009.

CIN rates remain Too High

- Hydration is the most recommended prevention-- CIN rates still unacceptably high[1]
- N-acetylcysteine provides no benefit[2]
- Sodium Bicarbarbonate provides no clear benefit[3]
- Recent, well conducted US trials have still reported rates as high as 25% in at-risk patients. [4]

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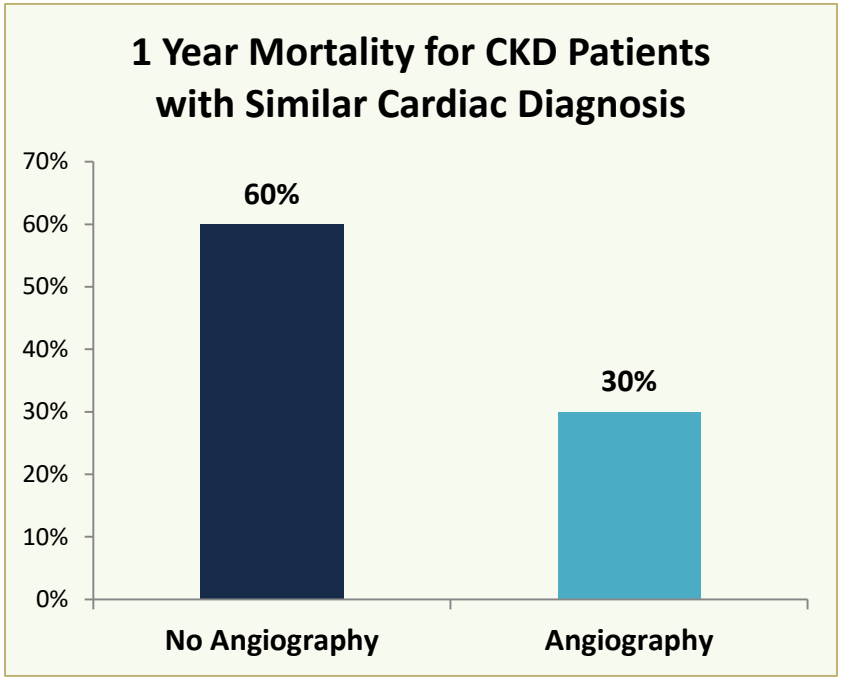
[1] Wijns et al. *Euro Heart J* 2010;31:2501-2555
[2] ACT Investigators. *Circulation* 2011;124(11):1250-9.
[3] Brar et al. *JAMA* 2008;300(9):1038–46.
[4] CARIN *ACC* 2016, AVERT *SCAI* 2016

Withholding Catheterization Not the Answer

- In a review of matched group of Medicare patients with cardiac diagnosis, 25% of patients with chronic kidney disease (CKD) received catheterization, compared to 47% of patients with similar cardiac diagnosis without CKD
- This “Renalism”, resulted in one year mortality for CKD patients who did not receive angiography of 60%, compared to 30% mortality for patients who did receive angiography
- In many cases, patient is still better off receiving catheterization than not
- Often, CKD patients have worsened cardiac disease due to their renal dysfunction



Need a solution that allows patients with poor renal function and cardiac disease to safely undergo procedures using contrast

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Chertow Am Soc of Nephrology 2004.

Dusting off an Old Solution: High Urine Flow

As urine flow increases, so should benefit:

- Shorter exposure time to contrast as urine moves more rapidly through tubules
- Lower concentration of contrast in the urine
- Decreased risk of medullary ischemia
- Less sludging/plugging of the tubules from direct toxicity of contrast to the tubular epithelium
- Should reduce incidence of apoptosis

Long History of Induced Diuresis Trials that Do Not Support the Theory

Study	Total Patients	CIN Rate-Control Group	CIN Rate-Furosemide Group	Favors?
Weinstein [1]	18	n/a	n/a	Control
Solomon[2]	58	11%	40%	Control
Dussol[3]	156	7%	15%	Control
Majumdar[4]	92	28%	50%	Control

What went wrong?

What do they have in common?

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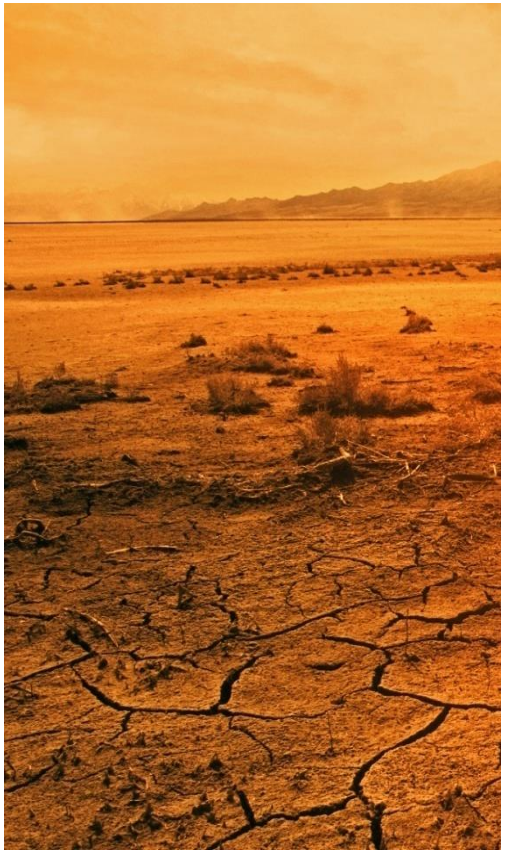
[1]Weinstein *Nephron* 1992; [2]Solomon *NEJM* 1994;
[3]Dussol *Nephrol Dial Transplant* 2006; [4]Majumdar *Am J Kidney Dis.* 2009

What Went Wrong?

Study	Dose of Furosemide	Weight change Control	Weight change Furosemide
Weinstein [1]	110 mg	+1.30 kg	-0.70 kg
Solomon[2]	80 mg	-0.49 kg	-0.78 kg
Dussol[3]	3 mg/kg	+0.13 kg	-0.46 kg
Majumdar[4]	100 mg	Control gained 266 ml more than furosemide group	



In the first three studies, no formal attempt was made to replace the fluid. In the Majumdar study, an attempt was made (hourly replacement) but still less fluid was given than was lost.

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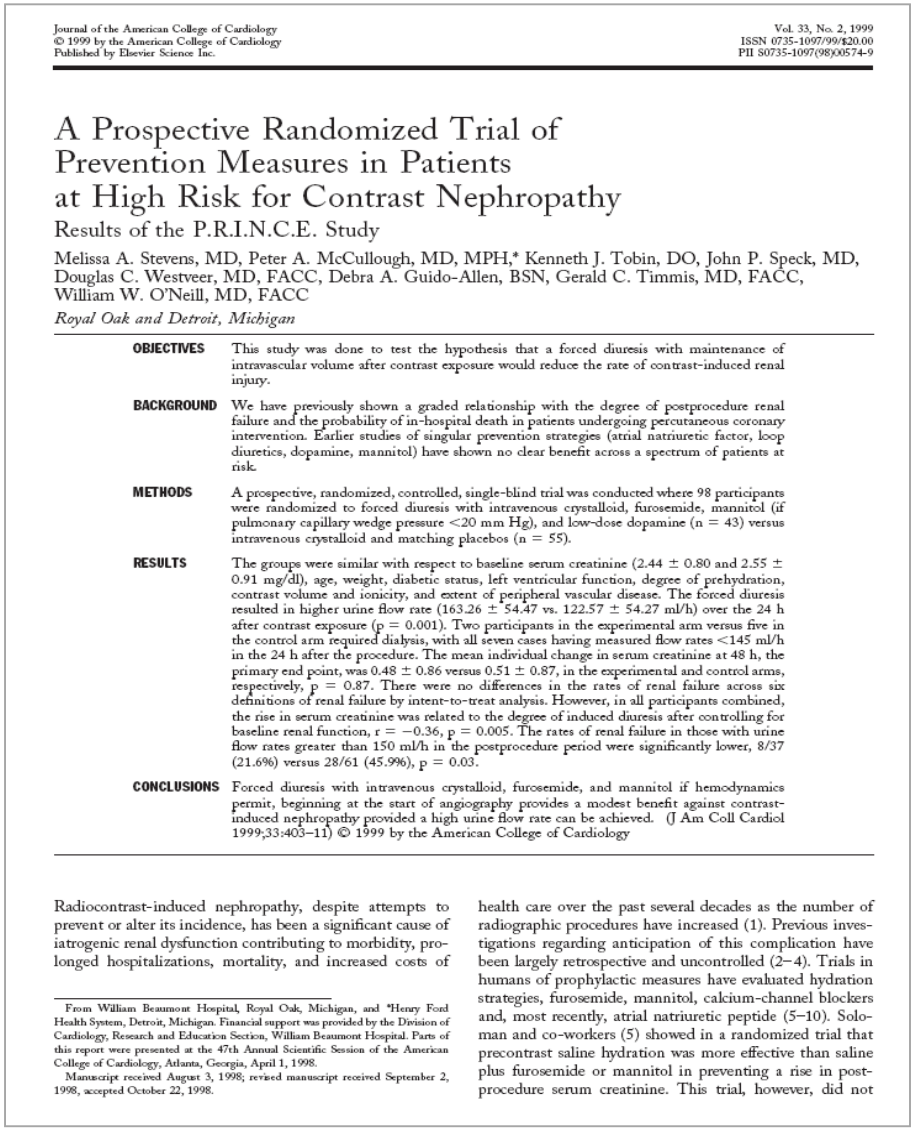
[1]Weinstein *Nephron* 1992; [2]Solomon *NEJM* 1994;
[3]Dussol *Nephrol Dial Transplant* 2006; [4]Majumdar *Am J Kidney Dis.* 2009

Promising Direction
Prince Study 1999

Prince Study demonstrated high urine flow may provide a benefit against contrast-induced nephropathy:

- Urine flow rates above 150 ml/hr showed a 50% reduction in rates of acute renal failure
- Most patients not able to reach 150 ml/hr urine rate
- Not optimal because the hydration protocol was a fixed amount and not matched to each individual's response



Journal of the American College of Cardiology
© 1999 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 33, No. 2, 1999
ISSN 0735-1097/99/$20.00
PII S0735-1097(98)00574-9

A Prospective Randomized Trial of Prevention Measures in Patients at High Risk for Contrast Nephropathy

Results of the P.R.I.N.C.E. Study

Melissa A. Stevens, MD, Peter A. McCullough, MD, MPH,* Kenneth J. Tobin, DO, John P. Speck, MD, Douglas C. Westveer, MD, FACC, Debra A. Guido-Allen, BSN, Gerald C. Timmis, MD, FACC, William W. O'Neill, MD, FACC

Royal Oak and Detroit, Michigan

OBJECTIVES This study was done to test the hypothesis that a forced diuresis with maintenance of intravascular volume after contrast exposure would reduce the rate of contrast-induced renal injury.

BACKGROUND We have previously shown a graded relationship with the degree of postprocedure renal failure and the probability of in-hospital death in patients undergoing percutaneous coronary intervention. Earlier studies of singular prevention strategies (atrial natriuretic factor, loop diuretics, dopamine, mannitol) have shown no clear benefit across a spectrum of patients at risk.

METHODS A prospective, randomized, controlled, single-blind trial was conducted where 98 participants were randomized to forced diuresis with intravenous crystalloid, furosemide, mannitol (if pulmonary capillary wedge pressure <20 mm Hg), and low-dose dopamine (n = 43) versus intravenous crystalloid and matching placebos (n = 55).

RESULTS The groups were similar with respect to baseline serum creatinine (2.44 ± 0.80 and 2.55 ± 0.91 mg/dl), age, weight, diabetic status, left ventricular function, degree of prehydration, contrast volume and ionicity, and extent of peripheral vascular disease. The forced diuresis resulted in higher urine flow rate (163.26 ± 54.47 vs. 122.57 ± 54.27 ml/h) over the 24 h after contrast exposure ($p = 0.001$). Two participants in the experimental arm versus five in the control arm required dialysis, with all seven cases having measured flow rates <145 ml/h in the 24 h after the procedure. The mean individual change in serum creatinine at 48 h, the primary end point, was 0.48 ± 0.86 versus 0.51 ± 0.87, in the experimental and control arms, respectively, $p = 0.87$. There were no differences in the rates of renal failure across six definitions of renal failure by intent-to-treat analysis. However, in all participants combined, the rise in serum creatinine was related to the degree of induced diuresis after controlling for baseline renal function, $r = -0.36$, $p = 0.005$. The rates of renal failure in those with urine flow rates greater than 150 ml/h in the postprocedure period were significantly lower, 8/37 (21.6%) versus 28/61 (45.9%), $p = 0.03$.

CONCLUSIONS Forced diuresis with intravenous crystalloid, furosemide, and mannitol if hemodynamics permit, beginning at the start of angiography provides a modest benefit against contrast-induced nephropathy provided a high urine flow rate can be achieved. (J Am Coll Cardiol 1999;33:403–11) © 1999 by the American College of Cardiology

Radiocontrast-induced nephropathy, despite attempts to prevent or alter its incidence, has been a significant cause of iatrogenic renal dysfunction contributing to morbidity, prolonged hospitalizations, mortality, and increased costs of health care over the past several decades as the number of radiographic procedures have increased (1). Previous investigations regarding anticipation of this complication have been largely retrospective and uncontrolled (2–4). Trials in humans of prophylactic measures have evaluated hydration strategies, furosemide, mannitol, calcium-channel blockers and, most recently, atrial natriuretic peptide (5–10). Soloman and co-workers (5) showed in a randomized trial that precontrast saline hydration was more effective than saline plus furosemide or mannitol in preventing a rise in postprocedure serum creatinine. This trial, however, did not

From William Beaumont Hospital, Royal Oak, Michigan, and *Henry Ford Health System, Detroit, Michigan. Financial support was provided by the Division of Cardiology, Research and Education Section, William Beaumont Hospital. Parts of this report were presented at the 47th Annual Scientific Session of the American College of Cardiology, Atlanta, Georgia, April 1, 1998.

Manuscript received August 3, 1998; revised manuscript received September 2, 1998, accepted October 22, 1998.

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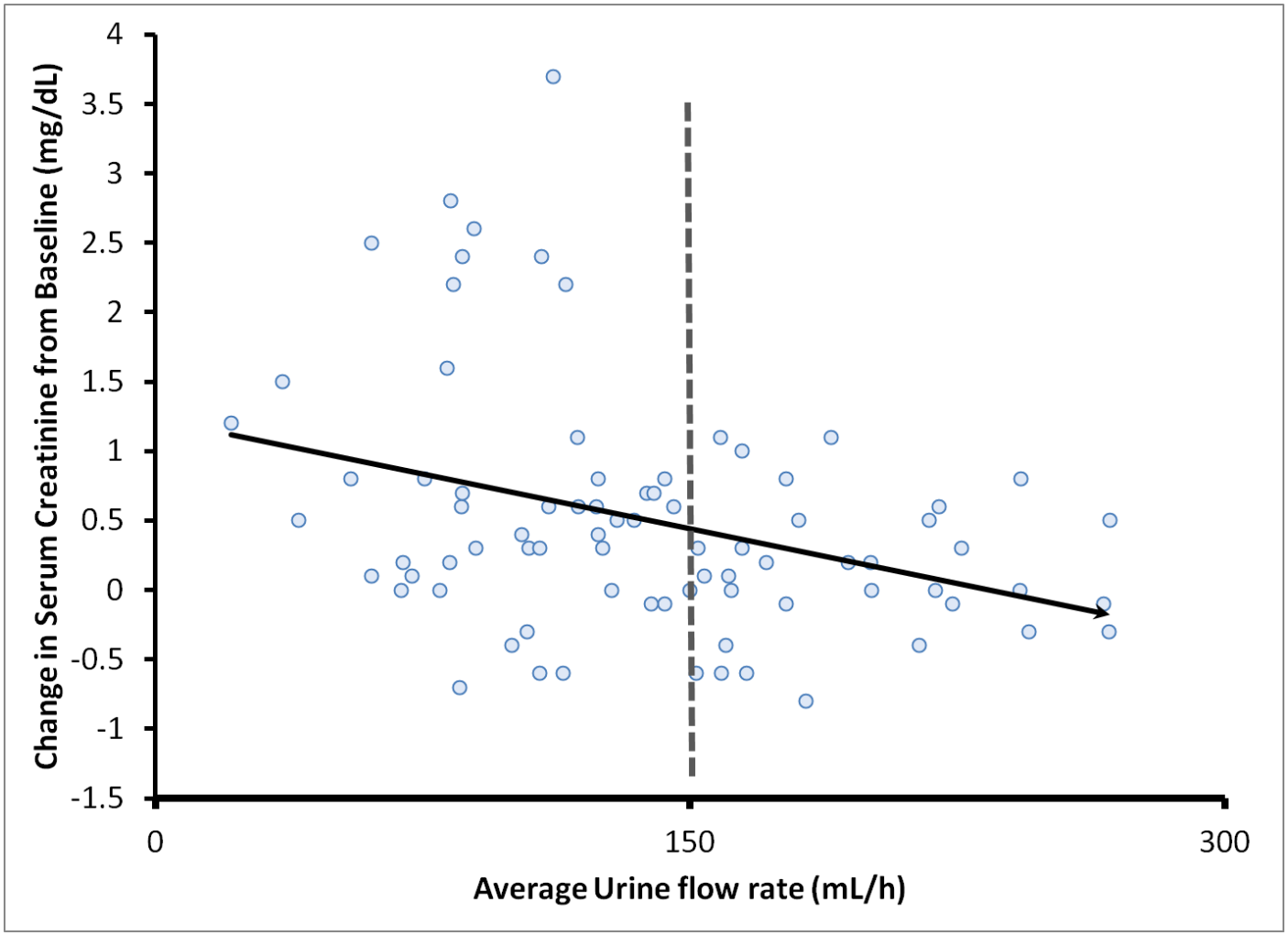
Stevens MA et al. *J Am Coll Cardiol.* 1999. 33:403-411.

Prince: Urine Rates Vs. Change in Creatinine



Rise in serum creatinine decreases as urine rate increases.

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Stevens MA et al. *J Am Coll Cardiol.* 1999. 33:403-411.

Why did PRINCE Results Fail to Impact Clinical Practice?

- Guidelines listed target urine output of 150 ml/hr as a goal for reducing CIN, but no one knew how to help patients actually achieve it.
- No simple way to consistently get patients to reach the urine rates needed to provide protection
- Every patient responds differently to Furosemide
- Tools available at the time to drive high urine rates came with risks:
  - Furosemide: Overwhelming data link the drug to higher rates of CIN
  - High volumes of Saline: Patient variability makes dosing very difficult- too much fluid risks fluid overload, too little risks dehydrating the patient

RenalGuard for CI-AKI prevention

RenalGuard® enables the benefits of high urine flows while preventing the negative effects of dehydration:

- **Automated fluid replacement**
  - Enables administration of diuretics
  - Mitigates risk of over/under hydration
- **Matched replacement + diuretic induces high urine flow**
  - Helps to rapidly clear renal toxins
  - Flushing prevents contrast from clogging tubules
- **Seamless integration**
  - Easily incorporated into existing lab workflow

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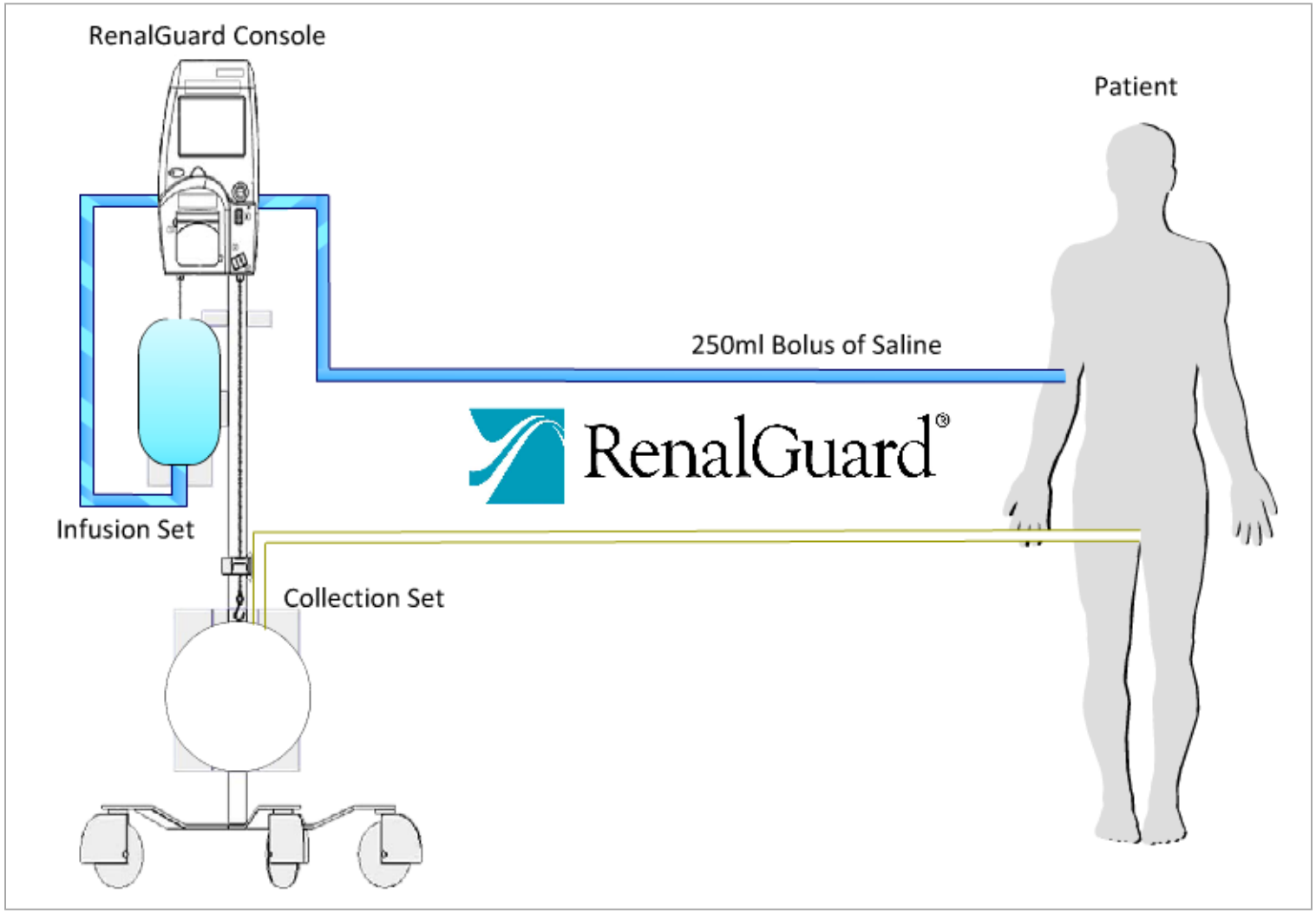
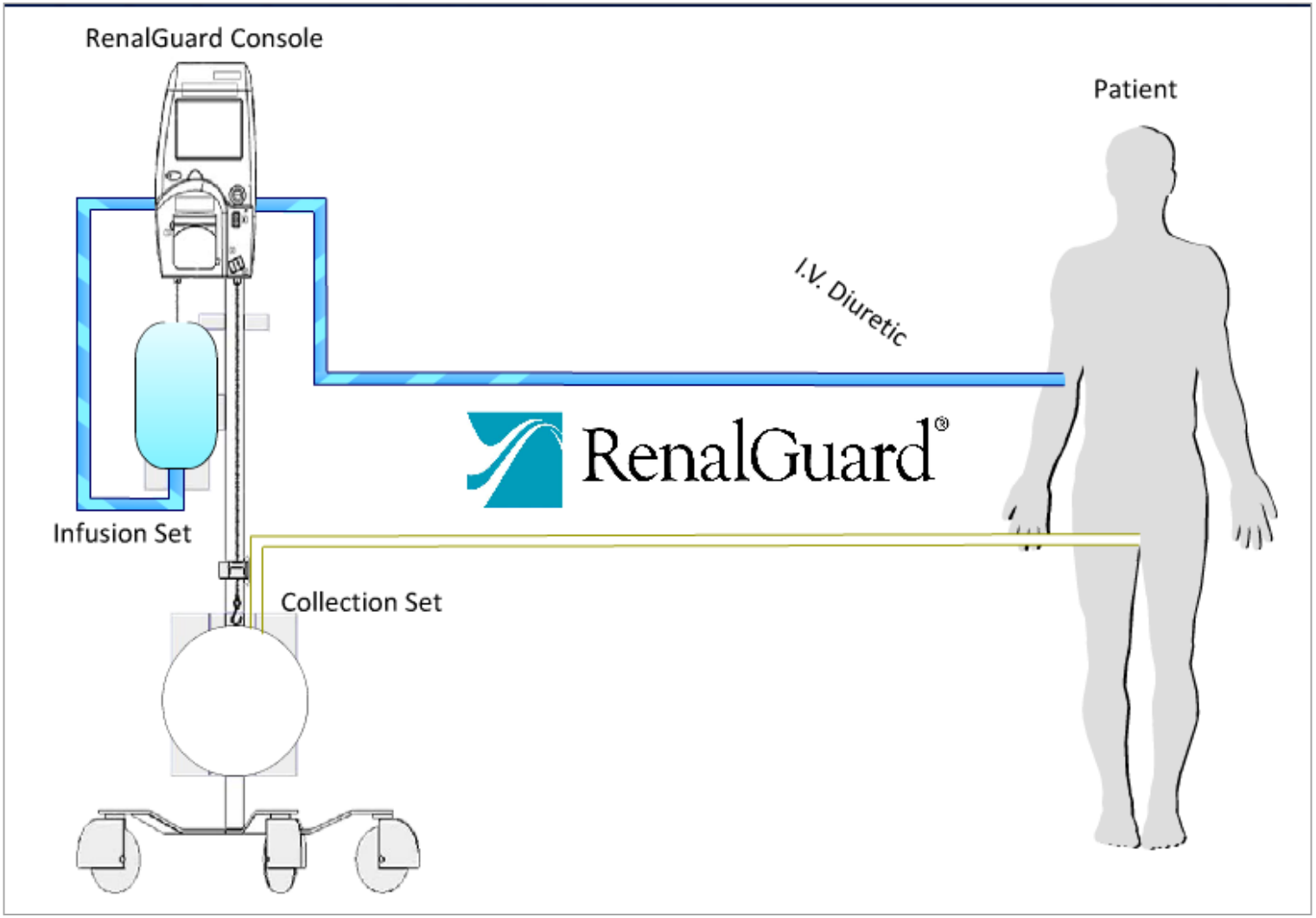
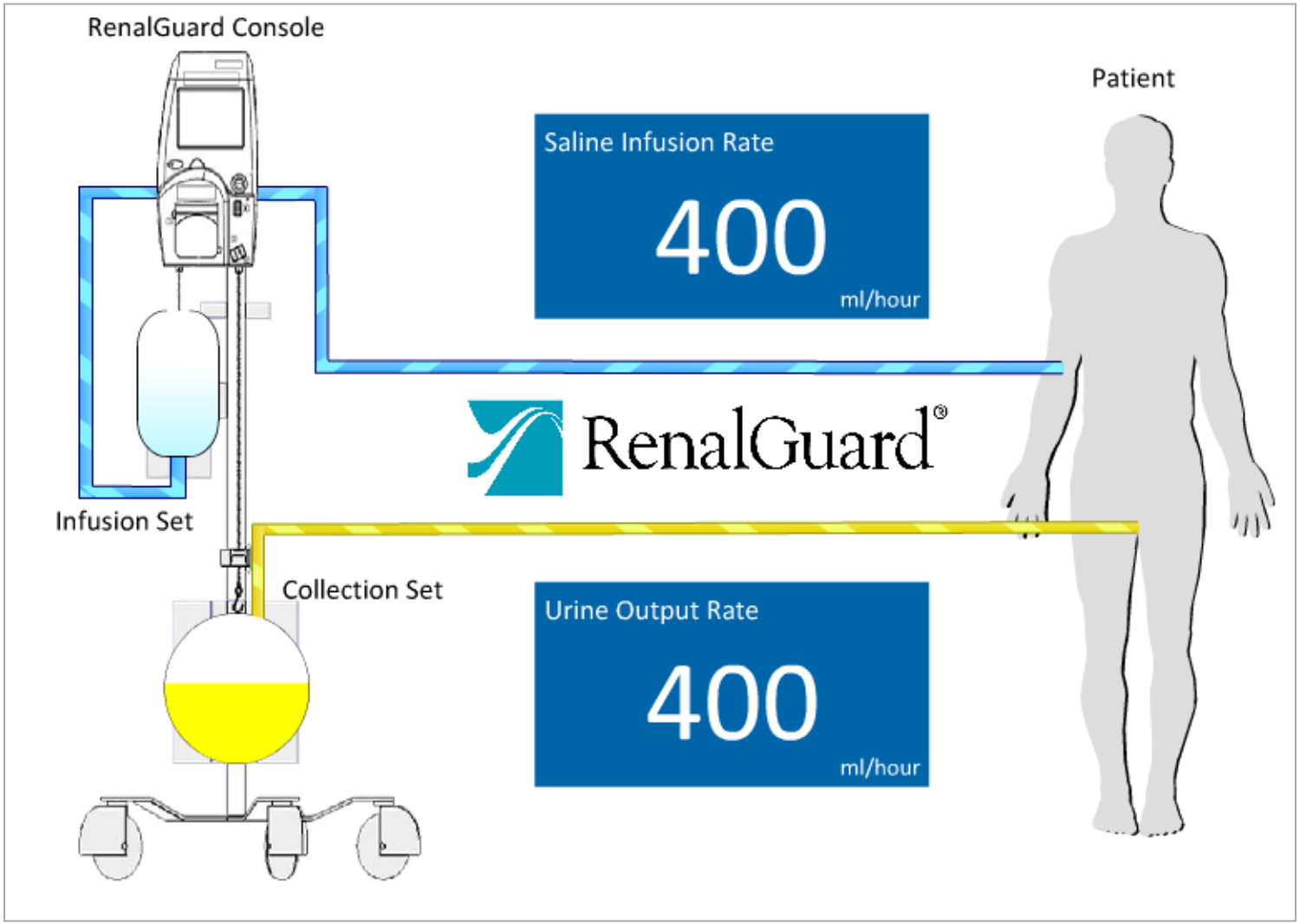
RenalGuard in Clinical Use



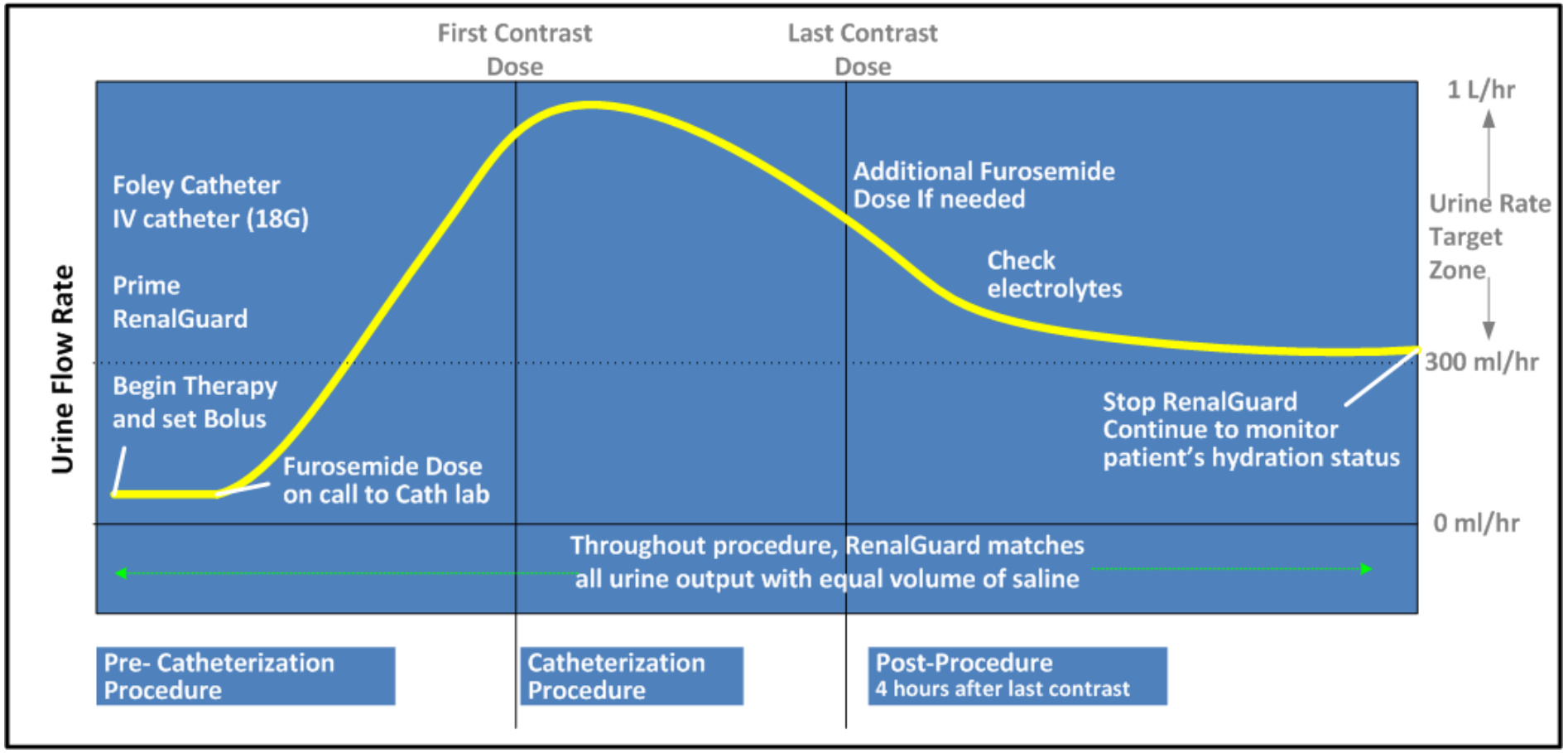
RenalGuard in Clinical Use



RenalGuard in Clinical Use



RenalGuard Therapy:
Integrates into current Cath Lab Flow



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RenalGuard for AKI prevention mechanism of action

Flush poisons out of kidneys

Reduces Oxidative stress

Promote and monitor urine output

- Creates and maintains high urine flow rates
- Rapidly clears renal toxins
- Prevents contrast from clogging tubules
- Avoids injury to kidneys

- High urine flow rates make the kidney work less
- Lowers kidneys oxygen requirement
- Less damage from low blood flow
- Less oxidative stress

US Pilot Study

Study Design:

- Single arm feasibility study
- RenalGuard treatment + Cath
- 23 patients eGFR ≤ 50
- 4 Sites

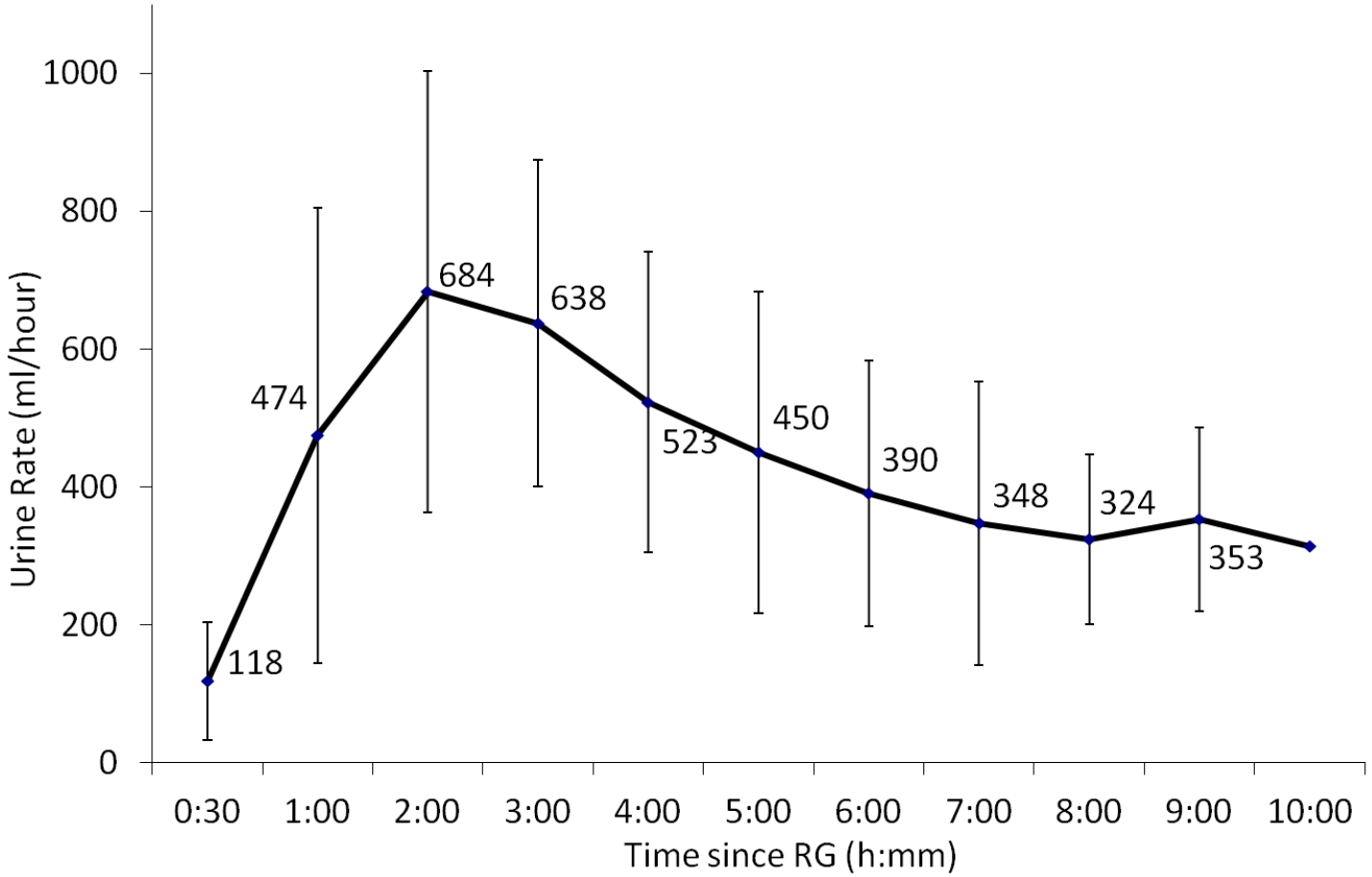
Results:

- All patients achieved the target urine flow at time of contrast exposure

RenalGuard®

Dorval J-F, et al. *International Journal of Cardiology.* 2011.

Pilot Study Urine Rates: High Flow. Large Variability.



Screening eGFR(MDRD): 39.1 + 9.3 (15.5 - 49.9)

RenalGuard®

Dorval J-F, et al. *International Journal of Cardiology.* 2011.

First Randomized Control Trial: MYTHOS

Centro Cardiologico Monzino
Milan, Italy

Patients:

- N=170
- PCI (elective/urgent: 100/70) using Iomeron®
- eGFR ≤ 60 ml/min/1.73m2

Design:

- Primary endpoint:

  CIN (≥0.5 mg/dl, ≥25%, or both within 72 h)
- Secondary endpoint:

  In-hospital major adverse events

Protocol for RenalGuard:

- Standard RenalGuard Therapy
- Furosemide 0.5 mg/kg

Protocol for Control Group:

- Normal saline (1 ml/kg/h for 12 before and 12h after procedure)

RenalGuard®

Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.

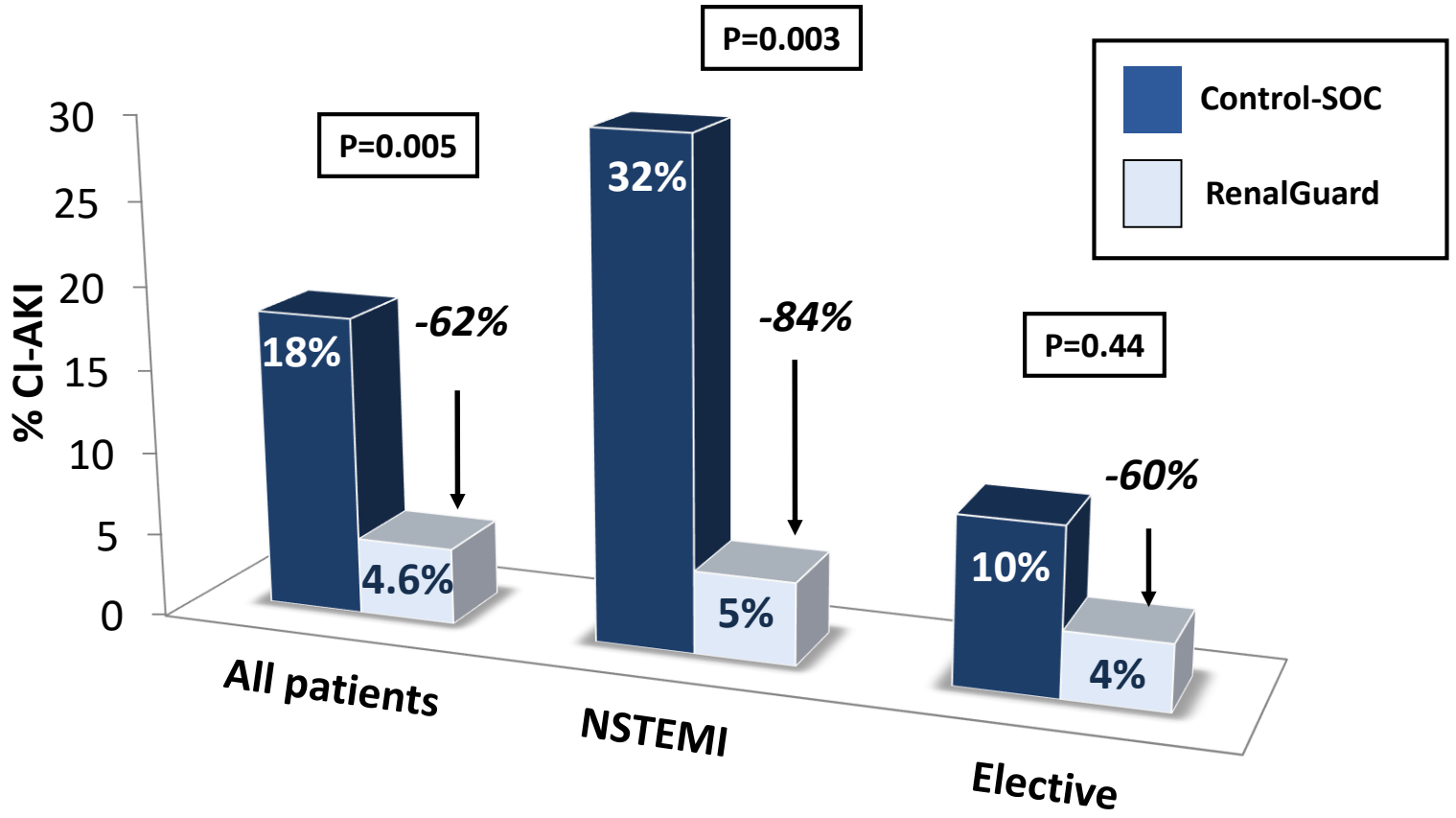
MYTHOS Baseline Clinical and Procedural Characteristics

	RG Group (N=87)	Control Group (n=83)	P-Value
Diabetes mellitus	38 (44%)	29 (35%)	0.24
Serum creatinine (mg/dl)	1.8±0.6	1.7±0.5	0.12
eGFR (ml/min/1.73 m^2)	38±11	41±10	0.17
Contrast volume (ml)	181±104	158±109	0.17

RenalGuard®

Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.

MYTHOS: RenalGuard Reduced the Rate of CI-AKI



RenalGuard-protected patients have over a 60% lower rate of CI-AKI than Standard of Care

RenalGuard®

Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.

RenalGuard significantly reduced in-hospital complications

	RenalGuard Group (N=87)	Control Group (n=83)	P Value
CI-AKI Requiring dialysis	1 (1.1%)	3 (4%)	NS
Acute myocardial infarction	0 (0%)	1 (1.2%)	NS
Atrial fibrillation/VT	1 (1.1%)	2 (2.4%)	NS
Emergency CABG	0 (0%)	0 (0%)	-
Acute pulmonary edema	5 (6%)	10 (12%)	NS
Hypotension/shock	0 (0%)	0 (0%)	-
In-hospital death	1 (1.1%)	3 (4%)	NS
All adverse events (per protocol)	7 (8%)	15 (18%)	0.05

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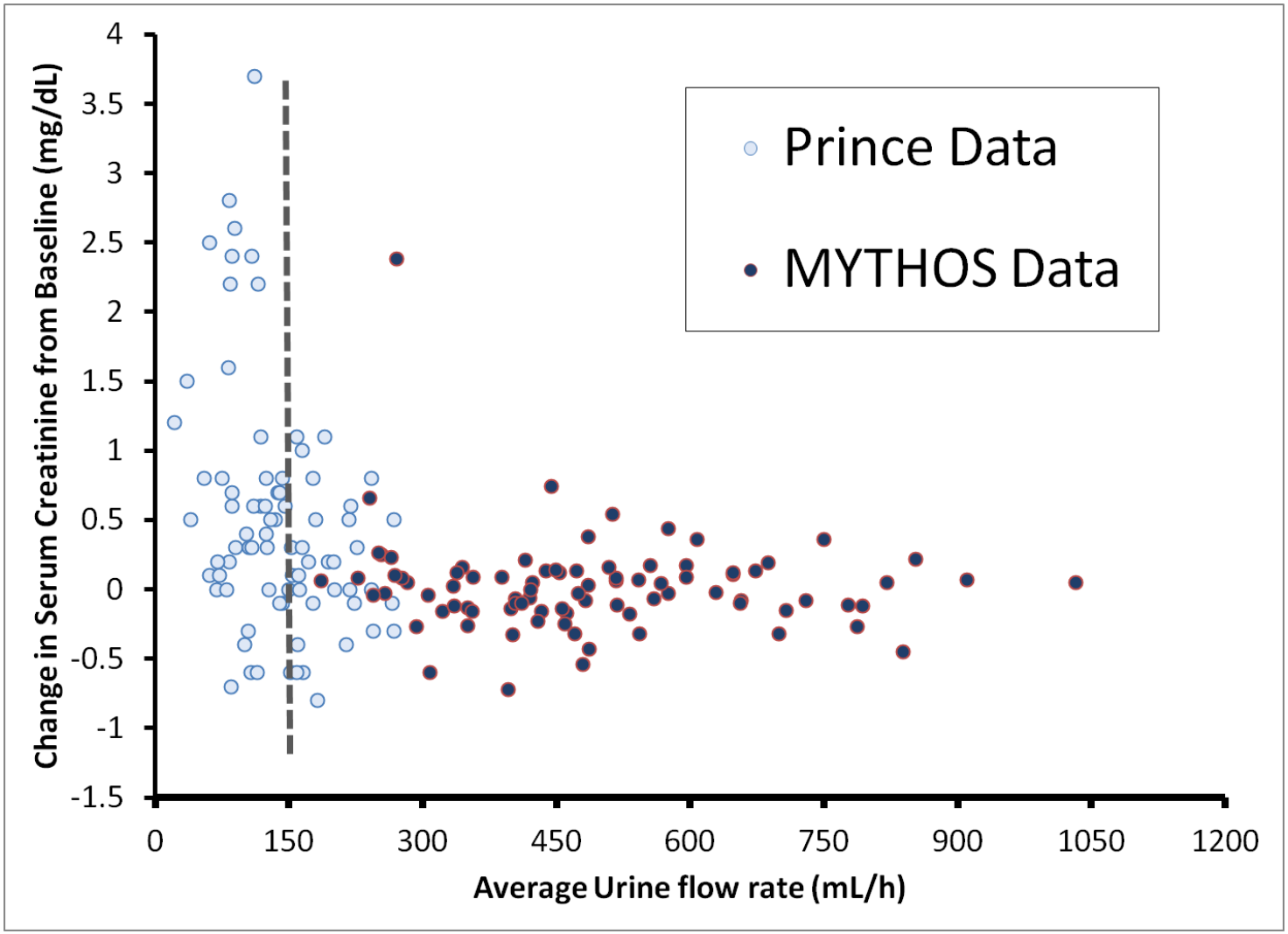
Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.

Comparison of PRINCE Results to MYTHOS



RenalGuard®

Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.
Stevens MA et al. J Am Coll Cardiol. 1999. 33:403-411.

Multi-Center Study: REMEDIAL II

Patients:

- Four Italian Centers
- N=292
- CA ± PCI (elective) or peripheral procedures using Iodixanol
- eGFR ≤ 30 ml/min/1.73m2 or Mehran score ≥ 11

Design:

- Primary endpoint: CIN (≥0.3 mg/dl at 48 h)
- Secondary endpoint: CIN (≥25% increase at 48 h)

Protocol for Control:

- Sodium Bicarbonate (3ml/kg/hr 1 hr, then 1ml/kg/hr until 6 hours post cath)
- N-acetylcysteine (NAC) 1200 mg orally 2x day before and day of cath

Protocol for RenalGuard:

- Standard RenalGuard Therapy
- Furosemide 0.25 mg/kg
- NAC 1.5 g/L IV given with bolus

RenalGuard®

Briguori et al. *Circulation* 2011;124(11):1260-9.

REMEDIAL II
Baseline Characteristics

	Control (n=146)	RenalGuard (n= 146)	P Value
Age	75±9	76±8	0.31
Male	70.5%	60.5%	0.065
BMI (kg/m^2)	29±5	28±5	0.16
LVEF%	48±10	46±11	0.10
Diabetes	71%	69%	0.51
eGFR	32±7	32±9	0.83
Procedure:			
Coronary Angio	41%	35%	0.36
PCI	40%	49%	
Coronary Angio + PCI	11%	7.5%	
Peripheral	6%	9%	
Contrast Volume	145±79	135±76	0.29
Contrast ratio >1	24%	19%	0.32

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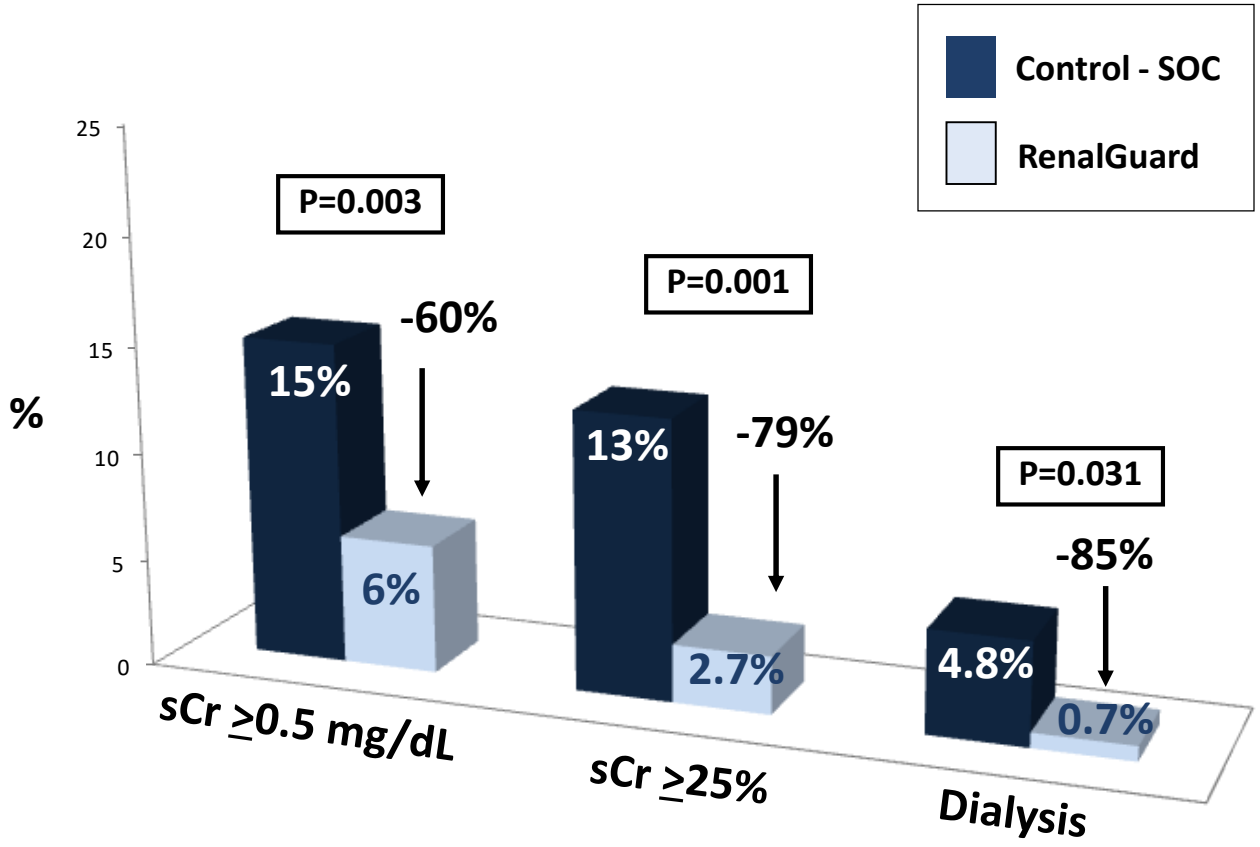
Briguori et al. *Circulation* 2011;124(11):1260-9.

RenalGuard Proven more Effective than Standard of Care



RenalGuard - more effective than standard of care at preventing CI-AKI and Dialysis in at-risk patients

RenalGuard®

Briguori et al. *Circulation* 2011;124(11):1260-9.

Prevention of Post Procedural Acute Kidney Injury in the Catheterization Laboratory in a Real-World Population

Patients:

- Ichilov Medical Center, Tel Aviv, Israel
- Angiography (16%), PCI (51%) and TAVI (33%) procedures using Iodixanol
- Determined by clinicians to be at high-risk of CI-AKI

Design:

- Primary endpoint: CIN (≥0.5 mg/dl, ≥25%, or both within 72 h)
- Compared to matched controls

Protocol for Control:

- Saline prior to procedure and 12 hours post-procedure

Protocol for RenalGuard:

- Standard RenalGuard Therapy
- Furosemide 0.25-0.5 mg/kg
- Followed by normal saline hydration to complete 12 hours post-procedure

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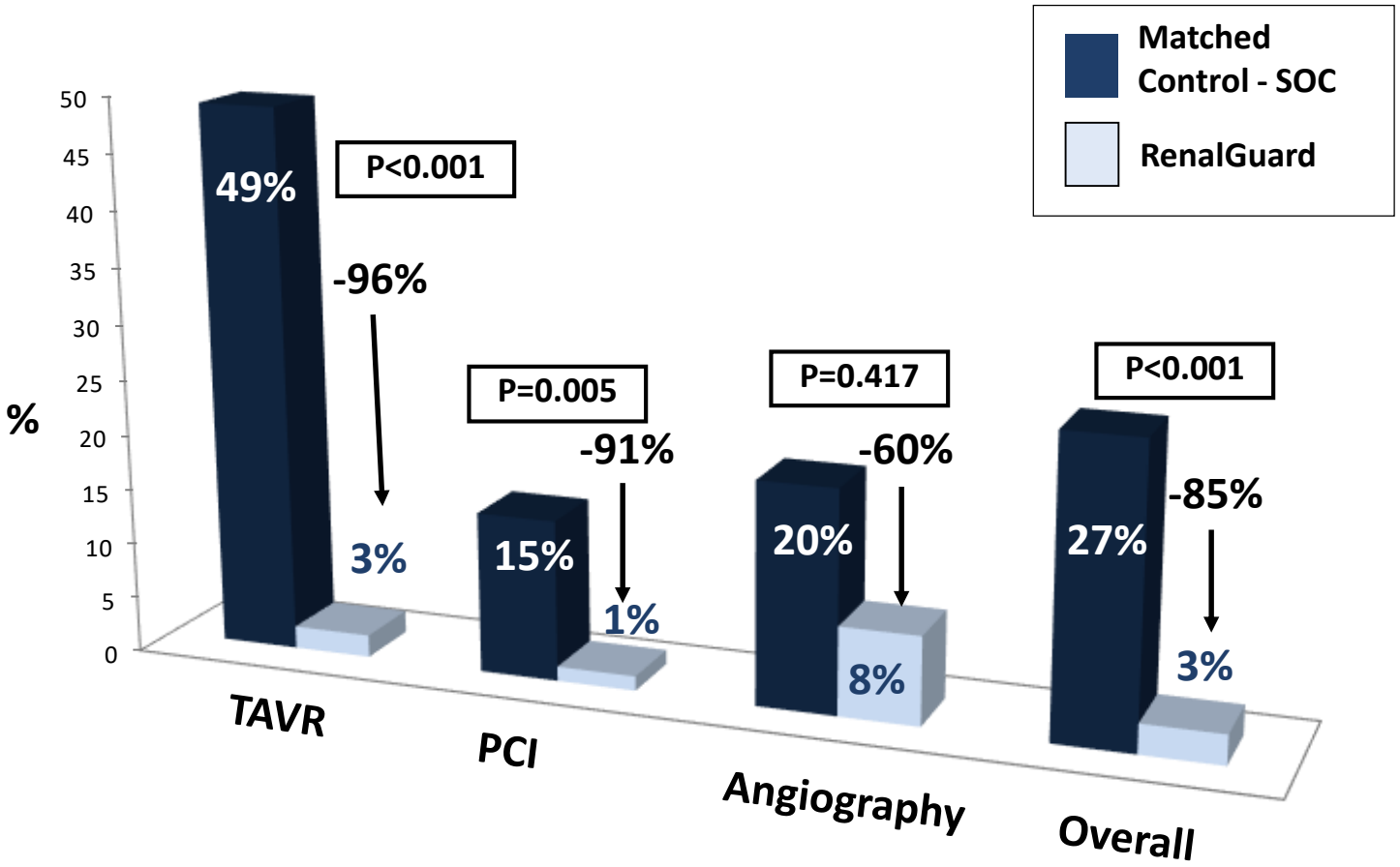
Chorin, et al. Prevention of post procedural acute kidney injury in the catheterization laboratory in a real-world population. *Int J Cardiol*. 2016.

Prevention of Post Procedural Acute Kidney Injury in the Catheterization Laboratory in a Real-World Population



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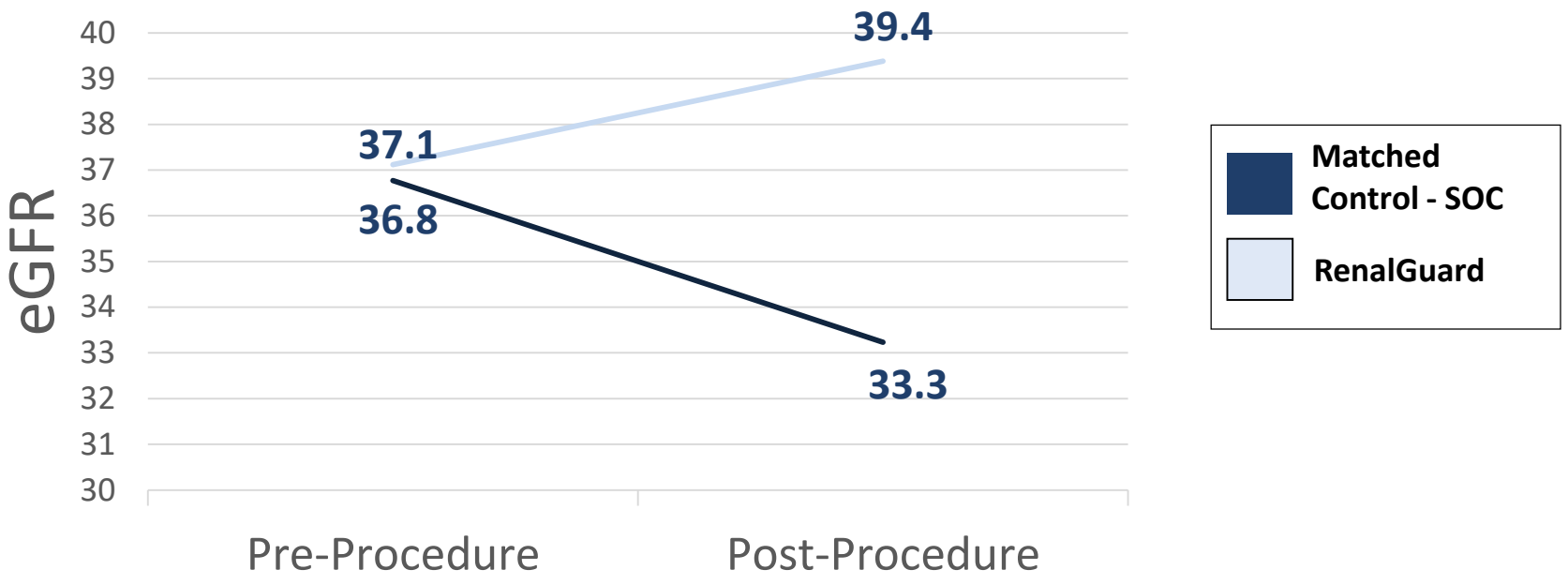
Chorin, et al. Prevention of post procedural acute kidney injury in the catheterization laboratory in a real-world population. *Int J Cardiol*. 2016.

Intriguing Results:



Contrast Volume

"In the present study, we found that contrast volume did not correlate with the incidence of AKI following interventional cardiology procedures."

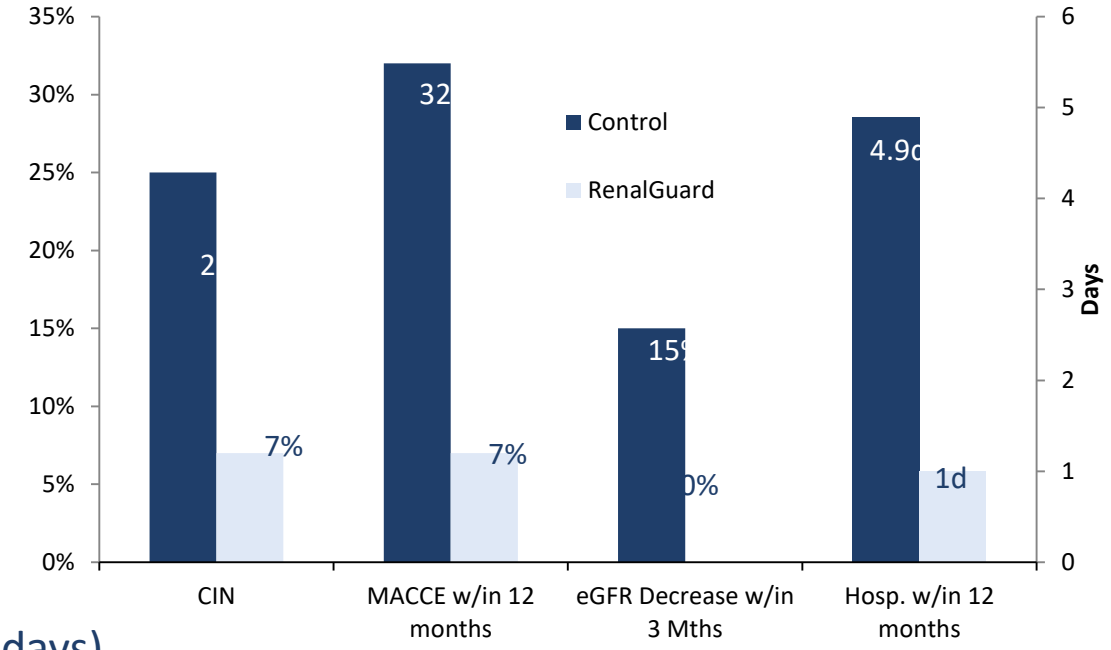
	Control (n=150)	RenalGuard (n= 150)	P Value
Contrast Volume	90±40	96±44	0.087

RenalGuard®

Chorin, et al. Prevention of post procedural acute kidney injury in the catheterization laboratory in a real-world population. *Int J Cardiol*. 2016.

AKIGUARD: Long term follow-up

Investigator Sponsored Trial
Torino, Italy



Patients

- N=133
- CA or PCI (elective) with Iodixanol
- eGFR ≤ 60 (avg eGFR 42)

Design

- RenalGuard vs. Overnight Hydration
- Primary endpoint: CIN (≥0.3 mg/dl at 48 h or 50% w/in 7 days)

Results

- CIN Reduced 72% (p=0.01)
- 12-months MACCE reduced 78 % (p<0.01)
- 12-month days in hospital reduced 80 % (p=0.01)

RenalGuard®

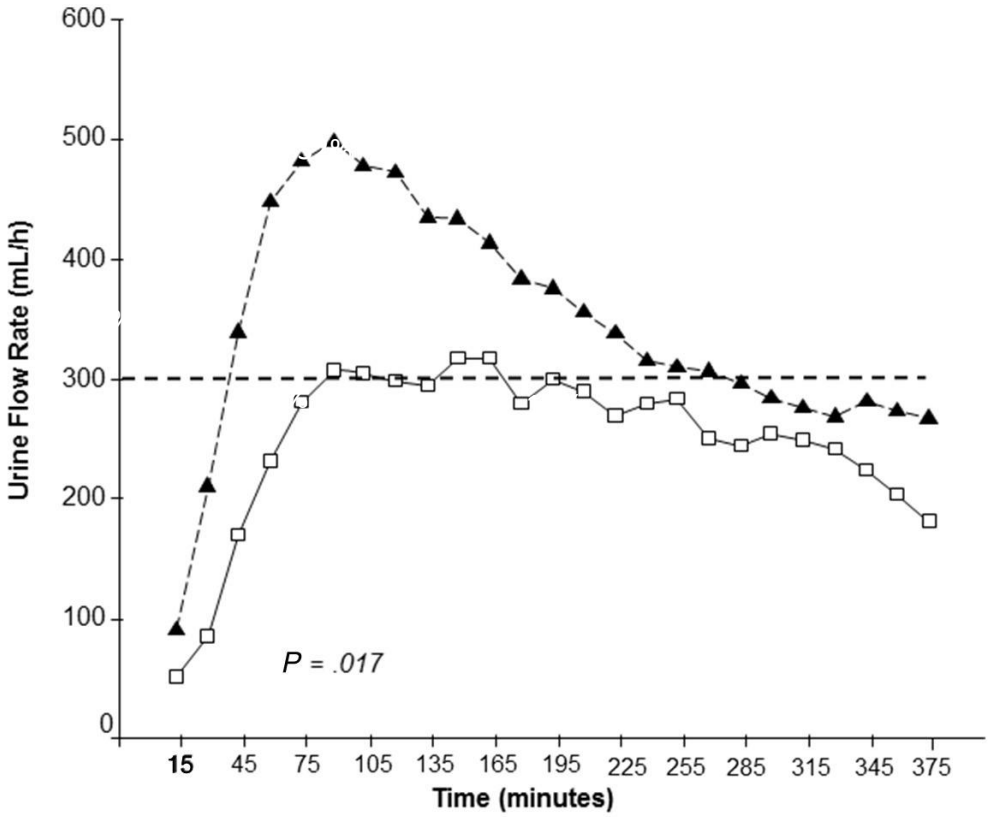
Usmiani T, et al. AKIGUARD (Acute Kidney Injury GUARding Device) trial: in-hospital and one-year outcomes. J Cardiovasc Med. 2015.

RenalGuard System in High-Risk Patients for Contrast-Induced Acute Kidney Injury

Study by Dr. Carlo Briguori (author of REMDIAL II) followed 400 high-risk patients treated with RenalGuard confirmed safety and effectiveness of RenalGuard in normal use.

Reported intriguing relationship between urine output profile and the development of AKI. Suggests:

- High urine output key (>450 ml/hr at peak)
- May be possible to improve RenalGuard Therapy's effectiveness by increasing urine response
- RenalGuard Therapy also has diagnostic potential. In the few patients with low urine output response, clinician may consider being more cautious with contrast usage.



	Pre-CM phase	CM phase	Post-CM phase
CIAKI group □	61±19 min	55 ±40 min	245 ±3 min
No CIAKI group ▲	60 ±23 min	51 ±30 min	243 ±5 min

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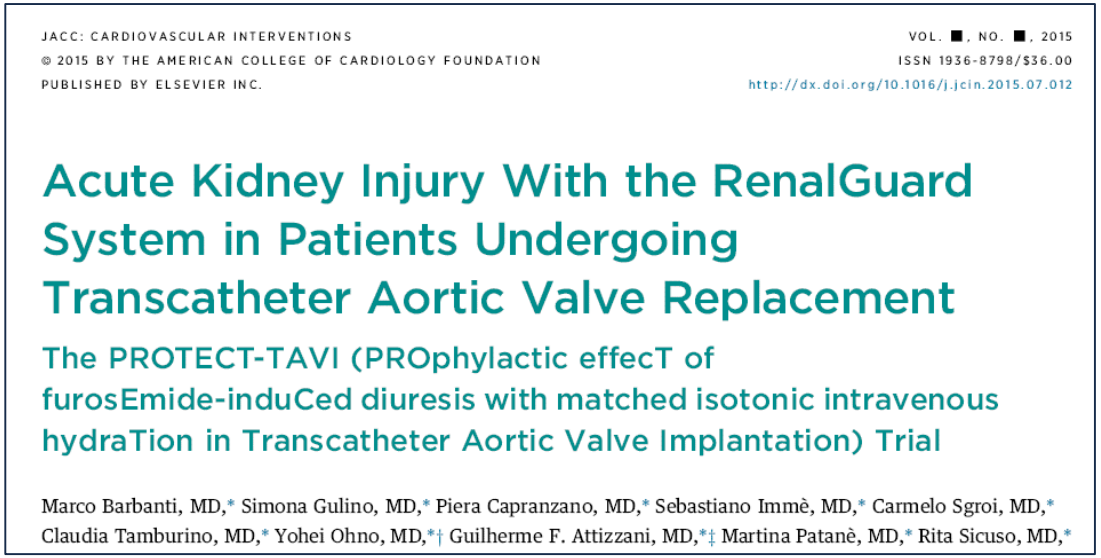
PROTECT-TAVI:
RenalGuard and TAVR[1]

- Rate of AKI after TAVI reported in literatures ranges between 10%-30%[2]
- AKI strong predictor of 1-year mortality (47.9% vs. 15.7% p<0.001) [2]



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PUBLISHED BY ELSEVIER INC.
VOL. ■, NO. ■, 2015
ISSN 1936-8798/$36.00
http://dx.doi.org/10.1016/j.jcin.2015.07.012

Acute Kidney Injury With the RenalGuard System in Patients Undergoing Transcatheter Aortic Valve Replacement

The PROTECT-TAVI (PROphylactic effecT of furosEmide-induCed diuresis with matched isotonic intravenous hydraTion in Transcatheter Aortic Valve Implantation) Trial

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Patients:

- N=112 patients scheduled for elective Transcatheter aortic valve replacement (TAVR)
- Excluded patients with LVEF <30%, unable to place Foley, or urgent TAVI, or RenalGuard unavailable

Design:

- Primary endpoint: Occurrence of AKI within 72 hours of procedure

Protocol for Control:

- IV Saline 12 hours pre-TAVR
- Continued 6 hours post-TAVR

Protocol for RenalGuard:

- IV Saline 10 hours pre-TAVR, then RenalGuard Therapy 2 hours pre-TAVR) (12 hours total
- Furosemide 0.25 mg/kg
- RenalGuard continued 4 hours post-TAVR

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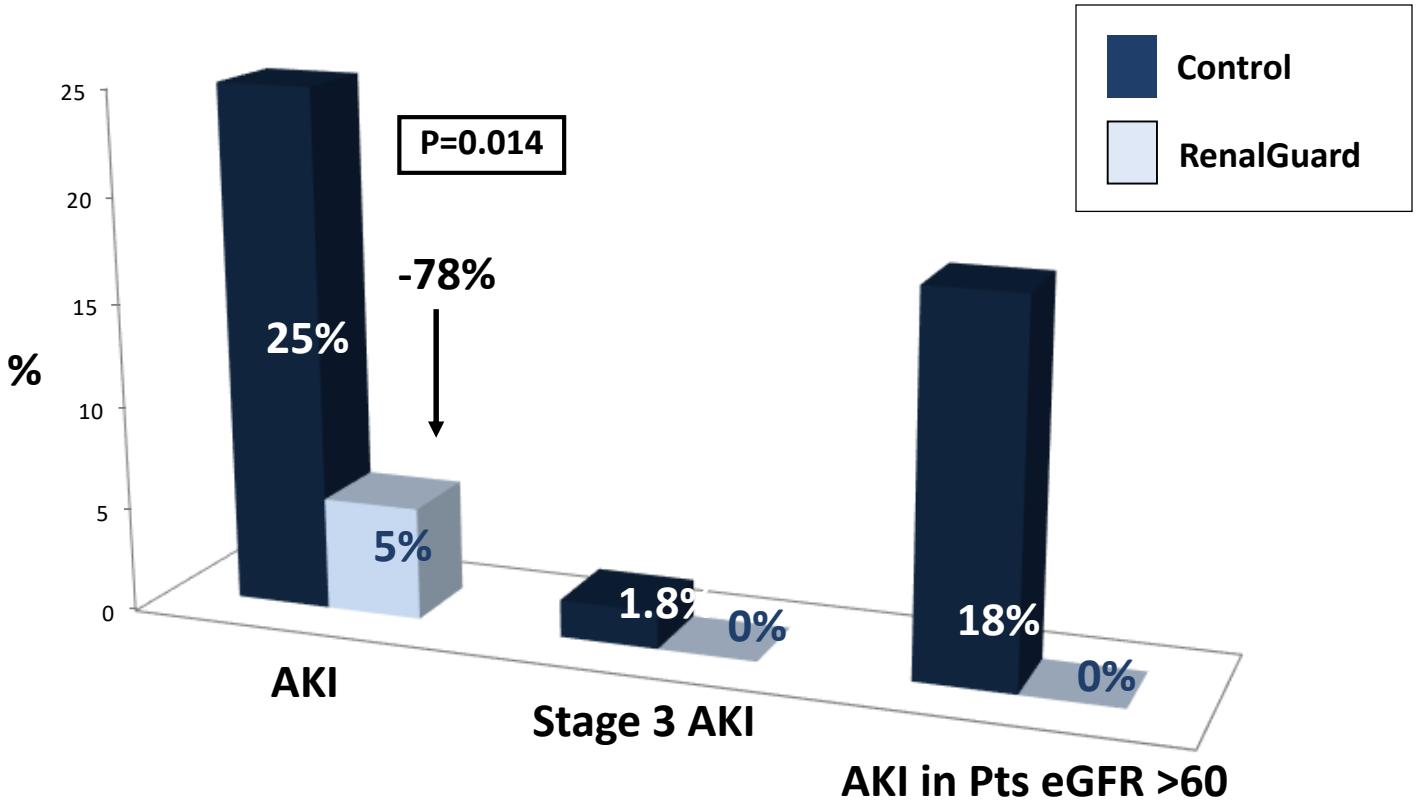
[1]Barbanti et al. *JACC: Cardiovascular Interventions* 2015;On-line ahead of print.
[2]Yamamoto. *JACC Cardiovasc Interv*. 2013;6(5):479–86.

PROTECT-TAVI
Procedural Characteristics

	Control (n=56)	RenalGuard (n= 56)	P Value
Device success	52 (92.8)	55 (98.2)	0.17
Device			
CoreValve, Medtronic	31 (55.3)	40 (71.4)	0.116
SAPIEN, Edwards	22 (39.3)	10 (17.8)	0.021
Portico, St. Jude	1 (1.8)	2 (3.6)	0.558
Lotus, Boston	1 (1.8)	2 (3.6)	0.558
Rapid pacing use	56 (100)	56 (100)	1
Concomitant PCI	5 (8.9)	6 (10.7)	0.751
Post-dilation	7 (12.5)	12 (21.4)	0.314
Contrast dye (ml)	170 (130–230)	180 (140–220)	0.633

Barbanti et al. *JACC: Cardiovascular Interventions* 2015;On-line ahead of print.

RenalGuard Found to be More Effective than Standard of Care in TAVI Patients



RenalGuard - more effective than standard of care at preventing AKI in CKD and non-CKD patients

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Barbanti et al. *JACC: Cardiovascular Interventions* 2015;On-line ahead of print.

RenalGuard for the prevention of AKI in patients undergoing TAVI
Visconti et al. Investigator Sponsored Trial, Naples, Italy

Patients

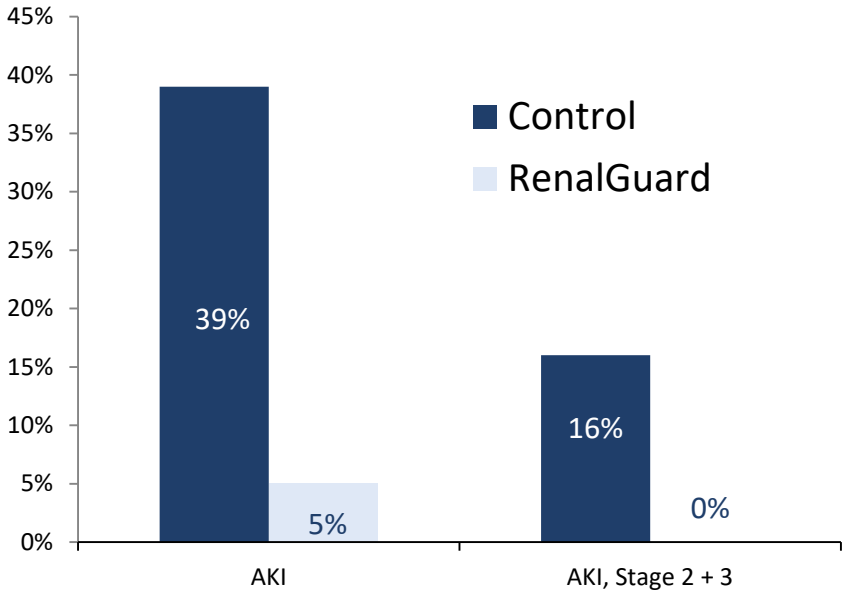
- N=48
- TAVI

Design

- RenalGuard vs. Sodium Bicarb + NAC
- Primary endpoint: CIN
  (≥0.3 mg/dl within 7 days)

Results

- AKI Reduced 87% (p=0.005)
- Severe AKI (Stage 2 + 3) eliminated
  - Control group: 16%
  - RenalGuard Group: 0%



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Visconti G, et al. RenalGuard system for the prevention of acute kidney injury in patients undergoing TAVI. EuroIntervention. 2016.

RenalGuard Clinical Data Review

Study	Control	Lasix Dose (mg/kg)	N	RenalGuard CI-AKI	Control CI-AKI	P
MYTHOS	Overnight Hydration	0.5	170	4.6%	18%	0.005
REMEDIAL II	Sodium Bicarbonate	0.25	292	6%	15%	0.025
AKIGUARD	Overnight Hydration	0.5	133	7%	25%	0.02
PROTECT-TAVI	Hydration	0.25	112	5%	25%	0.014
Visconti, et al	Sodium Bicarbonate	Not reported	48	5%	39%	0.005
Briguori (2015)	n/a	0.25	400	7.7%	n/a	n/a
Chorin, et al	Hydration	0.25-0.5	300	2.7%	26.7%	<0.001
		Total	1455			

Prof. Antonio Bartorelli on the Importance of Preventing CI-AKI

Why have you made preventing CIN a focus of your research?

In our cath lab, we are treating more and more elderly patients with several comorbidities, including chronic kidney disease, who are at high risk of developing acute renal failure after the procedure. Dialysis is a disaster for these patients. If your patient goes to dialysis, he is a "dead man walking" over 75 years of age.

How well integrated is RenalGuard into your cath lab?

The RenalGuard system at Monzino is in the flow of the cath lab. Last Friday, I saw two patients on stretchers going into the cath lab with two RenalGuard systems in a row. I believe this is a sign that this preventative treatment is now embedded in the flow.

All of the nurses in the CCU, ICU, cath lab and the ward know how to setup the system and how to connect the system to the patient. It's a routine treatment now.

European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)[1]

2014 Guidelines:
Recommendations for prevention of contrast-induced nephropathy

Recommendations	Dose	Class[a]	Level[b]	Ref[c]
Patients with moderate-to-severe CKD				
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.	Initial 250ml intravenous bolus of normal saline over 30 min (reduced to ≤150 mL in case of LV dysfunction) followed by an i.v. Bolus (0.25-0.5mg/kg) of furosemide. Hydration infusion rate has to be adjusted to replace the patient's urine output. When the rate of urine output is >300 mL/h, patients undergo the coronary procedure. Matched fluid replacement maintained during the procedure and for 4 hours post-treatment.	**IIb**	A	403.404

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[1]Windecker S, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2014.
[403] Marenzi et al. *JACC Cardiovasc Interv.* 2012;5(1):90-7.
[404] Briguori et al. *Circulation* 2011;124(11):1260-9.

Economics of CI-AKI and RenalGuard

- CI-AKI has been estimated to cost €9,000 per patient impacted
- Added costs include:
  - Extended hospital stay
  - Acute Dialysis
  - Earlier need for chronic dialysis
  - Need for overnight hydration
- RenalGuard provides the potential for reducing the additional costs of CI-AKI without requiring an additional hospital bed for overnight hydration
- Our calculations estimate investing in RenalGuard can save a Cath Lab that treats 1000 patients a year with 25% at-risk patients over €400,000/year

Cost of CIN Calculator

Number of Patients Treated in Your Cath Lab	1000
Number of Patients at risk for CIN (eGFR < 60)[1]	25 %
Total at Risk Population	250 patients
Incidence of CIN within at-risk population[1]	20 %
Nights Pre- and Post- Cath at-risk patients are hospitalized for hydration	1 night(s)
Average additional hospitalization days for CIN[1]	3.75 day(s)
Cost Per ICU Day for CIN patient (take into account dialysis, etc)	$ 2654
Cost Per Hospital day for pre- and post- hydration	$ 500
Cost of Hydration Per Patient	$500
Cost Per CIN Patient	$8,862.60
Number CIN Patients	60 patients
Total CIN Cost (prevention and treatment)	$597,625
Cost Per At-risk Patient	$2,391

http://www.plcmed.com/educational/cost-of-cin-calculator

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Subramanian S et al. Economic burden of contrast-induced nephropathy *Journal of Medical Economics*. 2007;10(2):119–134

Realizing The Promise of RenalGuard

- RenalGuard enables the promise of high urine flow with a therapy matched to the patient to reduce the risk of CIN.
- MYTHOS, REMEDIAL II, AKIGUARD, Briguori, and Ichilov study demonstrate RenalGuard safely reduces CIN and adverse events.
- AKIGUARD demonstrates that reducing CIN leads to improved long-term outcomes at 1 year
- PROTECT-TAVI and Visconti show RenalGuard's Impact in TAVI patients.
- Used in over 10,000 procedures around the world to-date
- Latest ESC/EACTS Guidelines endorse RenalGuard Therapy in Very High Risk Patients

RenalGuard
Preventing Acute Kidney Injury

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