



# 31 GIORNATE CARDIOLOGICHE TORINESI

TURIN  
October  
24<sup>th</sup>-26<sup>th</sup>  
2019

HOW TO REDUCE TIME, CONTRAST MEDIA AND RADIATION DOSE IN  
CARDIOVASCULAR IMAGING AND PROCEDURES  
**HEART FAILURE AND RENAL FAILURE**



*Federico Ronco*

*Interventional Cardiology - Department of Cardiac, Thoracic and Vascular Sciences*  
**AZIENDA ULSS 3 SERENISSIMA – MESTRE - VENEZIA - ITALY**





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I HAVE NO CONFLICT OF INTEREST FOR THIS PRESENTATION



*Federico Ronco*

*Interventional Cardiology - Department of Cardiac, Thoracic and Vascular Sciences*  
**AZIENDA ULSS 3 SERENISSIMA – MESTRE - VENEZIA - ITALY**



# HEART FAILURE AND RENAL FAILURE THE SIZE OF THE PROBLEM

Heart failure (HF) and chronic kidney disease (CKD) have increasing incidence and prevalence owing in part to the aging population and increasing rates of hypertension, diabetes, and other cardiovascular and kidney disease risk factors. **HF and CKD often coexist**

### Prevalence of CKD in HF patients

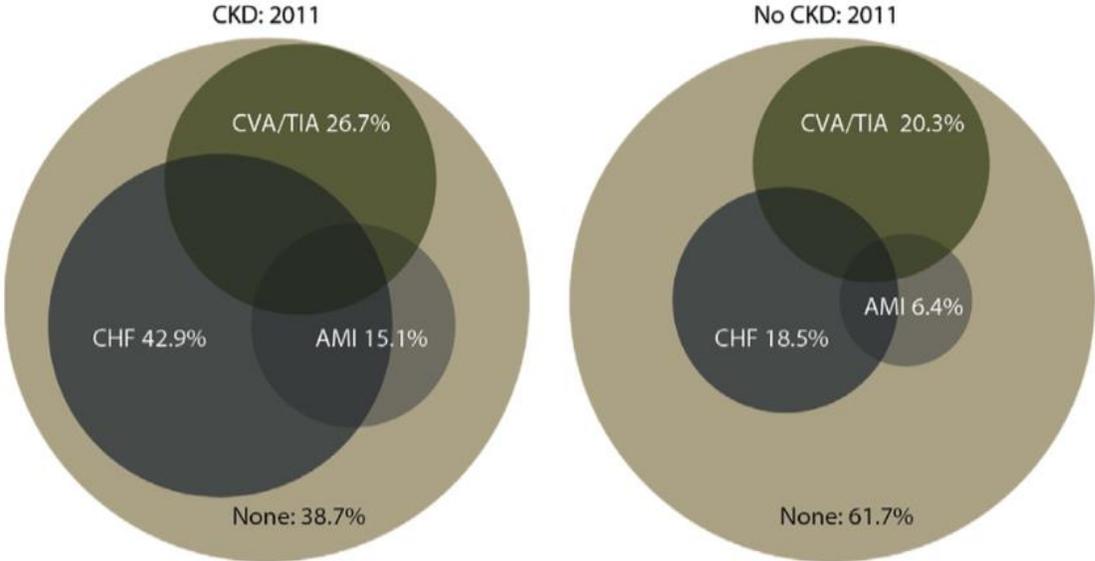
**Table 4** Prevalence and hazard of chronic kidney disease in patients with chronic heart failure.

Ref. no.	Study	Year	No. of pts	NYHA I-IV	Age, years	Male, %	EF, %	BP or HTN	DM, %	RASI, %	eGFR <60, %	Follow-up	Outcome	Adjusted hazard comparing with pts without CKD for the outcome
17	SOLVD-T	2000	2,161	I-IV	60.7	81.5	24.7	40.4%	24.9	50.3			CV death + HF hospitalization	1.41 for eGFR <60 <sup>a</sup>
18	PRIME-II	2000	1,906	III-IV	64.7	80.4	26.2	121.6/					All-cause mortality + HF hospitalization	1.91 for eGFR 44-58
19	DIG	2002	585	II/III: 85%	65								All-cause mortality + HF hospitalization	1.85 for eGFR <44
20													All-cause mortality + HF hospitalization	1.64 <sup>a</sup> for eGFR 44-58
21													All-cause mortality + HF hospitalization	1.8 <sup>a</sup> for eGFR <44
22												34.4 months	CV death + HF hospitalization	1.54 for eGFR 45-59.9
23	AN										39.2	2.07 years (median)	All-cause mortality + HF hospitalization	1.86 for eGFR <45
24	CHART				68.3	65.1	49.3 <sup>c</sup>	39.2% <sup>c</sup>	19.3 <sup>c</sup>	69.1 <sup>c</sup>	42.7	3.45 years	All-cause mortality + HF hospitalization	1.39 for eGFR 30-44
25	JCARE-CARD	2009	2,013	1.8 (mean)	71.5	58.7	44.8	54.5%	30.7	ACEI: 36.7	70.3	2.4 years	All-cause mortality	2.28 for eGFR 15-29
										ARB: 46.1				1.31 for eGFR 30-59
														1.56 for eGFR <30
														1.26 for eGFR 30-59
														2.48 for eGFR <30

CKD was present in 35-70% of HF patients evaluated in cohort studies or subanalyses of randomized controlled trials

Shiba N, J Cardiol 2010

### Prevalence of HF in CKD vs non-CKD patients (age > 66yo)



House A.A. Am J Kidney Disease 2017





# THE CARDIORENAL SYNDROME

## Definition of CRS

Journal of the American College of Cardiology  
© 2008 by the American College of Cardiology Foundation  
Published by Elsevier Inc.

Vol. 52, No. 19, 2008  
ISSN 0735-1097/08/\$34.00  
doi:10.1016/j.jacc.2008.07.051

STATE-OF-THE-ART PAPER

### Cardiorenal Syndrome

Claudio Ronco, MD,\* Mikko Haapio, MD,† Andrew A. House, MSc, MD,‡ Nagesh Anavekar, MD,§  
Rinaldo Bellomo, MD¶

Vicenza, Italy; Helsinki, Finland; London, Ontario, Canada; and Melbourne, Australia

*“A complex pathophysiologic disorder of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ”*

Acute  
Heart  
Disease



TYPE 1



Acute  
Kidney  
Injury

Chronic  
Heart  
Disease



TYPE 2



Progressive  
Kidney  
Injury

Acute  
Kidney  
Injury



TYPE 3



Acute  
Heart  
Disease

Chronic  
Kidney  
Disease



TYPE 4



Progressive  
Heart  
Disease



TYPE 5

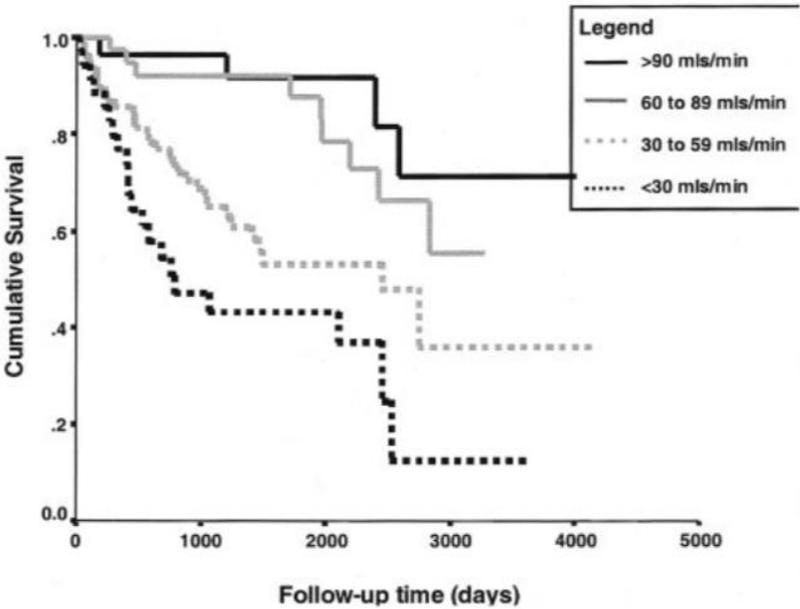
**combined** cardiac and renal dysfunction due to acute or chronic systemic disorders



# HEART FAILURE AND RENAL FAILURE THE SIZE OF THE PROBLEM

The presence of one condition has a strong influence on the other, leading to greater risks for hospitalization, morbidity, and death, as well as very high health care costs.

**CKD is a powerful independent prognostic factor in HF**

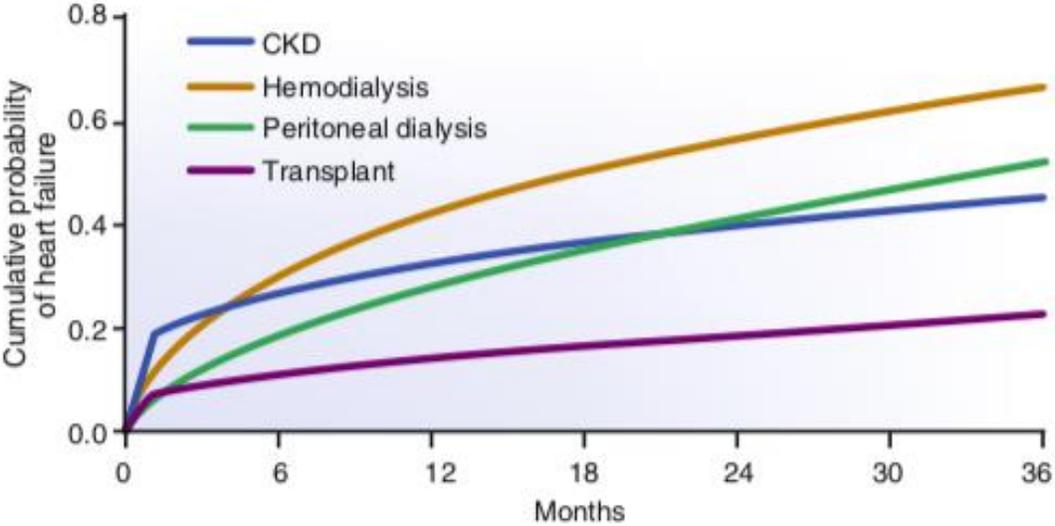


Survival stratified by baseline creatinine clearance. Log-rank statistic=27.98 ( $P<0.0001$ ).

McAlistar FA, Circ 2004

**HF is a powerful independent prognostic factor in CKD**

The mortality rate after HF was 83% at 3 years



Am J Kidney Disease 2003, 2008



# CLINICAL CASE

89 yo Male **admitted for ADHF**

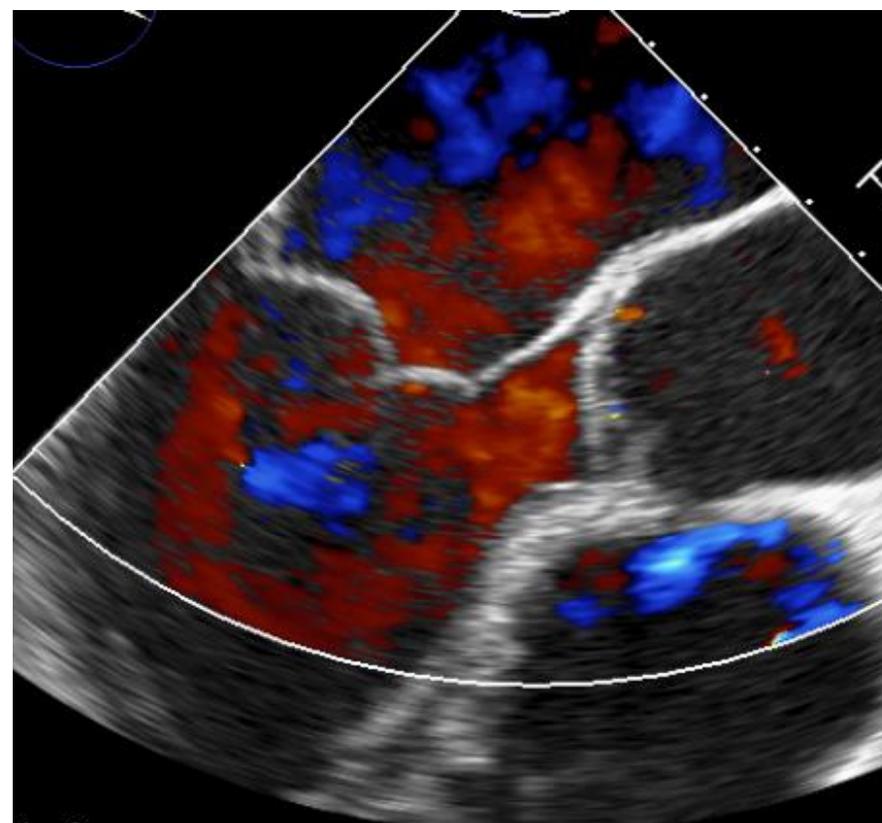
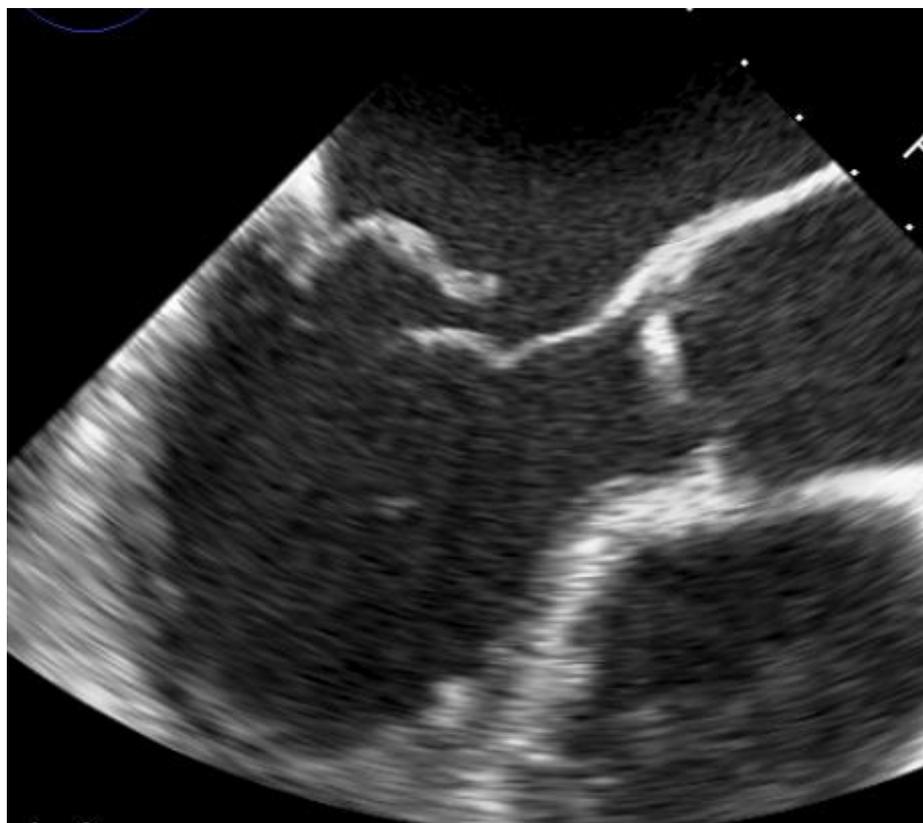
**Complicated by AKI**

Massive degenerative MR

Flail of posterior leaflet

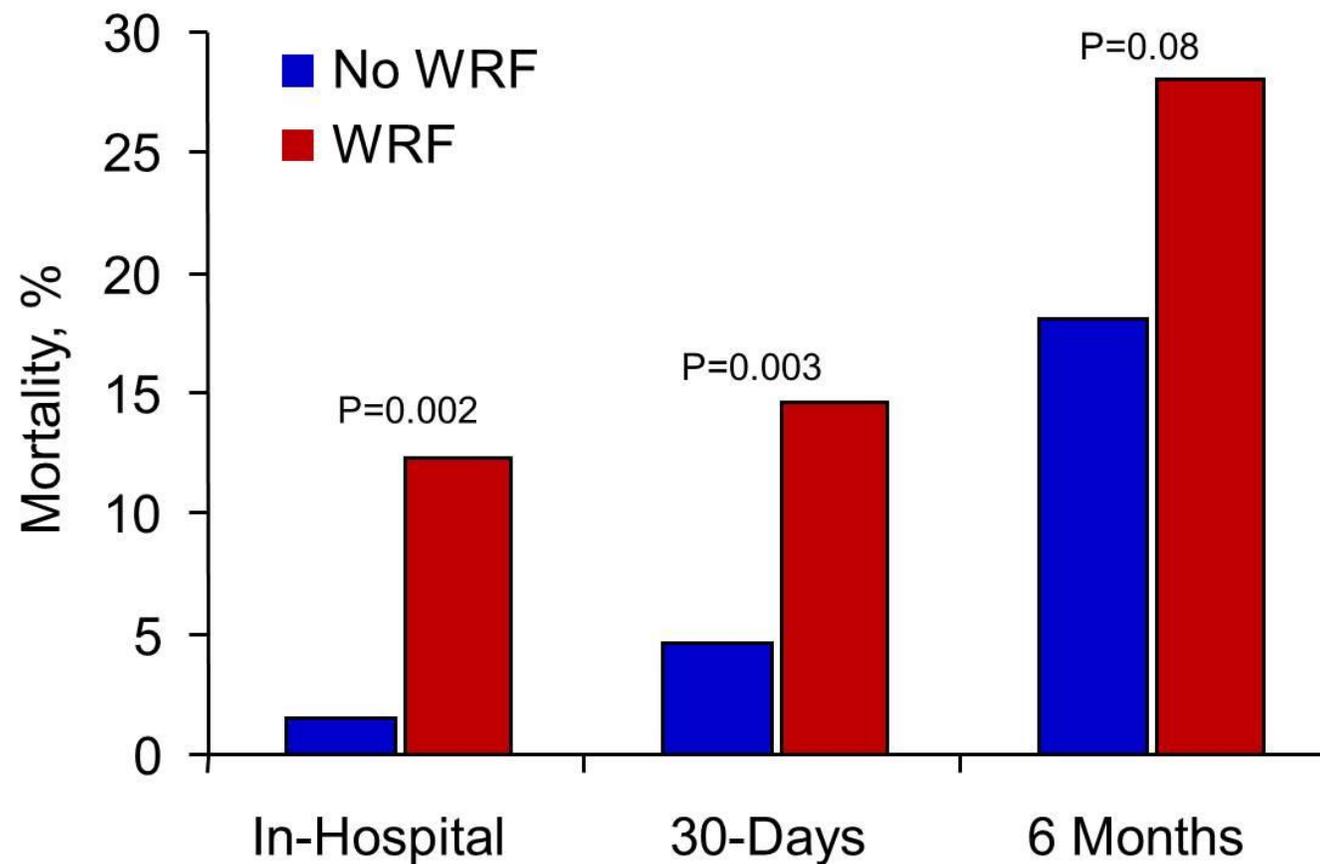
HEART TEAM decision:

**PMVR with MitraClip**



# DEVELOPMENT OF WORSENING RENAL FUNCTION DURING ADHF

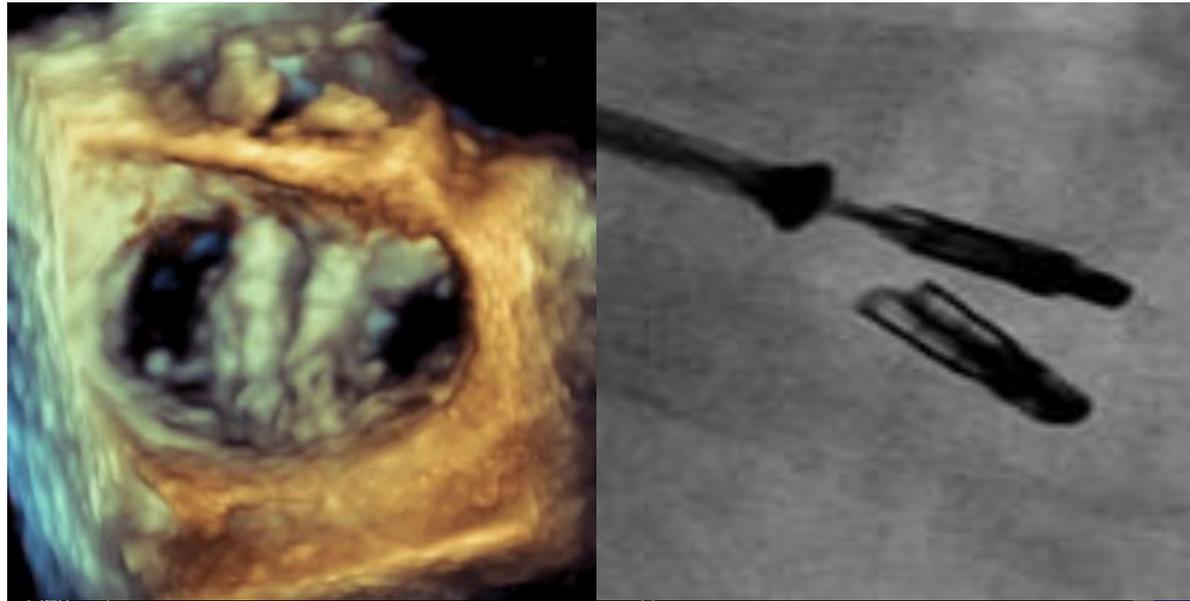
\*WRF = Cre  $\uparrow$  > 0.3



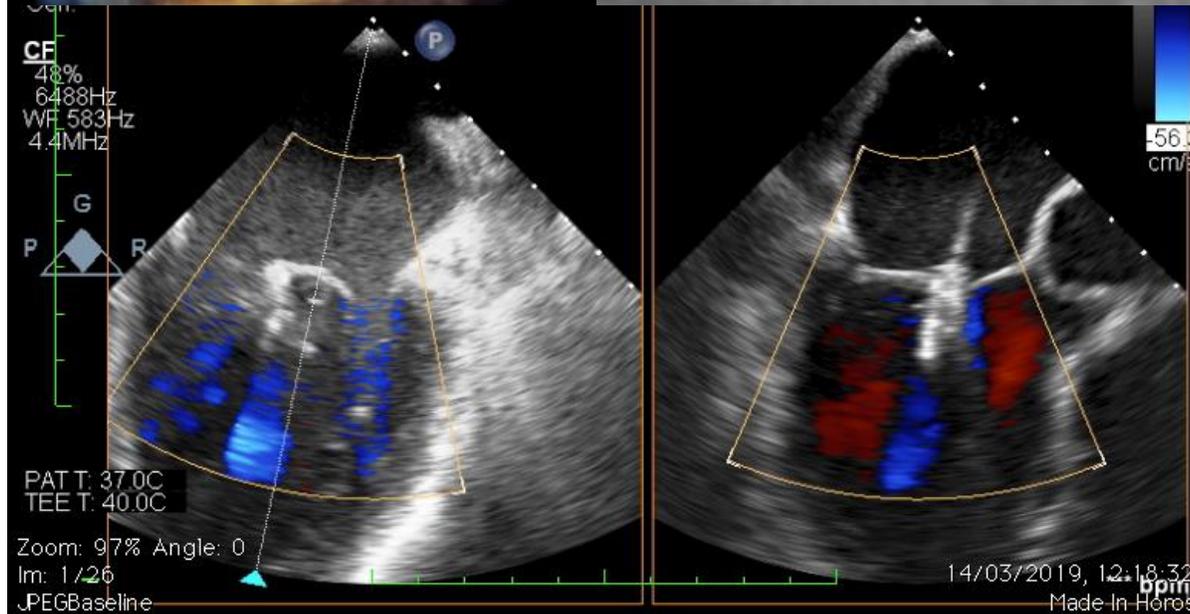
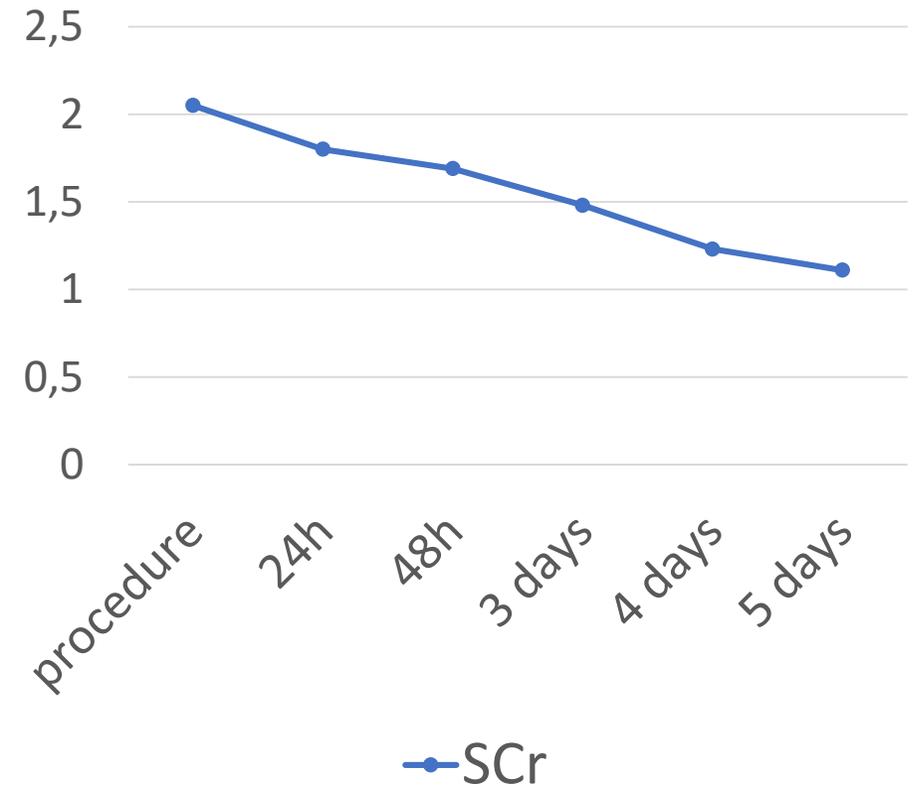
Cowle et al., Eur Heart J 2006;27:1216



# CLINICAL CASE



Serum Creatinine (mg/dl)



# EFFECT OF PMVR ON RENAL FUNCTION

Reduction in MR severity by the MitraClip device is associated with improvement in renal function at 1 year in patients with baseline renal dysfunction.

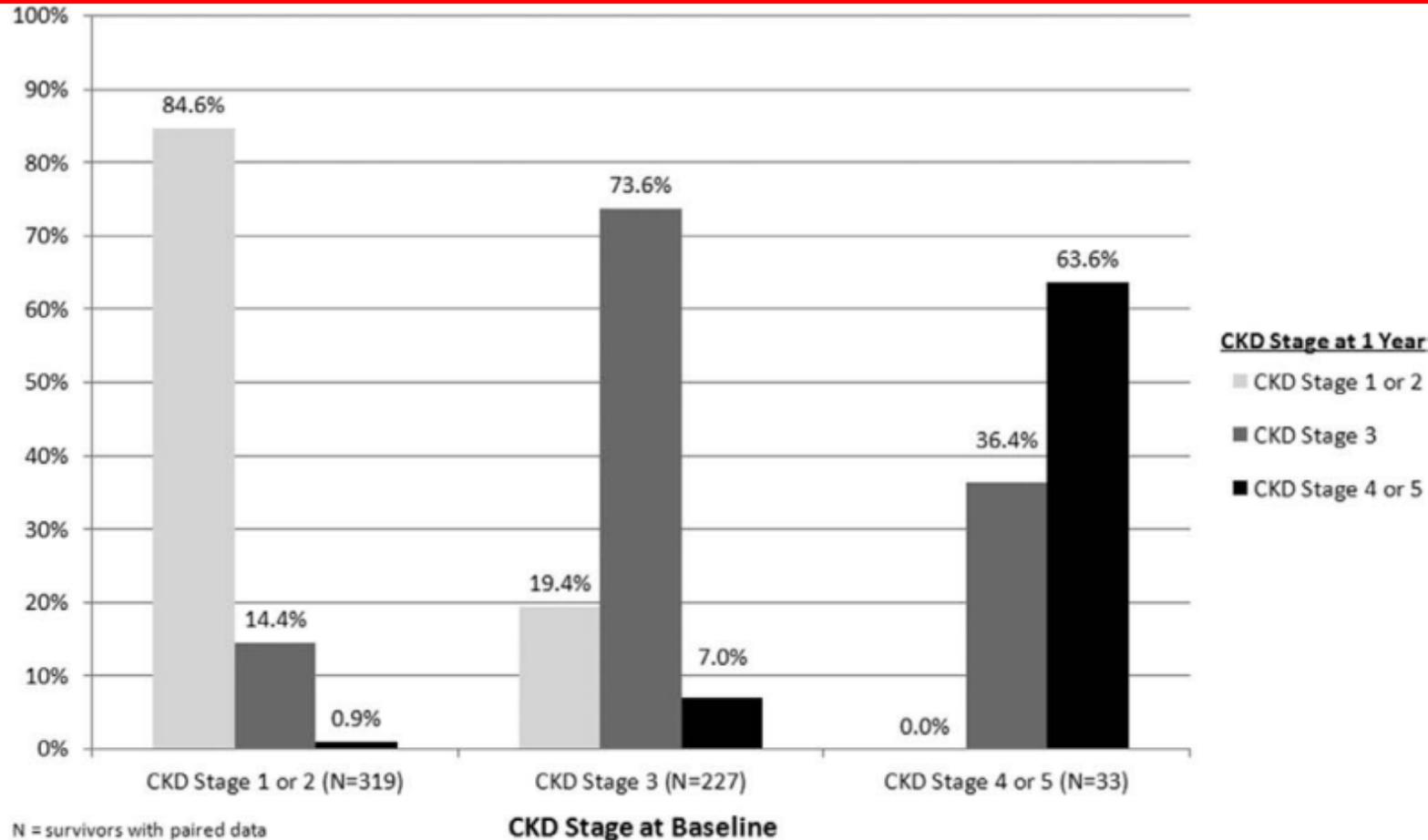


Figure 2. Paired comparisons of chronic kidney disease (CKD) severity across subgroups from baseline to 1 year.

Wang et al. Circ Cardiovasc Int 2015



# DIFFERENT CAUSES FOR RENAL FUNCTION DETERIORATION IN "CATH-LAB PATIENTS"

- LOW CARDIAC OUTPUT
- PRE-EXISTING CKD
- DRUGS
- COMORBIDITIES
- AGE
- EMBOLIC RENAL DAMAGE

CONTRAST ADMINISTRATION

Biomarker



Time Frame



CONTRAST INDUCED  
ACUTE KIDNEY INJURY  
**CI-AKI**

Differential Diagnosis



HOUSE



# CI-AKI DEFINITION

## In interventional cardiology

- An increase in serum creatinine by more than **0.5 mg/dl (44 µmol/l)** or **25% relative increase**
- Within **72 hours** of the intravascular administration of contrast medium

*Old definition*

- An increase in serum creatinine by more than **0.3 mg/dl (26.5 µmol/l)** or **1.5–1.9 times baseline**
- Within **48 hours** of the intravascular administration of contrast medium
- **Urine output < 0,5ml/Kg/h for 6-12 h**
- **No alternative aetiology**

*Current KDIGO 2012*

- An increase in **novel biomarkers** (NGAL...CyC...Cyr 61... IL18...)
- Within **few hours** of the intravascular administration of contrast medium

*Future definition?*



# CI-AKI CONSENSUS PROJECT



## Documento di consenso SICI-GISE/SIN: Danno renale acuto da mezzo di contrasto in cardiologia interventistica

Federico Ronco<sup>1</sup>, Lorenzo Azzalini<sup>2</sup>, Carlo Briguori<sup>3</sup>, Laura Cosmai<sup>4</sup>, Maurizio D'Amico<sup>5</sup>, Marina Di Luca<sup>6</sup>, Giovanni Esposito<sup>7</sup>, Antonino Granatelli<sup>8</sup>, Nicola Maddestra<sup>9</sup>, Federico De Marco<sup>10</sup>, Alessio La Manna<sup>11</sup>, Mauro Maioli<sup>12</sup>, Giuseppe Musumeci<sup>13</sup>, Fabio Tarantino<sup>14</sup>, Chiara Venturelli<sup>15</sup>, Giuliano Brunori<sup>15</sup>, Giuseppe Tarantini<sup>16</sup>

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Marina Di Luca  
Chiara Venturelli

Contrast-induced acute kidney injury (CI-AKI) is a serious complication that can affect outcome and prognosis of patients undergoing percutaneous diagnostic and interventional procedures. The Italian Society of Interventional Cardiology (SICI-GISE) has promoted a consensus project on the subject of CI-AKI in order to disseminate and implement nephroprotection strategies in interventional cardiology. The initiative was conducted in partnership with the Italian Society of Nephrology (SIN).

**Key words.** Acute kidney injury; Contrast dye; Contrast-induced acute kidney injury; Contrast-induced nephropathy; Interventional cardiology; Nephroprotection.

# CI-AKI IN DIFFERENT PROCEDURES

PROCEDURE	PCI	PPCI	CTO	TAVI	TEVAR	EVAR	AAA	AAO
<b>INCIDENCE CI-AKI</b>	3.3-10.2%	10.5%-18.3%	9.4%	22%				
<b>CLINICAL RELEVANCE</b>	Increased risk of death (9.5% at 1y) and	Increased	In hospital Increased	In hospital increased mortality (OR 14.35), life threatening bleeding (OR 2.9)	hospitalization (p=0.008) higher mortality (29%, p<0,001)	hospital death (14.3% p=0.013), ICU stays (p=0,029), 1y mortality (21.4%, p=0.005)	Increased risk of death in hospital death (OR 18.1), MI (OR 16.2), TIA-stroke (OR 5.5%) bleeding with transfusion (OR 7)	<b>Mortality</b> 23% (2 fold increase) at 1y
<b>REF</b>	Am J Cardiol 2009 Lindsay CCI 2003	Silvain Heart 2017	Demir Am J Cardiol 2018 Azzalini Can J Card 202018)	Gargiulo CCI 2015	Piiffaretti J Vas Surg 2012	Kawatani J Med Inv 2018	Prasad CCI 2016 Pucciarelli Euroint 2018 Grossman J int C 2017	Nombela-Franco JACC Int 2018

**CI-AKI is associated with worse procedural outcomes**

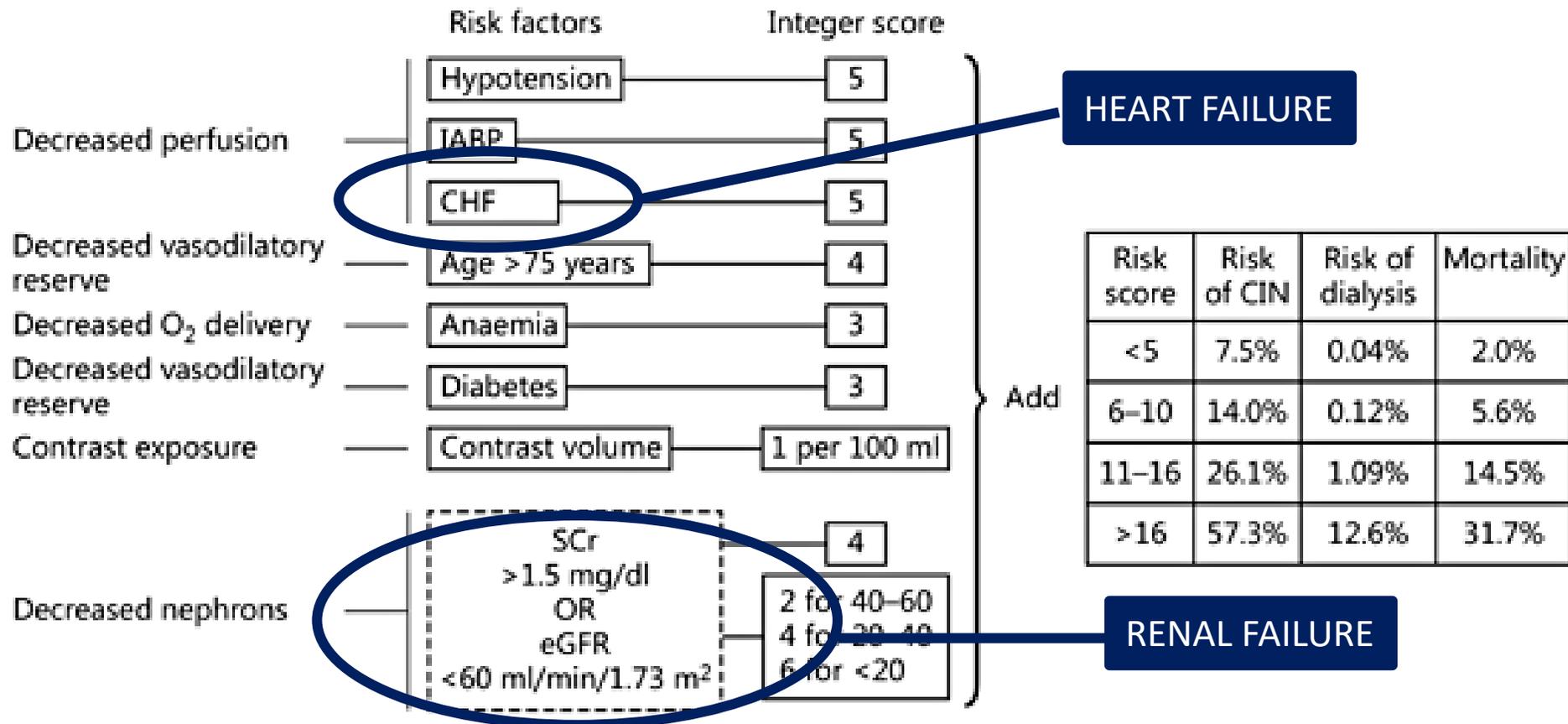


# RISK SCORE FOR CI-AKI

Pathophysiology

Univariate risk factors

Risk score



Mehran JACC 2004



# STRATEGIES TO REDUCE RISK OF CI-AKI

20 re

<p>Pre- and post-hydration with isotonic saline should be considered if the expected contrast volume is &gt;100 mL.</p>	<p>1 mL/kg/h 12 h before and continued for 24 h after the procedure (0.5 mL/kg/h if LVEF ≤35% or NYHA &gt;2).</p>	<p><b>IIa</b></p>	<p><b>C</b></p>
<p>As an alternative to the pre- and post- hydration regimen, tailored hydration regimens<sup>d</sup> may be considered.<sup>295–297</sup></p>		<p><b>IIb</b></p>	<p><b>B</b></p>

ent



# STRATEGIES TO REDUCE RISK OF CI-AKI

## Tailored Hydration



Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial *Lancet* 2014

Somjot S Brar, Vicken Aharonian, Prakash Mansukhani, Naing Moore, Albert Y-J Shen, Michael Jorgensen, Aman Dua, Lindsay Short, Kevin Kane

fluid protocol based on the left ventricular end-diastolic pressure

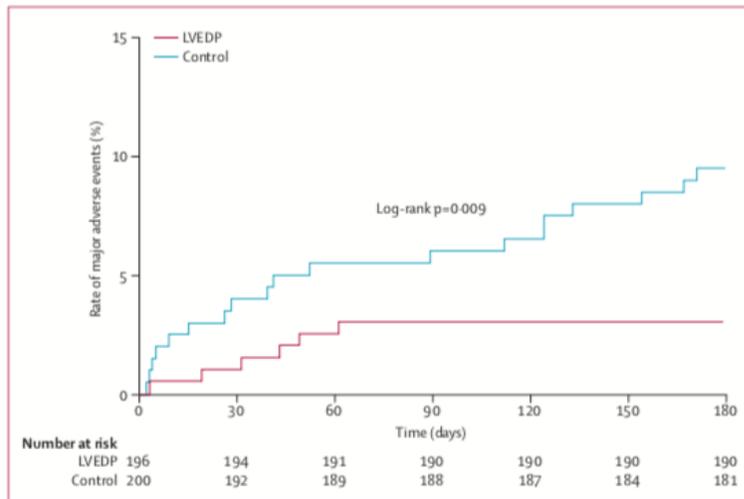


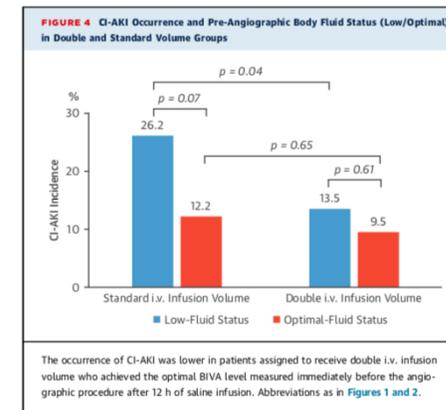
Figure 3: Rate of major adverse events in each group  
The graph shows the 6-month rate of major adverse events, defined as a composite of all-cause mortality, myocardial infarction, or dialysis. LVEDP=left ventricular end-diastolic pressure.

Bioimpedance-Guided Hydration for the Prevention of Contrast-Induced Kidney Injury

The HYDRA Study

JACC 2018

Mauro Maioli, MD,<sup>a</sup> Anna Toso, MD,<sup>a</sup> Mario Leoncini, MD,<sup>a</sup> Nicola Musilli, MD,<sup>a</sup> Gabriele Grippo, MD,<sup>a</sup> Claudio Ronco, MD,<sup>b</sup> Peter A. McCullough, MD, MPH,<sup>c,d,e,f</sup> Francesco Bellandi, MD<sup>a</sup>



Evaluation of BIVA levels on admission in patients with stable coronary artery disease allows adjustment of intravascular volume expansion, resulting in lower CI-AKI occurrence after angiographic procedures.





# STRATEGIES TO REDUCE RISK OF CI-AKI

## Tailored Hydration

### RenalGuard

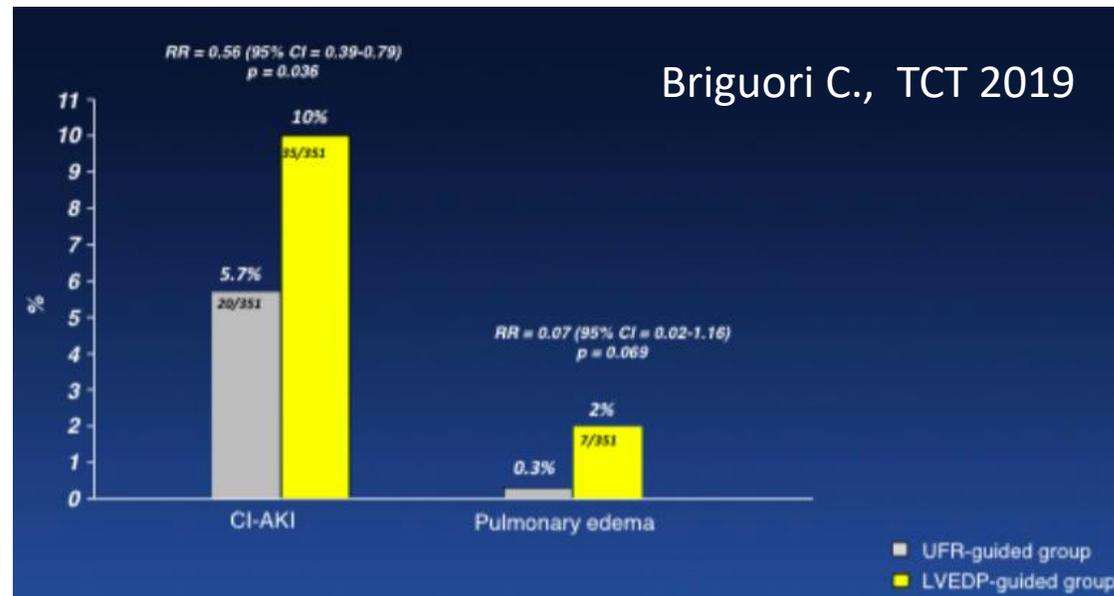


The RenalGuard system (RenalGuard Solutions, Milford, Massachusetts) is a device that allows the **maximization of intravenous hydration by matching the infused volume to the patient's urine output.**

### REMEDIAL III

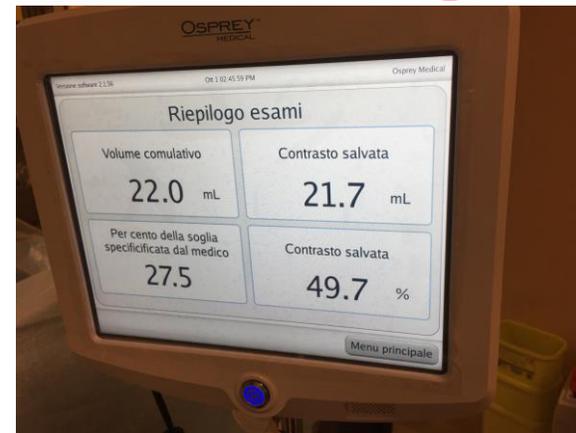
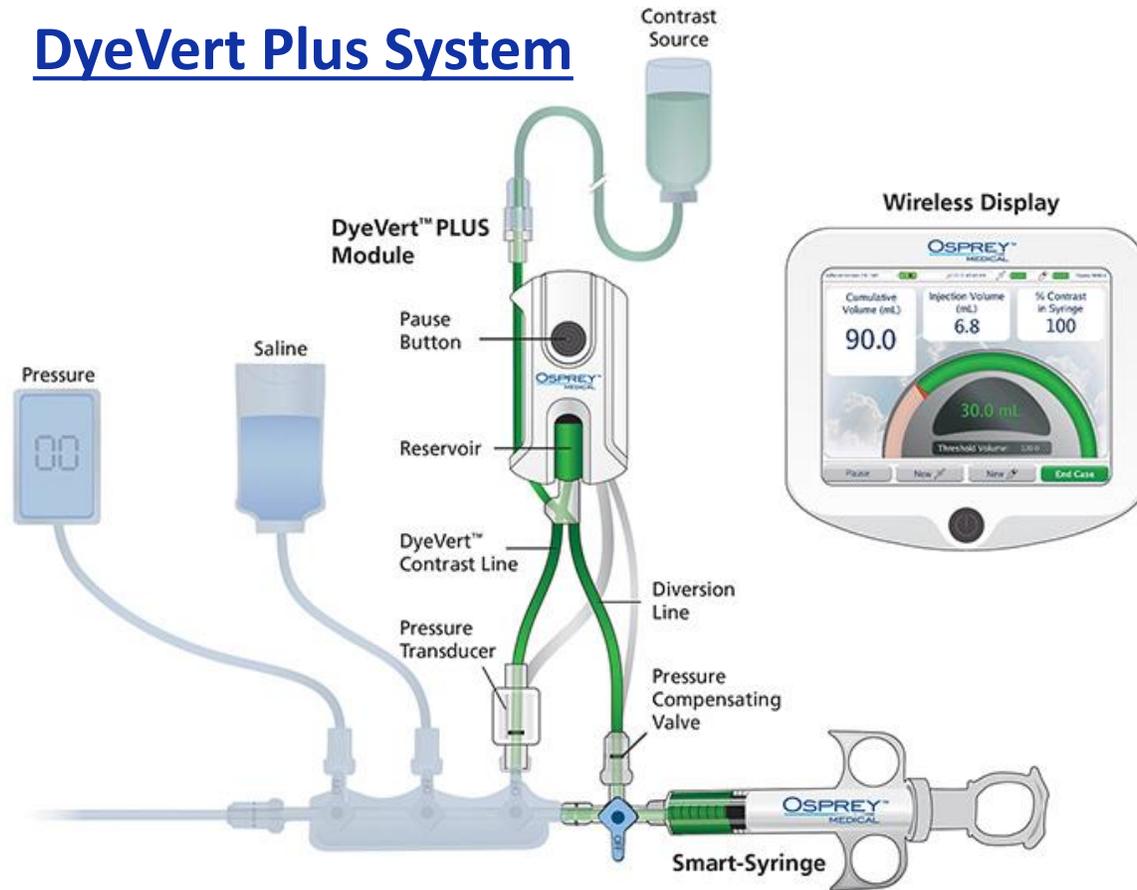
Multicenter, randomized, single-blind, phase 3, investigator-initiated trial comparing 2 tailored-hydration regimens:

- LVEDP-guided hydration
- UFR-guided hydration



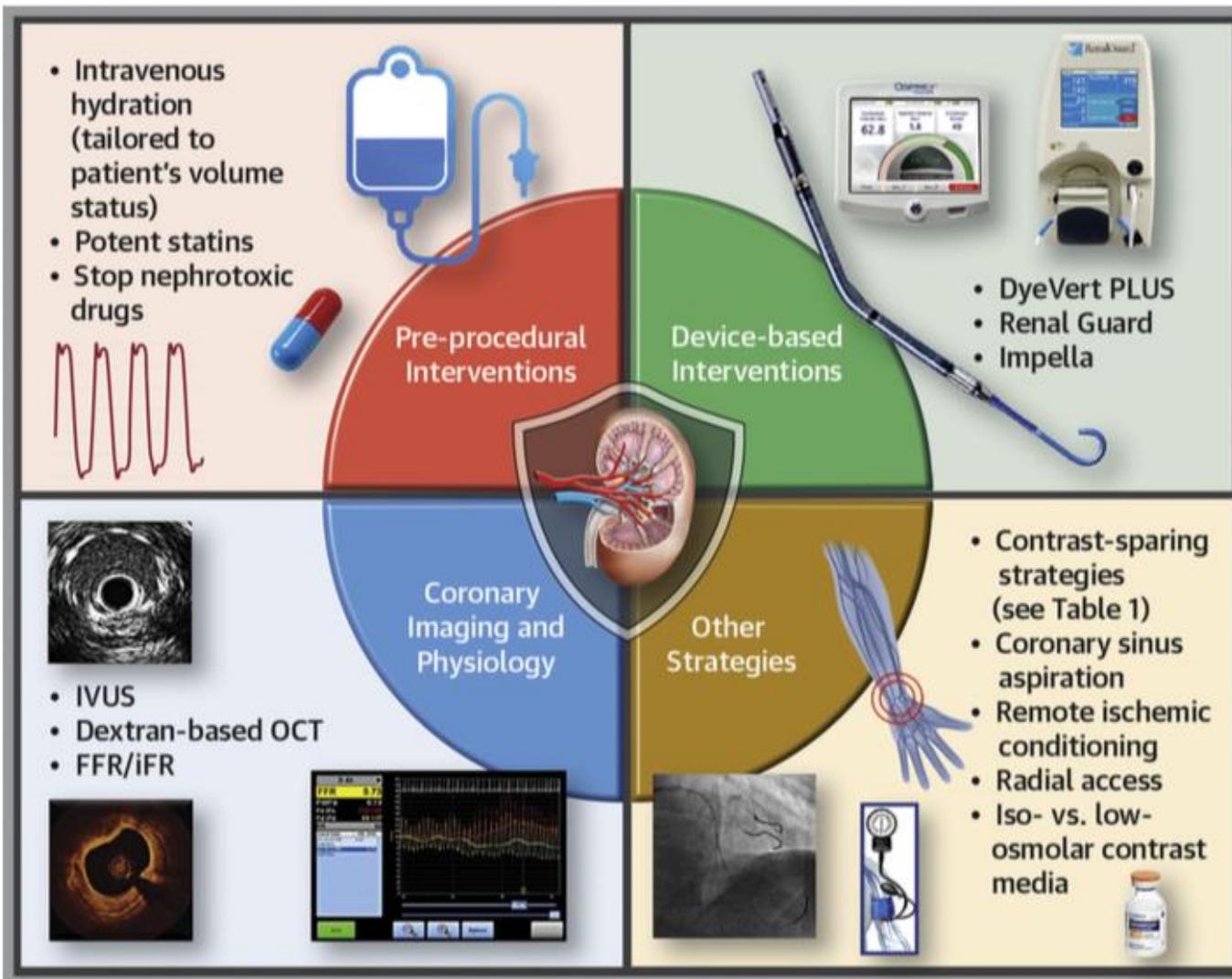
# AMOUNT OF CONTRAST MEDIUM *LESS IS MORE*

## DyeVert Plus System



# STRATEGIES TO REDUCE RISK OF AKI IN THE CATH LAB

**CENTRAL ILLUSTRATION** Measures to Decrease the Risk of CI-AKI Before and During PCI

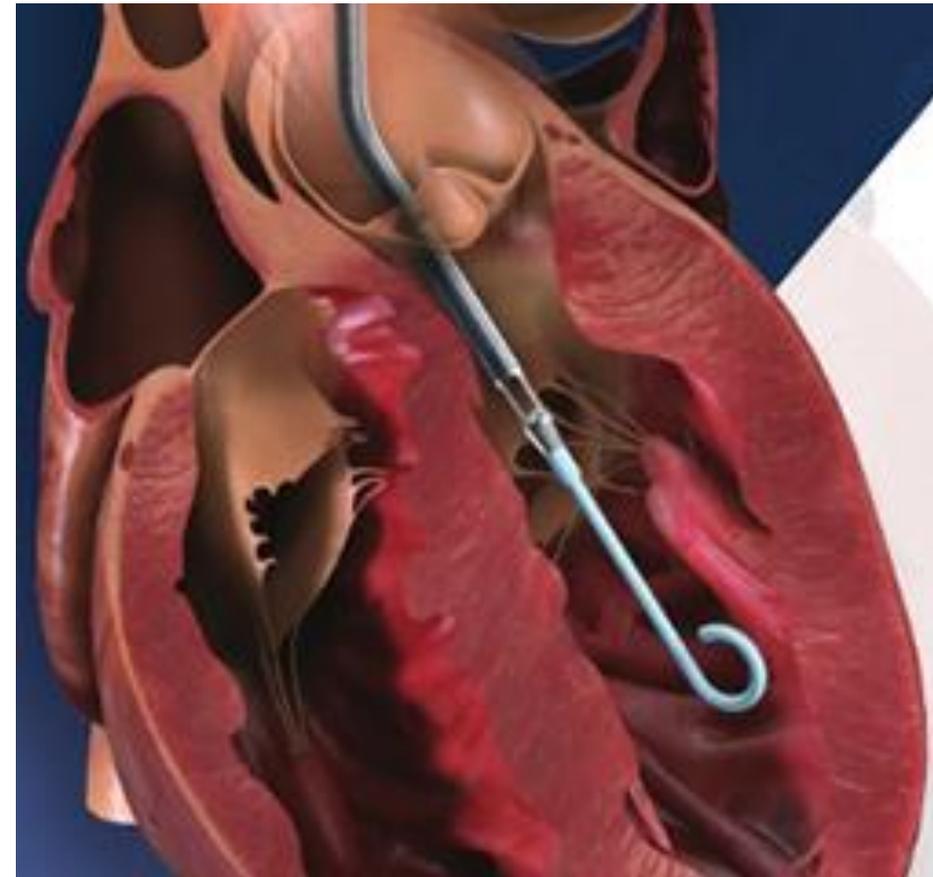


# IMPELLA

The Impella is a heart pump that pulls blood from the left ventricle through an inlet area near the tip and expels blood from the catheter into the ascending aorta.

## INDICATIONS

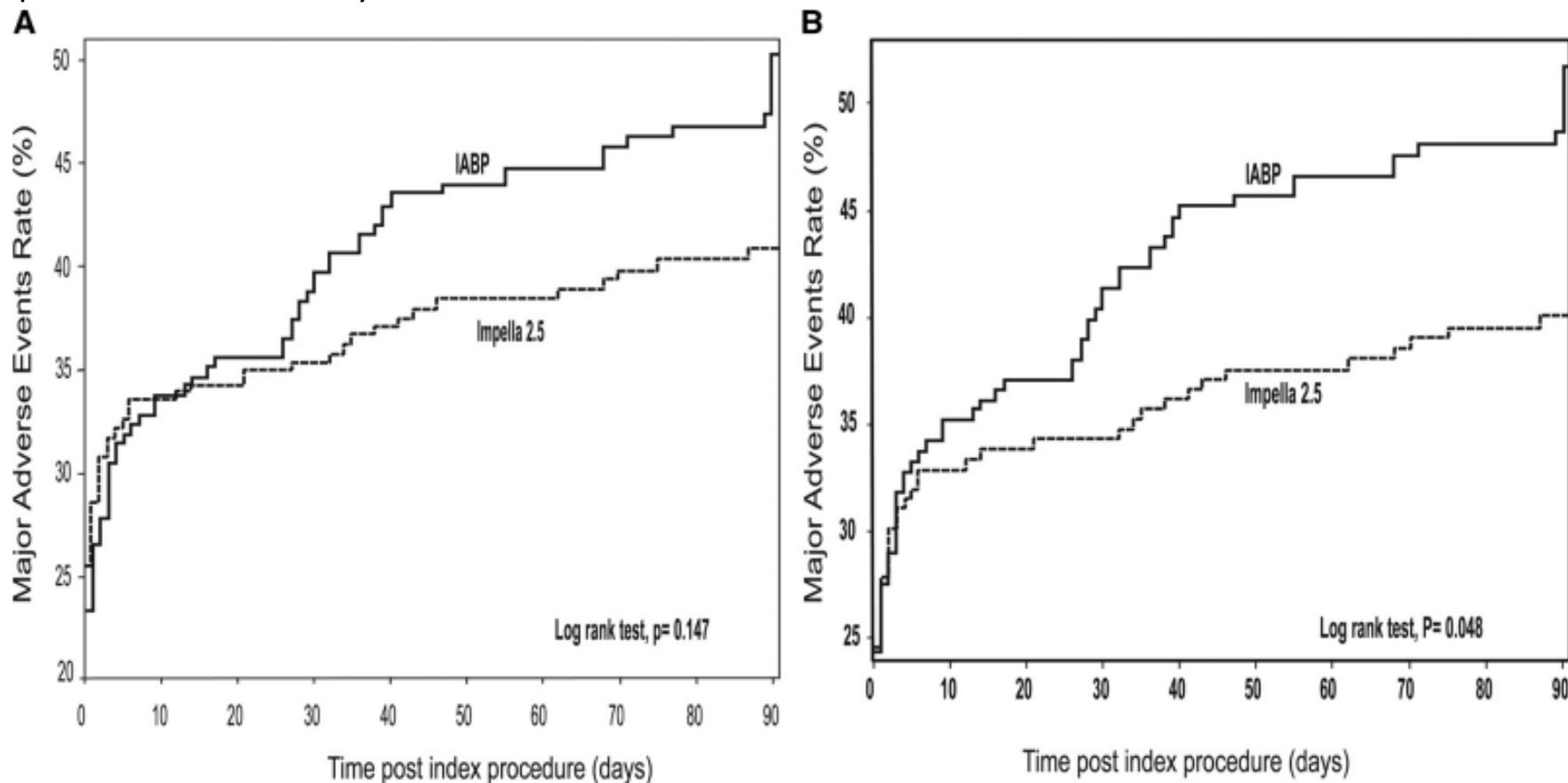
- *High risk PCI*
- *ADHF, Cardiogenic Shock*
- *Coronary artery bypass surgery without ECC.*





# IMPELLA

452 symptomatic patients with complex coronary artery disease and severely depressed left ventricular function randomly assigned to IABP (n226) or Impella 2.5 (n226) support during nonemergent high-risk percutaneous coronary intervention



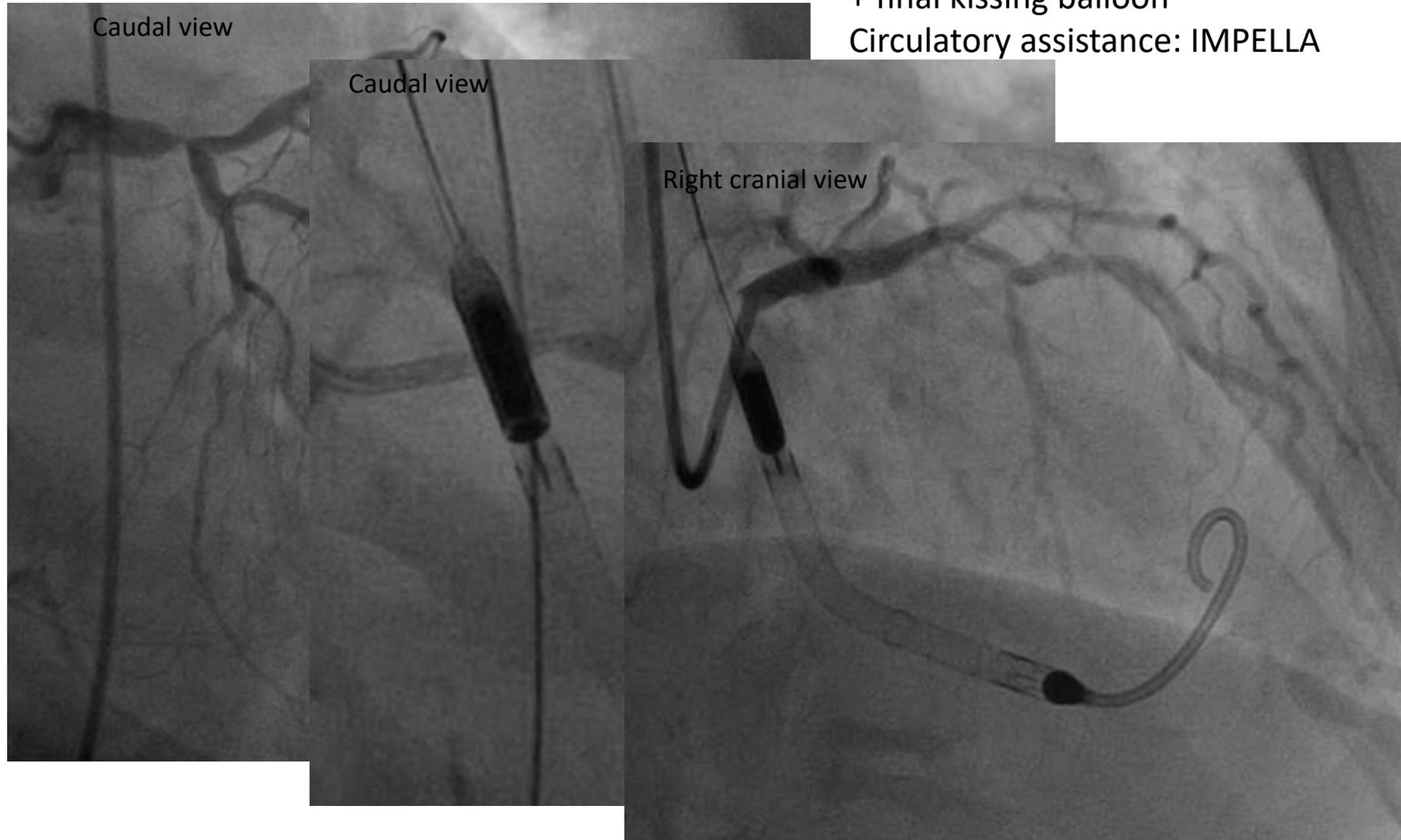
**Figure 2.** Kaplan–Meier curves of major adverse events to 90 days. **A**, intent-to-treat population. **B**, per protocol population. IABP indicates intra-aortic balloon pump.



# IMPELLA

Male 75 yo admitted for cardiogenic shock  
ECG: SR, LBBB

PCI with 2 DES LM-LAD-Circ  
+ final kissing balloon  
Circulatory assistance: IMPELLA





# MECHANICAL CIRCULATORY SUPPORT

## Effect of Percutaneous Ventricular Assist Devices on Renal Function

Huijuan Mao<sup>a, b, e</sup> Anna Giuliani<sup>a-c</sup> Lourdes Blanca-Martos<sup>a, b, f</sup>  
Jeong Chul Kim<sup>a, b</sup> Akash Nayak<sup>b, d</sup> Grazia Virzi<sup>a, b</sup> Alessandra Brocca<sup>a, b</sup>  
Elisa Scalzotto<sup>a, b</sup> Mauro Neri<sup>a, b</sup> Nevin Katz<sup>g</sup> Claudio Ronco<sup>a, b</sup>

pVAD insertion with hemodynamic improvement **should improve kidney function** as a result of the restoration of perfusion.

However, there are only a **few studies reporting the effect of pVADs on kidney function**, and the patient numbers studied are small.

Nevertheless, the **available clinical data support pVAD as a means to reverse and prevent renal failure** in patients with marked hemodynamic compromise.

In that kidney function is one of the most reliable predictors of outcome in the setting of acute heart disease, the pVAD should be chosen depending on its expected renal effects.



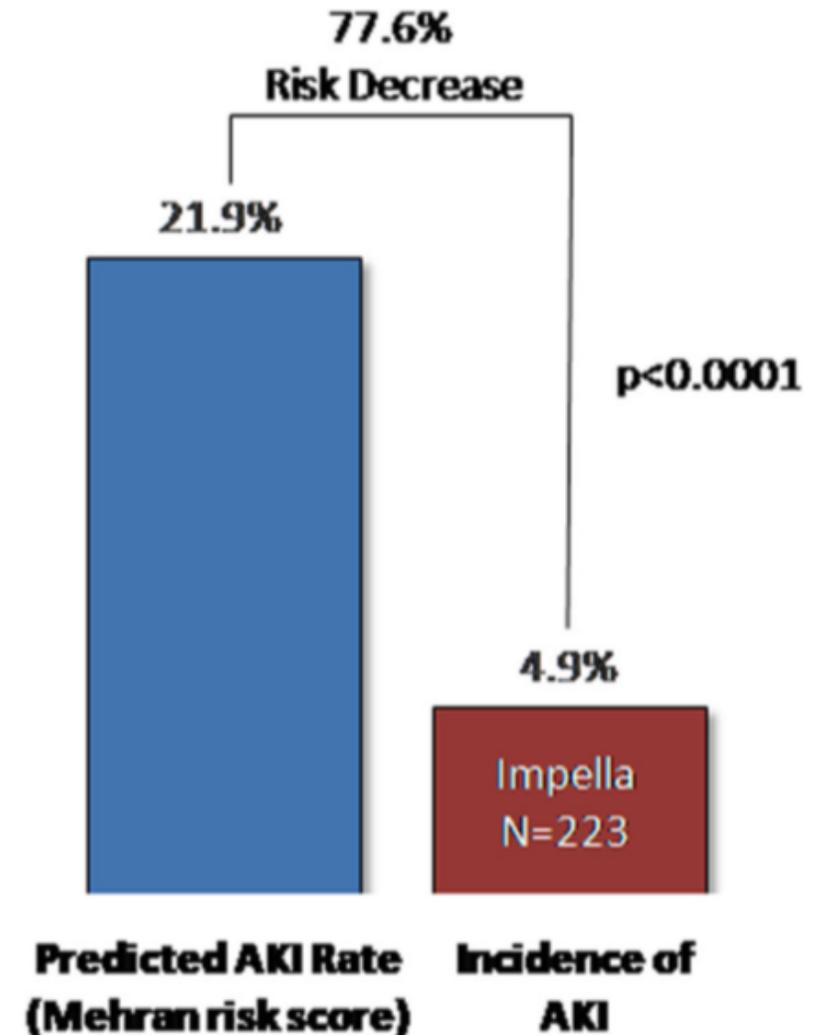
# IMPELLA

## Impella support and acute kidney injury during high-risk percutaneous coronary intervention: The Global cVAD Renal Protection Study

CCI 2019

Michael P. Flaherty MD, PhD<sup>1</sup> | Jeffrey W. Moses MD<sup>2</sup> | Ralf Westenfeld MD<sup>3</sup> | Igor Palacios MD<sup>4</sup> | William W. O'Neill MD<sup>5</sup> | Theodore L. Schreiber MD<sup>6</sup> | Michael J. Lim MD<sup>7</sup> | Amir Kaki MD<sup>8</sup> | Ioana Ghiu MD<sup>9</sup> | Roxanna Mehran MD<sup>10</sup>

**Conclusion:** The incidence of AKI was lower during HR-PCI than expected from current risk models. Although further exploration of this finding is warranted, these data support a **new protective strategy against AKI during HR-PCI.**



# CONTRAST DYES: IOCM vs LOCMs

## *RCTs*

LOCMs safer	Neutral	IOCM safer
	ICON (Mehran JACC 2009)	NEPHRIC (Aspelin NEJM 2013)
	VALOR (Rudnik AHJ 2008)	Recover (Jo JACC 2006)
	CARE (Solomon Circ 2007)	Nie CCI 2009
	Feldkamp (Clin Nephrol 2006)	Song Int J Cardiol 2017

## *Metanalysis*

LOCMs safer	Neutral	IOCM safer
	Reed (JACC 2009)	McCollough (CRM 2011)
	Heinrich (Radiology 2009)	Dong (JNephrol 2012)
	Biondi-Zoccai (IJC 2014)	Mc Collough (JACC 2006)
	Pandya IJC 2016	



# IOCM or LOCMs?

## Documento di consenso SICI-GISE/SIN: Danno renale acuto da mezzo di contrasto in cardiologia interventistica

Federico Ronco<sup>1</sup>, Lorenzo Azzalini<sup>2</sup>, Carlo Briguori<sup>3</sup>, Laura Cosmai<sup>4</sup>, Maurizio D'Amico<sup>5</sup>,  
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Alessio La Manna<sup>11</sup>, Mauro Maioli<sup>12</sup>, Giuseppe Musumeci<sup>13</sup>, Fabio Tarantino<sup>14</sup>, Chiara Venturelli<sup>15</sup>,  
Giuliano Brunori<sup>15</sup>, Giuseppe Tarantini<sup>16</sup>

Il Panel non ritiene vi siano evidenze per raccomandare l'utilizzo di IOCM vs LOCM nella popolazione generale dei pazienti sottoposti a procedure diagnostiche o interventistiche endovascolari. Tuttavia, nei pazienti giudicati clinicamente ad alto rischio di CI-AKI (Tabella 1), considerando che i dati esprimono l'equivalenza o comunque la superiorità dello IOCM vs LOCM in termini di riduzione del rischio di CI-AKI, il Panel accoglie il riportato trend di maggior sicurezza a favore del MCI iso-osmolare.

**Tabella 1.** Principali fattori di rischio per danno renale acuto da mezzo di contrasto.

### Dati anamnestici

Età avanzata

Insufficienza renale cronica

Diabete

Anemia

Scompenso cardiaco

Ridotta FEVS

### Presentazione clinica

Urgenza/emergenza

Shock

Concomitante insufficienza renale acuta da altre cause

Ipovolemia

Concomitante utilizzo di farmaci nefrotossici

### Aspetti procedurali

Volume di MCI

Tipo di MCI

IABP

Accesso arterioso femorale



# HEART AND KIDNEY OUTCOMES IN CATH-LAB

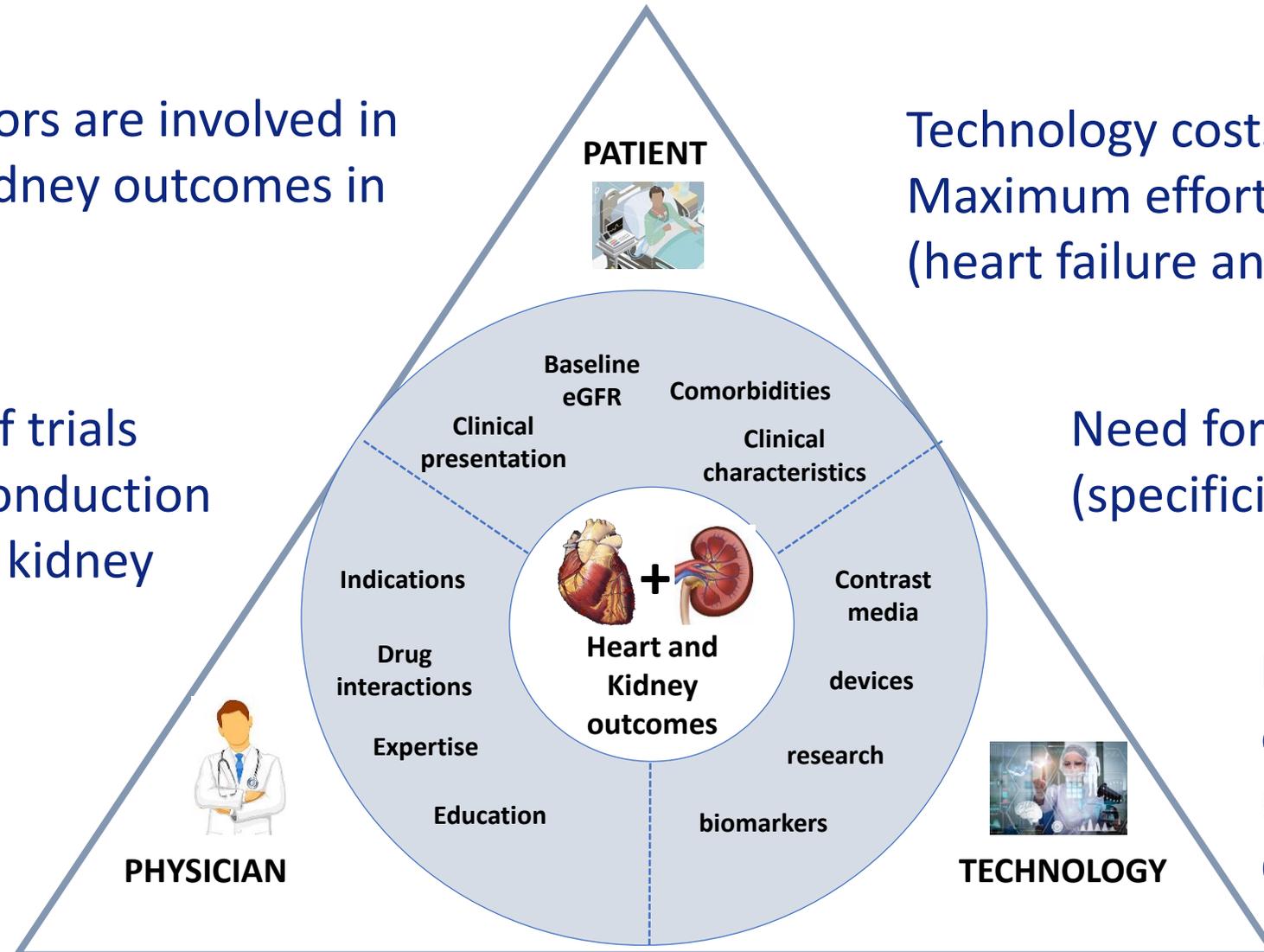
Multiple actors are involved in heart and kidney outcomes in the cath lab

Technology costs effectiveness: Maximum effort in high risk patients (heart failure and renal failure)

Complexity of trials design and conduction on heart and kidney outcomes

Need for novel biomarkers (specificity)

New combined end points (subclinical AKI and CI-AKI, MARCE)



Modified from Ronco F et al GIC 2019





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TURIN  
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2019

# THANK YOU



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