A Prospective, Randomized Trial of Sliding-Scale Hydration for Prevention of Contrast Nephropathy

The POSEIDON (Prevention of Contrast Renal Injury with Different Hydration Strategies) trial

Somjot S. Brar, MD, MPH

on behalf of the *POSEIDON* investigators

Disclosures

I, Somjot S. Brar DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Contrast Nephropathy

Common complication of contrast exposure associated with increased:

- Morbidity
- Mortality
- Cost

Hallmark of therapy is prevention yet preventive strategies remain limited.

Contrast Nephropathy

Unknowns Regarding Hydration

Hydration, with normal saline (0.9% saline), remains the cornerstone of CN prevention, yet important questions remain:

- Rate of hydration?
- Duration of hydration?
- Uniform rate for everyone or can the rate be optimized to the patients needs?

Study Hypothesis

Personalized Hydration for Prevention of Contrast Nephropathy

Does LVEDP guided hydration reduce the incidence of contrast induced acute kidney injury in patients undergoing coronary angiography or PCI?

LVEDP

Left Ventricular End Diastolic Pressure

- Hemodynamic parameter routinely measured in the cardiac cath lab
- Provides insight into volume status

Methods

Investigator Initiated RCT

Masking: Single blind

Study period: November 2010 to July 2012

Population: Patients undergoing coronary angiography or PCI (inpatient & outpatient)

Location: High volume tertiary care center in Los Angeles, CA

Funding: Kaiser Permanente (KP-RCCL-5718)

Principal Investigator: Somjot S. Brar, MD, MPH

Methods

Inclusion Criteria

Estimated GFR < 60 mL/min/1.73 m^2 (by MDRD equation)

And at least *one* of the following:

- Diabetes mellitus
- Age > 75
- Hypertension (>140/90 or treatment)
- History of CHF

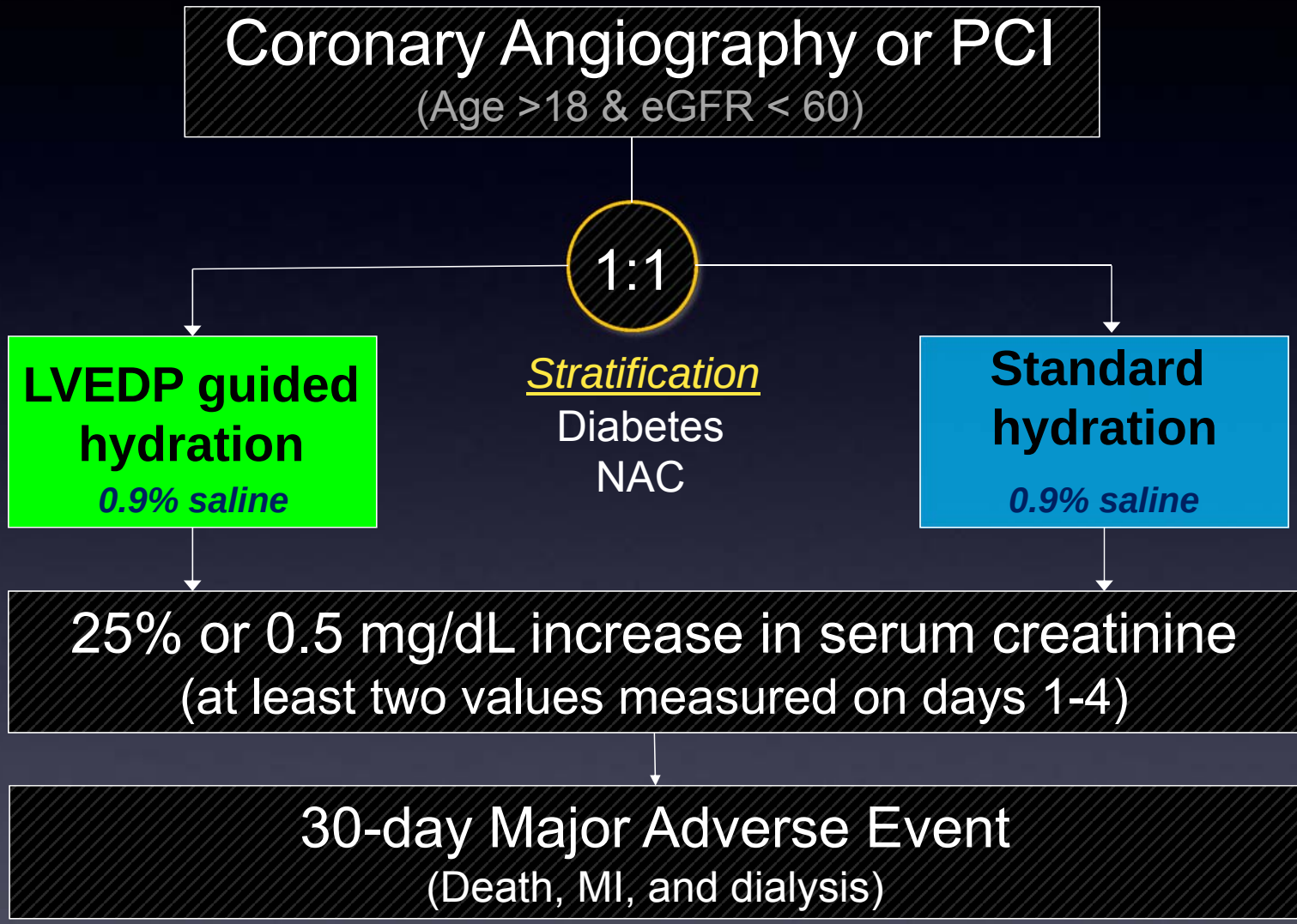
Methods

Exclusion Criteria

- Pulmonary edema or acute decompensated heart failure
- Contrast exposure within 48 hours
- Severe valvular heart disease or mechanical aortic valve
- Heart or Kidney transplant status
- Primary PCI
- >15% change in serum creatinine in previous 2 days

Methods

Study Design & Endpoints



Methods

Sliding Scale Hydration Protocol

	LVEDP Guided Hydration	Standard Hydration
Pre-procedure	3 mL/kg x 1 hr	3 mL/kg x 1 hr
During procedure	LVEDP / Rate <13 — 5 mL/kg/hr 13-18 — 3 mL/kg/hr >18 — 1.5 mL/kg/hr	1.5 mL/kg/hr
Post-procedure	Continued x 4hrs	Continued x 4hrs

LVEDP assessed prior to contrast administration

Methods

Additional Protocol Details

- LVEDP measured systematically using a pigtail catheter (prior to contrast administration).
- Ioxilan, a non-ionic, low-osmolar contrast medium used for all procedures.
- Power injector (Acist medical) used for contrast administration and measuring contrast volumes in 1mL increments.
- N-Acetylcysteine use at discretion of referring physician. If started, 2 day course was continued.

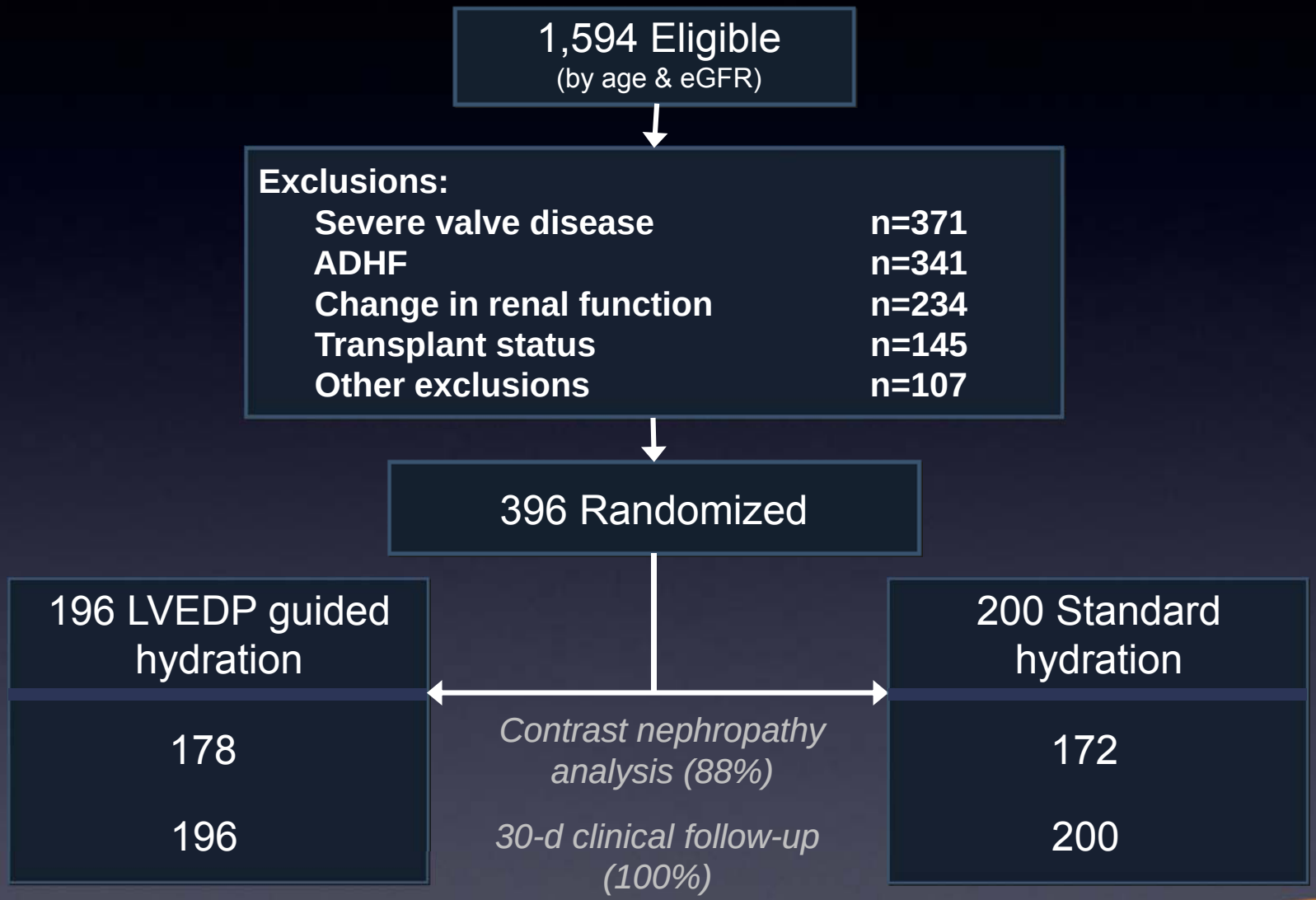
Methods

Data Quality & Analysis

- Intention-to-treat analysis
- All events adjudicated (blinded to treatment allocation)
- Independent oversight & auditing
- Sample size: assumed an event rate of 18% in control and 8% in treatment; with an α 0.05 and β 0.20; 10% loss to follow-up; => ~390 patients.

Methods

Study Flow



Baseline Characteristics

Demographics

	LVEDP Guided (n=196)	Control (n=200)	P-value
Age	71 ± 9	72 ± 8	0.14
Female	36%	41%	0.35
Race / Ethnicity			0.54
White	57%	57%	
Black	14%	14%	
Hispanic	9%	12%	
Asian	14%	15%	
Body Mass Index	30 ± 6	29 ± 6	0.27
Diabetes mellitus	52%	51%	0.76
Hypertension	98%	98%	0.49
Heart failure	11%	10%	0.54

Baseline Characteristics

Laboratory Data & Medications

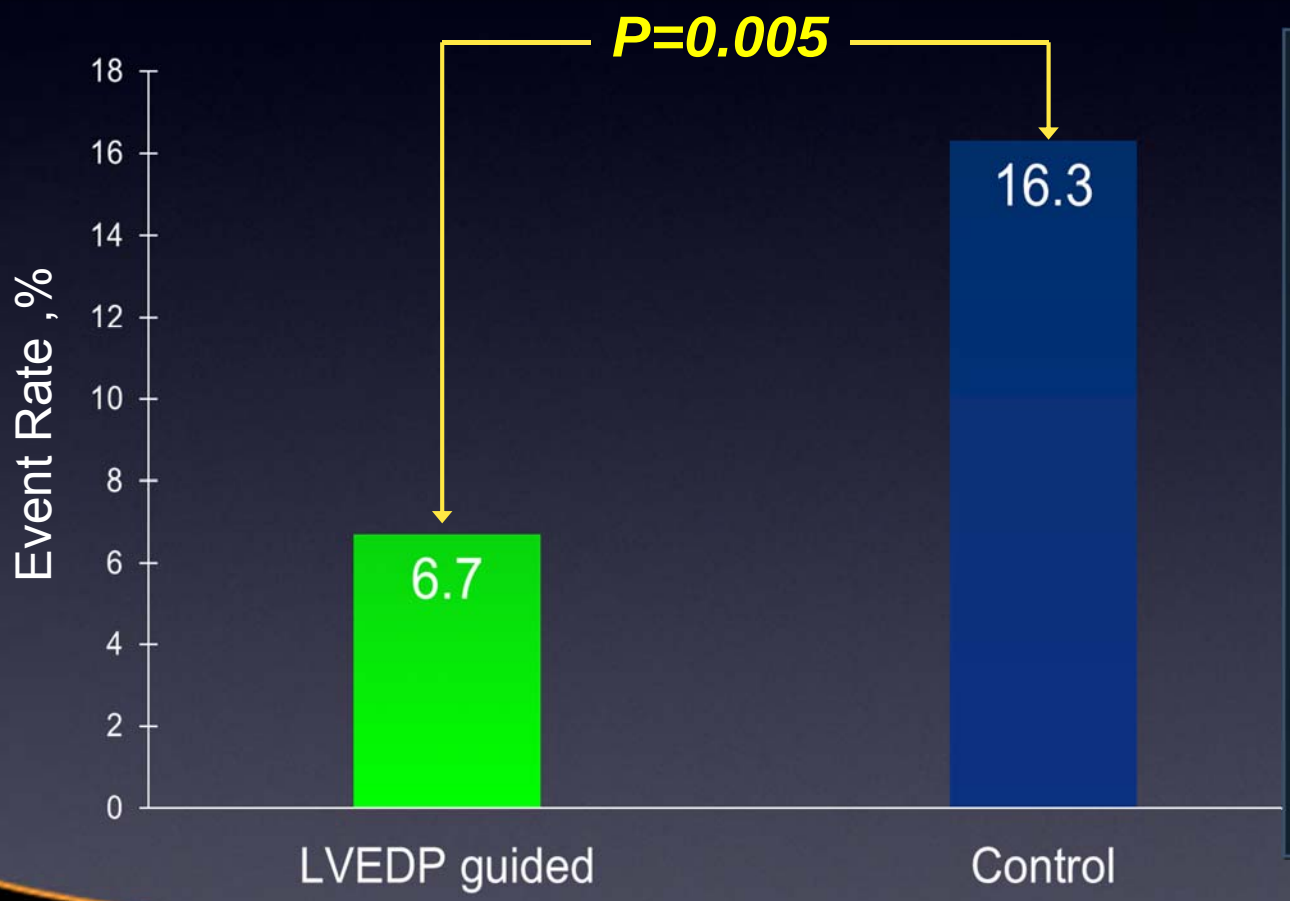
	LVEDP Guided (n=196)	Control (n=200)	P-value
Serum creatinine, mg/dL	1.4 ± 0.4	1.4 ± 0.3	0.87
Estimated GFR	48 ± 9	47 ± 9	0.39
Hemoglobin, g/dL	12.7 ± 1.8	12.7 ± 2.1	0.78
N-acetylcysteine	38%	37%	0.80
Beta blocker	79%	72%	0.13
ACE inhibitor / ARB	81%	77%	0.39
Diuretic, thiazide	20%	19%	0.63
Diuretic, loop	25%	22%	0.55

Hemodynamics & Procedural Data

	LVEDP Guided (n=196)	Control (n=200)	P-value
LVEDP, mmHg	12 ± 7	12 ± 7	0.36
Systolic BP	136 ± 20	134 ± 21	0.40
Diastolic BP	69 ± 12	68 ± 13	0.49
Ejection fraction	56 ± 12	57 ± 11	0.60
Contrast volume, mL	105 (84-188)	111 (79-209)	0.73
Procedure dur., min	35 ± 23	37 ± 25	0.77
PCI	24%	32%	0.08
No. of stents	1.2 ± 0.6	1.3 ± 0.6	0.55
Acute coronary syn.	39%	45%	0.31

Primary Endpoint

25% or 0.5 mg/dL increase in Serum Creatinine



RR (95% CI):

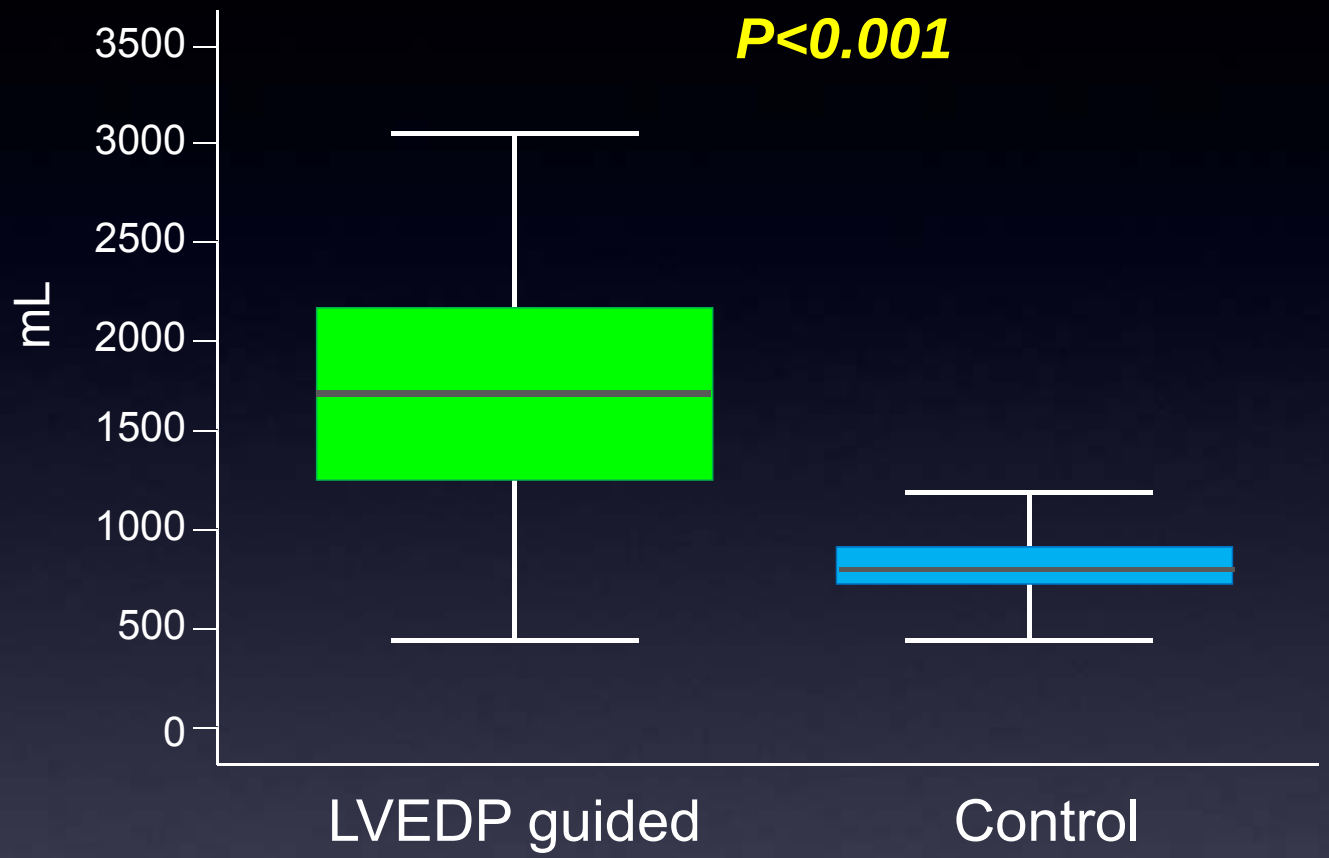
0.41 (0.22 – 0.79)

RD (95% CI):

-9.5% (-16.3 to -2.9)

NNT = 11

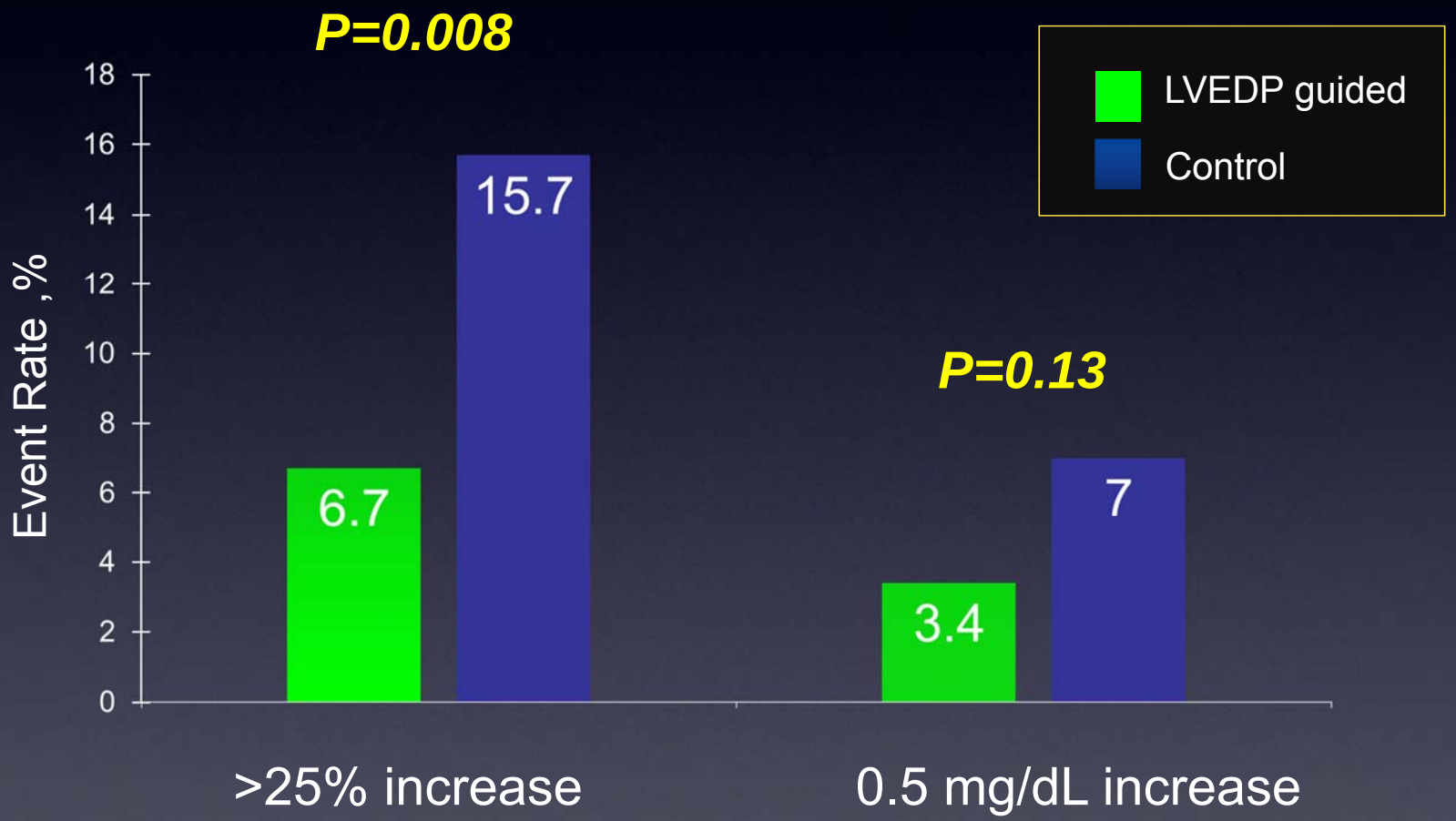
Hydration Volume



	LVEDP guided	Control
Maximum:	3055 mL	1200 mL
Median:	**1711 mL**	**807 mL**
Minimum:	473 mL	448 mL

Primary Endpoint

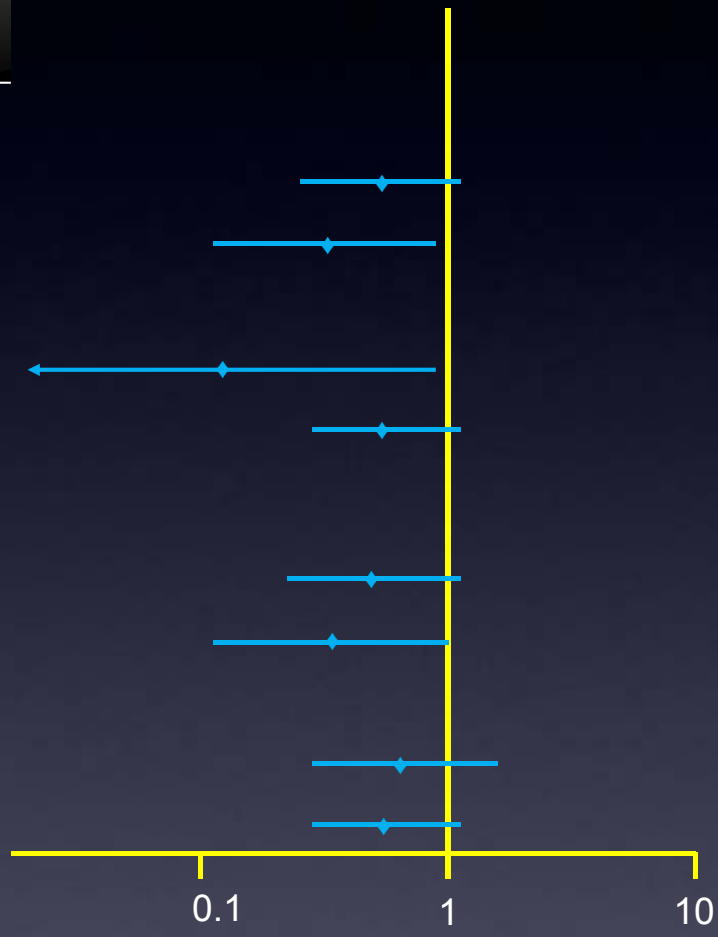
Components



Pre-Specified Subgroups

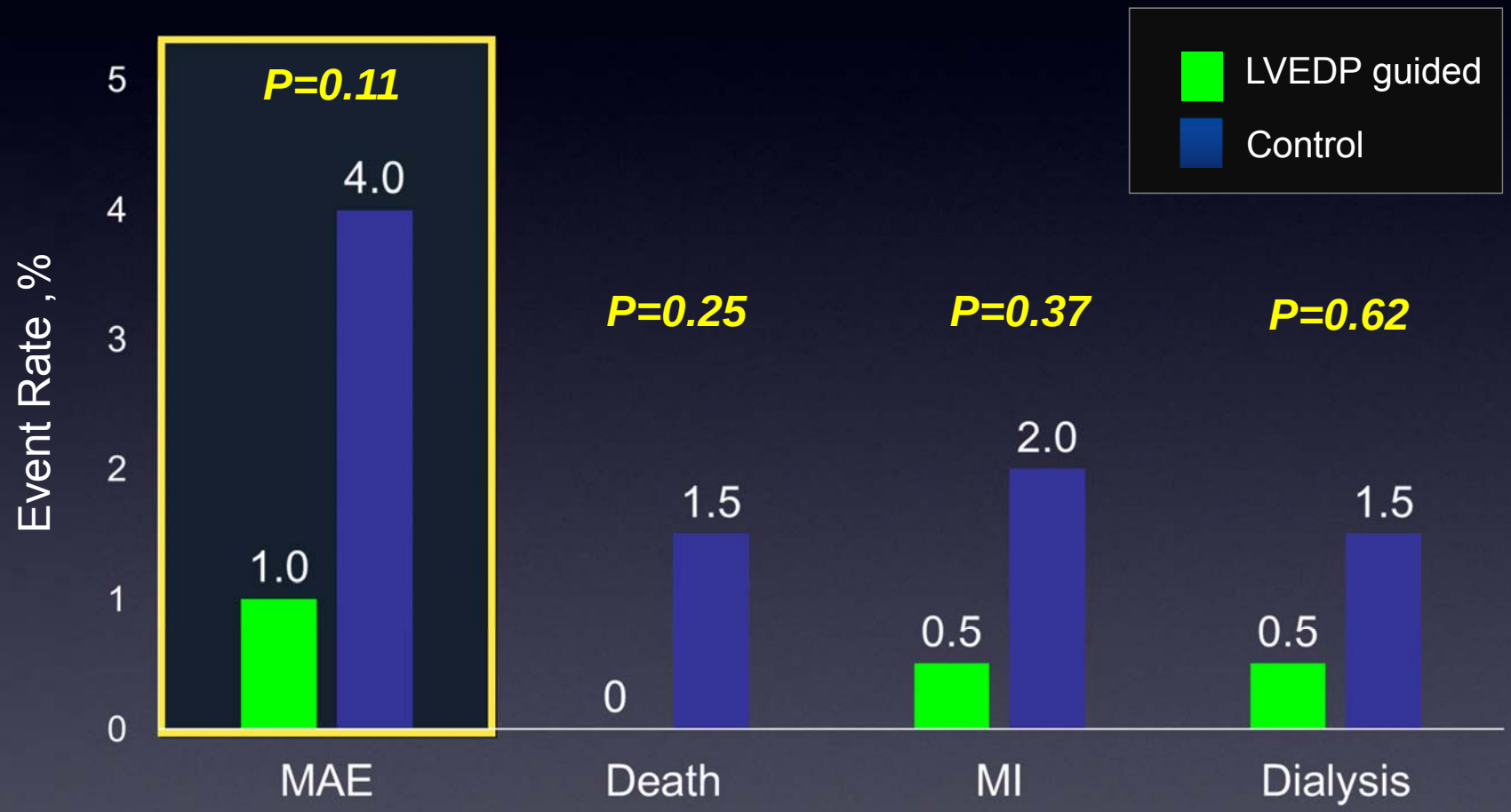
Primary Endpoint

SUBGROUP	RR	95% CI	P interaction
Gender			
Female	**0.54**	0.25 – 1.16	0.44
Male	**0.32**	0.10 – 0.96	
Diabetes			
No	**0.12**	0.02 – 0.92	0.17
Yes	**0.54**	0.54 – 1.07	
N-acetylcysteine			
No	**0.47**	0.21 – 1.05	0.64
Yes	**0.34**	0.11 – 0.99	
Contrast volume			
< 100 mL	**0.64**	0.26 – 1.58	0.74
≥ 100 mL	**0.54**	0.27 – 1.06	



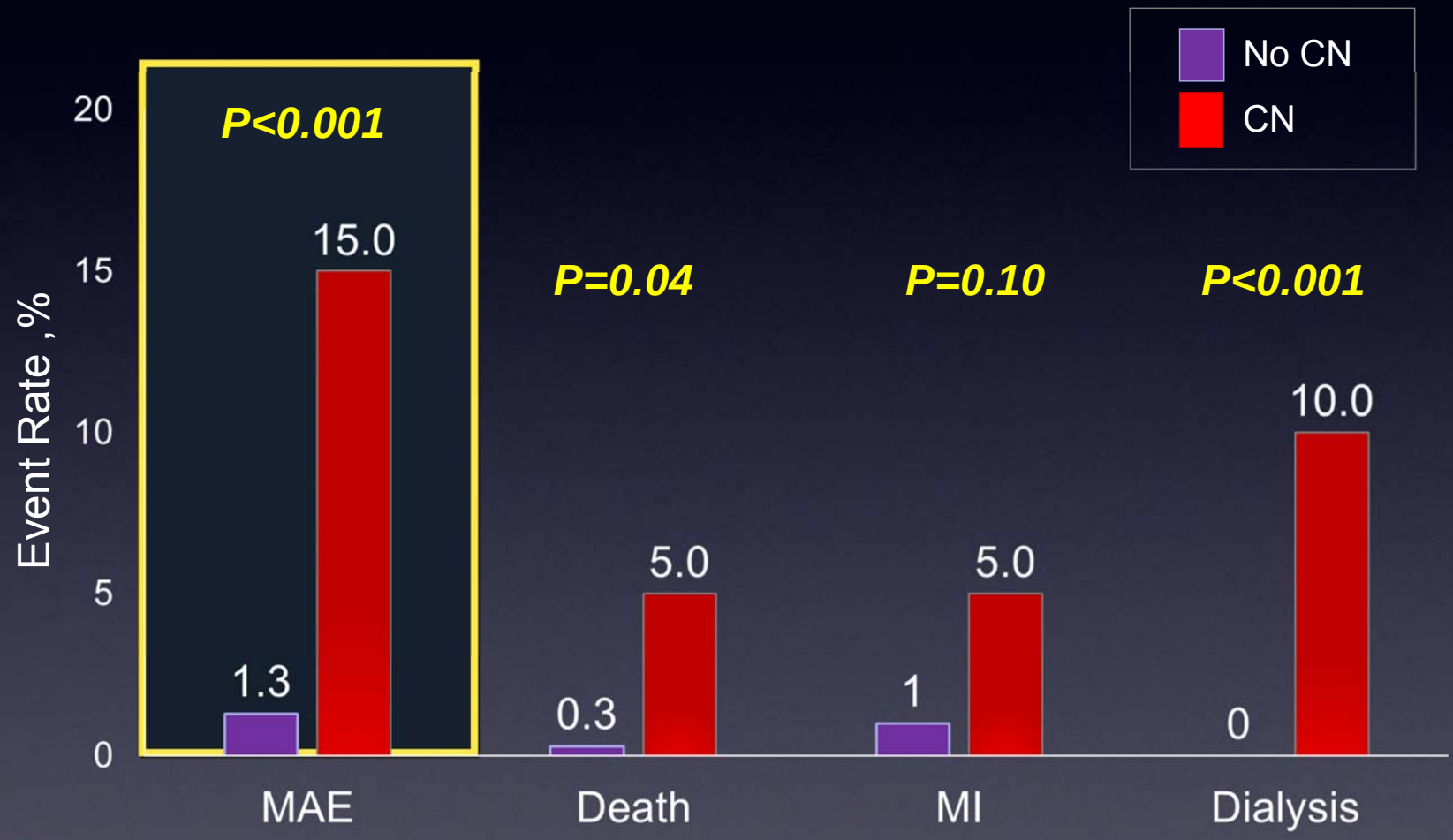
30-day MAE

Composite of Death, MI, & Dialysis



30-day MAE

by Contrast Nephropathy (CN) status



KAISER PERMANENTE
Regional Cardiac Cath Lab

POSEIDON

Safety

IV hydration terminated in 6 patients or 1.5% of the full study cohort (3 patients in each group).

LVEDP values:

LVEDP guided	3, 7, 26 mmHg
Control group	3, 23, 31 mmHg

Reason for termination:

- Shortness of breath
- 2 patients treated with diuretics (1 LVEDP guided; 1 control group)

Conclusions

Sliding Scale Hydration

- This is the first trial to test the hypothesis of a LVEDP guided hydration strategy for prevention of contrast nephropathy.
- LVEDP guided hydration resulted in a significant 59% relative and 10% absolute reduction in contrast nephropathy (p=0.005).
- In subgroup analyses, the treatment effect was consistently in favor of LVEDP guided hydration.

Conclusions

Sliding Scale Hydration

- Easily implemented protocol that can be readily adopted in the outpatient and inpatient settings.
- Personalized strategy of sliding scale hydration guided by the LVEDP was safe. IV hydration was terminated in 1.5% of subjects.
- Reaffirm, contrast nephropathy, as defined, is associated with a significant increase in MAE ($p<0.001$), including mortality ($p=0.04$) and dialysis ($p<0.001$) after cardiac catheterization.

CARDIAC
CATHETERIZATION
SPECIALTY SERVICES
KAISER PERMANENTE LOS ANGELES MEDICAL CENTER

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POSEIDON team

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