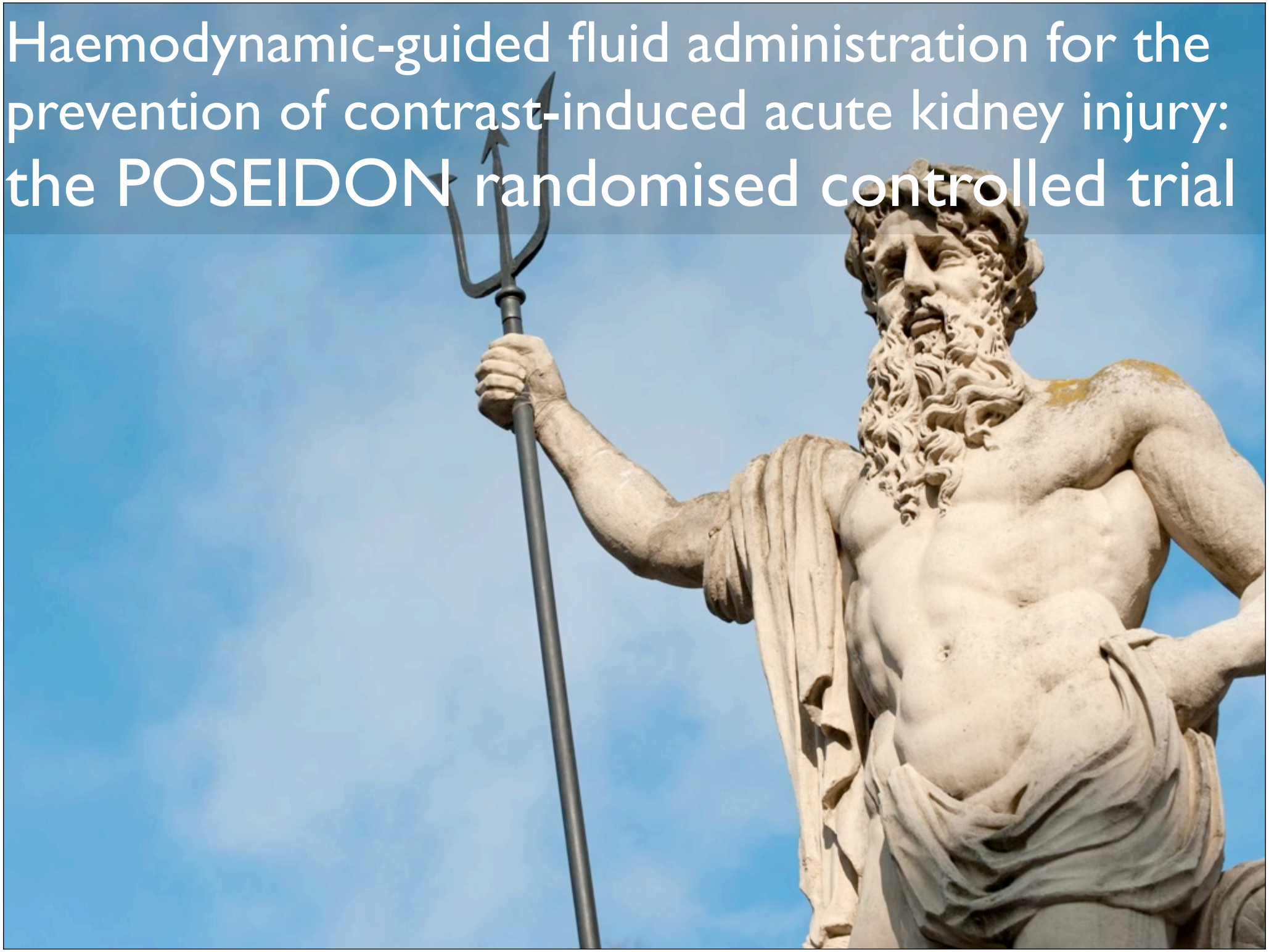
Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial



goal: prevent contrast nephropathy

"So far, no trial has directly compared volume expansion with isotonic saline at different rates or durations in at- risk populations."

"The aim of the POSEIDON trial was to investigative different rates of fluid administration guided by the left ventricular end-diastolic pressure in patients undergoing cardiac catheterisation."

methods: inclusion criteria

- estimated GFR of less than or equal to 60 mL/min
- plus at least one of the following:
  - diabetes mellitus
  - history of congestive heart failure
  - hypertension
  - age older than 75 years

methods: exclusion criteria

- inability to obtain consent
- emergency cardiac catheterisation
- dialysis patient
- exposure to contrast within the previous 2 days
- allergy to contrast media
- acute decompensated heart failure
- severe valvular heart disease
- mechanical aortic prosthesis
- LV thrombus
- kidney or heart transplant
- change in eGFR of ≥7.5% per day or a cumulative change of 15% or more during the preceding 2 or more days.

intervention

- 0.9% saline for all patients
- 3 mL/kg over 1 hour for all patients
- Control group: 1.5 mL/kg/hr
- Treatment group:
  - LVEDP < 13 mmHg: 5 mL/kg/hr
  - LVEDP 13-18 mmHg: 3 mL/kg/hr
  - LVEDP >18 mmHg: 1.5 mL/kg/h

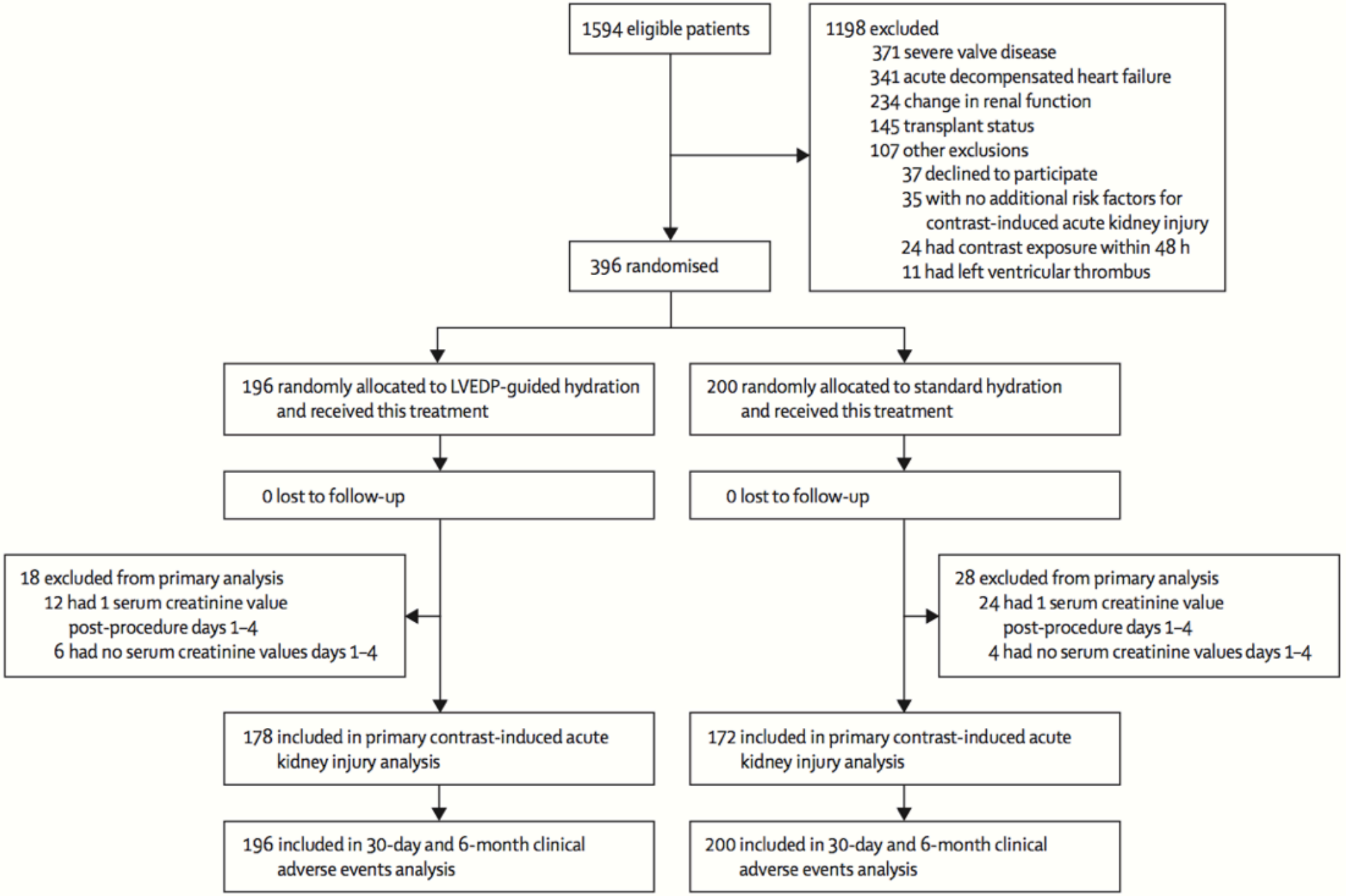
- Before the procedure, patients were instructed to discontinue anticoagulants, non-steroidal anti-inflammatory drugs, and diuretics
- Randomisation was stratified by diabetes mellitus status and N-acetylcysteine use
- Study was partially blinded.
  - Patients were not told which group they were in
  - Laboratory personnel processing the samples also had no knowledge of each patient's group
  - The physicians who did the procedures were not masked

primary endpoint

- Fraction of patients with greater than 25% or 0.5 mg/dL increase in the serum creatinine, based on:
  - baseline value obtained before the procedure
  - and the highest post-procedure value on days 1–4 in patients with two or more post-procedure serum creatinine values.

secondary endpoint

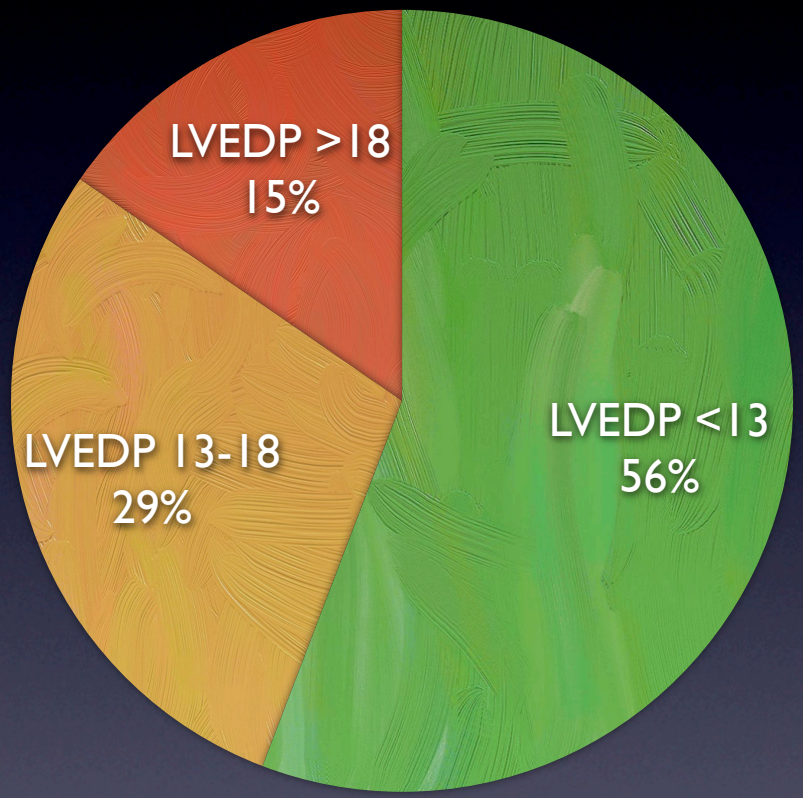
- components of the primary endpoint
- occurrence of major adverse events
  - composite of all-cause mortality, myocardial infarction, or dialysis
    - 30 days
    - 6 months


1594 eligible patients
1198 excluded
371 severe valve disease
341 acute decompensated heart failure
234 change in renal function
145 transplant status
107 other exclusions
37 declined to participate
35 with no additional risk factors for contrast-induced acute kidney injury
24 had contrast exposure within 48 h
11 had left ventricular thrombus
396 randomised
196 randomly allocated to LVEDP-guided hydration and received this treatment
200 randomly allocated to standard hydration and received this treatment
0 lost to follow-up
0 lost to follow-up
18 excluded from primary analysis
12 had 1 serum creatinine value post-procedure days 1–4
6 had no serum creatinine values days 1–4
28 excluded from primary analysis
24 had 1 serum creatinine value post-procedure days 1–4
4 had no serum creatinine values days 1–4
178 included in primary contrast-induced acute kidney injury analysis
172 included in primary contrast-induced acute kidney injury analysis
196 included in 30-day and 6-month clinical adverse events analysis
200 included in 30-day and 6-month clinical adverse events analysis

	LVEDP-guided hydration group (n=196)	Control group (n=200)
Age (years)*	71 (9)	72 (8)
Female sex	70 (36%)	81 (41%)
Race		
Black	27 (14%)	28 (14%)
Asian	28 (14%)	29 (15%)
Latino/Hispanic	17 (9%)	24 (12%)
White	111 (57%)	113 (57%)
Left ventricular end-diastolic pressure (mm Hg)	12 (7)	12 (7)
Left ventricular end-diastolic pressure category		
<13 mm Hg	113 (58%)	108 (54%)
13–18 mm Hg	52 (27%)	62 (31%)
>18 mm Hg	31 (16%)	30 (15%)
Renal function		
Estimated GFR (mL/min/1·73 m²)	48 (9)	48 (9)
Serum creatinine concentration (mg/dL)	1·4 (0·4)	1·4 (0·3)
Blood pressure (mm Hg)		
Systolic	136 (20)	134 (21)
Diastolic	69 (12)	68 (13)
Weight (kg)	86 (20)	83 (18)
Height (cm)	169 (12)	170 (26)
BMI (kg/m²)	30 (6)	29 (6)
Medical history		
Diabetes mellitus	102 (52%)	101 (51%)
Dyslipidaemia (use of statin therapy or LDL>160 mg/dL)	181 (92%)	190 (95%)
Congestive heart failure†	31 (16%)	50 (25%)
Hypertension	193 (99%)	195 (98%)
Previous percutaneous coronary intervention	79 (40%)	70 (35%)
Previous coronary artery bypass graft	38 (19%)	35 (18%)

	LVEDP-guided hydration group (n=196)	Control group (n=200)
Laboratory data		
Haemoglobin concencration (g/dL)	12·7 (1·8)	12·7 (2·1)
Platelets (×10³/μL)	213 (67)	210 (66)
LDL concentration (mg/dL)	89 (38)	89 (33)
HDL concentration (mg/dL)	45 (12)	47 (13)
Haemoglobin A_{1c} (%)	7·2% (1·2%)	7·1% (1·4%)
Medications		
HMG-CoA reductase inhibitors	155 (79%)	146 (73%)
Aspirin	167 (85%)	168 (84%)
Insulin	48 (25%)	60 (30%)
N-acetylcysteine	75 (38%)	74 (37%)
Procedural details		
Contrast total (mL)	104 (84–187)	112 (79–209)
Procedure duration (min)	26 (18–48)	30 (17–54)
Fluoroscopy duration (min)	5·0 (2·6–11·4)	6·1 (2·5–11·4)
Percutaneous coronary intervention*	47 (24%)	65 (33%)
Acute coronary syndrome	77 (39%)	89 (45%)

Data are mean (SD), n (%), or median (IQR). LVEDP=left ventricular end-diastolic pressure. GFR=glomerular filtration rate. LDL=low-density lipoprotein. HDL=high-density lipoprotein. *p=0·05–0·10. †p=0·01–0·05.



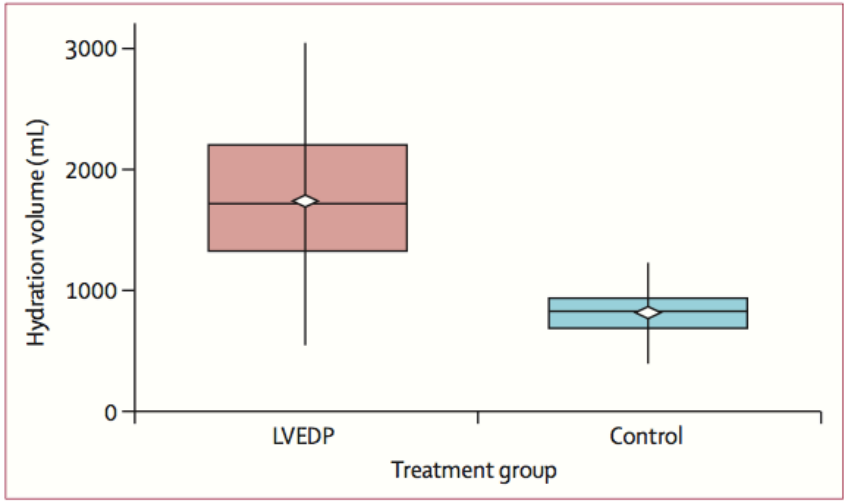


Figure 2: **Hydration volumes of normal saline administered in each group**
The box for each group represents the 25th percentile to the 75th percentile of the data (ie, the IQR). The line in the middle of the box indicates the median (50th percentile) of the data. The whiskers start from the edge of the box and extend to the furthest datapoint that is within 1·5-times the IQR. The diamonds represent the mean volume of fluid administered. LVEDP=left ventricular end-diastolic pressure.

The overall incidence of contrast-induced acute kidney injury was 11.4% (40/350)

- LVEDP: 6.7% (12/178)
- Control: 16.3% (28/172) (p=0.005)
- Relative risk 0.41 (95% CI 0.22–0.79)
- Absolute risk difference was –9 ·5% (–2.9 to –16.2%)

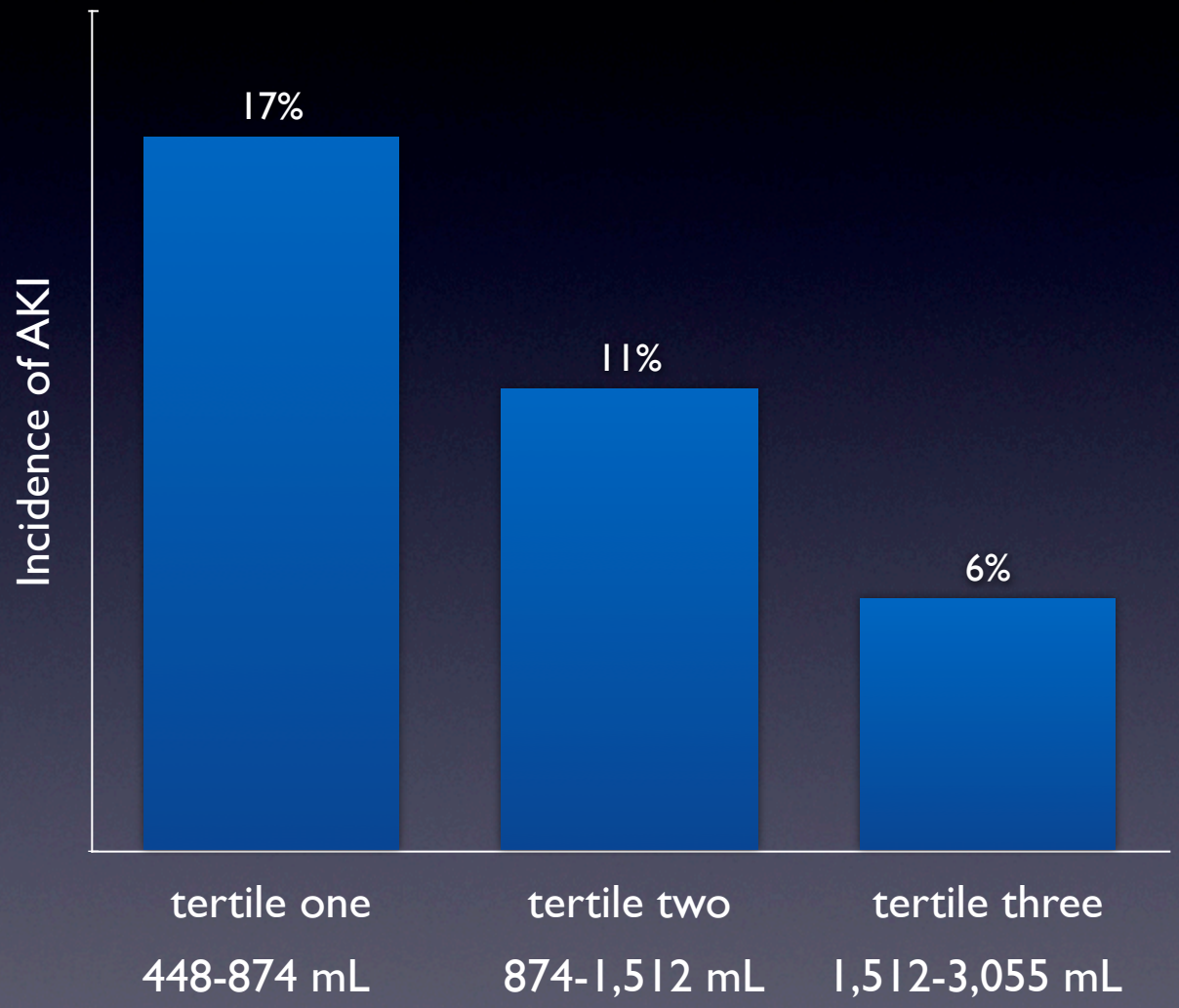
In participants with an eGFR less than 45 mL/min, the incidence of contrast-induced acute kidney injury:

- LVEDP: 8% (5/60)
- Control: 23% (14/61)
- relative risk: 0 ·36 (95% CI 0 ·14–0 ·95, p=0 ·03)

From the discussion:

...as compared with standard treatment resulted in a *significant* 68% relative reduction in the primary endpoint of contrast-induced acute kidney injury, and a *significant* 59% relative reduction in major adverse clinical events.

AKI based on volume of fluid given



Persistent renal impairment

2–8 weeks after the procedure

- LVEDP: 3.4% (6/178) of 12 with CIAKI
- Control: 7.0% (12/172) of 28 with CIAKI
- Relative risk 0.48 (95% CI 0.19–1.26)

Persistent renal impairment was recorded in 46% (18/39) of patients who developed contrast-induced acute kidney injury.

Major adverse events

	LVEDP-guided group (n=196)	Control group (n=200)	Relative risk (95% CI)	Risk difference (95% CI)	p value
At 30 days					
All-cause mortality	0	3 (1·5%)	..	..	0·25
Myocardial infarction	1 (0·5%)	4 (2·0%)	..	..	0·37
Renal replacement therapy	1 (0·5%)	3 (1·5%)	..	..	0·62
Cumulative major adverse events	2 (1·0%)	8 (4·0%)	0·26 (0·05–1·19)	–3·0 (–6·0 to 0·1)	0·11
At 6 months					
All-cause mortality	1 (0·5%)	8 (4·0%)	..	..	0·037
Myocardial infarction	4 (2·0%)	13 (6·5%)	..	..	0·029
Renal replacement therapy	1 (0·5%)	4 (2·0%)	..	..	0·37
Cumulative major adverse events	6 (3·1%)	19 (9·5%)	0·32 (0·13–0·79)	–6·4 (–11·2 to –1·7)	0·008

Data are n (%). LVEDP=left ventricular end-diastolic pressure.

Table 4: **Major adverse events at 30 days and 6 months**

In patients with contrast-induced acute kidney injury

Major adverse events

- CIAKI: 25% (10/40)
- Patients without injury: 3.5% (11/310)
- Relative risk 7.1 (95% CI 3.2–15.5; p<0.00001).

CIAKI was associated with:

- increased All-cause mortality (p=0.002)
- myocardial infarction (p=0.02)
- renal replacement therapy (p=0.0002)

- Six patients developed shortness of breath that required stopping the IV fluids

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

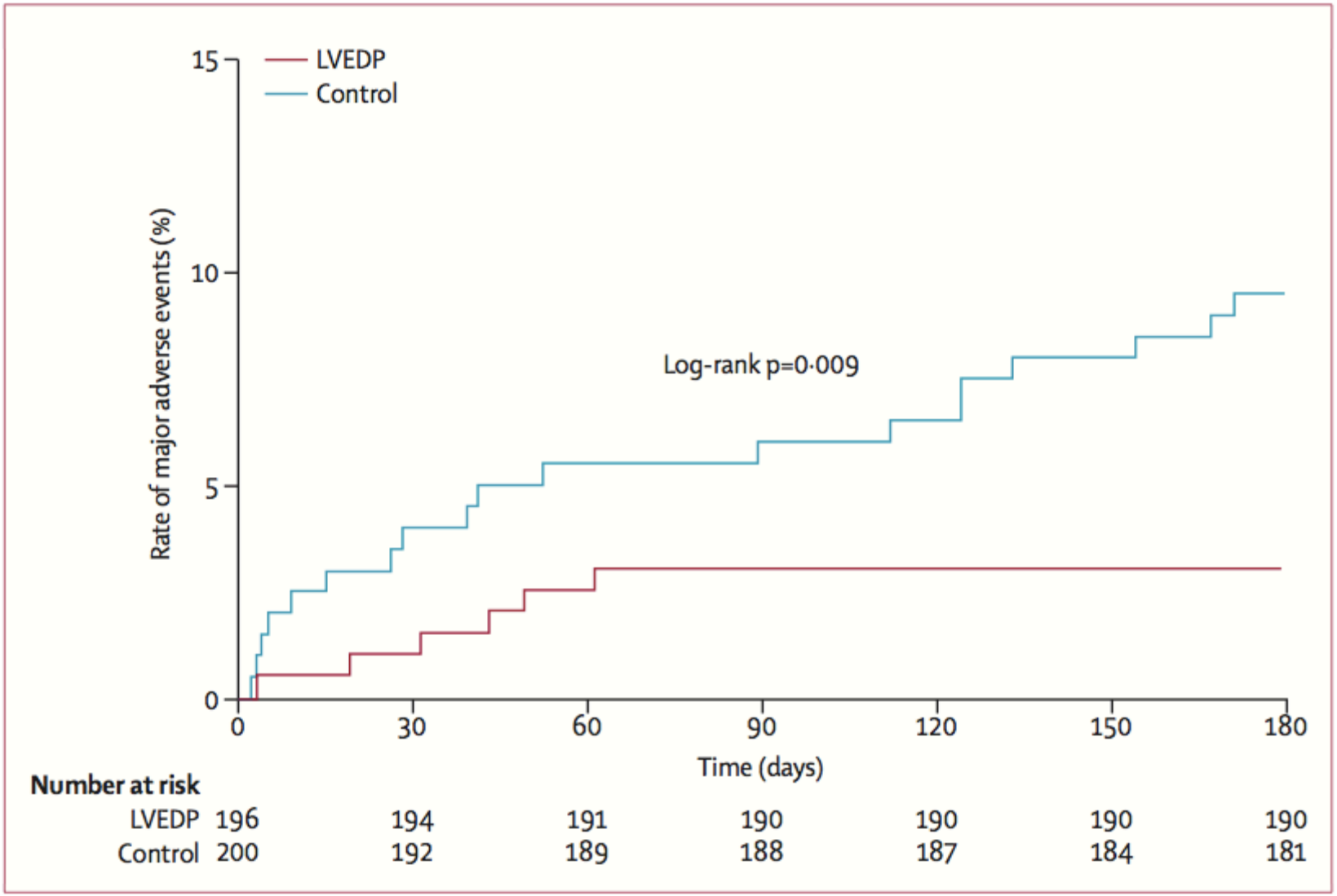


***Figure 3*: Rate of major adverse events in each group**

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.

Cox proportional hazards model for major adverse events at 6 months

This was done to see if minor imbalances in the rate of percutaneous coronary intervention and CHF were responsible for the differences in the observed results.

	LVEDP-guided hydration group (n=196)	Control group (n=200)
Medical history		
Diabetes mellitus	102 (52%)	101 (51%)
Dyslipidaemia (use of statin therapy or LDL>160 mg/dL)	181 (92%)	190 (95%)
Congestive heart failure†	31 (16%)	50 (25%)
Hypertension	193 (99%)	195 (98%)
Previous percutaneous coronary intervention	79 (40%)	70 (35%)

Odds ratio for contrast-induced acute kidney injury without the imbalance variables was 0.37 (95% CI 0.18–0.74) and with the imbalance variables was 0.40 (0.19–0.81)

Similarly, the hazard ratio for 6-month major adverse events without the imbalance covariates was 0.31 (95% CI 0.13–0.78) and with the imbalance covariates was 0.35 (0.14–0.89)

"Thus, the minor imbalances between treatment groups do not have a meaningful effect on the results."

	LVEDP hydration-guided group	Control group	Relative risk (95% CI)	Risk difference (95% CI)	p value
Primary endpoint					
>25% or 0·5 mg/dL increase in serum creatinine	12/178 (6·7%)	28/172 (16·3%)	0·41 (0·22–0·79)	−9·5 (-2·9 to −16·2)	0·005
Secondary endpoints					
>25% increase in serum creatinine	12/178 (6·7%)	27/172 (15·7%)	0·43 (0·22–0·82)	−9·0 (−2·5 to −15·5)	0·008
>0·5 mg/dL increase in serum creatinine	5/178 (2·8%)	11/172 (6·4%)	0·44 (0·16–1·24)	−3·6 (−8·0 to 0·8)	0·11
Sensitivity analyses					
≥0·3 mg/dL increase in serum creatinine	24/178 (13·5%)	43/172 (25·0%)	0·54 (0·34–0·85)	−11·5 (−3·3 to −19·7)	0·006
>25% or 0·5 mg/dL increase in serum creatinine in participants with ≥1 serum creatinine value available	12/190 (6·3%)	28/196 (14·3%)	0·44 (0·23–0·84)	−8·0 (−2·0 to −14·0)	0·01

Data are n/N (%). LVEDP=left ventricular end-diastolic pressure.

Table 2: **Occurrence of contrast-induced acute kidney injury**