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 investigate 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 $\geq 7.5\%$ 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/hr
• 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
- 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

178 included in primary contrast-induced acute kidney injury analysis

196 included in 30-day and 6-month clinical adverse events analysis

200 randomly allocated to standard hydration and received this treatment
- 0 lost to follow-up
- 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

172 included in primary contrast-induced acute kidney injury analysis

200 included in 30-day and 6-month clinical adverse events analysis
<table>
<thead>
<tr>
<th></th>
<th>LVEDP-guided hydration group (n=196)</th>
<th>Control group (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>71 (9)</td>
<td>72 (8)</td>
</tr>
<tr>
<td>Female sex</td>
<td>70 (36%)</td>
<td>81 (41%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>27 (14%)</td>
<td>28 (14%)</td>
</tr>
<tr>
<td>Asian</td>
<td>28 (14%)</td>
<td>29 (15%)</td>
</tr>
<tr>
<td>Latino/Hispanic</td>
<td>17 (9%)</td>
<td>24 (12%)</td>
</tr>
<tr>
<td>White</td>
<td>111 (57%)</td>
<td>113 (57%)</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td>12 (7)</td>
<td>12 (7)</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;13 mm Hg</td>
<td>113 (58%)</td>
<td>108 (54%)</td>
</tr>
<tr>
<td>13-18 mm Hg</td>
<td>52 (27%)</td>
<td>62 (31%)</td>
</tr>
<tr>
<td>&gt;18 mm Hg</td>
<td>31 (16%)</td>
<td>30 (15%)</td>
</tr>
<tr>
<td>Renal function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated GFR (mL/min/1.73 m²)</td>
<td>48 (9)</td>
<td>48 (9)</td>
</tr>
<tr>
<td>Serum creatinine concentration (mg/dL)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.3)</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>136 (20)</td>
<td>134 (21)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>69 (12)</td>
<td>68 (13)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>86 (20)</td>
<td>83 (18)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 (12)</td>
<td>170 (26)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30 (6)</td>
<td>29 (6)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>102 (52%)</td>
<td>101 (51%)</td>
</tr>
<tr>
<td>Dyslipidaemia (use of statin therapy or LDL&gt;160 mg/dL)</td>
<td>181 (92%)</td>
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</tr>
<tr>
<td>Congestive heart failure†</td>
<td>31 (16%)</td>
<td>50 (25%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>193 (99%)</td>
<td>195 (98%)</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>79 (40%)</td>
<td>70 (35%)</td>
</tr>
<tr>
<td>Previous coronary artery bypass graft</td>
<td>38 (19%)</td>
<td>35 (18%)</td>
</tr>
<tr>
<td></td>
<td>LVEDP-guided hydration group (n=196)</td>
<td>Control group (n=200)</td>
</tr>
<tr>
<td>--------------------------------</td>
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<td>-----------------------</td>
</tr>
<tr>
<td><strong>Laboratory data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin concentration (g/dL)</td>
<td>12.7 (1.8)</td>
<td>12.7 (1.1)</td>
</tr>
<tr>
<td>Platelets (×10^6/µL)</td>
<td>213 (67)</td>
<td>210 (66)</td>
</tr>
<tr>
<td>LDL concentration (mg/dL)</td>
<td>89 (38)</td>
<td>89 (33)</td>
</tr>
<tr>
<td>HDL concentration (mg/dL)</td>
<td>45 (12)</td>
<td>47 (13)</td>
</tr>
<tr>
<td>Haemoglobin A₁₃ (%)</td>
<td>7.2% (1.2%)</td>
<td>7.1% (1.4%)</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors</td>
<td>155 (79%)</td>
<td>146 (73%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>167 (85%)</td>
<td>168 (84%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>48 (25%)</td>
<td>60 (30%)</td>
</tr>
<tr>
<td>N-acetylcysteine</td>
<td>75 (38%)</td>
<td>74 (37%)</td>
</tr>
<tr>
<td><strong>Procedural details</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast total (mL)</td>
<td>104 (84-187)</td>
<td>112 (79-209)</td>
</tr>
<tr>
<td>Procedure duration (min)</td>
<td>26 (18-48)</td>
<td>30 (17-54)</td>
</tr>
<tr>
<td>Fluoroscopy duration (min)</td>
<td>5.0 (2.6-11.4)</td>
<td>6.1 (2.5-11.4)</td>
</tr>
<tr>
<td>Percutaneous coronary intervention*</td>
<td>47 (24%)</td>
<td>65 (33%)</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>77 (35%)</td>
<td>89 (45%)</td>
</tr>
</tbody>
</table>

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 (i.e., 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

Incidence of AKI

<table>
<thead>
<tr>
<th>Tertile</th>
<th>Volume Range</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tertile One</td>
<td>448-874 mL</td>
<td>17%</td>
</tr>
<tr>
<td>Tertile Two</td>
<td>874-1,512 mL</td>
<td>11%</td>
</tr>
<tr>
<td>Tertile Three</td>
<td>1,512-3,055 mL</td>
<td>6%</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th></th>
<th>LVEDP-guided group (n=196)</th>
<th>Control group (n=200)</th>
<th>Relative risk (95% CI)</th>
<th>Risk difference (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At 30 days</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0</td>
<td>3 (1.5%)</td>
<td>..</td>
<td>..</td>
<td>0.25</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (0.5%)</td>
<td>4 (2.0%)</td>
<td>..</td>
<td>..</td>
<td>0.37</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>1 (0.5%)</td>
<td>3 (1.5%)</td>
<td>..</td>
<td>..</td>
<td>0.62</td>
</tr>
<tr>
<td>Cumulative major adverse events</td>
<td>2 (1.0%)</td>
<td>8 (4.0%)</td>
<td>0.26 (0.05-1.19)</td>
<td>-3.0 (-6.0 to 0.1)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>At 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>1 (0.5%)</td>
<td>8 (4.0%)</td>
<td>..</td>
<td>..</td>
<td>0.037</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>4 (2.0%)</td>
<td>13 (6.5%)</td>
<td>..</td>
<td>..</td>
<td>0.029</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>1 (0.5%)</td>
<td>4 (2.0%)</td>
<td>..</td>
<td>..</td>
<td>0.37</td>
</tr>
<tr>
<td>Cumulative major adverse events</td>
<td>6 (3.1%)</td>
<td>19 (9.5%)</td>
<td>0.32 (0.13-0.79)</td>
<td>-6.4 (-11.2 to -1.7)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

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

*Table 4: Major adverse events at 30 days and 6 months*
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<0.0001).

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

<table>
<thead>
<tr>
<th>LVEDP group</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mmHg</td>
<td>3 mmHg</td>
</tr>
<tr>
<td>7 mmHg</td>
<td>23 mmHg</td>
</tr>
<tr>
<td>26 mmHg</td>
<td>31 mmHg</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Medical history</th>
<th>LVEDP-guided hydration group (n=196)</th>
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<tr>
<td>Diabetes mellitus</td>
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<td>195 (98%)</td>
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<tr>
<td>Previous percutaneous coronary intervention</td>
<td>79 (40%)</td>
<td>70 (35%)</td>
</tr>
</tbody>
</table>
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.”
<table>
<thead>
<tr>
<th></th>
<th>LVEDP hydration-guided group</th>
<th>Control group</th>
<th>Relative risk (95% CI)</th>
<th>Risk difference (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;25% or 0.5 mg/dL increase in serum creatinine</td>
<td>12/178 (6.7%)</td>
<td>28/172 (16.3%)</td>
<td>0.41 (0.22–0.79)</td>
<td>-9.5 (-2.9 to -16.2)</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;25% increase in serum creatinine</td>
<td>12/178 (6.7%)</td>
<td>27/172 (15.7%)</td>
<td>0.43 (0.22–0.82)</td>
<td>-9.0 (-2.5 to -15.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>&gt;0.5 mg/dL increase in serum creatinine</td>
<td>5/178 (2.8%)</td>
<td>11/172 (6.4%)</td>
<td>0.44 (0.16–1.24)</td>
<td>-3.6 (-8.0 to 0.8)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Sensitivity analyses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0.3 mg/dL increase in serum creatinine</td>
<td>24/178 (13.5%)</td>
<td>43/172 (25.0%)</td>
<td>0.54 (0.34–0.85)</td>
<td>-11.5 (-3.3 to -19.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>&gt;25% or 0.5 mg/dL increase in serum creatinine in participants with ≥1 serum creatinine value available</td>
<td>12/190 (6.3%)</td>
<td>28/196 (14.3%)</td>
<td>0.44 (0.23–0.84)</td>
<td>-8.0 (-2.0 to -14.0)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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

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