HYDration and bicarbonate to prevent acute Renal injury after EVAR

HYDRA trial

Athanasios Saratzis MBBS MRCS FHEA PhD
NIHR Academic Clinical Lecturer
NIHR Leicester Biomedical Research Centre

Virginia Chiocchia; Ahamed Jiffry; Neelam Hassanali; Surjeet Singh; Chris Imray; Matthew Bown; Asif Mahmood
Disclosures

Salary: National Institute for Health Research (NIHR)

CONSULTANCIES

General Electric: consultancy, trial steering committee
Novartis: consultancy, trial planning
Amgen: investigator in clinical trial (paid)

TRAVEL, BURSARIES, AWARDS, PRIVATE GRANTS

Maquet
British Society for Endovascular Therapy
Vascutek Terumo (educational grant)
AKI → abrupt loss of kidney function

Potential mechanisms in EVAR

Renal arteries
- Coverage of accessory arteries in 10%
- Occlusion of orifice
- Dissection or stenosis

AAA
- Significant inflammatory infiltrate (not excised as in open repair)

Lower limbs
- Ischaemic during the procedure (45-120 minutes)
- Ischaemia reperfusion injury

Implications of AKI in EVAR

Series of 950 EVARs with long-term FU

Incidence: 20 - 25%

<table>
<thead>
<tr>
<th>Implications</th>
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<tbody>
<tr>
<td>Short term mortality</td>
<td>HR: <strong>4.8</strong> (95% CI: 2.3-5.6)</td>
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<tr>
<td>Long term mortality</td>
<td>HR: <strong>2.4</strong> (95% CI: 1.4-3.1)</td>
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AKI after EVAR associated with:

- Short-term survival
- Long-term survival
- Long-term cardiovascular events

£4.2 million extra treatment costs
5,180 bed days

Saratzis et al. EJVES 2016
Saratzis et al. CJASN 2015
Saratzis et al. Kidney International 2017
Research question

How can we prevent AKI in EVAR?

- Mechanisms and patient co-morbidities in EVAR-related AKI very different to other interventions

- No RCT investigating AKI prevention in EVAR
Methods:

1) Create an EVAR specific AKI intervention:
   Evidence review, patient input (interviews), national survey of anaesthetists, focus groups → Delphi
   • 10ml/kg/hr before & 2ml/kg/hr after (Hartmann’s)
   • 8.4% NaHCO3 1ml/kg over 1 hour @ induction

2) RCT to test it
• Blinded placebo controlled prospective multicentre randomised controlled trial

• Supported by Oxford CTU

• Primary outcome: AKI incidence (AKIN criteria)

• Reporting 1 year pilot-trial data today
Randomisation: 2 centres in the pilot 1\textsuperscript{st} year

GROUP 1: hydration

GROUP 2: hydration & bicarbonate 1mmol/kg bolus

EVAR

2 hours: urine sample

6 hours: urine sample

24 hours: urine and blood sample

48 hours: blood sample

FOLLOW-UP
84% eligible patients recruited = 58 participants

Enrolment

Assessed for eligibility (n=109)
- Excluded (n=51)
  - Not meeting inclusion criteria (n=42)
  - Declined to participate (n=3)
  -Incomplete screening (n=6)

Randomised and consented (n=58)

Standard hydration

Allocated to intervention (n=28)
- Received allocated intervention (n=28)
- Did not receive allocated intervention (n=0)

Follow-Up
- Completed post-operative outcome (n=28)
- Completed 30 day follow-up (n=25)
  Reasons for non-completion:
  - 3 patients attended 30-day follow-up outside the permitted window

Analysis
- Analysed (As treated) (n=30)
  - Excluded from analysis (n=0)
  - 30 day follow-up (As treated) (n=27)

Standard hydration + bolus bicarbonate

Allocated to intervention (n=30)
- Received allocated intervention (n=28)
- Did not receive allocated intervention (n=2)
  Reasons:
  - Unavailability of study medication – crossover to control group (n=2)

Completed post-operative outcome (n=30)
Completed 30 day follow-up (n=28)
  Reasons for non-completion:
  - 2 patients attended 30-day follow-up outside the permitted window

Analysed (As treated) (n=28)
- Excluded from analysis (n=0)
- 30 day follow-up (As treated) (n=26)
## Demographics & anatomy

**PILOT ROUND: 1st YEAR**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Control</th>
<th>Intervention</th>
<th>Total (N = 58)</th>
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<tbody>
<tr>
<td>Age</td>
<td>75.5 (70, 80)</td>
<td>74.5 (73, 80)</td>
<td>75 (71, 80)</td>
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<tr>
<td>Female</td>
<td>3 (10%)</td>
<td>3 (10.7%)</td>
<td>6 (10.3%)</td>
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<tr>
<td>AAA diameter</td>
<td>6.2 (5.9, 6.6)</td>
<td>6.7 (5.8, 8.1)</td>
<td>6.3 (5.8, 6.9)</td>
</tr>
<tr>
<td>Neck length</td>
<td>2.1 (1.5, 2.6)</td>
<td>2.0 (1.6, 2.6)</td>
<td>2.0 (1.6, 2.6)</td>
</tr>
<tr>
<td>Neck calcification</td>
<td>4 (14.3%)</td>
<td>3 (10.0%)</td>
<td>7 (12.1%)</td>
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Baseline characteristics

• Patients **comparable** in terms of:

  Cardiovascular risk factors
  Major **established AKI risk-factors** including eGFR
  **Contrast** volume
  **Duration** of procedure

97% of patients had a suprarenal fixation device

**PILOT ROUND: 1st YEAR**
Results

- 84% recruitment rate
- No NaHCO3 AEs $\rightarrow$ high-dose NaHCO3 safe

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<thead>
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<th>AKI incidence</th>
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<tbody>
<tr>
<td>Controls</td>
<td>33%</td>
</tr>
<tr>
<td>Intervention</td>
<td>7%</td>
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<th>Major complications</th>
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<tr>
<td>Controls</td>
<td>10% (2 life-threatening)</td>
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<tr>
<td>Intervention</td>
<td>0</td>
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URINE and PLASMA markers of tubular ischaemia & inflammation over 2 days.
Conclusions

High-dose NaHCO3 promising AKI prevention strategy

• Safe
• Cheap
• Easily reproducible
• Acceptable by patients & clinicians

• Definitive RCT: currently in planning; 782 recruits
Acknowledgements

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