Cardiac Remodelling Following Ligation of Arteriovenous Fistula in Stable Renal Transplant Recipients: A Randomized Controlled Study

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Background

• Kidney Transplantation is the optimal long-term management of end-stage kidney disease

• Cardiovascular (CV) disease is responsible for up to 40% of deaths in kidney transplant recipients

• Left Ventricular Mass (LVM) is strongly associated with CV disease and CV mortality
Background

• Arteriovenous fistula contribute adversely to cardiac remodelling and function

• No guideline consensus on management of a redundant arteriovenous fistula following successful kidney transplantation

• No previous randomized controlled trials have been performed that study the CV effects of ligation of arteriovenous fistulas following successful kidney transplantation
Aim

To study the effects of ligation of arteriovenous fistula on cardiovascular structure and function in stable kidney transplant recipients utilizing cardiac magnetic resonance imaging (CMR)
Primary Hypothesis:

• Ligation of arteriovenous fistula in stable kidney transplant recipients would result in improvement in cardiac structure with a significant reduction in LVM, compared with control subjects not undergoing arteriovenous fistula ligation

Secondary Hypothesis:

• Ligation of arteriovenous fistulas in stable kidney transplant recipients would result in reductions in both ventricular and atrial volumes, NT-pro BNP levels and peak pulmonary artery velocity
Methods

- **Study Design**: Open-label, multi-centre, two group, parallel-design, randomized controlled trial. Prospectively registered with Australian and New Zealand clinical trials registry. **ACTRN12613001302741**

- **Inclusion Criteria**: Adult ($\geq$ 18 years) kidney transplant recipients; $\geq$ 12 months post successful transplant; stable kidney function; a persistent & functioning arteriovenous fistula; deemed at low risk of graft failure.

- **Exclusion Criteria**: Contraindication to MRI scan; claustrophobia; unstable or deteriorating post-transplant kidney anticipated to require re-institution of haemodialysis within 24 months.
Methods

• Procedure:

![Diagram showing the procedure with First CMR, AVF Ligation, and Second CMR]

• **Sample size:** To obtain a 9% change in LV mass with 80% power, it was calculated that 64 study participants were required, accounting for a dropout rate of 10%.
93 patients were assessed for eligibility

29 excluded
- 17 did not meet criteria
- 10 declined to participate
- 2 were claustrophobic

64 underwent randomization

33 patients assigned to intervention (AVF Ligation with repeat CMR in 6 months)
- 32 underwent first CMR scan
- 31 received ligation
- 1 moved interstate
- 1 withdrew consent.

1 died
3 declined second scan

27 included in the analysis of primary and secondary outcomes

31 patients assigned to no intervention (Observation with repeat CMR in 6 months)

1 died
3 lost to follow up

27 were included in the analysis of primary and secondary outcomes
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>AVF ligation arm (n = 32)</th>
<th>Control arm (n = 31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.3 ± 11.8</td>
<td>60.4 ± 9.5</td>
<td>0.70</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>20 (62.5)</td>
<td>22 (70.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>AVF creation to first scan (months)</td>
<td>113.3 ± 86.5</td>
<td>138.7 ± 99.4</td>
<td>0.32</td>
</tr>
<tr>
<td>Transplantation until first scan (months)</td>
<td>92.3 ± 71.7</td>
<td>115.0 ± 97.9</td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>9 (28.1)</td>
<td>9 (29)</td>
<td>0.83</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>25 (78.1)</td>
<td>23 (71.8)</td>
<td>0.25</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>7 (21.8)</td>
<td>9 (29)</td>
<td>0.32</td>
</tr>
<tr>
<td>Peripheral Vascular Disease, n (%)</td>
<td>2 (6.2)</td>
<td>2 (6.4)</td>
<td>0.83</td>
</tr>
<tr>
<td>Prior ischaemic heart disease, n (%)</td>
<td>4 (12.5)</td>
<td>2 (6.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>Location of AVF, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Forearm AVF</td>
<td>14 (43.7)</td>
<td>16 (51.6)</td>
<td>0.59</td>
</tr>
<tr>
<td>• Upper arm AVF</td>
<td>18 (56.2)</td>
<td>15 (48.3)</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD
### Baseline Cardiac Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>AVF ligation arm (n=32)</th>
<th>Control arm (n=31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV Mass (gm)</td>
<td>151.2 ± 36.5</td>
<td>153.4 ± 47.8</td>
<td>0.85</td>
</tr>
<tr>
<td>LV EDV (ml/min)</td>
<td>161.5 ± 52.3</td>
<td>171.7 ± 45.5</td>
<td>0.45</td>
</tr>
<tr>
<td>LV ESV (ml/min)</td>
<td>56.3 ± 25.7</td>
<td>52.4 ± 18.9</td>
<td>0.52</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>67.7 ± 9.9</td>
<td>69.3 ± 6.7</td>
<td>0.50</td>
</tr>
<tr>
<td>RV EDV (ml/min)</td>
<td>166.4 ± 53.0</td>
<td>179.8 ± 52.2</td>
<td>0.35</td>
</tr>
<tr>
<td>RV ESV (ml/min)</td>
<td>63.1 ± 21.1</td>
<td>65.6 ± 24.4</td>
<td>0.69</td>
</tr>
<tr>
<td>RV EF (%)</td>
<td>62.4 ± 6.9</td>
<td>64.0 ± 6.3</td>
<td>0.36</td>
</tr>
<tr>
<td>LA Area (cm²)</td>
<td>25.2 ± 5.5</td>
<td>27.0 ± 5.2</td>
<td>0.22</td>
</tr>
<tr>
<td>RA Area (cm²)</td>
<td>22.1 ± 4.8</td>
<td>23.8 ± 4.8</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Data are mean ± SD
Primary end point

AVF Non-ligated

Mean LV mass (gm)

LVM increase of 1.2gm (95% CI -4.8 to 7.2); p = 0.69

AVF ligated

LVM decrease of 22.1gm (95% CI -29.1 to -15.0); p < 0.001

Indexed to BSA, LVM reduction was 11.8 gm/m² (95% CI 15.2 to 7.8); p < 0.001

14.7 % decrease in LV mass with AVF closure

Scan 1            Scan 2
LV End Diastolic Volume (ml)
AVF Non ligated: p = 0.19
AVF Ligated: p = 0.26

LV End Systolic Volume (ml)
AVF Non ligated: p < 0.01
AVF Ligated: p = 0.30

Left Atrial Area (cm²)
AVF Non ligated: p = 0.43
AVF Ligated: p < 0.001

RV End Diastolic Volume (ml)
AVF Non ligated: p = 0.10
AVF Ligated: p < 0.001

RV End Systolic Volume (ml)
AVF Non ligated: p = 0.30
AVF Ligated: p < 0.01

Right Atrial Area (cm²)
AVF Non ligated: p = 0.16
AVF Ligated: p < 0.001

Scan 1                   Scan 2
Secondary End Points:

**NT-pro BNP Level (ng/L)**
- AVF Non Ligated: 500 ng/L
- AVF Ligated: 450 ng/L
- Reduction in NT-pro BNP from 411 ng/L to 166 ng/L with AVF ligation (p < 0.01)

**Left Atrial Volume (ml)**
- AVF Non Ligated: 60 ml
- AVF Ligated: 45 ml
- Reduction in left atrial volume by 17.5 ml with AVF ligation (p < 0.001)

**Pulmonary Artery peak velocity (m/sec)**
- AVF Non Ligated: 0.5 m/sec
- AVF Ligated: 0.3 m/sec
- Non-significant reduction in peak pulmonary artery flow by 0.19 m/sec with AVF ligation (p = 0.07)
Complications of Arteriovenous Fistula Ligation:

- **Thrombosis** causing pain and erythema over the proximal venous segment in 6 participants - resolved with rest and anti-inflammatory medication

- **Infection** over the suture lines in 2 patients (managed with oral antimicrobial therapy)

- No patients required admission or surgical re-intervention

- There was **no significant change in eGFR at follow-up** comparing AVF ligation versus controls
Summary:

Arteriovenous fistula ligation resulted in:

1. A significant reduction in LV mass
2. A significant reduction in the volume of all four cardiac chambers
3. A significant reduction in NT-pro BNP levels

• Control patients face persisting and substantial deleterious cardiac remodelling

• Further investigation would clarify the impact of AVF ligation on clinical outcomes following kidney transplantation