Arterial Revascularization Trial (ART)

Randomized comparison of single versus bilateral internal thoracic artery grafts in 3102 CABG patients: Major cardiovascular outcomes at ten years of follow up

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for the Arterial Revascularization Trial Investigators
(No conflicts declared)

ESC 2018

MRC
Medical Research Council

British Heart Foundation

National Institute for Health Research

University of Oxford

NHS
Declaration of interest

- I have nothing to declare
Background: What We Already Know

① Coronary artery bypass grafting (CABG) is highly effective for symptoms and/or prognosis in multi-vessel and left main coronary artery disease (SYNTAX, CORONARY, PRECOMBAT, BEST, EXCEL, NOBLE: 2013-2016)

② Over 1 million CABG performed worldwide each year; standard operation in >90% is CABG x 3 (1 internal thoracic artery (ITA) and 2 vein grafts)

③ Strong angiographic evidence of increasing failure of vein grafts over time (due to progressive atherosclerosis) that accelerates after 5 years and that increases overall mortality and cardiac morbidity

④ Strong angiographic evidence that ITA grafts have excellent long term patency rates (> 90% at 20 years)

⑤ Left ITA is established as the standard of care for grafting the left anterior descending (LAD) coronary artery during CABG

⑥ Numerous observational studies have estimated a 20% reduction in mortality with Bilateral versus Single ITA grafts over the long-term

⑦ Low use of Bilateral ITA (<10% in Europe, <5% in USA) due to 3 concerns
   (i) increased technical complexity
   (ii) potentially increased mortality and morbidity
   (iii) lack of evidence from RCTs
• Enrolment from June 2004 to December 2007
• 28 cardiac surgery centres
• 7 countries (UK, Poland, Australia, Brazil, India, Italy, Austria)
• 3102 patients randomized (1554 patients to single and 1548 to bilateral ITA)
• At 10 years high use of guideline based medical therapy: aspirin (81%), statins (89%), ACE-inhibitor or Angiotensin receptor blockers (73%), beta blockers (74%)

(Much higher than other contemporary PCI vs CABG trials)
Analysis of Results at 10 Years:

98.4% of Patients With Vital Status

1. **Intention To Treat (ITT):**

2. **As Treated (AT):** Non-Randomized

   - 36% of Patients Received A ‘Different’ Treatment Strategy
   - 14% of Bilateral ITA crossed to Single ITA
   - 22% of Single ITA received a 2\textsuperscript{nd} Arterial Graft (Radial Artery)
MORTALITY AT 10 YEARS (Intention To Treat)

HR (95% CI) = 0.96 (0.82, 1.12)

\[ p = 0.62 \]

No. at risk
- Bilateral graft: 1548, 1481, 1417, 1359, 1283, 882
- Single graft: 1554, 1484, 1432, 1370, 1283, 894
MORTALITY AT 10 YEARS (As Treated)

HR (95% CI) = 0.81 (0.68, 0.95)

No. at risk
MAG  1690  1632  1567  1510  1430  1430  998
SAG  1330  1270  1222  1163  1081  1081  750
Patients With Event (%)  

<table>
<thead>
<tr>
<th>Time from randomisation (years)</th>
<th>No. at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1548</td>
</tr>
<tr>
<td>2</td>
<td>1435</td>
</tr>
<tr>
<td>4</td>
<td>1362</td>
</tr>
<tr>
<td>6</td>
<td>1299</td>
</tr>
<tr>
<td>8</td>
<td>1214</td>
</tr>
<tr>
<td>10</td>
<td>830</td>
</tr>
</tbody>
</table>

DEATH, MI, STROKE AT 10 YEARS (Intention To Treat)  

HR (95% CI) = 0.90 (0.78, 1.03)  
p = 0.12
DEATH, MI, STROKE AT 10 YEARS (As Treated)

HR (95% CI) = 0.80 (0.69, 0.93)

No. at risk
MAG  1690  1591  1510  1442  1353  934
SAG  1330  1212  1162  1101  1006  692
Why No Difference in Bilateral vs Single ITA Grafts @ 10 years (Intention To Treat)?

① Genuinely NO Difference:
   (Concept of Complete vs Incomplete Revascularization ?)

② Guideline Based Medical Therapy:
   in > 80% (slows vein graft failure ?)

③ Radial Artery Use:
   22% of Single ITA: (superior 5yr patency and clinical outcomes)

④ Differential X-over:
   14% of Bilateral ITA → Single ITA; 4% Single ITA → Bilateral ITA

⑤ Surgeon Experience:
   Individual Surgeon X-over from Bilateral ITA to Single ITA: 0%-100%
# Radial-Artery or Saphenous-Vein Grafts in Coronary-Artery Bypass Surgery

Mario Gaudino, M.D., Umberto Benedetto, M.D., Stephen Frenes, M.D., Giuseppe Biondi-Zoccai, M.D., M.Stat., Art Sedrakyan, M.D., Ph.D., John D. Puskas, M.D., Gianni D. Angelini, M.D., Brian Buxton, M.D., Giacomo Frati, M.D., David L. Hare, M.D., Philip Hayward, M.D., Giuseppe Nasso, M.D., Neil Moat, M.D., Miodrag Peric, M.D., Kyung J. Yoo, M.D., Giuseppe Speziale, M.D., Leonard N. Girardi, M.D., and David P. Taggart, M.D., for the RADIAL Investigators*

## Table 3. Main Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Radial-Artery Group (N = 534)</th>
<th>Saphenous-Vein Group (N = 502)</th>
<th>Treatment Effect†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, myocardial infarction, or repeat revascularization</td>
<td>67 (12.5)</td>
<td>94 (18.7)</td>
<td>0.67 (0.49–0.90)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>40 (7.5)</td>
<td>42 (8.4)</td>
<td>0.90 (0.59–1.41)</td>
<td>0.68</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>16 (3.0)</td>
<td>21 (4.2)</td>
<td>0.72 (0.53–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Repeat revascularization</td>
<td>23 (4.3)</td>
<td>43 (8.6)</td>
<td>0.50 (0.40–0.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Graft occlusion§</td>
<td>28/345 (8.1)</td>
<td>61/307 (19.9)</td>
<td>0.44 (0.28–0.70)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

§ Only within 2 months.
Effects of Surgeon Volume in ART

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Bilateral ITA</th>
<th>Single ITA</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 operations</td>
<td>172/829 (20.8)</td>
<td>151/846 (17.9)</td>
<td>1.17 (0.94, 1.46)</td>
<td>0.015</td>
</tr>
<tr>
<td>≥ 50 operations</td>
<td>127/637 (19.9)</td>
<td>159/634 (25.1)</td>
<td>0.79 (0.62, 0.99)</td>
<td></td>
</tr>
<tr>
<td><strong>Composite – Death/MI/Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 operations</td>
<td>210/829 (25.3)</td>
<td>207/846 (24.5)</td>
<td>1.03 (0.85, 1.25)</td>
<td>0.058</td>
</tr>
<tr>
<td>≥ 50 operations</td>
<td>156/637 (24.5)</td>
<td>195/634 (30.8)</td>
<td>0.78 (0.63, 0.96)</td>
<td></td>
</tr>
</tbody>
</table>

Favors Bilateral ITA  Favors Single ITA
Incidence and clinical implications of intraoperative bilateral internal thoracic artery graft conversion: Insights from the Arterial Revascularization Trial [JTCVS 2018]

Umberto Benedetto, MD, PhD, a Douglas G. Altman, DSc, b Marcus Flather, MD, c Stephen Gerrry, MSc, b Alastair Gray, PhD, d Belinda Lees, BSc, PhD, a and David P. Taggart, MD, PhD, e on behalf of the Arterial Revascularization Trial Investigators

Conversion rate from Bilateral to Single ITA: 14%
(Single to Bilateral ITA 4%)
Individual Surgeon: 0-100%
Individual Centres: 0-49%
✗ INFERIOR CLINICAL OUTCOMES AT 5 YEARS
Intention to Treat
10-Year MORTALITY FOR HIGHEST VOLUME SURGEON IN ART

1.2% X-Over BITA to SITA

HR (95% CI) = 0.69 (0.46, 1.03)

No. at risk
Bilateral graft 211 202 195 188 175 175 122
Single graft 205 196 188 175 161 114
Summary: Ten Year Analysis of the ART

- ART Largest CABG trial with long term follow-up (>98% @ 10 yrs)
- Excellent 10 year outcomes for CABG in both groups
- 14% allocated to Bilateral ITA actually received Single ITA, and 22% of single ITA received additional radial artery graft
- Intention To Treat: Confirms safety of Bilateral ITA grafts @ 10 years
- Intention To Treat: No significant differences in all cause mortality or composite of mortality, myocardial infarction or stroke
- As Treated (Non randomized): Potential for multiple arterial grafts to provide superior outcomes
- Surgeon experience appears to be a crucial factor for outcomes with Bilateral ITA grafts
- Need for further trials of Single vs Multiple arterial grafts
Acknowledgements:

- In Memoriam Prof Doug Altman: RIP June 2018
- Presented on behalf of all investigators and patients participating in ART
- Trial Steering Committee: Peter Sleight, Doug Altman, Keith Channon, John Dark, Barbara Farrell, Marcus Flather, Alastair Gray, John Pepper, Rod Stables, David Taggart, Geza Vermez, Jeremy Pearson, Mark Pitman, Belinda Lees, Umberto Benedetto
- Data Monitoring Committee: Salim Yusuf, Stuart Pocock, Desmond Julian, Tom Treasure
- Clinical Events Adjudicators, Luckasz Krzych (Poland)
- Trial Management: Belinda Lees, Carol Wallis, Jo Cook, Edmund Wyatt, Surjeet Singh (SITU), Stephen Gerry (Statistical Support)
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- Design, conduct and analysis conducted independently of funding agencies and sponsor
Randomized comparison of the clinical outcome of single versus multiple arterial grafts: the ROMA trial—rationale and study protocol