Arterial Revascularization Trial (ART)
Randomized comparison of single versus bilateral internal mammary artery grafting in 3102 patients: Effects on major cardiovascular outcomes after five years of follow up

AHA 2016

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for the Arterial Revascularization Trial Investigators
(No conflicts declared)
Background: What We Already Know

① Coronary artery bypass grafting (CABG) is highly effective for the symptomatic and/or prognostic management of 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 is CABG x 3 (using 1 internal mammary artery (IMA) and 2 vein grafts)

③ Strong *angiographic* evidence of increasing failure of vein grafts with time (due to progressive atherosclerosis) that accelerates after 5 years

④ Strong *angiographic* evidence that internal mammary (thoracic) arteries (IMA) have excellent long term patency rates (> 90% at 20 years)

⑤ Left IMA (LIMA) 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 IMA grafts over the long-term

⑦ Low use of bilateral IMA (<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
While some contemporary studies show superior vein graft patency the largest current angiographic study (PREVENT IV) show similar patency rates
The right internal thoracic artery: is it underutilized? 
James Tatoulis\textsuperscript{a,c}, Brian F. Buxton\textsuperscript{b,c} and John A. Fuller\textsuperscript{b} [2011]
15,583 patients followed for a mean of >9 years

<10% of CABG in Europe and <5% in USA use BIMA !!!

> 60% in several Asian countries
Randomized comparison of Left IMA (plus vein grafts) versus Bilateral IMA (plus vein grafts) grafting on:

- All-cause mortality at ten years (primary outcome in 2018)
- All-cause mortality at five years (interim outcome)
- Sternal wound complications
- Mortality, myocardial infarction and stroke at five and ten years (secondary outcomes)
Sample Size

- **Estimate**: that at 10 years, bilateral IMA grafting will result in an absolute 5% reduction in mortality (i.e. from 25% to 20%) compared with single IMA grafting
- **Confirm**: with 90% power at the 5% significance level requires 2928 patients
- **Aim**: to enrol >3000 patients (1500 in each arm) over a 2- to 3-year recruitment period
Eligibility

INCLUSION:
✓ Patients with multi-vessel coronary artery disease scheduled for CABG on symptomatic and/or prognostic grounds
✓ Urgent cases for acute coronary syndrome (not evolving MI)
✓ CABG could be performed “on-pump or off-pump”

EXCLUSION:
✗ Patients with evolving myocardial infarction
✗ Patients requiring single graft
✗ Patients requiring concomitant valve surgery
✗ Patients requiring redo CABG
Results

- Enrolment from June 2004 to December 2007
- 28 cardiac surgery centres
- 7 countries (UK, Poland, Australia, Brazil, India, Italy, Austria)
- 3102 patients in total
- 1554 patients randomized to single and 1548 to bilateral IMA
- At 5 years high use of guideline based medical therapy: aspirin (89%), statins (89%), ACE-inhibitor or Angiotensin receptor blockers (73%), beta blockers (75%)

(Much higher than other contemporary PCI vs CABG trials)
Total randomized =3102

Single IMA graft group n=1554

1546 received CABG (99.5%)
  Single IMA graft n=1494
  Bilateral IMA graft n=38 [2.4%]
  Other n=14
  No surgery n=8
  (death, cancelled surgery, PCI withdrawals)

At five years
  129 died
  62 lost to follow-up [4%]
  (mean 3 years follow-up)
  9 withdrew
  Known to be alive n=1349

Bilateral IMA graft group n= 1548

1531 received CABG (98.9%)
  Bilateral IMA graft n=1294
  Single IMA graft n=215 [14%]
  Other n=22
  No surgery n=16
  (death, cancelled surgery, PCI withdrawals)

At five years
  133 Died
  71 lost to follow up [4.6%]
  (mean 3 years follow-up)
  5 Withdrew
  Known to be alive n= 1330
<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Single graft (n=1554)</th>
<th>Bilateral graft (n=1548)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>86%</td>
<td>85%</td>
</tr>
<tr>
<td>Age mean (SD) years</td>
<td>64 (9)</td>
<td>64 (9)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>14 %</td>
<td>15 %</td>
</tr>
<tr>
<td>Systolic BP mean (SD) [mmHg]</td>
<td>132 (19)</td>
<td>132 (18)</td>
</tr>
<tr>
<td>Body Mass index mean (SD)</td>
<td>28 (4)</td>
<td>28 (4)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>92 %</td>
<td>92 %</td>
</tr>
<tr>
<td>South Asian</td>
<td>5 %</td>
<td>5 %</td>
</tr>
<tr>
<td>Insulin dependent diabetes</td>
<td>5 %</td>
<td>6 %</td>
</tr>
<tr>
<td>Non insulin dependent diabetes</td>
<td>18 %</td>
<td>18 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78 %</td>
<td>77 %</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>93 %</td>
<td>94 %</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>8 %</td>
<td>7 %</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>3 %</td>
<td>3 %</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>44 %</td>
<td>40 %</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>16 %</td>
<td>16 %</td>
</tr>
<tr>
<td>NYHA class 1 and 2</td>
<td>79%</td>
<td>78%</td>
</tr>
<tr>
<td>CCS class 1-3</td>
<td>84%</td>
<td>84%</td>
</tr>
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### Surgical Details, Post-operative Care and Length of Stay

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Single graft (n=1546)</th>
<th>Bilateral graft (n=1531)</th>
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<tbody>
<tr>
<td>Details of operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>On pump</td>
<td>60 %</td>
<td>58 %</td>
</tr>
<tr>
<td>Off pump</td>
<td>40 %</td>
<td>42 %</td>
</tr>
<tr>
<td>Conversion to bypass</td>
<td>2 %</td>
<td>2 %</td>
</tr>
<tr>
<td>CABG duration minutes mean (SD)</td>
<td>199 (58)</td>
<td>222 (61)</td>
</tr>
<tr>
<td>Number of grafts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>18 %</td>
<td>18 %</td>
</tr>
<tr>
<td>3</td>
<td>49 %</td>
<td>50 %</td>
</tr>
<tr>
<td>4+</td>
<td>33 %</td>
<td>31 %</td>
</tr>
<tr>
<td>Cell saver</td>
<td>32 %</td>
<td>31 %</td>
</tr>
<tr>
<td>Aprotinin during surgery</td>
<td>24 %</td>
<td>24 %</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>12 %</td>
<td>12 %</td>
</tr>
<tr>
<td>Return to operating theatre</td>
<td>4 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Intra-aortic balloon pump use</td>
<td>4 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Renal support therapy</td>
<td>4 %</td>
<td>6 %</td>
</tr>
<tr>
<td>Hospital stay Mean days (SD)</td>
<td>8 (8)</td>
<td>8 (7)</td>
</tr>
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</table>
Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART)

David P. Taggart¹*, Douglas G. Altman², Alastair M. Gray³, Belinda Lees⁴, Belinda Lees⁵, Fiona Nugara⁴, Ly-Mee Yu², Helen Campbell³ and Marcus Flather⁴,⁵, on behalf of the ART Investigators

3102 patients randomized to single or bilateral IMA grafts

- primary outcome is 10 year survival (available 2018)
- 67 surgeons, 28 centres, seven countries

- 30 day mortality 1.2%, 1 yr mortality 2.4%
- 1 year incidence of stroke, MI, repeat revasc all < 2%

- Sternal wound reconstruction: 0.6% SIMA vs 1.9% BIMA (NNH = 78)
All Cause Mortality at 5 years

CABG MORTALITY @ 5 YEARS in SYNTAX 9%; BEST 12%; NOBLE 9%; CORONARY 14%

Single IMA: 8.4%
Bilateral IMA: 8.7%
HR: 1.04 (0.81-1.32) p = 0.77

Time from randomization (years)

Number at risk

Single IMA 1554 1502 1467 1435 1389 1332
Bilateral IMA 1548 1496 1468 1425 1370 1321
Death, Myocardial Infarction or Stroke at 5 years

Death / myocardial infarction / stroke (%)

Time from randomization (years)

Number at risk

Single IMA: 12.7%
Bilateral IMA: 12.2%
HR: 0.96 (0.79, 1.17) p=0.69

Single mammary
Bilateral mammary
<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Single graft (n=1554)</th>
<th>Bilateral graft (n=1548)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRIMARY: MORTALITY</strong></td>
<td>130 (8.4%)</td>
<td>134 (8.7%)</td>
<td>1.04 (0.81, 1.32)</td>
<td>0.77</td>
</tr>
<tr>
<td>Composite – Death, myocardial infarction, stroke</td>
<td>198 (12.7%)</td>
<td>189 (12.2%)</td>
<td>0.96 (0.79, 1.17)</td>
<td>0.69</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>54 (3.5%)</td>
<td>52 (3.4%)</td>
<td>0.97 (0.66, 1.41)</td>
<td>0.86</td>
</tr>
<tr>
<td>Stroke</td>
<td>49 (3.2%)</td>
<td>38 (2.5%)</td>
<td>0.78 (0.51, 1.19)</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>ADVERSE EVENTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Bleed</td>
<td>41 (2.6%)</td>
<td>48 (3.1%)</td>
<td>1.18 (0.78, 1.77)</td>
<td>0.44</td>
</tr>
<tr>
<td>Repeat Revascularisation</td>
<td>103 (6.6%)</td>
<td>101 (6.5%)</td>
<td>0.98 (0.76, 1.28)</td>
<td>0.91</td>
</tr>
<tr>
<td>Sternal wound complication</td>
<td>29 (1.9%)</td>
<td>54 (3.5%)</td>
<td>1.87 (1.20, 2.92)</td>
<td>0.005</td>
</tr>
<tr>
<td>Sternal wound reconstruction</td>
<td>10 (0.6%)</td>
<td>29 (1.9%)</td>
<td>2.91 (1.42, 5.95)</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Summary: Five Year Analysis of the ART

- Excellent 5 year outcomes for CABG in both groups
- Confirmation of safety of bilateral IMA grafts over medium term
- No significant differences in all cause mortality or composite of mortality, myocardial infarction or stroke
- No significant differences in major bleeds, need for repeat revascularization, angina status and quality-of-life measures (angina and QoL data not shown)
- Early excess of sternal wound reconstruction with bilateral IMA (1.9% vs 0.6%) mainly in Diabetes Mellitus with high BMI
- Differential non-adherence to randomization (4% SIMA to BIMA vs 14% BIMA to SIMA): ? Surgeon experience with BIMA
- Primary outcome is 10 year survival (available in 2018)
- Acknowledgements
Acknowledgements

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