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)







NHS National Institute for Health Research

Background: What We Already Know



- Coronary artery bypass grafting (CABG) is highly effective for the Arterial Revascularisation To symptomatic and/or prognostic management of multi-vessel and left main coronary artery disease (SYNTAX, CORONARY, PRECOMBAT, BEST, EXCEL, NOBLE: 2013-2016)
- 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 <u>angiographic</u> evidence of increasing failure of vein grafts with time (due to progressive atherosclerosis) that accelerates after 5 years
- Strong <u>angiographic</u> 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

Coronary Bypass Graft Fate and Patient Outcome: Angiographic Follow-Up of 5,065 Grafts Related to Survival and Reopcration in 1,388 Patients During 25 Years

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In current practice of > 1 million CABG per year > 80% of all grafts are SVG



While some contemporary studies show superior vein graft patency the largest current angiographic study (PREVENT IV) show similar patency rates



Original Article

Effect of Bilateral Internal Mammary Artery on Long-Term Survival A Mate Analysis Approach [CIRC 2014]

A Meta-Analysis Approach

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Design and Outcome Measures



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)





- 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 2to 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:

- X Patients with evolving myocardial infarction
- X Patients requiring single graft
- X Patients requiring concomitant valve surgery
- X 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)



Patient flow



Known to be alive n = 1330

Known to be alive n=1349

9 withdrew

Other n=14

No surgery n=8

withdrawals)

At five years

129 died

Baseline Characteristics Well Matched	Single graft (n=1554)	Bilateral graft (n=1548)
Male	86%	85%
Age mean (SD) years	64 (9)	64 (9)
Current smoker	14 %	15 %
Systolic BP mean (SD) [mmHg]	132 (19)	132 (18)
Body Mass index mean (SD)	28 (4)	28 (4)
Caucasian	92 %	92 %
South Asian	5 %	5 %
Insulin dependent diabetes	5 %	6 %
Non insulin dependent diabetes	18 %	18 %
Hypertension	78 %	77 %
Hyperlipidemia	93 %	94 %
Peripheral arterial disease	8 %	7 %
Prior stroke	3 %	3 %
Prior myocardial infarction	44 %	40 %
Prior PCI	16 %	16 %
NYHA class 1 and 2	79%	78%
CCS class 1-3	84%	84%

Surgical Details, Post-operative Care and Length of Stay

Procedures	Single graft	Bilateral graft
Details of operation	(n=1546)	(n=1531)
On pump	60 %	58 %
Off pump	40 %	42 %
Conversion to bypass	2 %	2 %
CABG duration minutes mean (SD)	199 (58)	222 (61)
Number of grafts		
2	18 %	18 %
3	49 %	50 %
4+	33 %	31 %
Cell saver	32 %	31 %
Aprotinin during surgery	24 %	24 %
Blood transfusion	12 %	12 %
Return to operating theatre	4 %	4 %
Intra-aortic balloon pump use	4 %	4 %
Renal support therapy	4 %	6 %
Hospital stay Mean days (SD)	8 (8)	8 (7)





European Heart Journal doi:10.1093/eurheartj/ehq318

FASTIRACK ESC HOT LINE

Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART)

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O3102 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%



terial Revascularisation Trial

Death, Myocardial Infarction or Stroke at 5 years



Arterial Revascularisation Trial

Clinical Outcomes and Adverse Events

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

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

- 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
- Data Monitoring Committee: Salim Yusuf, Stuart Pocock, Desmond Julian, Tom Treasure
- Funded by UK Medical Research Council, British Heart Foundation, National Institute of Health Research Efficacy and Mechanism Evaluation, sponsored by University of Oxford
- Design, conduct and analysis conducted independently of funding agencies and sponsor



British Heart

Foundation

MRC

Medical

Council

Research

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts

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