Randomized comparison of single versus double mammary coronary artery bypass grafting: 5 year outcomes of the Arterial Revascularization Trial

David Taggart
Professor of Cardiac Surgery
University of Oxford, UK
On behalf of Arterial Revascularization Trial investigators

British Heart Foundation

Arterial Revascularisation Trial

NHS
National Institute for Health Research

Funding and declarations

Arterial Revascularisation Trial

- No conflicts of interest declared by presenter
- Funded by UK Medical Research Council, British Heart Foundation, UK National Institute of Health Research Efficacy and Mechanistic Evaluation
- Sponsored by University of Oxford, UK
- Design, conduct and analysis conducted independently of funding agencies and sponsor
- Authors (David Taggart, Doug Altman, Alastair Gray, Belinda Lees, Stephen Gerry, Umberto Benedetto, Marcus Flather) take full responsibility for conduct and results from the trial
- Presented on behalf of all investigators and patients participating in ART

British Heart Foundation

NHS
National Institute for Health Research

Background

Arterial Revascularisation Trial

- Coronary artery bypass grafting (CABG) is effective for management of symptomatic multi-vessel coronary artery disease
- Left internal mammary artery has excellent long term patency rates and is established as standard of care for CABG
- Evidence that vein grafts fail over time especially >5 years
- Long term excellent patency of the right internal mammary
- Observational studies have estimated up to 20% reduction in mortality with bilateral versus single mammary artery grafts

British Heart Foundation

NHS
National Institute for Health Research

Design and outcome measures

Arterial Revascularisation Trial

Randomized multi-center comparison of left internal mammary artery (plus vein grafts) versus bilateral internal mammary artery grafting on

- All-cause mortality at five years (interim outcome: this analysis)
- Sternal wound complications
- All-cause mortality at ten years (primary outcome)
- Mortality, myocardial infarction or stroke at five and ten years (secondary outcomes)

British Heart Foundation

NHS
National Institute for Health Research

Sample size

Arterial Revascularisation Trial

- Estimated that bilateral internal mammary artery grafting would result in an absolute 5% reduction in 10-year mortality (i.e. from 25% to 20%) compared with single internal mammary artery grafting.
- To detect this expected reduction with 90% power at the 5% significance level requires 2928 patients.
- Aim was to enrol at least 3000 patients (1500 in each arm) over a 2- to 3-year recruitment period.

British Heart Foundation

NHS
National Institute for Health Research

Eligibility

Arterial Revascularisation Trial

INCLUSION

- Patients with symptomatic multi-vessel coronary artery disease scheduled for coronary artery bypass grafting (including urgent cases and planned “off pump” surgery)

EXCLUSIONS

- Single graft planned
- Redo CABG
- Evolving myocardial infarction
- Concomitant valve surgery

British Heart Foundation

NHS
National Institute for Health Research

Results

Arterial Revascularisation Trial

- 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 the single-graft group
- 1548 to the bilateral-graft group
- Use of aspirin (89%), statins (89%), ACE-inhibitor/ Angiotensin receptor blockers (73%), beta blockers (75%) at 5 years

British Heart Foundation

NHS
National Institute for Health Research

Patient flow

Arterial Revascularisation Trial

British Heart Foundation

NHS National Institute for Health Research

Baseline characteristics

	Single mammary (n=1554)	Bilateral mammary (n=1548)
Male [n (%)]	1338 (86.1%)	1318 (85.1%)
Mean (SD) age at randomization, years	63.5 (9.1)	63.7 (8.7)
Smoking status [n (%)]		
Current smoker	214 (13.8%)	237 (15.3%)
Ex-smoker	898 (57.8%)	834 (53.9%)
Never smoked	442 (28.4%)	477 (30.8%)
Ethnic origin [n (%)]		
Caucasian	1431 (92.1%)	1418 (91.6%)
East Asian	1 (0.1%)	5 (0.3%)
South Asian	76 (4.9%)	74 (4.8%)
Afro-Caribbean	2 (0.1%)	0
African	1 (0.1%)	4 (0.3%)
Other	42 (2.7%)	47 (3.0%)
Mean (SD) height [cm]	170.4 (8.4)	170.0 (8.5)
Mean (SD) weight [kg]	81.9 (14.2)	82.0 (13.5)
Mean (SD) body mass index (BMI)	28.1 (4.1)	28.3 (4.0)
Mean (SD) systolic blood pressure [mmHg]	131.8 (18.5)	131.7 (18.0)
Mean(SD) diastolic blood pressure [mmHg]	74.8 (11.1)	75.0 (11.0)
Diabetes [n (%)]		
No history	1191 (76.6%)	1177 (76.0%)
Insulin dependent diabetes	79 (5.1%)	95 (6.1%)
Non insulin dependent diabetes	284 (18.3%)	276 (17.8%)
Hypertension treated with drugs [n (%)]	1217 (78.3%)	1193 (77.1%)
Hyperlipidemia treated with drugs [n (%)]	1448 (93.2%)	1457 (94.1%)
Documented peripheral arterial disease [n (%)]	118 (7.6%)	103 (6.6%)
Documented transient ischemic attack [n (%)]	57 (3.7%)	53 (3.4%)
Prior stroke [n (%)]	48 (3.1%)	42 (2.7%)
Prior myocardial infarction [n (%)]	681 (43.8%)	619 (40.0%)
Prior percutaneous coronary intervention ± stent [n (%)]	248 (16.0%)	242 (15.6%)
NYHA class [n (%)] 1 and 2	1228 (79%)	1203 (78%)
CCS class [n (%)] 1-3	1304 (84%)	1298 (84%)

Arterial Revascularisation Trial

British Heart Foundation

NHS National Institute for Health Research

Surgical details, post-op care and length of stay

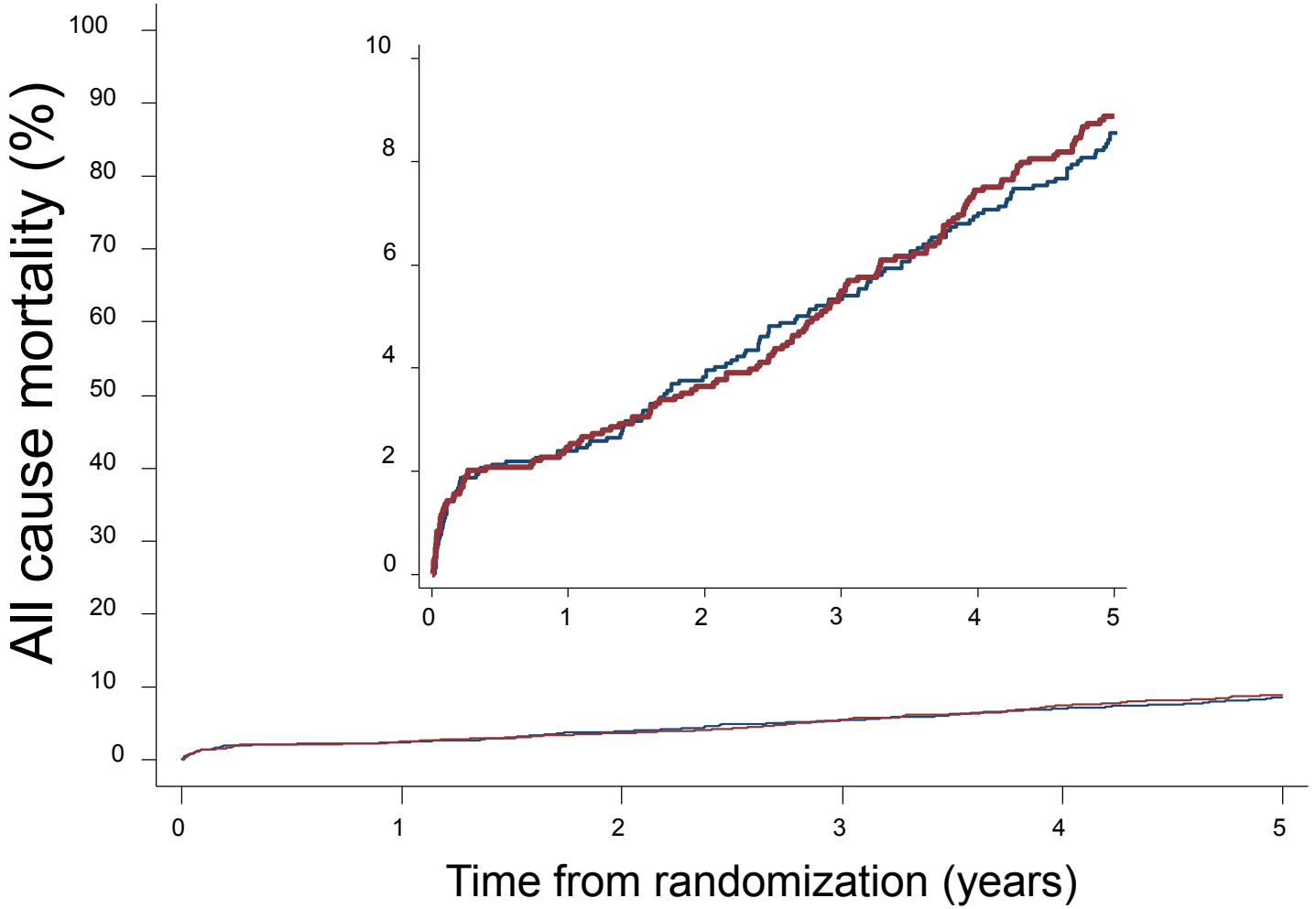
Procedures	Single mammary artery	Bilateral mammary artery
Details of operation	(n=1546)	(n=1531)
On pump	928 (60.0%)	890 (58.1%)
Off pump	618 (40.0%)	641 (41.9%)
Intra-operative conversions to bypass	13/618 (2.1%)	15/641 (2.3%)
Mean (SD) duration of operation, mins	199 (58)	222 (61)
Number of vessels grafted	(n=1546)	(n=1530)
1	11 (0.7%)	8 (0.5%)
2	273 (17.7%)	272 (17.8%)
3	749 (48.54%)	771 (50.4%)
4+	513 (33.2%)	479 (31.3%)
Aprotinin started during surgery	372/1545 (24.1%)	368/1531 (24.0%)
Aprotinin given after surgery	89/1545 (5.8%)	98/1530 (6.4%)
Blood transfusion	184/1515 (12.2%)	179/1492 (12.0%)
Median (IQR) blood (red cells)	500 (300 to 600))	500 (300 to600)
Platelets	35/1512 (2.3%)	46/1494 (3.1%)
Fresh Frozen Plasma (FFP)	53/1513 (3.5%)	66/1493 (4.4%)
Cell saver	474/1500 (31.6%)	461/1479 (31.2%)
Immediate post-operative period		
Return to theatre and reason	54/1546 (3.5%)	66/1532 (4.3%)
Bleeding	44	51
Tamponade	2	6
Other	8	9
Unknown	3	6
Intra-aortic balloon pump used (IABP)	57/1546 (3.7%)	68/1532 (4.4%)
Renal support therapy	68/1545 (4.4%)	91/1532 (5.9%)
	(n=1539)	(n=1524)
Mean (SD) Duration of ventilation (min)	863 (3293)	968 (3029)
ITU admissions: 0	8 (0.6%)	8 (0.6%)
1	1390 (96.1%)	1362 (95.3%)
Mean (SD) ITU length of stay (hours)	38 (106)	41 (94)
Mean (SD) HDU length of stay (days)	2 (3.7)	2 (3.8)
Mean (SD) post op hospital stay (days)	7.5 (7.6)	8.0 (7.4)

Arterial Revascularisation Trial

British Heart Foundation

NHS National Institute for Health Research

All cause mortality at 5 years



Number at risk

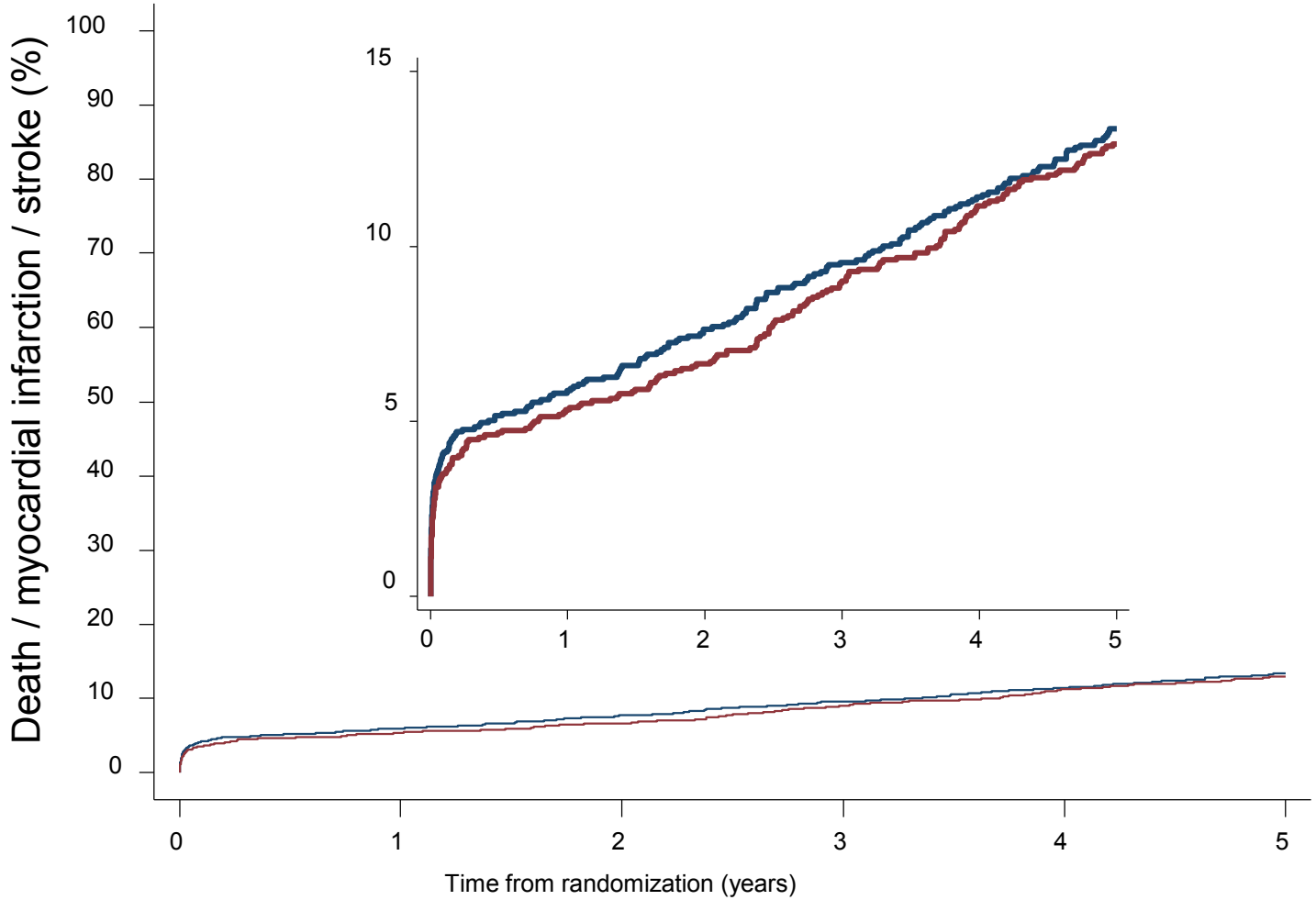
Single mammary	1554	(37)	1502	(24)	1467	(22)	1435	(24)	1389	(23)	1332
Bilateral mammary	1548	(38)	1496	(18)	1468	(28)	1425	(29)	1370	(21)	1321

Single mammary

Bilateral mammary

Arterial Revascularisation Trial

Death, myocardial infarction or stroke at 5 years



Number at risk

Single mammary	1554	(91)	1448	(27)	1410	(29)	1371	(28)	1322	(29)	1261
Bilateral mammary	1548	(82)	1452	(20)	1422	(36)	1373	(32)	1317	(26)	1266

Single mammary

Bilateral mammary

Arterial Revascularisation Trial

Clinical outcomes and adverse events

	Single mammary (n=1554)	Bilateral mammary (n=1548)	Hazard Ratio (95% CI)	P value
Clinical Outcomes				
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

Arterial Revascularisation Trial

Summary: five year analysis of arterial revascularization trial

Arterial Revascularisation Trial

- No significant differences in all cause mortality
- No significant differences in composite of mortality, myocardial infarction or stroke
- Early excess of sternal wound complications with bilateral mammary artery grafting
- No significant differences in major bleeds, need for repeat revascularization, angina status and quality-of-life measures (QoL data not shown)
- These data demonstrate medium term safety of bilateral mammary approach

British Heart Foundation

NHS
National Institute for Health Research

Discussion

Arterial Revascularisation Trial

- 5 year outcomes comparing single versus bilateral mammary artery grafting does not show any significant differences on clinical outcomes with an early excess of sternal wound complications
- Approximately 14% of patients assigned bilateral mammary group received a single mammary artery only
- This is an interim analysis which has limited power to detect differences in clinical outcomes
- Longer term follow up will determine if there are benefits from the bilateral mammary approach

British Heart Foundation

On line publication in New England Journal of Medicine
14 November 2016 Taggart et al

NHS
National Institute for Health Research