SUPPLEMENTAL MATERIAL

Table S1: Number and percentage of patients by age category

| Distribution of age | |
|---|---|
| Age<=65 | 820 (68%) |
| 65<Age<=70 | 191(16%) |
| 70<Age<=75 | 126 (10%) |
| 75<Age<=80 | 60 (5%) |
| Age>80 | 15 (1%) |

**Table S2 Baseline Characteristics by Age**

| Variable | Baseline Age Quartiles | | | | |
|---|---|---|---|---|---|
| | Q1 (Age≤54 years) (n=330) | Q2 (54<Age≤60 years) (n=295) | Q3 (60<Age≤67 years) (n=279) | Q4 (Age>67 years) (n=308) | P-value for trend[1] |
| Age (year) | 50(47, 53) | 57(56, 58) | 64(62, 65) | 72 (69, 75) | |
| Female | 35 (11%) | 26 (9%) | 37 (13%) | 50 (16%) | 0.011 |
| White race | 187 (57%) | 189 (64%) | 200 (72%) | 251 (82%) | <0.001 |
| BMI (kg/m$^2$) | 27 (24, 31) | 27 (24, 30) | 27 (24, 30) | 26 (24, 29) | 0.178 |
| **Medical History:** | | | | | |
|    Diabetes | 103 (31%) | 121 (41%) | 124 (44%) | 130 (42%) | 0.003 |
|    Hypertension | 178 (54%) | 177 (60%) | 159 (57%) | 214 (70%) | <0.001 |
|    PVD | 36 (11%) | 40 (14%) | 42 (15%) | 66 (21%) | <0.001 |
|    Renal insufficiency | 10 (3%) | 16 (5%) | 25 (9%) | 43 (14%) | <0.001 |
|    Stroke | 23 (7%) | 14 (5%) | 21 (8%) | 34 (11%) | 0.028 |
|    Atrial flutter/ fibrillation | 19 (6%) | 25 (9%) | 42 (15%) | 67 (22%) | <0.001 |
|    Previous MI | 250 (76%) | 229 (78%) | 208 (75%) | 247 (80%) | 0.320 |
|    Hyperlipidemia | 190 (58%) | 174 (59%) | 181 (65%) | 185 (60%) | 0.286 |
|    Depression | 24 (7%) | 17 (6%) | 15 (5%) | 20 (7%) | 0.646 |
|    Current smoker | 104 (32%) | 64 (22%) | 50 (18%) | 34 (11%) | <0.001 |
|    Previous PCI | 45 (14%) | 38 (13%) | 38 (14%) | 35 (11%) | 0.465 |
|    Previous CABG | 8 (2%) | 10 (3%) | 11 (4%) | 7 (2%) | 0.974 |
| **CCS angina class:** | | | | | |
|    No angina | 106 (32%) | 97 (33%) | 91 (33%) | 148 (48%) | <0.001 |
|    I | 42 (13%) | 44 (15%) | 52 (19%) | 49 (16%) | 0.145 |
|    II | 169 (51%) | 141 (48%) | 119 (43%) | 96 (31%) | <0.001 |
|    III | 10 (3%) | 12 (4%) | 15 (5%) | 11 (4%) | 0.551 |
|    IV | 3 (1%) | 1 (<1%) | 2 (1%) | 4 (1%) | 0.583 |
| **NYHA class:** | | | | | |
|    I | 35 (11%) | 50 (17%) | 22 (8%) | 32 (10%) | 0.276 |
|    II | 185 (56%) | 134 (45%) | 157 (56%) | 150 (49%) | 0.318 |
|    III | 100 (30%) | 106 (36%) | 93 (33%) | 113 (37%) | 0.152 |
|    IV | 10 (3%) | 5 (2%) | 7 (3%) | 13 (4%) | 0.315 |
| Median systolic BP (mmHg) | 120 (110, 130) | 120 (110, 130) | 120 (110, 130) | 122 (110, 136) | <0.001 |
| Median heart rate (bpm) | 76 (68, 84) | 75 (68, 82) | 74 (66, 82) | 71 (63, 80) | <0.001 |
| Median 6 minute walk distance (meter) | 352 (259, 434) | 360 (273, 415) | 340 (270, 400) | 321 (250, 385) | <0.001 |
| **Lab measures:** | | | | | |
|    Hemoglobin (g/dL) | 14.3 (13.2, 15.4) | 13.9 (12.7, 14.9) | 13.7 (12.6, 14.8) | 13.6 (12.3, 14.6) | <0.001 |
|    Creatinine (mg/dL) | 1.02 (0.90, 1.18) | 1.10 (0.97, 1.23) | 1.10 (0.94, 1.30) | 1.17 (1.00, 1.40) | <0.001 |
|    Sodium (mEq/L) | 139 (137, | 140 (137, 142) | 140 (138, 142) | 140 (137, | 0.086 |

|  | 142) |  |  | 142) |  |
|---|---|---|---|---|---|
| BUN (mg/dL) | 22 (15, 37) | 21 (16, 34) | 21 (16, 36) | 24 (18, 39) | 0.016 |

1. P-values for categorical variables are based on Cochran-Armitage Trend test. Spearman correlation test is performed to get the p-values for continuous variables and the continuous age variable.

**Table S3 Baseline Left Ventricular Structure and Function and Coronary Anatomy by Age**

| Variable | Q1 (Age≤54 years) (n=330) | Q2 (54<Age≤60 years) (n=295) | Q3 (60<Age≤67 years) (n=279) | Q4 (Age>67 years) (n=308) | P-value for Trend[1] |
|---|---|---|---|---|---|
| | **Baseline Age Quartiles** | | | | |
| **Structure and function:** | | | | | |
| LVEF (%) | 28 (22, 33) | 28 (23, 35) | 26 (21, 33) | 28 (22, 34) | 0.518 |
| ESVI | 81 (62, 103) | 81 (61, 98) | 77 (60, 105) | 77 (61, 98) | 0.190 |
| EDVI | 117 (92, 144) | 113 (90, 139) | 109 (87, 141) | 108 (87, 135) | 0.020 |
| E velocity (m/s) | 0.70 (0.30, 0.90) | 0.70 (0.50, 0.90) | 0.70 (0.50, 0.90) | 0.60 (0.50, 0.85) | <0.001 |
| A velocity (m/s) | 0.60 (0.40, 0.80) | 0.70 (0.50, 0.80) | 0.73 (0.60, 0.90) | 0.70 (0.60, 0.90) | <0.001 |
| E/A ratio | 1.00 (0.75, 2.25) | 1.00 (0.71, 1.78) | 0.80 (0.63, 1.57) | 0.75 (0.57, 1.33) | <0.001 |
| E/e' ratio (septal) | 14 (11, 20) | 17 (12, 23) | 15 (12, 24) | 17 (11, 23) | 0.129 |
| E/e' ratio (lateral) | 11 (8, 15) | 12 (9, 16) | 13 (9, 17) | 12 (8, 17) | 0.222 |
| Anterior akinesia or dyskinesia (%) | 43 (30, 57) | 43 (20, 50) | 43 (29, 57) | 40 (14, 57) | 0.146 |
| **MR severity:** | | | | | |
| None or trace | 123 (37%) | 110 (37%) | 106 (38%) | 96 (31%) | 0.145 |
| Mild | 149 (45%) | 130 (44%) | 128 (46%) | 147 (48%) | 0.456 |
| Moderate | 43 (13%) | 47 (16%) | 38 (14%) | 53 (17%) | 0.240 |
| Severe | 14 (4%) | 8 (3%) | 7 (3%) | 10 (3%) | 0.460 |
| **Coronary anatomy:** | | | | | |
| **No of vessels with stenosis ≥ 50%** | | | | | |
| 1 | 46 (14%) | 24 (8%) | 24 (9%) | 18 (6%) | <0.001 |
| 2 | 101 (31%) | 94 (32%) | 87 (31%) | 84 (27%) | 0.362 |
| 3 | 183 (56%) | 177 (60%) | 168 (60%) | 205 (67%) | 0.006 |
| Stenosis of proximal LAD ≥75% | 242 (73%) | 200 (68%) | 185 (66%) | 199 (65%) | 0.020 |
| Duke CAD severity index | 52 (39, 65) | 65 (39, 77) | 65 (39, 77) | 65 (39, 77) | 0.039 |

1. P-values for categorical variables are based on Cochran-Armitage Trend test. Spearman correlation test is performed to get the p-values for continuous variables and the continuous age variable.

LVEF – left ventricular ejection fraction, ESVI – end systolic volume indexed, EDVI  - end diastolic volume indexed, E - early diastolic filling velocity, A – atrial contraction induced diastolic filling velocity wave, e′ - early diastolic myocardial velocity, MR – mitral regurgitation, LAD – left anterior descending , CAD – coronary artery disease

**Table S4 Procedural Details and Perioperative Complications by Age**

| Variable | Baseline Age Quartiles | | | | P-value for Trend[1] |
|---|---|---|---|---|---|
| | Q1 (Age≤54 years) (n=149) | Q2 (54<Age≤60 years) (n=127) | Q3 (60<Age≤67 years) (n=131) | Q4 (Age>67 years) (n=148) | |
| Number of conduits: | | | | | |
| 1 | 26 (17%) | 10 (8%) | 15 (12%) | 18 (12%) | 0.284 |
| 2 | 49 (33%) | 37 (29%) | 42 (32%) | 47 (32%) | 0.958 |
| 3 | 60 (40%) | 60 (47%) | 52 (40%) | 64 (43%) | 0.894 |
| ≥4 | 14 (9%) | 20 (16%) | 22 (17%) | 19 (13%) | 0.362 |
| Number of arterial conduits: | | | | | |
| 0 | 11 (7%) | 9 (7%) | 12 (9%) | 18 (12%) | 0.123 |
| 1 | 123 (83%) | 104 (82%) | 104 (79%) | 115 (78%) | 0.249 |
| ≥2 | 15 (10%) | 14 (11%) | 15 (12%) | 15 (10%) | 0.957 |
| Number of distal anastomoses: | | | | | |
| 0 | 2 (1%) | 2 (2%) | 2 (2%) | 1 (1%) | 0.631 |
| 1 | 23 (15%) | 10 (8%) | 14 (11%) | 16 (11%) | 0.319 |
| 2 | 41 (28%) | 27 (21%) | 30 (23%) | 30 (20%) | 0.185 |
| 3 | 57 (38%) | 55 (43%) | 50 (39%) | 59 (40%) | 0.982 |
| 4 | 22 (15%) | 23 (18%) | 22 (17%) | 31 (21%) | 0.211 |
| ≥5 | 4 (3%) | 10 (8%) | 12 (9%) | 11 (7%) | 0.090 |
| Off-pump bypass | 40 (27%) | 24 (19%) | 25 (19%) | 27 (18%) | 0.083 |
| Total minutes on bypass | 83 (63, 110) | 92 (72, 125) | 93 (66, 110) | 89 (70, 126) | 0.262 |
| Cross—clamp time in minutes | 50 (33, 67) | 55 (41, 79) | 54 (35, 72) | 56 (39, 80) | 0.097 |
| Intensive Care Unit length of stay in hours | 52 (43, 87) | 61 (42, 94) | 49 (27, 97) | 65 (40, 112) | 0.124 |
| **Perioperative complications** | | | | | |
| Return to operating room | 7 (5%) | 9 (7%) | 7 (5%) | 12 (8%) | 0.326 |
| Mediastinitis | 3 (2%) | 4 (3%) | 2 (2%) | 2 (1%) | 0.516 |
| Other infection | 9 (6%) | 10 (8%) | 8 (6%) | 19 (13%) | 0.061 |
| New onset Atrial Fibrillation | 10 (7%) | 20 (16%) | 22 (17%) | 38 (26%) | <0.001 |
| Worsening renal impairment | 2 (1%) | 4 (3%) | 12 (9%) | 16 (11%) | <0.001 |
| Intra-aortic balloon pump | 25 (17%) | 22 (17%) | 24 (18%) | 18 (12%) | 0.335 |
| Inotropes for low cardiac output | 45 (30%) | 44 (35%) | 56 (43%) | 71 (48%) | <0.001 |
| Cardiac arrest requiring cardiopulmonary resuscitation | 3 (2%) | 3 (2%) | 10 (8%) | 7 (5%) | 0.079 |
| Pulmonary edema requiring intubation | 3 (2%) | 3 (2%) | 4 (3%) | 4 (3%) | 0.640 |
| **Mortality within 30 days after CABG** | 3 (2%) | 5 (4%) | 10 (8%) | 8 (5%) | 0.081 |

1. P-values for categorical variables are based on Cochran-Armitage Trend test. Spearman correlation test is performed to get the p-values for continuous variables and the continuous age variable.

Table S5: Medical therapy at randomization and at 10 years in each quartile of age by randomized therapy

| | | Q1 (Age≤54 years) N(%) | | | | Q2 (54<Age≤60 years) N(%) | | | | Q3 (60<Age≤67 years) N(%) | | | | Q4 (Age>67 years) N(%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Overall | MED | CABG | P | Overall | MED | CABG | P | Overall | MED | CABG | P | Overall | MED | CABG | P |
| Betablocker | Randomization | 282 (85) | 148 (87) | 134 (84) | 0.39 | 247 (84) | 135 (89) | 112 (78) | 0.01 | 250 (90) | 124 (92) | 126 (88) | 0.23 | 257 (83) | 122 (84) | 135 (83) | 0.76 |
| | At 10 year follow up | 280 (91) | 143 (91) | 137 (91) | 0.80 | 246 (89) | 130 (92) | 116 (87) | 0.24 | 228 (91) | 117 (91) | 111 (91) | 0.94 | 223 (79) | 110 (80) | 113 (78) | 0.63 |
| ACE inhibitor or ARB | Randomization | 288 (87) | 149 (88) | 139 (87) | 0.83 | 263 (89) | 132 (87) | 131 (92) | 0.19 | 252 (90) | 121 (90) | 131 (91) | 0.70 | 282 (92) | 129 (89) | 153 (94) | 0.12 |
| | At 10 year follow up | 269 (87) | 142 (90) | 127 (85) | 0.17 | 233 (85) | 119 (84) | 114 (86) | 0.66 | 226 (90) | 118 (91) | 108 (89) | 0.44 | 211 (75) | 104 (76) | 107 (74) | 0.68 |
| Statin | Randomization | 271 (82) | 147 (86) | 124 (78) | 0.03 | 242 (82) | 126 (83) | 116 (81) | 0.69 | 230 (82) | 118 (87) | 112 (78) | 0.03 | 240 (78) | 109 (75) | 131 (80) | 0.27 |
| | At 10 year follow up | 264 (86) | 135 (85) | 129 (86) | 0.89 | 230 (84) | 118 (83) | 112 (84) | 0.80 | 225 (90) | 115 (89) | 110 (90) | 0.79 | 230 (82) | 110 (80) | 120 (83) | 0.59 |
| Aspirin | Randomization | 273 (83) | 145 (85) | 128 (80) | 0.20 | 250 (85) | 129 (85) | 121 (85) | 0.95 | 232 (83) | 116 (86) | 116 (81) | 0.23 | 247 (80) | 123 (85) | 124 (76) | 0.05 |
| | At 10 year follow up | 272 (88) | 141 (89) | 131 (87) | 0.60 | 237 (86) | 118 (83) | 119 (89) | 0.13 | 203 (81) | 110 (85) | 93 (76) | 0.07 | 203 (72) | 97 (71) | 106 (73) | 0.67 |
| Warfarin | Randomization | 25 (8) | 17 (10) | 8 (5) | 0.09 | 23 (8) | 17 (11) | 6 (4) | 0.03 | 35 (13) | 20 (15) | 15 (10) | 0.27 | 44 (14) | 22 (15) | 22 (13) | 0.67 |
| | At 10 year follow up | 39 (13) | 18 (11) | 21 (14) | 0.49 | 47 (17) | 26 (18) | 21 (16) | 0.58 | 45 (18) | 24 (19) | 21 (17) | 0.77 | 74 (26) | 36 (26) | 38 (26) | 0.99 |
| Potassium sparing diuretic | Randomization | 161 (49) | 84 (49) | 77 (48) | 0.82 | 137 (46) | 70 (46) | 67 (47) | 0.89 | 136 (49) | 67 (50) | 69 (48) | 0.77 | 122 (40) | 55 (38) | 67 (41) | 0.57 |
| | At 10 year follow up | 173 (56) | 86 (54) | 87 (58) | 0.53 | 147 (53) | 75 (53) | 72 (54) | 0.83 | 150 (60) | 80 (62) | 70 (57) | 0.45 | 127 (45) | 59 (43) | 68 (47) | 0.52 |

Table S6: Cross overs from each treatment arm by quartile of age

| Randomized Treatment | Baseline Age Quartiles | | | | Total (n=1212) | P Value |
| --- | --- | --- | --- | --- | --- | --- |
| | Q1 (Age≤54 years) (n=330) | Q2 (54<Age≤60 years) (n=295) | Q3 (60<Age≤67 years) (n=279) | Q4 (Age>67 years) (n=308) | | |
| MED patients who crossed over to CABG | 24/170 (14.1) | 13/152 (8.6) | 16/135 (11.9) | 13/145 (9.0) | 66/602 (11.0) | 0.25 |
| CABG patients who crossed over to MED | 11/160 (6.9) | 16/143 (11.2) | 13/144 (9.0) | 15/163 (9.2) | 55/610 (9.0) | 0.62 |

Table S7: Hazard ratios and 95% confidence intervals for CABG plus optimal medical therapy versus optimal medical therapy alone by quartile of age

| | Q1 (Age≤54 years) (n=330) | Q2 (54<Age≤60 years) (n=295) | Q3 (60<Age≤67 years) (n=279) | Q4 (Age>67 years) (n=308) |
|---|---|---|---|---|
| All-cause death | 0.66 (0.49, 0.89) | 0.87 (0.64, 1.18) | 1.00 (0.75, 1.33) | 0.82 (0.63, 1.06) |
| Cardiovascular death | 0.61 (0.43, 0.85) | 0.88 (0.63, 1.24) | 1.02 (0.73, 1.44) | 0.70 (0.50, 0.97) |
| Death or cardiovascular hospitalization | 0.55 (0.43, 0.71) | 0.81 (0.62, 1.05) | 0.85 (0.66, 1.09) | 0.73 (0.57, 0.92) |

Figure S1 Hazard ratio (solid line) and 95% confidence interval (grey area) for the effect of CABG vs medical therapy across the range of age- as treated analysis accounting for cross overs