Supplementary Data

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Positron Emission Tomography

15O-water positron emission tomography (PET) stress scanning was performed using a whole-body PET/computed tomography (CT) scanner (Gemini TF 64; Philips Healthcare, Cleveland, OH, USA) at Hokkaido University Hospital before and after treatment. Patients were instructed to fast for at least 4 h and to abstain from caffeine and methylxanthine for at least 24 h. Routine antianginal medications were continued and CT scans for coronary artery calcium scoring, as well as attenuation and scatter correction, were performed. A 6 min list-mode scan was then initiated with simultaneous administration of 500 MBq of 15O-water. An identical acquisition was performed during hyperemia using intravenous adenosine triphosphate administration (0.16 mg/kg/min) 3 min before the scan and 10 min after the first administration of 15O-water. Emission data were reconstructed using a 3D row-action-maximum-likelihood algorithm into 24 frames (18×10-s and 6×30-s).

Cardiovascular Magnetic Resonance Imaging

Cardiovascular magnetic resonance imaging was performed using a 3 Tesla whole-body scanner (Achieva TX; Philips Medical Systems, Best, The Netherlands) with a 32-channel phased-array receiver torso-cardiac coil. Cine images were acquired using a retrospectively gated, balanced steady-state, free precession pulse sequence with the following parameters: field of view, 380 mm; repetition time, 3 ms; echo time, 1.43 ms; flip angle, 60°; slice thickness, 8 mm; acquisition matrix, 128×136 pixels; sensitivity encoding parallel imaging factor, 2; and 20 phases per cardiac cycle. Late gadolinium enhancement images were acquired 10-15 min after administration of 0.1 mmol/kg of gadolinium contrast media using an inversion-recovery prepared, 3-dimensional fast field echo pulse sequence with the following parameters: field of view, 380 mm; repetition time, 3.5 ms; echo time, 2.3 ms; flip angle, 10°; slice thickness, 5 mm without gap; acquisition matrix, 256×84 pixels; and sensitivity encoding parallel imaging factor, 2. Inversion time was optimized to null normal myocardial signal using a Look-Locker sequence.

**Supplementary Figure 1.** Representative images of 99mTc-tetrofosmin SPECT in a 70-year-old man with 3-vessel disease



**Supplementary Table 1.** Medications at baseline and follow-up on a per-patient basis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **No revascularization**  **(n=16)** | **PCI**  **(n=18)** | **CABG**  **(n=13)** | **P** |
| Antiplatelet agents |  |  |  |  |
| Baseline | 16 (100) | 17 (94) | 10 (77) | 0.09 |
| Follow-up | 16 (100) | 18 (100) | 13 (100) | 1.00 |
| P | 1.00 | 1.00 | 0.25 |  |
| Angiotensin inhibitors |  |  |  |  |
| Baseline | 11 (69) | 11 (61) | 6 (46) | 0.45 |
| Follow-up | 12 (75) | 13 (72) | 6 (46) | 0.22 |
| P | 0.32 | 0.16 | 1.00 |  |
| Beta-blockers |  |  |  |  |
| Baseline | 11 (69) | 10 (56) | 9 (69) | 0.69 |
| Follow-up | 13 (81) | 12 (67) | 11 (85) | 0.51 |
| P | 0.32 | 0.41 | 0.41 |  |
| Calcium-channel blockers |  |  |  |  |
| Baseline | 9 (56) | 8 (44) | 3 (23) | 0.21 |
| Follow-up | 6 (38) | 8 (44) | 6 (46) | 0.87 |
| P | 0.18 | 1.00 | 0.18 |  |
| Statins |  |  |  |  |
| Baseline | 15 (94) | 16 (89) | 11 (85) | 0.84 |
| Follow-up | 12 (75) | 15 (83) | 12 (92) | 0.49 |
| P | 0.08 | 0.65 | 0.32 |  |
| Nitrates |  |  |  |  |
| Baseline | 7 (44) | 6 (33) | 6 (46) | 0.81 |
| Follow-up | 6 (38) | 4 (22) | 6 (46) | 0.36 |
| P | 0.32 | 0.16 | 1.00 |  |
| Diuretics |  |  |  |  |
| Baseline | 5 (31) | 2 (11) | 5 (38) | 0.18 |
| Follow-up | 5 (31) | 2 (11) | 5 (38) | 0.18 |
| P | 1.00 | 1.00 | 1.00 |  |
| Insulin |  |  |  |  |
| Baseline | 1 (6) | 2 (11) | 2 (15) | 0.84 |
| Follow-up | 2 (13) | 2 (11) | 3 (23) | 0.68 |
| P | 0.32 | 1.00 | 0.32 |  |
| Warfarin |  |  |  |  |
| Baseline | 2 (13) | 1 (6) | 1 (8) | 0.82 |
| Follow-up | 2 (13) | 1 (6) | 2 (15) | 0.61 |
| P | 1.00 | 1.00 | 0.32 |  |
| Direct oral anticoagulants |  |  |  |  |
| Baseline | 1 (6) | 4 (22) | 4 (31) | 0.23 |
| Follow-up | 1 (6) | 4 (22) | 4 (31) | 0.23 |
| P | 1.00 | 1.00 | 1.00 |  |

Data are presented as the median (interquartile range) or n (%).

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

**Supplementary Table 2.** Comparisons of changes in quantitative myocardial perfusion in vessel territories without revascularization

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **%DS <50%**  **(n=43)** | **%DS 50–69%**  **(n=7)** | **%DS ≥70%**  **(n=33)** | **P** | **P for interaction (group×time)** |
| Rest MBF |  |  |  |  |  |
| Baseline | 0.85 (0.60–1.05) | 0.97 (0.61–1.22) | 0.80 (0.63–0.98) | 0.59 | 0.86 |
| Follow-up | 0.80 (0.67–0.99) | 0.92 (0.71–1.07) | 0.84 (0.70–0.97) | 0.71 |
| P | 0.09 | 0.81 | 0.23 |  |  |
| Stress MBF |  |  |  |  |  |
| Baseline | 2.03 (1.50–2.47) | 1.88 (1.46–2.36) | 1.80 (1.36–2.11) | 0.16 | 0.75 |
| Follow-up | 2.15 (1.61–2.90) | 1.81 (1.39–2.43) | 1.95 (1.39–2.18) | 0.07 |
| P | 0.09 | 0.81 | 0.25 |  |  |
| MFR |  |  |  |  |  |
| Baseline | 2.67 (2.04–3.16) | 2.22 (1.76–2.43) | 2.07 (1.73–2.71) | 0.008 | 0.96 |
| Follow-up | 2.53 (1.84–3.31) | 2.41 (1.29–2.68) | 2.15 (1.75–2.52) | 0.06 |
| P | 0.51 | 0.69 | 0.81 |  |  |

Values are presented as the median (interquartile range).

DS, diameter stenosis.

**Supplementary Table 3.** Hemodynamic data during positron emission tomography on a per-patient basis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **No revascularization**  **(n=16)** | **PCI**  **(n=18)** | **CABG**  **(n=13)** | **P** |
| **Heart rate (bpm)** |  |  |  |  |
| Rest |  |  |  |  |
| Baseline | 61 (57–68) | 60 (51–68) | 63 (60–70) | 0.36 |
| Follow-up | 65 (57–73) | 60 (54–68) | 66 (57–71) | 0.58 |
| P | 0.94 | 0.25 | 0.49 |  |
| Stress |  |  |  |  |
| Baseline | 76 (71–82) | 71 (63–78) | 77 (69–83) | 0.32 |
| Follow-up | 75 (70–85) | 71 (63–81) | 76 (67–87) | 0.40 |
| P | 0.41 | 0.99 | 0.78 |  |
| **Systolic blood pressure (mmHg)** |  |  |  |  |
| Rest |  |  |  |  |
| Baseline | 119 (107–141) | 124 (109–137) | 113 (107–133) | 0.69 |
| Follow-up | 126 (112–147) | 123 (103–139) | 106 (99–124) | 0.08 |
| P | 0.11 | 0.58 | 0.16 |  |
| Stress |  |  |  |  |
| Baseline | 107 (88–124) | 98 (88–111) | 102 (84–121) | 0.65 |
| Follow-up | 107 (97–119) | 92 (84–107)\* | 88 (83–109) | 0.024 |
| P | 0.21 | 0.058 | 0.12 |  |
| **Diastolic blood pressure (mmHg)** |  |  |  |  |
| Rest |  |  |  |  |
| Baseline | 63 (51–75) | 63 (58–74) | 63 (54–69) | 0.82 |
| Follow-up | 68 (58–75) | 64 (53–73) | 58 (53–68) | 0.21 |
| P | 0.34 | 0.41 | 0.27 |  |
| Stress |  |  |  |  |
| Baseline | 54 (45–60) | 53 (47–61) | 58 (44–65) | 0.97 |
| Follow-up | 54 (50–63) | 51 (44–59) | 46 (43–55) | 0.13 |
| P | 0.61 | 0.37 | 0.14 |  |
| **Rate-pressure product (bpm·mmHg)** |  |  |  |  |
| Rest |  |  |  |  |
| Baseline | 7078 (6199–9123) | 6851 (5967–8225) | 7810 (6806–8381) | 0.61 |
| Follow-up | 7397 (6669–10746) | 7530 (5881–9226) | 6996 (6057–8318) | 0.37 |
| P | 0.25 | 0.73 | 0.41 |  |
| Stress |  |  |  |  |
| Baseline | 7448 (6395–9481) | 7002 (6336–7923) | 7140 (6479–9068) | 0.74 |
| Follow-up | 7785 (6909–9988) | 6276 (5233–7601)\* | 6960 (5709–8407) | 0.040 |
| P | 0.18 | 0.11 | 0.31 |  |

Values are presented as the median (interquartile range).

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

\*P<0.05 vs. patients without revascularization.

**Supplemental Table 4.** Multilevel mixed-effects model analysis including medications at follow-up to predict changes in regional stress MBF and MFR after coronary revascularization on a per-vessel basis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1: absolute change** | | |  | **Model 2: percent change** | | |
|  | **β** | **95%CI** | **P** |  | **β** | **95%CI** | **P** |
| **Dependent variable: change in regional stress MBF** | | | | | | | |
| Intercept | −0.01 | −0.75 to 0.72 | 0.97 |  | −3.8 | −68.3 to 60.7 | 0.91 |
| Pretest likelihood of obstructive CAD (per 10%) | 0.02 | −0.05 to 0.09 | 0.57 |  | 1.4 | −4.8 to 7.6 | 0.65 |
| **Medications at follow-up** |  |  |  |  |  |  |  |
| Angiotensin inhibitors | −0.24 | −0.48 to 0.0003 | 0.050 |  | −18.7 | −39.8 to 2.3 | 0.08 |
| Beta-blockers | 0.23 | −0.07 to 0.52 | 0.13 |  | 16.7 | −9.1 to 42.5 | 0.20 |
| Calcium-channel blockers | 0.02 | −0.23 to 0.27 | 0.87 |  | 1.2 | −20.5 to 22.9 | 0.91 |
| Statins | −0.14 | −0.45 to 0.17 | 0.38 |  | −1.4 | −28.8 to 25.9 | 0.92 |
| Nitrates | 0.09 | −0.16 to 0.35 | 0.46 |  | 12.0 | −10.4 to 34.5 | 0.29 |
| **Regional factors** |  |  |  |  |  |  |  |
| Log (1+Leaman score reduction) (per 1) | 0.10 | 0.02 to 0.18 | 0.015 |  | 9.9 | 3.5 to 16.2 | 0.003 |
| **Dependent variable: change in regional MFR** | | | | | | | |
| Intercept | −1.08 | −2.12 to −0.03 | 0.044 |  | −45.7 | −101.4 to 9.9 | 0.10 |
| Pretest likelihood of obstructive CAD (per 10%) | 0.05 | −0.05 to 0.15 | 0.33 |  | 2.6 | −2.8 to 8.0 | 0.34 |
| **Medications at follow-up** |  |  |  |  |  |  |  |
| Angiotensin inhibitors | −0.07 | −0.41 to 0.28 | 0.70 |  | −7.2 | −25.3 to 10.9 | 0.43 |
| Beta-blockers | 0.39 | −0.03 to 0.81 | 0.06 |  | 19.1 | −3.1 to 41.4 | 0.09 |
| Calcium-channel blockers | −0.23 | −0.58 to 0.12 | 0.19 |  | −9.0 | −27.7 to 9.7 | 0.34 |
| Statins | 0.50 | 0.06 to 0.95 | 0.028 |  | 21.7 | −1.9 to 45.3 | 0.07 |
| Nitrates | 0.09 | −0.28 to 0.45 | 0.63 |  | 8.9 | −10.5 to 28.2 | 0.36 |
| **Regional factors** |  |  |  |  |  |  |  |
| Log (1+Leaman score reduction) (per 1) | 0.16 | 0.05 to 0.28 | 0.005 |  | 11.0 | 5.4 to 16.6 | <0.001 |

CAD, coronary artery disease; CI, confidence interval

**Supplemental Table 5.** Sensitivity analyses using a stepwise variable selection procedure to predict changes in regional stress MBF and MFR after coronary revascularization on a per-vessel basis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1: absolute change** | | |  | **Model 2: percent change** | | |
|  | **β** | **95%CI** | **P** |  | **β** | **95%CI** | **P** |
| **Dependent variable: change in regional stress MBF** | | | | | | | |
| Intercept | −0.40 | −1.02 to 0.22 | 0.20 |  | −0.6 | −103.0 to 101.8 | 0.99 |
| Age (per 10 years) | – | – | – |  | −6.0 | −16.2 to 4.2 | 0.24 |
| Body mass index (kg/m2) | 0.02 | −0.005 to 0.04 | 0.13 |  | 1.7 | −0.5 to 4.0 | 0.13 |
| Diabetes | – | – | – |  | 3.0 | −13.8 to 19.8 | 0.72 |
| Hyperlipidemia | −0.03 | −0.27 to 0.20 | 0.78 |  | 0.5 | −19.1 to 20.0 | 0.96 |
| **Medications at follow-up** |  |  |  |  |  |  |  |
| Angiotensin inhibitors | −0.27 | −0.49 to −0.04 | 0.024 |  | −16.5 | −37.3 to 4.4 | 0.12 |
| Beta-blockers | 0.27 | 0.02 to 0.53 | 0.037 |  | 20.8 | −0.5 to 42.1 | 0.056 |
| **Regional factors\*** |  |  |  |  |  |  |  |
| Log (1+Leaman score reduction) (per 1) | 0.11 | 0.02 to 0.19 | 0.012 |  | 11.1 | 4.5 to 17.7 | 0.001 |
| Right coronary artery† | 0.15 | −0.08 to 0.38 | 0.19 |  | 16.8 | −2.9 to 36.5 | 0.09 |
| Left circumflex artery† | 0.09 | −0.13 to 0.32 | 0.40 |  | 9.7 | −8.1 to 27.6 | 0.28 |
| **Dependent variable: change in regional MFR** | | | | | | | |
| Intercept | −0.12 | −1.37 to 1.13 | 0.85 |  | 9.5 | −55.0 to 74.0 | 0.77 |
| Age (per 10 years) | −0.10 | −0.25 to 0.06 | 0.22 |  | −6.5 | −14.5 to 1.4 | 0.10 |
| Diabetes | – | – | – |  | 4.7 | −9.4 to 18.7 | 0.51 |
| Hyperlipidemia | −0.02 | −0.36 to 0.32 | 0.89 |  | 2.0 | −14.4 to 18.5 | 0.80 |
| Current smoker at follow-up | −0.58 | −1.14 to −0.02 | 0.044 |  | −37.0 | −66.0 to −7.9 | 0.014 |
| **Medications at follow-up** |  |  |  |  |  |  |  |
| Beta-blockers | 0.47 | 0.10 to 0.83 | 0.014 |  | 21.9 | 2.6 to 41.3 | 0.027 |
| Statins | 0.40 | −0.04 to 0.83 | 0.07 |  | 13.0 | −9.0 to 35.1 | 0.24 |
| Nitrates | – | – | – |  | 12.4 | −5.5 to 30.4 | 0.17 |
| **Regional factors\*** |  |  |  |  |  |  |  |
| Log (1+Leaman score reduction) (per 1) | 0.19 | 0.08 to 0.31 | 0.001 |  | 12.8 | 7.2 to 18.4 | <0.001 |
| Right coronary artery† | 0.31 | −0.03 to 0.66 | 0.08 |  | 20.9 | 4.1 to 37.8 | 0.016 |
| Left circumflex artery† | 0.24 | −0.07 to 0.55 | 0.12 |  | 15.4 | 0.2 to 30.6 | 0.047 |

CAD, coronary artery disease; CI, confidence interval

**\***Regional factors were forced into the multivariate model as a clinically meaningful variable, and other variables were selected from patient factors (age, sex, body mass index, hypertension, diabetes, hyperlipidemia, and current smoker at follow-up) and medications at follow-up (angiotensin inhibitors, beta-blockers, calcium-channel blockers, statins, and nitrates) on the basis of the corrected Akaike’s information criterion score.

†Left anterior descending artery serves as the reference.