Online supplemental material

Positron Emission Tomography protocols and data acquisition

Two ^{15}O-H_2O perfusion scans were initiated at time = 0 min as 6-min scans with the following time-frame sequence: 1×10, 8×5, 4×20, 2×15, 3×20, 2×30, and 2×60 s. To reconstruct images a 3-dimensional (D) iterative algorithm was used (3 iterations (Vision 4), 21 subsets (Vision 5), 5-mm Gaussian postfilter), applying all appropriate corrections for normalization, dead time, scatter, random coincidences, and attenuation. The first ^{15}O-H_2O scan was an examination for resting MBF (n=10) whereas the second scan was performed as an adenosine stress test to determine maximal MBF (n=9) and MFR (n=9).

The 27-minute ^{11}C-acetate scan (n=10) was begun at time = 30 min with frame structure: 1x10, 12x5, 5x10, 2x30, 3x60, 3x120, and 3x300 s. Data were reconstructed with a 3D iterative algorithm (3 iterations (Vision 4), 21 subsets (Vision 5), 5-mm Gaussian postfilter). Blood pressure and heartrate was measured during the examination at time = 1, 5, 10, and 20 minutes.

The ^{11}C-palmitate scan (n=12) was initiated at time = 130 min in a 50-minute list mode scan (frame structure 6×5, 6×10, 3×20, 5×30, 5×60, 8×150, 4×300 s). Data were reconstructed with a 3D iterative algorithm (3 iterations (Vision 4), 21 subsets (Vision 5), 5-mm Gaussian postfilter). Blood and dynamic PET data were decay corrected to scan start.

The 50-minute ^{18}F-FDG scan (n=11)) was initiated at time = 230 min. 200 MBq ^{18}F-FDG was injected and a 50-minute list mode scan (frame structure 1×10, 8×5, 4×10, 3×20, 5×30, 5×60, 4×150, 4×300, and 1×600 s) was performed using 3D iterative reconstruction (3 iterations (Vision 4), 21 subsets (Vision 5), 4-mm Gaussian postfilter).

PET image analysis

Myocardial fatty acid metabolism was analyzed using a 3-tissue compartment model in which 3 rate constants was fitted. The input function was corrected for ^{11}C-metabolites using validated population-based estimates(1) The efflux rate of $^{11}CO_2$ was fixed to the oxidation rate and a slow esterification compartment was included. Macroparameters myocardial fatty acid oxidation (MFAO), myocardial fatty acid esterification (MFAE), and total myocardial fatty acid uptake (MFAU) were defined according to the suggestions by Bergmann(2):

$$MFAE = C_{NEFA} = \frac{k_{p1}k_{12}}{k_{1p} + k_{12} + k_{13}}$$

$$MFAO = C_{NEFA} = \frac{k_{p1}k_{13}}{k_{1p} + k_{12} + k_{13}}$$

$$MFAU = MFAE + MFAO$$

Myocardial glucose uptake (MGU) was estimated by Patlak analysis as previously described(3), with automatic segmentation of the left ventricle performed using K1 parametric images (due to low myocardial FDG retention). The relative uptake rate, Ki, was multiplied by the plasma glucose concentration to obtain absolute MGU (µmol/100 g /min). The lumped constant was not assumed to change between the two visits and was hence fixed at 1.

Myocardial oxygen consumption and efficiency were measured by ^{11}C-acetate PET. The examination was performed to obtain the global clearance rate (k_2) and to calculate MVO_2 as previously described(4)

$$MVO_2 = \frac{135xk2 - 0.96}{100}$$

Myocardial external efficiency, MEE, was calculated as:

$$MEE = \frac{LVexternal\ work}{Total\ LV\ MVO_2} = \frac{(FCO\ x\ MAP\ x\ 1.33x\ 10^{-4})}{MVO_2\ x\ LVmass\ x\ 20}$$

Left ventricular mass (LV_{mass}) and forward cardiac output (FCO) was obtained from the PET dataset, whereas MAP was measured manually during the PET scan.

Rest and stress MBF were measured by ^{15}O-H_2O and analyzed using a previously described method allowing for highly automated calculation of parametric MBF imaging(5). In brief, parametric MBF images were generated using cluster analysis and implementation of a basis function method of the single-tissue model with additional RV spillover correction. All parametric images were automatically segmented according to the 17-segment model advocated by the American Heart Association (AHA)(6).

Left ventricular ejection fraction (LVEF) was calculated using the 11C-acetate scans as previously reported (7). In brief, the left ventricle was segmented automatically using parametric images of K_1 (myocardial 11C-acetate uptake rate) and V_A (Arterial blood fraction). End Systolic Volumes (ESV) were calculated based on V_A>0.7 and End Diastolic Volume (EDV) on V_A>0.175. LVEF calculated this way has been shown to correlate very well with LVEF measured by the Gold Standard of CMR (7).

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