Supplementary Appendix

METHODS

Image acquisition

Parameters of CT image acquisition

The parameters were as follows: detector collimation 64 × 0.6 mm, equaling a slice acquisition of 128 × 0.6 mm using the flying focal spot technique; table pitch adapted to heart rate (0.17–0.38); rotation time 275 ms; tube current time product 360 mA; and tube voltage 120 kVp, according to automatic tube voltage selection. A test bolus CT acquisition was performed at the level of the ascending aorta following administration of 10 ml contrast medium followed by 20 ml saline, with low-dose images obtained every 1 s. The delay before the formal scan was calculated as the time to peak enhancement in the ascending aorta plus 3 s to ensure enhancement of the ventricule. For the final scan, contrast agents (Omnipaque 350, Daiichi Sankyo, Japan) were injected with an injection time of 10 s, followed by a second bolus of 80% of the amount of contrast medium diluted 50%, and then a chaser bolus of saline. All injections were done at the same flow rate, calculated as body weight × 0.07 ml/s.[1]

Image acquisition during nuclear stress testing

All stress and rest nuclear SPECT examinations were performed according to standard institutional clinical protocols with ^{99m}Tc or ^{201}Tl as the tracer using a dual detector cardiac gamma camera with 60 views, each for 30 s, in a noncircular 180° orbit (DISCOVERY, NM/CT 670 GE Healthcare). As a stress, exercise or a pharmacological stress test (intravenous adenosine infusion at 135 μg/kg/min for 6 min) was performed. The average exercise time was 6 min and 50 s. The average percent of maximal predicted heart rate (MPHR) was 80.3%. One patient who had ≥85% MPHR complained of chest pain during the examination. We defined an adequate stress test as: 1) any test using adenosine, 2) achieving

≥85% of MPHR, or 3) patient complaining of chest pain during exercise testing. Although only 50% of exercise tests achieved MPHR ≥85%, 94% of stress tests were considered adequate. None of the patients who failed to achieve an adequate test had substantial electrocardiogram changes during exercise. Gated SPECT using ^{99m}Tc as the tracer was performed in 32 patients, and ^{201}Tl as the tracer was used in three patients. No algorithms for attenuation correction or resolution recovery were applied. Among the 35 study participants who underwent this test, 31 were evaluated with adenosine SPECT-MPI, and the remaining four were evaluated with exercise SPECT-MPI.

Image processing and interpretation

Reference standard: Quantitative coronary angiography

One reader (H.K.) who was blinded to the clinical information and the results from CCTA and SPECT-MPI examined each catheter angiography using computerized quantitative coronary artery angiography analysis software (CAAS II system, Pie Medical, Maastricht, the Netherlands) to determine the percent stenosis in each coronary segment according to the 16-segment classification model of the American Heart Association [2]. Coronary artery stenosis was defined as "significant" if the mean luminal diameter narrowing exceeded 50%.

Coronary artery CT angiography: CCTA

For each patient, axial slices were optimally reconstructed within the mid- to end-diastolic phase using retrospective electrocardiography gating and cardiac reconstruction software (Virtual Place, Raijin, AZE Inc., Tokyo, Japan). Evaluation of the presence of significant coronary artery stenosis was performed on axial source images. One senior cardiologist (K.O.) and two senior CT technicians (Y.M. and N.A.) who were blinded to all patient and clinical data, including first-pass CT-MPI and SPECT-MPI data, performed the analysis, and evaluation was made on a per-segment basis using the established American Heart

Association segment model.[2] The presence of coronary artery stenosis was defined as a luminal obstruction of greater than 50% of the diameter. Moreover, the presence of severe coronary artery stenosis was defined as obstruction of greater than 70% of the diameter. All coronary artery segments were assessed for the presence of significant stenosis.

CT-MPI

These were smooth filtered based on a prediction and collection algorithm to eliminate the helical artifact noise. From 20 image data sets, the image data set with the fewest artifacts (both motion artifacts and beam hardening) was carefully selected at the mid-diastolic phase. The minimum and maximum thresholds for segmentation of the myocardium were approximately set between 0 and 180 Hounsfield Unit (HU), although these depended on contrast enhancement. The right ventricular myocardium and papillary muscle were automatically removed using 3D spline interpolation of endocardial and epicardial boundaries. Twenty percent of the wall thickness from the endocardial boundary and 40% of the wall thickness from the epicardial boundary were removed to reduce partial volume effects of an enhanced left ventricular cavity and epicardial coronary arteries (e.g., bridging coronary arteries, large coronary artery, and/or vein). Finally, the mean CT attenuation was calculated from the apex to the base of the shaped short-axis slice image at 3-degree increments, and values were demonstrated on a bulls-eye map. The maximum and minimum myocardial thresholds were determined from the whole-heart CT value. The window center value and window width were defined as follows:

Window center (HU) = k × (maximum myocardial threshold − minimum myocardial threshold) + minimum myocardial threshold (k = 0.4, 0.45, 0.5). Window width = Window center ± 50 (HU).

At first, the constant k was 0.4. If halation such as "excessive contrast enhancement" was detected, the constant k was stepped up to obtain an adequate image for assessment. Warm

colors represented hyper-enhanced areas with high CT values (more than the center value), and cold colors represented hypo-enhanced areas with low CT values (less than the center value). Furthermore, each hypo-enhanced area was colored automatically according to the CT values, and the ratio of the cold colors area in each segment was visually evaluated. Based on the tone of cold colors and the ratio of the cold color area, the hypo-enhanced areas were graded according to a three-point scale: 1: mild reduction or equivocal, 2: moderately reduced (cold colors but less than 50% of the area), 3: severely reduced (more than 50% of the area and/or a bright blue color, i.e., very low attenuation). A grade of more than 2 in the three-point scale was defined as significant hypo-enhancement. The intra- and inter-observer correlation coefficients were high (r = 0.91 and 0.90, respectively).

Twenty short axial myocardial images were automatically analyzed by one senior reader (Y.K.) in a core laboratory (Sakurabashi Watanabe Hospital, Osaka, Japan). The reader was blinded with respect to any clinical information of the patients or results of other examinations including CCTA and SPECT-MPI data. The same raw data used for CCTA were used to create short-axis images via reconstruction at the mid- to end-diastolic phase of the cardiac cycle and were finally expressed in a bulls-eye map. Assignment of the left ventricular segment was based on the 16 myocardial segment models, excluding the apical segment.[3] Perfusion imaging was expressed with color maps coded according to the CT value. Warm colors represented hyper-enhanced areas with high CT values, and cold colors represented hypo-enhanced areas with low CT values. We evaluated the variation in myocardial enhancement during the diastolic phase.

SPECT-MPI

SPECT-MPI data were analyzed by two independent experienced readers (S.S. and T.M.) who were blinded to the clinical information and results from cardiac CT examination and invasive coronary angiography. Data were evaluated using short axial, horizontal long axial,

and vertical long axial source images. Gated SPECT data, if acquired, were also presented to the readers. Disagreements in data analysis between the two observers were resolved by consensus reading. Visual assessment of myocardial perfusion was performed using the 17–myocardial segment classification model of the American Heart Association.[2]

REFERENCES

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