Relation of Change in Wall Motion and Glucose Metabolism After Coronary Artery Bypass Grafting

— Assessment with positron emission tomography —

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Regional myocardial glucose metabolism was assessed by positron emission tomography (PET) in stunned myocardium. PET perfusion and metabolic imaging using N-13 ammonia and F-18 deoxyglucose (FDG) was performed before and 5–7 weeks after coronary artery bypass grafting (CABG) in 23 patients with coronary artery disease. Of 22 asynergy segments showing increased FDG uptake preoperatively, the postoperative PET showed a decrease in FDG uptake in 16 segments (73%) and persistent uptake in 6 segments (27%). The improvement in asynergy was observed in all of the segments showing postoperative decrease in FDG uptake, while it was observed in only 50% of those with persistent FDG uptake ($p < 0.01$). On the other hand, 4 of 5 segments showing a new FDG uptake postoperatively revealed deterioration of wall motion abnormality. These data suggest that an increase in exogenous glucose utilization may often persist in postischemic myocardium. Improvement in regional function seems to be associated with the improvement in metabolic abnormality after CABG.

POSITRON emission tomography (PET) permits assessment of regional myocardial perfusion and metabolism in vivo.^{1,2} Hypoperfused myocardium with increased uptake of fluorine-18 fluorodeoxyglucose (FDG) as an indicator of exogenous glucose utilization is considered to be an ischemic but viable region which is likely to improve in regional function after restoration of blood flow.^{3–6} On the other hand, a considerable variation in functional recovery has been observed after revascularization. Similarly, sustained regional metabolic abnormalities are considered to be present after

revascularization.^{10–11} We hypothesized that prolonged postischemic dysfunction may be associated with persistent metabolic abnormality. To support this hypothesis, PET using FDG was performed in coronary patients before and after coronary artery bypass grafting (CABG) and the metabolic findings were compared with change of regional myocardial function.

MATERIALS AND METHODS

Patients

Twenty-three patients who underwent PET before and after CABG were selected for this study. There were twenty-one men and two women aged 36 to 68 years. PET was performed within 4 weeks before CABG

Key words:

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TABLE I RELATION OF CHANGES IN F-18 DEOXYGLUCOSE (FDG) UPTAKE WITH CHANGES IN WALL MOTION IN 49 PREOPERATIVE ASYNERGIC SEGMENTS.

Pre CABG FDG	Post CABG FDG	n	Postoperative wall motion		
			improved	unchanged	deteriorated
FDG (+)	decreased	16	16	0	0
FDG (+)	unchanged	6	3	3	0
FDG (-)	unchanged	22	7	15	0
FDG (-)	increased	5	0	1	4
Total		49	26	19	4

and repeated 5 to 7 weeks after CABG. Eighteen patients had a history of myocardial infarction with longer than one month after onset. All patients gave a written informed consent.

Positron emission tomography

PET was performed with a whole-body, multislice positron camera (Positologica III, Hitachi Medical Co)!² Following an accurate positioning of a patient in the positron camera, a transmission scan was performed for 15 min!³⁻¹⁵ Then, 370 to 740 MBq (10 to 20 mCi) of N-13 ammonia was intravenously injected at rest and myocardial perfusion imaging was performed for 5 min. Immediately after the first scan, the second scan was carried out for 8 min in a position 8 mm caudal to the first scan. These 2 scans provided a total of 14 contiguous transverse slices of the myocardium with 8 mm intervals!¹⁶

An FDG study was separately performed within a week after the N-13 ammonia study. All patients fasted for at least 5 h before the study. Then, 74 to 259 MBq (2 to 7 mCi) of FDG was injected at rest and 2 emission scans were obtained for each 8-10 min, 60 min after injection!¹³⁻¹⁵

Analysis of positron images

The regional myocardial perfusion was quantitatively assessed by the circumferential profile analysis from three transverse slices of N-13 ammonia distribution in a patient and the lower limit of a normal subject!⁷ The left ventricular myocardium was divided into 5 segments, including anterior, septal, apical, inferior and lateral segments. The segments with perfusion below the lower limits covering at least 30 degrees of the

profiles were considered as hypoperfused segments.

N-13 ammonia and FDG images were correlated in the corresponding segments. Three experienced observers visually interpreted the uptake on both images. The segments with normal perfusion were defined as normal areas. The hypoperfused segments with FDG uptake definitely higher than N-13 ammonia were defined as ischemic areas. The hypoperfused segments with FDG uptake less or similar to N-13 ammonia uptake were defined as myocardial scar!^{3,13-15} FDG uptake in the myocardium was also quantitatively measured as a % of the injected dose!⁸ The segments with FDG uptake less than 0.8% of injected dose were considered to be myocardial scars. The change in FDG uptake more than 0.2% after CABG was considered significant.

Wall motion analysis

Each patient received radionuclide ventriculography in the anterior and left anterior oblique projections following intravenous injection of 740 MBq (20 mCi) of Tc-99m in-vivo labeled red blood cells before and after CABG. The left ventricle was divided into 5 segments corresponding to those of the perfusion analysis. Wall motion was visually scored by three experienced observers from 2 to -1 (normal, hypokinetic, akinetic and dyskinetic) without knowledge of other radionuclide or postoperative results. When the score increased by one or more after the operation, the segment was defined as improved wall motion postoperatively, while the segment with score decreased by one or more postoperatively was defined as deteriorated wall motion.

Fig.1. Two representative slices of N-13 ammonia perfusion (top) and FDG (bottom) images before (a) and after (b) bypass surgery of a patient with inferior wall myocardial infarction. Note hypoperfusion with increased FDG uptake in posterolateral region preoperatively (arrows) where improvement in perfusion (small arrows) but persistent FDG uptake (arrow heads) was observed postoperatively.

RESULTS

Preoperative radionuclide ventriculography identified 49 segments with wall motion

abnormalities in 21 of the 23 patients (91%). Of these asynergic segments, 26 (53%) improved in wall motion postoperatively, while the wall motion abnormality was unchanged

Fig 2. End-diastolic (left) and end-systolic (right) images of radionuclide ventriculography in anterior (top) and left anterior oblique (LAO) projections before (a) and after (b) CABG in the same patient. Note hypokinetic wall motion in posterolateral and apical regions preoperatively where similar hypokinesis was observed postoperatively in spite of improvement in asynergy in anterior regions.

in 19 segments (38%) and deteriorated in 4 segments (8%). The preoperative PET was normal in 4 (8%), and revealed ischemia in 22 segments (45%), and scar in 23 (47%), in-

dicating 26 segments as metabolically viable regions.

Table I shows the changes of FDG uptake after CABG in the 49 preoperative asynergic

Fig.3. One representative slice of N-13 ammonia perfusion (top left) and FDG (top right) images before bypass surgery and FDG images at one month (bottom left) and 10 months (bottom right) after the surgery. Note persistent FDG uptake in anterior regions at one month which decreased at 10 months after the surgery.

segments. Of 22 segments showing positive FDG uptake preoperatively, the uptake decreased in 16 segments (73%) and persisted in the remaining 6 segments (27%) (Fig. 1). The improvement in wall motion was observed in all of the segments showing the decreased FDG uptake, while it was observed only in 50% of those showing persistent FDG uptake (Fig. 2) ($p < 0.01$). Of 27 asynergic segments exhibiting negative F-18 deoxyglucose uptake preoperatively, no uptake persisted in 22 segments (81%) (Table I). However, there were 5 segments showing a new FDG uptake postoperatively. Four of them (80%) revealed deteriorated wall motion after the surgery. All the segments showing deteriorated wall motion abnormality had a new FDG uptake postoperatively.

PET follow-up study was performed 1 year later in two patients who showed persistent FDG uptake after CABG. One patient revealed a decrease in FDG uptake at 10 months after CABG (Fig. 3), accompanied by recovery of regional function. The remaining patient showed a similar increase in FDG uptake even at 10 months after

CABG. He had occasional exertional chest pain, suggestive of dysfunction of the bypass grafts.

DISCUSSION

This study demonstrates persistent metabolic abnormality in FDG-PET in postischemic myocardium and a significant relation to change in regional function with improvement in metabolic abnormality.

In our data, persistent FDG uptake was observed 5–7 weeks after CABG in approximately one third of the segments, even though most grafts were patent. Only half of them showing persistent FDG uptake revealed an improvement in asynergy. In contrast, all the segments showing a decrease in FDG uptake after CABG were associated with an improvement in asynergy. This, the slow recovery of function in reversible ischemic segments appears to be in parallel with slow recovery of metabolism. These observations were consistent with the previous experimental study using PET and FDG by Schwaiger et al.¹⁰ showing sustained metabolic derangement after transient ische-

mia. In addition, PET studies demonstrated persistent abnormalities in fatty acid metabolism¹¹ and oxygen metabolism^{19,20} in postischemic myocardium.

There is a body of evidence to support the existence of persistent functional abnormalities after revascularization⁷⁻⁹. This phenomenon has been referred to in the literature as "stunned myocardium"⁸. Those with severe and intermittent ischemia, leading to regional depletion of glycogen or highenergy phosphate stores, may revascularization assessed by PET may explain such biochemical derangement^{10,11,19,20}. Recent preliminary study demonstrated that slow recovery of oxygen metabolism but enhanced glucose metabolism persisted as long as 1 month¹⁹, indicating anaerobic glucose metabolism or glucose utilization to glycogen. However, the precise mechanism of prolonged metabolic alterations long after revascularization remains unknown.

Interestingly, there were some segments showing a new appearance of FDG uptake after CABG. Most of them showed deteriorated hypoperfusion and asynergy, probably due to small perioperative myocardial infarction with occluded bypass grafts. Furthermore, one patient who showed sustained FDG uptake at 1 month revealed slow recovery of glucose metabolism at 1 year, as shown in Fig. 3. Although our study seems to be still preliminary, the follow-up PET using FDG permits valuable assessment of serial changes of tissue function and recovery of chronic ischemia after CABG.

There was relative heterogeneity in the relation of functional and metabolic changes after CABG in our study. This may be the result of qualitative analysis of FDG uptake instead of quantitative measurement of glucose utilization. Furthermore, it is often difficult to match the segment of planar radionuclide ventriculography and tomographic PET imaging, particularly in inferior segments.

We conclude that persistent FDG uptake was occasionally observed after successful CABG, which seems to be related to sustained abnormality in regional function. Thus, serial analysis of PET using FDG should provide insights into the understanding of tissue metabolic alterations which correlate well with improvement in regional

function after CABG.

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