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Prediction of reversible ischemia after coronary artery bypass grafting by positron emission tomography

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Summary

Metabolic imaging using positron emission tomography (PET) facilitates the identification of ischemic but viable myocardium. In this study, the predictive value of PET for identifying improvement in regional function after coronary artery bypass grafting (CABG) was assessed. PET perfusion and metabolic imagings using N-13 ammonia and F-18 deoxyglucose (FDG) were performed before and 5–7 weeks after CABG in 25 patients with coronary artery disease. Each of the 5 myocardial segments of the left ventricle was categorized as normal, ischemic and infarcted based on the findings of perfusion and PET metabolic images. Among 58 hypoperfused segments, abnormal perfusion in 17 of 25 ischemic segments was correctly predicted to be reversible (68% prediction accuracy), and that in 25 of 33 infarcted segments were correctly predicted to be irreversible (76% prediction accuracy) ($p<0.001$). Similarly, among 53 asynergy segments assessed by radionuclide ventriculography, abnormal wall motion in 21 of 27 asynergy segments was correctly predicted to be reversible (78% prediction accuracy), and that in 21 of 26 PET viable segments was correctly predicted to be irreversible (81% prediction accuracy) ($p<0.001$). Thus, preoperative metabolic imaging using PET appears to be useful for predicting responses to CABG.

Key words

Positron emission tomography　Coronary bypass surgery　F-18 fluorodeoxyglucose　Coronary artery disease

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Introduction

The identification of viable but compromised myocardium is important for identifying patients who may benefit from revascularization. Positron emission tomography (PET) has the unique capability to assess regional myocardial perfusion and metabolism[1,2]. Metabolic imaging should particularly be sensitive for estimating ischemic but viable myocardium as an area of persistent metabolic activity[3~5]. We hypothesized that metabolic imaging can accurately identify reversible ischemic segments which will improve in regional function after coronary artery bypass grafting (CABG). Thus, to determine the predictive value of PET for identifying improvement in hypoperfusion and wall motion abnormalities, PET using FDG was performed before and after CABG and the metabolic findings were compared with changes of regional myocardial function.

Materials and methods

Patient population

This study includes 25 patients who underwent PET before and after CABG. There were 23 men and 2 women whose ages ranged from 36 to 68 years. PET was performed during 4 weeks before and 5 to 7 weeks after CABG. Twenty patients had a history of myocardial infarction of more than one-month duration after onset. All patients gave their written informed consent according to a protocol approved by the Human Clinical Trial Committee of Kyoto University Hospital.

Positron emission tomography

PET was performed on the entire body using a multislice positron camera (Positologica III, Hitachi Medical Co)[6]. Following accurate positioning of a patient for the positron camera, a transmission scan was performed for 15 min. Then, 10 to 20 mCi N-13 ammonia was intravenously injected at rest, and myocardial perfusion imaging was performed for 5 min. Immediately after completion of the first scan, the second scan was performed for 8 min at a position 8 mm caudal to the first scan. These 2 scans provided a total of 14 contiguous transverse slices of the myocardium at 8 mm intervals[7].

The FDG study was performed separately within one week after the N-13 ammonia perfusion study. All patients fasted for at least 5 hours before each study. Two to 7 mCi FDG were administered at rest and 2 emission scans were obtained every 8–10 min each after 60 min of the injections[8~10].

Analysis of PET images

The regional myocardial perfusions were quantitatively assessed by circumferential profile analysis of 3 transverse slices of N-13 ammonia distribution in one patient using the lower limit for normal subjects. The lower limit was determined as the mean minus 2 standard deviations from the values of 10 normal volunteers[11]. An image of the left ventricular myocardium was divided into 5 segments (anterior septal, apical, inferior and lateral). The segments with perfusion below the lower limit covering at least 30 degrees of the profiles were considered hypoperfused segments.

The pre- and postoperative perfusion images were quantitatively analyzed to assess the improvement in perfusion after surgery. Based on the study of variations of perfusions in normal subjects[11], the perfusions were considered to have improved when the postoperative perfusion at rest increased by 10% or more compared to the preoperative perfusion on the profile curves. However, when the postoperative perfusion was decreased by 10% or more from the preoperative perfusion on the profile curves, the perfusion was considered to have deteriorated.

N-13 ammonia and FDG images were correlated with the corresponding segments. Three experienced observers visually interpreted the uptake on both images. The segments with normal perfusion were defined as normal regions. The hypoperfused segments with FDG uptake definitely higher than N-13 ammonia were defined as ischemic regions. The hypoperfused segments with FDG uptake less than or close to N-13 ammonia uptake were defined as myocardial scars[3~5,8~10].

Wall motion analysis

Each patient underwent radionuclide ventriculography in the anterior and left anterior oblique projections following the intravenous injection of 20 mCi of Tc-90 m in-vivo labeled red blood cells before and after CABG. The image of the left ventricle was divided into 5 segments corresponding to those of the perfusion analysis. Wall motion was visually scored by 3 experienced observers from 2 to –1 (normal, hypokinetic, akinetic and dyskinetic) without knowledge of any other radionuclide or postoperative results. When the score increased by one or more after the operation, the segment was defined as a region with improved wall motion postoperatively, while the segment with a score decreased by one or more postoperatively, it was defined as a region with deteriorated wall motion. The septal segment was excluded from the wall motion analysis because postoperative paradoxical motion was frequently observed[12].

Coronary bypass surgery

Each patient underwent a grafting of the saphenous vein or internal mammary artery. One patient received one bypass graft, 12 patients had 2 grafts and 12 patients had 3 grafts. Among a total of 61 bypass grafts, 51 (84%) were patent on the graftgraphy performed one month after the surgery. Two patients were believed to have had small perioperative myocardial infarction. Two patients underwent aneurysmectomies.

Statistical analysis

Comparisons of proportions were made using a chi-square test. Probability values less than 0.05 were considered to be significant.

Results

The N-13 ammonia perfusion study identified 58 hypoperfused segments in 23 of the 25 patients (92%) preoperatively. Among the hypoperfused segments, 25 (43%) improved in perfusion postoperatively, 27 segments remained unchanged (47%), and 6 segments deteriorated (10%). Preoperative PET revealed ischemia in 25 segments (43%) and scar in 33 segments (57%). Among 25 metabolically active segments, 17 (60%) improved in hypoperfusion, 8 segments did not improve (32%) after surgery. In contrast, among 33 metabolically-inactive segments, only 8 (24%) improved in hypoperfusion ($p<0.001$) (**Fig. 1**). Thus, the preoperative metabolic activity on PET correctly predicted the improvement in perfusion (60% accuracy), and no improvement in perfusion (76% accuracy) after CABG.

Preoperative radionuclide ventriculography identified 53 segments with wall motion abnormalities in 23 of the 25 patients (92%). Among these asynergy segments, 26 (49%) im-

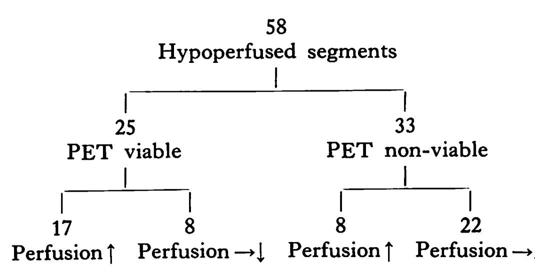

Fig. 1. Preoperative prediction of reversible ischemia by positron emission tomography (PET) **in 58 hypoperfused segments.**

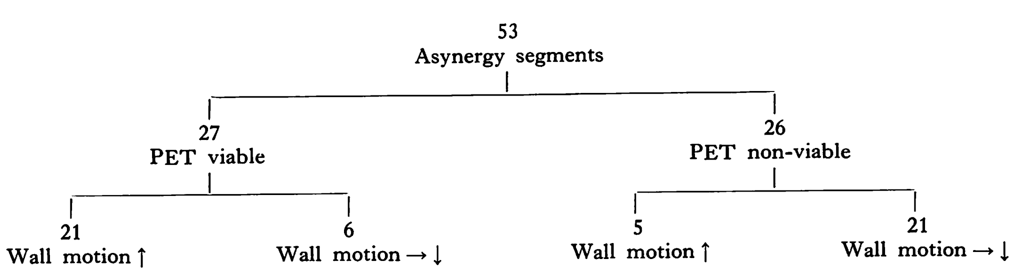

Fig. 2. Preoperative prediction of reversible asynergy by PET in 53 asynergy segments.

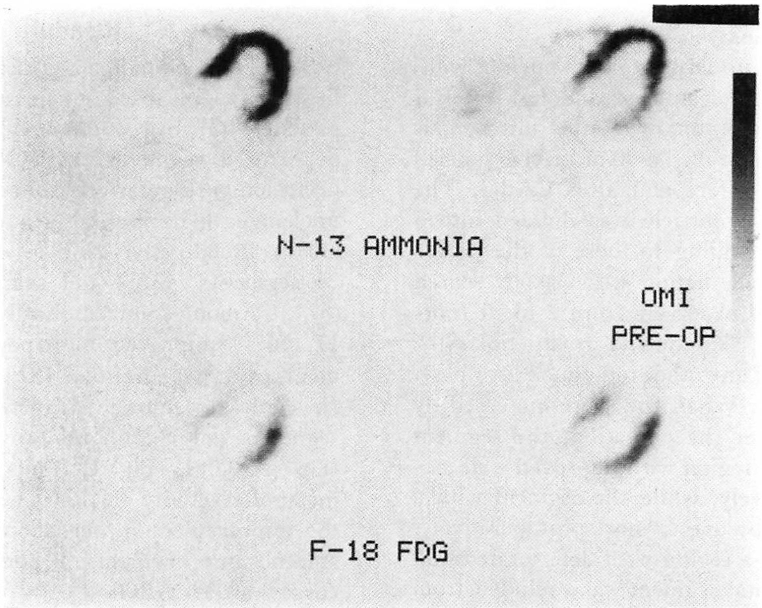

Fig. 3. Two representative transverse slices of N-13 ammonia perfusion (top) **and F-18 deoxyglucose** (FDG) (bottom) **images of a patient with inferior wall myocardial infarction before the bypass surgery.**

Hypoperfusion with increased FDG uptake in the posterolateral regions is noted.

proved in wall motion postoperatively, while the wall motion abnormalities remained unchanged in 23 segments (43%) and deteriorated in 4 segments (8%). Preoperative PET revealed normal segment in 4 segments (8%), ischemia in 23 (43%), and scar in 26 (49%). Thus, preoperative PET identified these 27 segments as metabolically viable regions. Among these segments, the wall motion abnormalities in 21 (78%) improved, while those in 6 segments (22%) did not improve postoperatively. In contrast, among 26 segments exhibiting no metabolic activity, in only 5 (19%) did the wall motion abnormality improve ($p<0.001$) (**Fig. 2**). Thus, preoperative metabolic PET imaging correctly predicted the improvement in wall motion abnormalities (81% prediction accuracy) and no improvement in wall motion abnormalities (78% prediction accuracy) after CABG. **Figs. 3, 4** show examples of PET and radionuclide ventriculography before and after CABG.

Figs. 3~6 illustrate an example of a patient with inferior wall myocardial infarction. The preoperative PET study revealed hypoperfusion in the posterolateral wall with increased FDG uptake (**Fig. 3**). The postoperative PET study demonstrated improvement in perfusion with decreased FDG uptake in the same region (**Fig. 4**). The preoperative (**Fig. 5**) and postoperative (**Fig. 6**) radionuclide ventriculography showed akinesis in the apex and hypokinesis in the posterolateral wall preoperatively, where wall motion improved after surgery. Thus, the areas with increased FDG uptake on preoperative PET improved on perfusion as did wall motion after CABG.

Discussion

Our data demonstrate the highlights of metabolic imaging using PET for predicting responses to CABG. The segments exhibiting metabolic activity preoperatively are expected to recover from hypoperfusion and asynergy after CABG.

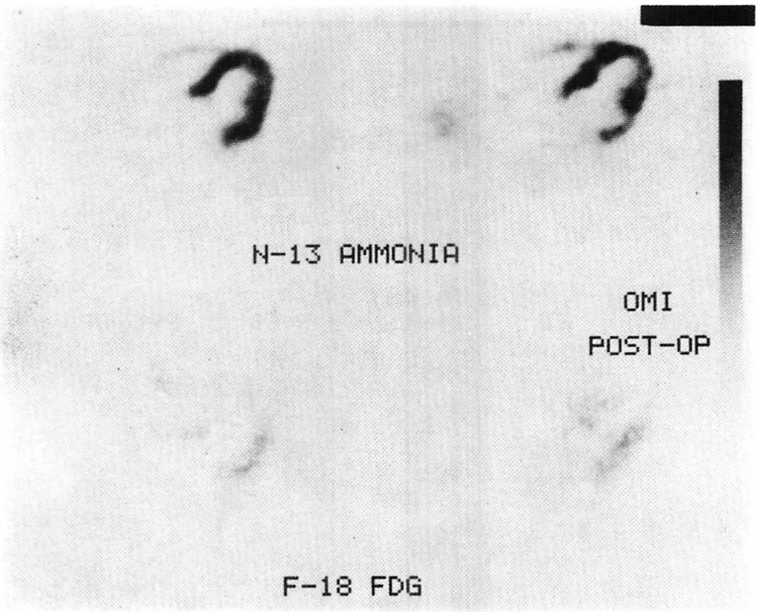

Fig. 4. The same slices of N-13 ammonia perfusion (top) **and FDG** (bottom) **images of the same patient after surgery** (Ref. Fig. 3).
Improvement in perfusion with decrease in FDG uptake in the posterolateral regions is observed.

Predicting reversible ischemia is of great importance in selecting patients for revascularization. Redistribution on thallium-201 imaging has been widely used to differentiate ischemic but viable myocardium from irreversibly infarcted myocardium[13~16]. However, recent studies have reported the limited value of PET for predicting non-redistribution segments to be irreversibly infarcted myocardium[17~19]. Persistent metabolic activity was often observed in the segments exhibiting persistent thallium-201 defects on PET[8,10,20], however, persistent metabolic activity in ischemic areas assessed by PET is expected to be a specific indicator of tissue viability[3~5]. An increase in FDG uptake was often observed in ECG infarcted areas with relatively preserved perfusion and wall motion[8,20,21], however, dyskinetic segments occasionally showed increased FDG uptakes[9,21]. Therefore, it is important to know whether these metabolically-active areas truly represent reversible ischemia which is likely to restore regional function after the restoration of blood flow. In addition, wall motion may not be a reliable indicator of tissue viability. Segments with severely depressed cardiac function often improve in terms of wall motion after the restoration of blood flow, which may be considered as hibernating myocardium[22].

The present study demonstrates that an accurate preoperative prediction of reversible asynergy and hypoperfusion can be made with PET using FDG. Segments showing metabolic activity, which may include a substantial amount of viable myocardium, have potential for improvement in regional function after CABG. These are consistent with earlier observations by Tillisch et al[4] describing the high predictive value of PET for identifying reversible asynergy.

Though metabolic imaging seems to be an ideal method for identifying hibernating myocardium where metabolic activity persists with severely depressed[22] blood flow and wall

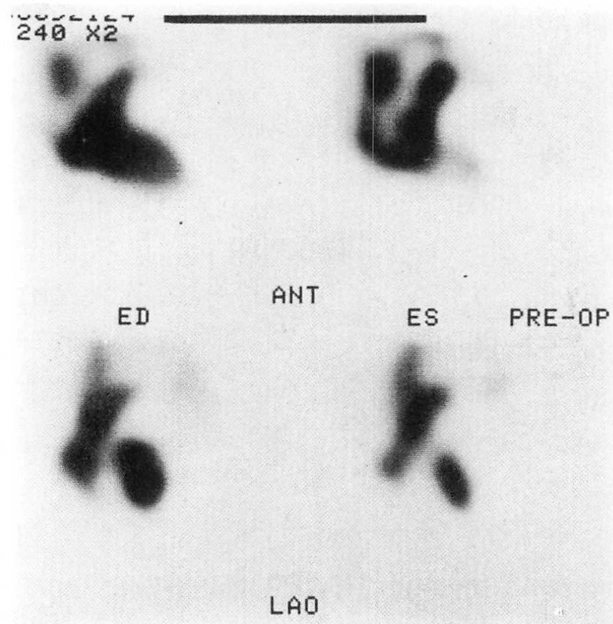

Fig. 5. End-diastolic (left) **and end-systolic** (right) **images of radionuclide ventriculography in the anterior** (ANT) (top) **and left anterior oblique** (LAO) (bottom) **projections of the same patient before the surgery** (Ref. Fig. 3).
Akinesis in the apical wall and hypokinesis in the posterolateral wall are shown.

motion, slow recovery of regional cardiac function in reversible ischemic segments may occasionally be observed after revascularization[23~25]. Our preliminary study also showed occasional persistent metabolic activity after CABG[26,27]. This phenomenon has been referred to in the literature as "stunned myocardium"[28]. This may suggest limitations of PET for identifying low predictive value of the improvement in regional function after CABG.

The improvement in regional perfusion did not as highly correlate with preoperative metabolic activity as did the improvement in regional wall motion. This may have been due to the analysis of perfusion at rest in the present study. An assessment of perfusions both at rest and during exercise after CABG might have presented clearer correlations[17~29], because CABG is associated with an increase in flow reserve. In addition, we did not apply quantitative measurements of glucose utilization, instead qualitative analysis of FDG uptakes was done. Furthermore, it is often difficult to match the segments or planar radionuclide ventriculography with those of tomographic PET imaging. In particular, the inferior segment may not be well delineated by ventriculography in the 2 standard projections. These factors may cause relative heterogeneity of the correlations between PET findings and postoperative responses.

In summary, reversible ischemia and asynergy after CABG can be accurately predicted by preoperative PET using FDG. The metabolically active segments are most likely to improve in regional function and tissue perfusion after CABG. Thus, metabolic PET imaging should be reliable means of identifying viable but compromised myocardium.

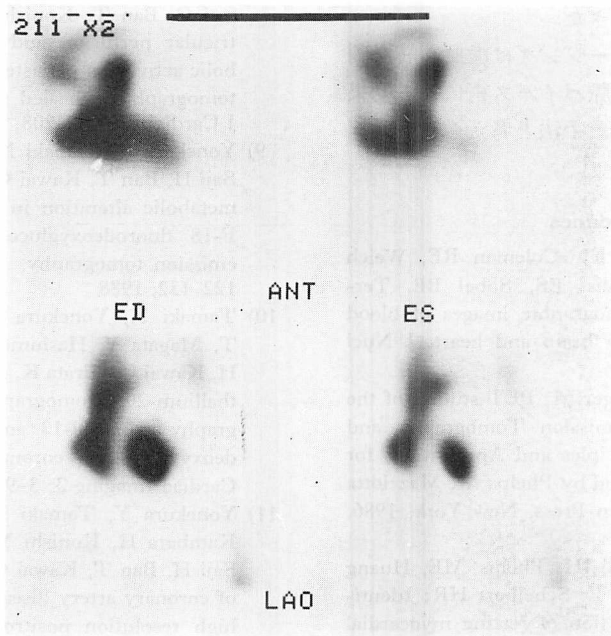

Fig. 6. End-diastolic (left) **and end-systolic** (right) **images of radionuclide ventriculography in the anterior** (ANT) (top) **and left anterior oblique** (LAO) (bottom) **projections of the same patient after the surgery** (Ref. Fig. 3).

Improvement in the asynergy in the apical and posterolateral regions is demonstrated.

要　　約

ポジトロン CT による冠動脈バイパス術後の可逆的虚血心筋の検出

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ポジトロン CT (PET) は心筋代謝の有無により虚血心筋を同定できる優れた手法と考えられる．本報告では，本法が冠動脈バイパス術後の局所心機能の回復をどの程度予測できるかを検討した．

虚血性心疾患 25 例に，バイパス術前および手術 5～7 週間後に，N-13 アンモニアによる血流イメージングと F-18 フルオロデオキシグルコースによる糖代謝イメージングを施行した．左室心筋 5 区域につき，血流が正常な健常心筋，血流が低下し糖代謝の亢進した虚血心筋，血流も糖代謝も低下した梗塞心筋の三つに区分し，前 2 者を蘇生可能 (viable) な心筋とした．

術前，血流の低下した 58 区域中，術後，血流の改善したのは，糖代謝の亢進した 25 区域中 17 区域 (68%) であったのに対し，糖代謝の低下した 33 区域では，わずかに 8 区域 (24%) であった ($p<0.001$)．同様に術前壁運動の低下した 53 区域中，術後，壁運動の改善したのは PET 上 viable であった 27 区域中 21 区域(78%) であったのに対し，梗塞心筋と判定された 26 区域ではわずかに 5 区域(19%) であった ($p<0.001$)．術前の PET により術後の血流の改善した区域を 68%，改善しなかった区域を 76% 正しく予測できた．また壁運動の改善した区域を 81%，改善しなかった区

域を 78% 正しく予測できた.

PET による代謝イメージングは虚血心筋を判定することにより，冠動脈バイパス術による効果を正しく予測できる優れた手法と考えられた.

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