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Proportion of viable myocardium is more reliable than semi-quantitative score in predicting functional recovery: a pilot study of PET myocardial viability imaging

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Abstract PET myocardial viability imaging is the "gold standard" for the non-invasive assessment of myocardial viability. The research aims to find out the best methods of imaging interpretation in predicting the postoperative functional recovery. Twenty-one CAD patients with multi-vessel involvement were recruited. All patients underwent gated myocardial perfusion imaging(G-MPI) and FDG PET myocardial imaging within 2 weeks before coronary artery bypass grafting. The postoperative G-MPI was performed in all patients 3 months after the surgery. Out of the total 420 segments, 164 segments of ischemic myocardium were detected by preoperative G-MPI. Among them, 93 ischemic segments were identified as non-viable(difference score≥0) and the rest 71 segments were identified as viable(difference score<0). The proportion of viable segments (the ratio of viable segments versus ischemic segments) and summed difference score of metabolism to perfusion were calculated. The patients were further divided into 2 groups according to the proportion of viable myocardium: group Ⅰ (the proportion≥50%, 12 cases) and group Ⅱ (the proportion<50%, 9 cases) while another division was made according to SDS: group A (SDS≥0), group B (-5≤SDS<0) and group C (SDS<-5). The diagnostic accuracy of proportion of viable segments and SDS in predicting the post-revascularization improvement in the left ventricular ejection fraction by at least 5 or more ejection fraction units was 88.89% (8/9) and 55.56% (5/9) respectively. It is concluded that both approaches allow accurate evaluation of myocardial viability. Furthermore, the proportion of viable myocardium is more reliable in predicting the postoperative functional recovery.

Key words Myocardial viability, Deoxyglucose, PET, Coronary artery disease

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1 Introduction

Coronary artery bypass grafting(CABG) is widely recognized as one of the best forms in treating coronary artery disease (CAD) and its short-, medium-, and long-term results are well documented[1]. In patients with CAD and impaired left ventricular (LV) function, the differentiation between dysfunctional but still viable myocardium and irreversible necrotic tissue has important clinical implications[2–4]. It is now clear that in many patients LV dysfunction may be reversible following coronary revascularization[5]. Therefore, the distinction of LV dysfunction caused by fibrosis from that arising from viable but dysfunctional myocardium is a relevant diagnostic issue and has important implications for patients with a low ejection fraction, in whom heart failure may be attributed to hibernation or stunning (or both) rather than to necrosis[6].

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Single-photon emission computed tomography (SPECT) with ^{201}Tl or $^{99}Tc^m$-labelled agents has been widely used in clinical practice to detect myocardial viability[7–9]. However, combined with myocardial perfusion imaging, positron emission tomography (PET) metabolic imaging with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) has been recognized as the non-invasive gold standard for differentiating viable from non-viable myocardium[10–12]. Nevertheless few articles focusing on the comparison of different image interpretation methods have been issued. In our research, we aimed to evaluate the clinical role of PET myocardial viability imaging in identifying the potential benefits from CABG and compare the semi-quantitative score system with proportion of viable segments in predicting the functional recovery.

2 Materials and methods

2.1 Patients population

Twenty-one consecutive patients with multi-vessel involved coronary artery disease (16 males and 5 females, mean age=65.38±8.48 years) were prospectively recruited from the department of Cardiac/Thoracic Surgery. The coronary artery stenosis or occlusion of all patients were identified by coronary angiography. All patients were proved to have at least 2 main coronary branches involvement and the major stenosis was greater than 80% (15 cases with LAD, RCA and LCX involvement, 4 cases with LAD and RCA involvement, 2 cases with LAD and LCX involvement). Gated myocardial perfusion imaging (G-MPI) using $^{99}Tc^m$-sestamibi and PET myocardial metabolic imaging using ^{18}F-FDG were performed in all patients within 2 weeks before surgery to identify the viability of ischemic myocardium. All patients underwent off pump coronary artery bypass (OPCAB) while 4 cases underwent ventricular aneurysm dissection simultaneously. G-MPI was performed as the major follow-up work-up in the 3rd month after surgery to check out the improvement of cardiac function and myocardial perfusion.

2.2 G-MPI data acquisition

Patients received an intravenous injection of $^{99}Tc^m$-sestamibi (925MBq) and were told to take a cup of milk 30-45 minutes afterward to minimize overlap of hepatobiliary with myocardial activity. Acquisition began 30-45 minutes after the ingestion of milk and a dual-head gamma camera system (ADAC Vertex V60) was employed for scan. The camera system was equipped with VXGP collimator. The energy window was centered at 140 keV photon peak of technetium-99m sestamibi with a 20% window. Data acquisition(step mode, circular orbit) was done in supine position over 180° (45°RAO to 45°LPO). A total number of 64 projections, of which the scan time was 40 seconds for each, were collected. Eight frames/cycle were acquired using an R wave-triggered electrocardiogram gated system and the allowable change of heart rate was 20%. Data were stored in a 64×64, 16bit matrix. A cine review was applied prior to reconstruction to verify the absence of patient motion.

2.3 G-MPI data reconstruction and interpretation

The raw data were reconstructed by filtered back projection using a Butterworth filter (cut off frequency at 0.5, order at 5). Attenuation correction was not applied. Further reconstruction and reorientation yielded standard short axis, vertical long axis and horizontal long axis planes.

The images were interpreted by two experienced nuclear physicians, who were blinded to any results of other work-ups. According to the interpretation guidelines for myocardial perfusion imaging issued by American Society of Nuclear Cardiology (ASNC), a 20-segment model and 5-point scoring system were employed in the study to evaluate the location, extent and severity of myocardial ischemia[13]. The severity of abnormal tracer uptake was graded as follows: 0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced and 4, absent. Resting score (RS) and summed resting score (SRS) were calculated. RS presented the tracer uptake grade of every single segment according to the criteria above. SRS=the sum of RS of all segments. Other parameters of left ventricular function, which included left ventricular ejection fraction (LVEF), wall thickening (WT), end diastolic volume (EDV) and end systolic volume (ESV), were generated automatically by cardiac processing software Autoquant4.21.

2.4 PET data acquisition

A dedicated PET scanner (ADAC C-PET 250) was employed in the study. The patients preparation protocol, which was proposed by Division of Nuclear Medicine of LAC+USC Medical Center, was followed[14]. Being fast for at least 6 hours, all patients underwent one-touch blood glucose test and oral glucose load or insulin were given according to the blood glucose concentration and presence of diabetes to maximize the myocardial uptake of FDG. ^{18}F-FDG was injected with the dose of 2.526 MBq/kg afterward and acquisition was started 90 minutes after the injection. Data acquisition was done in a supine position with arms-up in a total time of 30 minutes. A three-dimensional mode was applied in emission and transmission acquisition.

2.5 PET data reconstruction and interpretation

The raw data was reconstructed by row-action maximum likelihood algorithm (RAMLA). Attenuation correction was not applied. Further reconstruction and reorientation yielded standard short axis, vertical long axis and horizontal long axis planes.

The images were interpreted by two experienced nuclear physicians, who were blinded to any results of other work-ups except for G-MPI. According to the interpretation guidelines for myocardial glucose metabolism imaging issued by ASNC, a 5-point semi-quantitative scoring of metabolism images relative to perfusion images was used to calculate the normalized difference score (DS) of every ischemic myocardial segment as well as the summed difference score (SDS)[15]. The segmental scores on the FDG images were normalized to the perfusion scores (i.e., the scores need to be adjusted so that scores in myocardium with normal perfusion will be 0). The ischemic myocardial segments with DS<0 were assessed as viable while the segments with DS≥0 were assessed as non-viable. SDS≥0 is considered as perfusion-metabolism match while SDS<0 is considered as perfusion-metabolism mismatch. Besides, the proportions of viable myocardium (the ratio of viable segments versus ischemic segments) were calculated.

The population were further divided into 2 groups according to the proportion of viable myocardium: group Ⅰ (the proportion≥50%) and group Ⅱ (the proportion<50%) while another division was made according to SDS: group A (SDS≥0), group B (-5≤SDS<0) and group C (SDS<-5). The improvement of SRS, LVEF, EDV and ESV of each group was assessed.

2.6 Statistical analysis

All parameters were recorded as mean and standard deviation (SD) of the mean. Paired-samples T test was used for parametric samples while Wilcoxon test was used for non-parametric samples. A probability value of P<0.05 was considered significant.

3 Results

3.1 Preoperative G-MPI and PET imaging

The preoperative G-MPI revealed 164 segments of ischemic myocardium out of 420 segments. The mean SRS of 21 cases was 16.24±8.36 while the mean RS of all ischemic segments was 2.08±0.89. Among 164 ischemic segments, 71 segments (mean RS = 2.04±0.93, mean WT=(11.28±10.11)%) were considered as viable according to PET imaging while 93 segments (mean RS=2.11±0.93, mean WT=(10.61±8.63)%) were considered nonviable. The patients were further divided into 2 groups according to the proportion of viable myocardium: group Ⅰ (the proportion ≥50%, 12 cases) and group Ⅱ (the proportion <50%, 9 cases) while another division was made according to SDS: group A (SDS≥0, 5 cases), group B (-5≤SDS<0, 8 cases) and group C (SDS<-5, 8 cases). The perfusion, viability and functional parameters of each group are listed in Tables 1 and 2.

Table 1 The pre- and post-operative comparison of SDS, SRS, LVEF, EDV and ESV observed in patients of groups A, B and C

Groups	A (*n*=5)	B (*n*=8)	C (*n*=8)
SDS	1.80±1.79	-4.13±0.83	-9.25±2.60
Pre-SRS	18.20±3.35	14.50±11.01	16.75±8.10
Post-SRS	23.40±5.98	11.50±10.82	12.25±9.25
Pre-LVEF / %	33.40±7.57	30.50±8.68	28.38±10.39
Post-LVEF / %	29.80±8.47	33.88±8.56	35.63±11.19
Pre-EDV / mL	221.00±60.70	191.50±70.11	204.63±59.83
Post-EDV / mL	243.40±72.60	190.75±50.46	176.00±57.22
Pre-ESV / mL	149.20±40.80	137.63±62.70	150.13±59.89
Post-ESV / mL	173.20±62.90	129.38±43.06	118.13±49.41

Table 2 The preoperative comparison of SDS, SRS, LVEF, EDV and ESV observed in patients of groups Ⅰ and Ⅱ

Groups	Ⅰ	Ⅱ
Viable/ischemic / %	81.15±15.72	15.76±16.86
Pre-SRS	11.92±7.03	22.00±6.44
Pre-LVEF / %	28.50±10.17	32.89±6.67
Pre-EDV / mL	201.67±72.71	206.00±48.28
Pre-ESV / mL	149.58±65.13	139.22±38.18
SDS	-7.00±3.52	-1.56±4.42
Post-SRS	7.83±5.29	23.67±7.70
Post-LVEF / %	33.67±8.98	33.44±10.57
Post-EDV / mL	185.00±59.38	214.56±64.37
Post-ESV / mL	127.50±48.42	146.22±59.29

3.2 Postoperative G-MPI imaging

The postoperative G-MPI revealed 155 segments of ischemic myocardium. The mean SRS of 21 cases was 14.62±10.18 postoperatively while the mean RS of all ischemic segments was 1.76±1.21. The mean RS and WT of pre-operatively assessed viable segments was 1.00±0.89 and (14.17±11.76)% respectively, both of which were significantly improved. The mean RS and WT of pre-operatively assessed nonviable segments was 2.34±1.10 and (11.72±10.29)% respectively, of which RS was worse and WT was improved non-statistically (Table 3). The postoperative perfusion and functional parameters are listed in Tables 4 and 5.

Table 3 The mean preoperative and postoperative RS, WT of viable and nonviable segments and the improvement of RS, WT

Segments	Viable (*n*=71)	Nonviable (*n*=93)
Pre-RS	2.04±0.93	2.11±0.93
Post-RS	1±0.89	2.34±1.10
Reduce of RS	1.04±0.64*	-0.24±0.71*
Pre-WT / %	11.28±10.11	10.61±8.63
Post-WT / %	14.17±11.76	11.72±10.29
Increase of WT / unit	3.04±5.17*	1.11±6.69†

**P*<0.01, † *P*>0.05, compare viable segments with nonviable segments.

Table 4 SRS, LVEF, EDV and ESV improvement of groups A, B and C

Groups	A (*n*=5)	B (*n*=8)	C (*n*=8)
Decrease of SRS	-5.20±5.63*	3.00±1.69‡	4.50±3.74†
Increase of LVEF / unit	-3.60±2.70†	3.38±5.90*	6.88±5.62‡
Decrease of EDV / mL	-22.40±23.93*	0.88±27.11*	28.63±23.86†
Decrease of ESV / mL	-24.00±25.35*	8.25±28.57*	32.00±26.25†

* *P*>0.05, †*P*<0.05, ‡*P*<0.01, compare preoperative status with postoperative status.

Table 5 SRS, LVEF, EDV and ESV improvement of groups Ⅰ and Ⅱ

Groups	Ⅰ	Ⅱ
SRS	4.08±2.31‡	-1.67±6.42*
LVEF / %	5.08±5.37‡	0.33±7.07*
EDV / mL	16.75±29.58*	-8.55±28.31*
ESV / mL	22.08±30.22†	-7.00±32.37*

**P*>0.05, †*P*<0.05, ‡*P*<0.01, compare preoperative status with postoperative status.

3.3 Comparison of perfusion and functional improvement of different group

The study showed a significantly different performance of the recovery of perfusion and systolic function between groups (Tables 4 and 5). The patients of groups A and Ⅰ didn't show any improvement of perfusion and systolic function (Fig.1). A significant improvement of myocardial perfusion instead of systolic function was observed in the patients of group B. The SRS, LVEF, EDV and ESV were all significantly improved in the patients of groups C and Ⅱ (Figs.1 and 2).

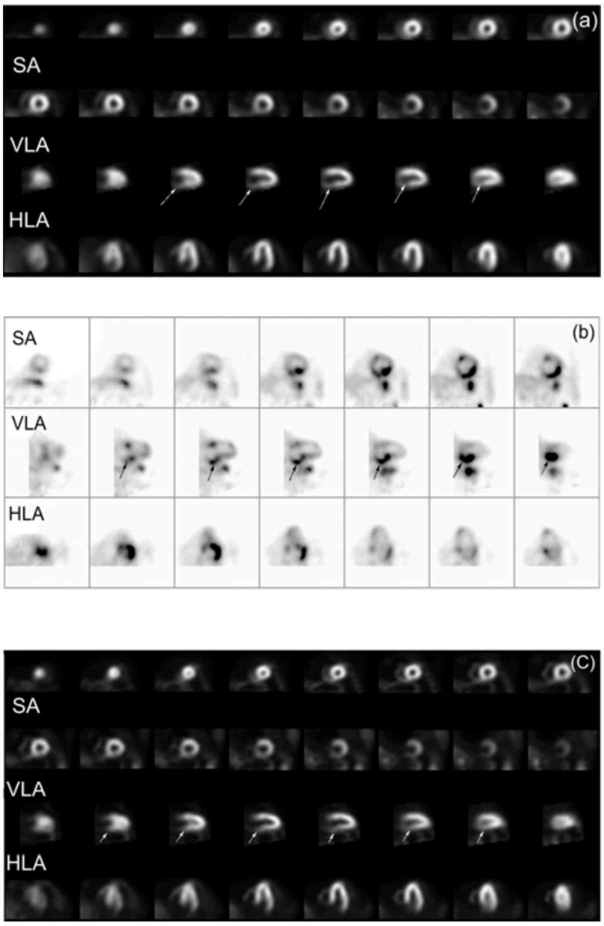

Fig.1 Myocardial viability imaging of a 77-year-old man with prior myocardial infarction of inferior wall. Preoperative G-MPI (vertical long axis): showed a moderately to severely reduced perfusion involving basal and mid inferior wall (solid arrow) (a). PET imaging (vertical long axis): The FDG uptake within basal and mid inferior wall (arrow) was significantly intensive compared to the rest segments. The proportion of viable segments=100% and SDS was -8 for this patient (b). Postoperative G-MPI (vertical long axis): revealed improvement of perfusion and wall thickening within those segments (arrow). The global LVEF elevated from 50% to 57% (c).

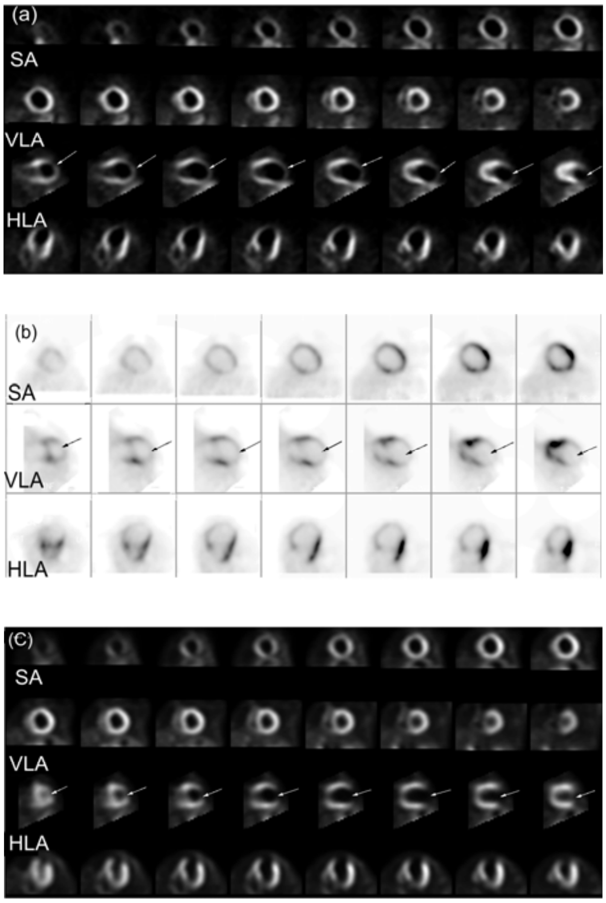

Fig.2 Myocardial viability imaging of a 75-year-old woman with prior myocardial infarction of apex and apical anterior wall. Preoperative G-MPI (vertical long axis): showed severely reduced uptake in anteroapical, inferoapical, apical anterior, apical inferior, apical anteroseptal, apical inferoseptal, apical anterolateral and apical inferolateral wall (arrow). Dyskinesis was observed in apex (a). PET imaging (vertical long axis): indicated a perfusion-metabolism match of those area (arrow) with the proportion of viable segments=0% and SDS=0 (b). Postoperative G-MPI (vertical long axis): showed neither perfusion nor functional improvement. There is absence of uptake in the preoperatively ischemic area (c).

4 Discussion

Myocardial perfusion imaging has a long and successful history in the diagnosis and risk stratification of CAD[16]. Semi-quantitative score of myocardial perfusion was recommended in ASNC imaging guidelines in 1999 and consists of summed resting score, summed stress score and summed difference score[13]. A large-scale clinical trial (2686 cases) has identify that the most powerful predictor of cardiac death was post-stress LVEF whereas the best predictor of myocardial infarction was summed difference score. Integration of the LVEF and summed difference score yielded effective stratification of patients into low-, intermediate- and high-risk subgroups[17].

^{18}F-FDG PET myocardial viability imaging is proved to be accurate in predicting the functional improvement after CABG[18-20]. However, there is a relatively short history of using semi-quantitative system in ^{18}F-FDG PET myocardial viability imaging, which was firstly introduced by ASNC in 2003[15]. On the basis of current knowledge, the potential of a post-revascularization improvement in the left ventricular ejection fraction by at least 5 or more ejection fraction units is high if the perfusion-metabolism mismatch affects 20% or more of the left ventricular myocardium[21-23]. So far, little work has been done to study whether the extent or magnitude of a perfusion-metabolism mismatch serves as a predictor of the degree of functional improvement and which one has better diagnostic accuracy.

As mentioned above, our study classifies the patients into 5 groups according to different proportion of viable myocardium and SDS to evaluate the clinical role of the extent or magnitude of a perfusion-metabolism mismatch in CABG. Our results indicate that the patients of group Ⅱ and C(SDS<-5) have the best postoperative perfusion and functional improvement. The patients of group B(-5≤SDS<0) have a significant improvement of myocardial perfusion while the functional improvement was found to be no statistically significant. No perfusion and functional improvement were revealed in the patients of group Ⅰ and A (SDS≥0). In the cases of group Ⅰ and A, the ischemic myocardium may mainly consist of viable myocardium, which benefit from CABG to the largest extent.

In the cases of group B, the ischemic myocardium may be a relatively balanced mixture of infarcted and hibernating/stunned myocardium, of which the degree of functional improvement is yet to be determined and requires further study with more samples. In the cases of group Ⅱ and C, the ischemic myocardium is rarely viable so that CABG may even worsen the cardiac function due to surgical trauma. Thus the proportion of viable myocardium and SDS were both found by our study to be a powerful predictor of the degree of functional improvement.

However, if we consider a postoperative LVEF increase by at least 5 unit as clinically significant, the proportion of viable myocardium has better diagnostic accuracy (88.9%) than SDS (55.6%). The population with few ischemic segments might contribute most to that different performance. Though all or most of the ischemic segments are viable, the patients with few ischemic segments might be classified into the group of -5≤SDS<0, which does not indicate a significant functional recovery. For instance, a patient with a total ischemic segments of 4, 3 all of which are viable and DS is -1 for each, might be considered equivocal as SDS>-5. Thus SDS might underestimate the functional recovery in patients with few ischemic segments. Though only 21 cases were included in the clinical trial, our study reveals that the patients, of which the proportion viable segments ≥50% or SDS <-5, benefit the most from CABG and should undergo the surgery. The patients, of which SDS≥0 or the proportion viable segments <50%, should maintain medical therapy as surgery is unbeneficial. The patients of -5≤SDS<0 may be underestimated as the cases with few ischemic segments were included in the population. Further study with more samples is required to verify our results.

Besides the global improvement of perfusion and function, the relationship between DS and segmental improvement was also studied. As showed above, a significant segmental improvement of perfusion and systolic function were observed in viable segments (DS<0) while the nonviable segments (DS≥0) showed no improvement of both. PET myocardial viability imaging was found to be accurate in differentiating the viable segments from infarcted segments as well as in predicting the segmental improvement of perfusion and systolic function.

5 Conclusion

Our preliminary study indicates that the proportion of viable myocardium is accurate in predicting the post-surgery improvement of myocardial perfusion as well as systolic function. Despite the relatively small sample number, the proportion of viable myocardium is proved by the study to be accurate in evaluating which group of patients might benefit from CABG. Thus it may play a significant role in deciding whether patients should undergo surgical treatment or maintain medical therapy.

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