

REVIEW ARTICLE—INTERNATIONAL CORNER

Clinical Application of Quantitative Myocardial Blood Flow Assessment Using Positron Emission Tomography

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Abstract

Epicardial coronary artery disease has been highly noticed in the traditional clinical examination, while myocardial microcirculation function has been neglected for a long time, which plays a nonnegligible role in quite a few patients' clinical manifestations and prognosis. Non-invasive quantitative PET myocardial perfusion imaging has become a unique and gold standard of evaluating myocardial microcirculation function. Its clinical applications in diagnosis, risk stratification, prognosis evaluation, efficacy evaluation and treatment guidance of cardiovascular diseases are given, together with its development status in China.

Keywords: Absolute quantification, Myocardial perfusion imaging, Positron emission tomography

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A follow-up study concluding 11,223 patients of stable angina pectoris (1) reported the incidence of microcirculation dysfunction in patients with myocardial ischemia but with non-obstructive coronary angiography was about 45%, whose major cardiovascular events and all-cause mortality were significantly higher than the control group. Epicardial coronary artery disease has been highly noticed in the traditional cardiovascular examination, while myocardial microcirculation function has been neglected for decades and globally.

In China, two myocardial perfusion PET imaging agents, ¹³N-ammonia, ¹⁵O-H₂O, have been approved by Chinese Food and Drug Administration. ¹³N-ammonia is the common one used in both clinical and research study for its proper half-life period and good image quality since the end of the 20th century. Adenosine triphosphate and dobutamine are the most commonly used stress drugs. For the past few years, about 10 hospitals or centers carried out more ¹³N-ammonia-related work of production optimization or clinical application. Currently, four departments of nuclear medicine carry out absolute quantitative cardiac PET for routine clinical program (Table 1). The earliest is the first hospital of Shanxi medical university, initiated from the end of 2015, the typical results diagrams of normal volunteer (Figure 1) and diabetes mellitus

(Figure 2) show as follows. Although the current status is not optimistic, it is gratifying that the Chinese Society of Nuclear Medicine is now paying great attention to the absolute quantitative technology, giving strong support and active promotion to adapt to clinical needs in future. In addition, as the installation of D-SPECT increases in China, more and more hospitals are expected to participate.

Since Gould K. Lance put forward the concept of coronary flow reserve (CFR) in 1974, non-invasive PET MPI has become a unique and gold standard of evaluating myocardial microcirculation function. In order to broad acknowledgement and better utilization of quantitative cardiac PET, the following summarizes its clinical applications.

Risk stratification, prognosis evaluation and decision-making optimization

Abnormal coronary microcirculation is an independent predictor of adverse cardiovascular events (2). The prognosis of CAD patients with reduced CFR was similar to that of patients with worse coronary morphology, and patients with lower CFR after CABG revascularization had unimproved prognosis (3). Cardiomyopathy were also found with abnormal myocardial blood flow (MBF) or CFR (4). CFR can perform more detailed risk stratification and prediction, not

Table 1 Related Chinese status of quantitative PET MPI

Approved perfusion PET agents by Chinese Food and Drug Administration	^{13}N -ammonia (Commonly used), ^{15}O -H ₂ O
Commonly used vasodilator	Adenosine triphosphate, dobutamine
Nuclear medicine departments carrying out quantitative cardiac PET in clinics currently	1. First hospital of Shanxi Medical University 2. Wuhan Union Medical College Hospital 3. Tianjin Teda International Cardiovascular hospital 4. Peking Union Medical College Hospital

only among common risk population, but also between different gender (5). The absolute quantitative analysis is the premise of individual precision therapy. In addition to the above clinical studies, derived PET indexes like coronary flow capacity (CFC) (6) and CFR ratio (ratio of CFR in single vessel coronary artery to overall maximum CFR) (7) were reported better diagnosis value when compared with traditional CFR and stress MBF.

Exploring of cardiovascular risk factors

In addition to traditional cardiovascular risk factors, more potential factors such as systemic lupus erythematosus (8), end-stage renal disease (9), elevated serum uric acid level (10) and early trauma (11) were found leading to microcirculatory abnormalities, which were of great significance for early clinical intervention and future improvement of prognosis of individuals.

Comparative studies with other imaging

Studies of coronary circulatory response to stenosis reported CFR even could successfully distinguish between 70%–89% and 50%–69% of coronary stenosis (12). There was a discrepancy between noninvasive and invasive indexes (13). Abnormal CFR and IMR (resistance index of microcirculation) may still be found in people with normal FFR (coronary flow reserve fraction). The prognosis of patients with decreased CFR and increased IMR is poor, which may be applied to further risk stratification (14). Combined coronary artery calcification score, total perfusion defect area and absolute quantitative index (MBF, CFR) are more valuable for accurate evaluation of obstructive CAD (15). CFR and other indexes can complement each other and provide the most accurate and overall information to the clinic.

Efficacy evaluation of treatments or interventions

Traditional interventions such as smoking cessation, blood glucose or pressure control, lipid lowering were reported to improve MBF or CFR. Ranolazine, drugs for chronic angina pectoris, was reported no significant influence on exercise-stimulated MBF or CFR but modestly improve diastolic function in suspected CAD (16). Some novel approaches to treat CAD like neutrophil inhibition can also be assessed by

PET MPI (17). On the other hand, Chemotherapy medicines were reported presence of cardiotoxicity, leading to decreased CFR, using mostly echocardiography (18–20). In addition, thoracic radiotherapy can induce a series of changes of MBF and CFR in the irradiated area, leading to radiation-induced heart disease (21, 22).

Development of acquisition and algorithm

As to acquisition, shorter scan time (23), new vasodilator like regadenoson as well as new ^{18}F -labeled myocardial perfusion tracers are being tried to realize more feasible clinical practice. Meanwhile, updated algorithms like post-reconstruction Gaussian filtering (24), time-of-flight (25), respiratory motion correction (26) were applied to obtain better image quality.

In conclusion, PET MPI plays an important role in the early assessment of the occurrence and development of coronary dysfunction and in revealing the pathogenesis of cardiovascular disease, it can provide more precise guidance for clinical decision-making. However, a large number of studies are still needed to further excavate and utilize the information provided by PET MBF and CFR to verify its clinical value and to better serve the patients.

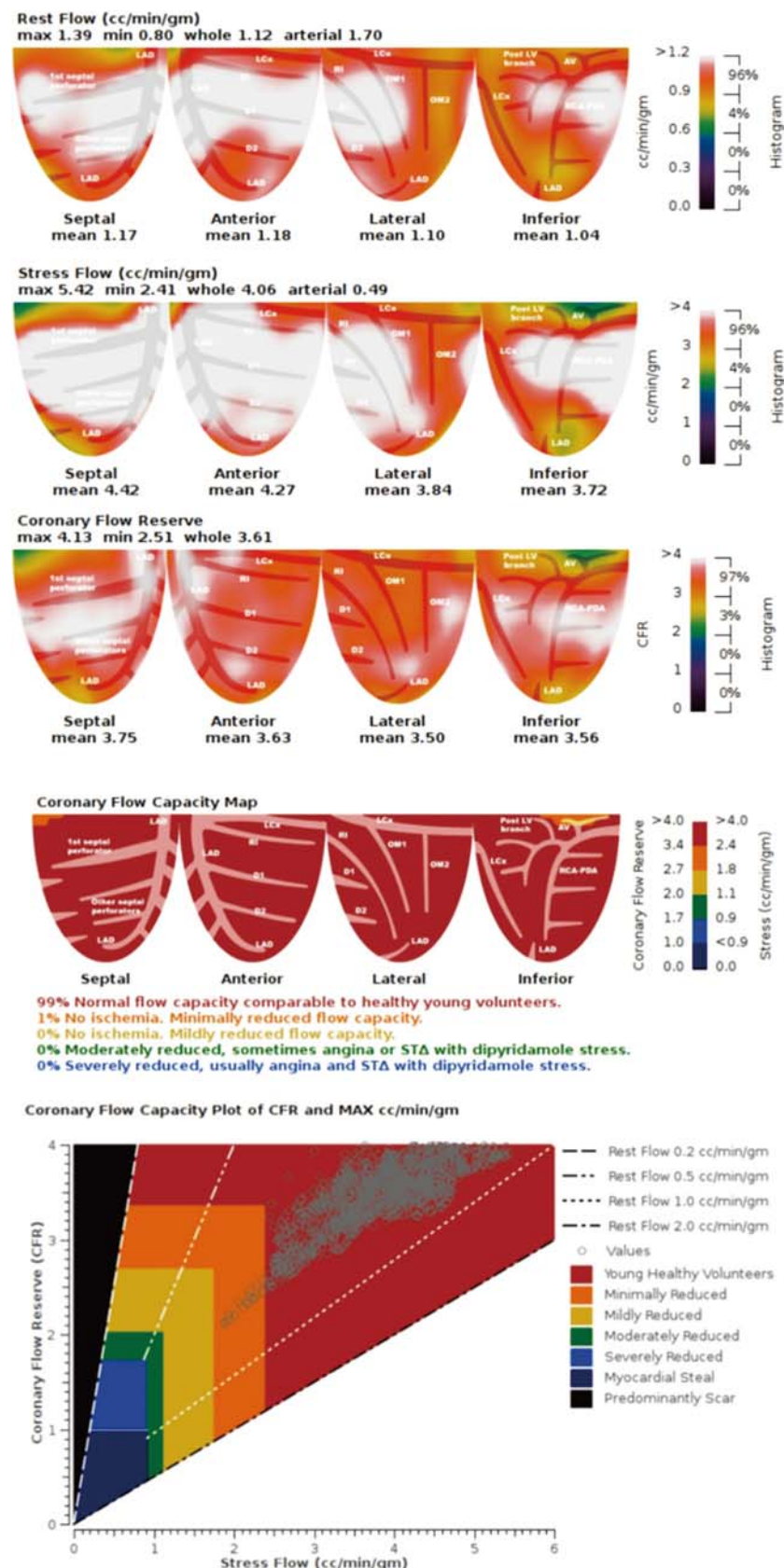


Figure 1 A 31-year-old male volunteer. The upper three rows display rest flow, stress flow and coronary flow reserve (CFR) of left ventricle. Max, min and whole represent the maximum, minimum and average value of the left ventricle as a whole, respectively. Mean represents the average value of a single chamber wall. The advantage of this diagram is to combine quantitative blood flow with anatomical coronary artery distribution, thus facilitating the intuitive judgment of criminal coronary vessels. The 4th row shows maps of the coronary flow capacity of each single wall, six different colors represent varying degrees of flow capacity. The coordinate diagram below is another display way, which projects each pixel point of the left ventricular myocardium into a different color block, the abscissa represents stress flow, and the ordinate represents CFR. Therefore, the rest flow information is actually covered in it.

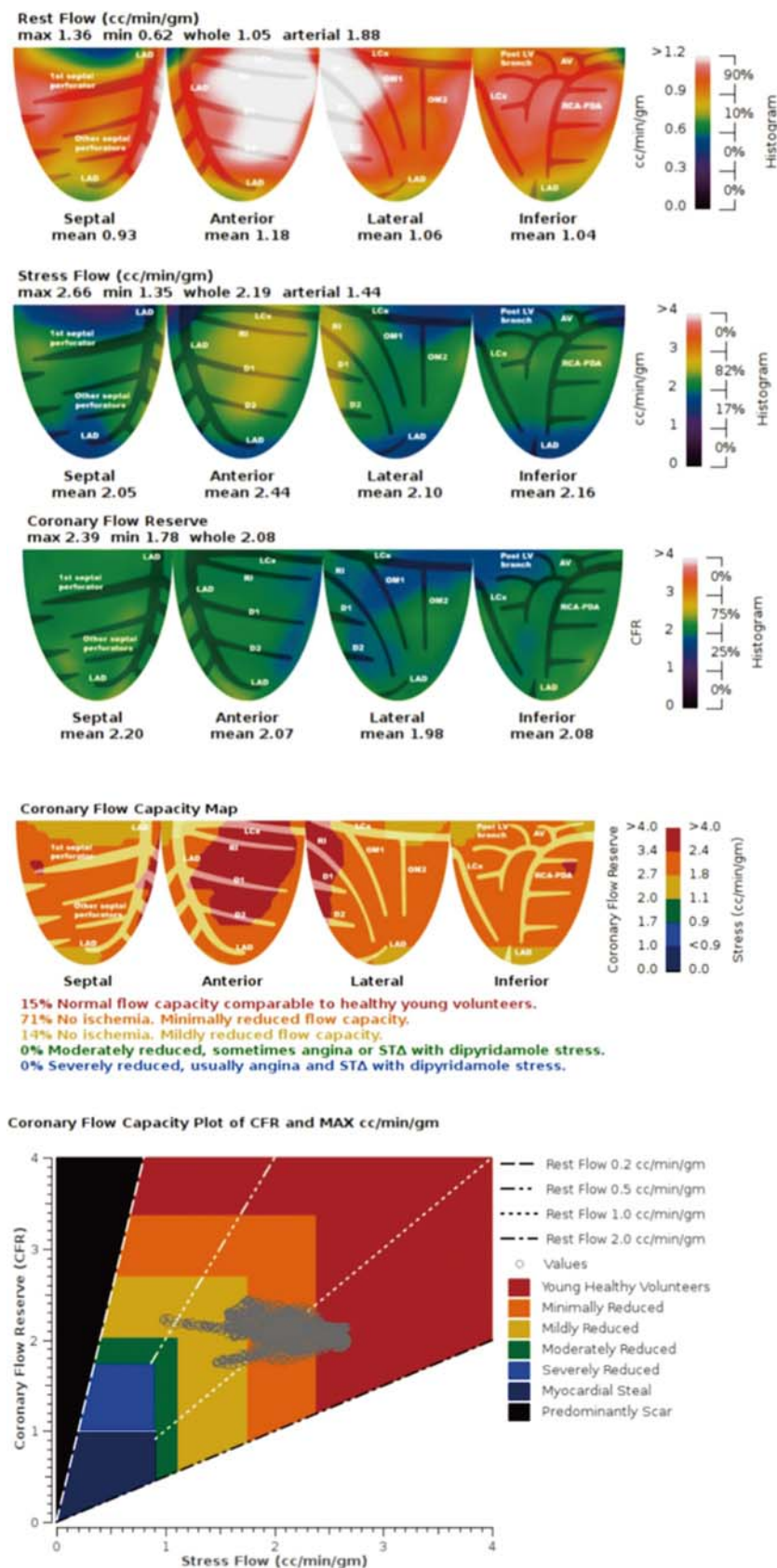


Figure 2 A 58-year-old male diagnosed with diabetes for 17 years, showed diffusely decreased stress flow and CFR, suggesting injured endothelial function. The following capacity map displayed large areas of minimally reduced flow capacity (orange zone), not reaching the standard of ischemia.

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Conflicts of interest

None.

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