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Detection Of Functional Significance of Coronary Stenoses Using Dynamic ^{13}N-Ammonia Stress-PET/CT With Absolute Values Of Myocardial Blood Flow And Coronary Flow Reserve

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Abstract

Objectives. The aim of the study was to compare the values of myocardial blood flow (MBF) at stress, MBF at rest and coronary flow reserve (CFR) obtained by ^{13}N-ammonia stress-PET/CT in patients with various degrees of coronary stenosis and in healthy patients. And thus to estimate the possible contribution of the stress-PET/CT quantitative data to the detection of functionally significant coronary stenoses in patients with coronary artery disease (CAD).

Materials and methods. 63 patients (mean age 64±9 years) with known CAD underwent dynamic ^{13}N-ammonia stress-PET/CT followed by calculation of MBF both at stress and at rest in absolute units and CFR. We compared quantitative values in two groups of patients with coronary artery stenosis: 1) ≥75% (n = 36) and 2) <75% (n = 27) confirmed by invasive coronary angiography and in group of healthy patients (n = 11).

Results. MBF at stress was significantly lower in group with ≥75% diameter stenoses (median 1,44 [1,21; 1,85] mL/min per g) compared with group with <75% diameter stenoses (2,42 [1,75; 2,89] mL/min/g) and the normal group (2,54 [2,31; 2,86] mL/min/g), (p <0,001). There was no reliable difference in MBF at rest between the three groups (p = NS). CFR was significantly lower in the group of patients with severe ≥75% stenoses (1,85 [1,54; 2,31]) in comparison with patients group with stenoses of intermediate <75% severity (2,73 [2,19; 3,21]), and also in comparison with the normal group (3,12 [2,75; 3,23]), (p <0,001).

Conclusion. The values of MBF at stress and CFR are significantly lower in patients with severe coronary arteries stenoses comparing with the group of patients with mild and moderate stenoses. The value of MBF at rest used independently has no diagnostic utility for detection of functional significance of coronary artery stenoses.

Keywords: myocardial blood flow, coronary flow reserve, PET/CT, ^{13}N-ammonia, coronary stenosis.

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1. Introduction

The ability to obtain quantitative values of myocardial blood flow (MBF) and coronary flow reserve (CFR) has been perceived as an important advantage of positron emission tomography combined with computed tomography (PET/CT) over semiquantitative myocardial perfusion imaging. Recent results of different studies suppose that diagnostic accuracy of semiquantitative myocardial perfusion imaging for the detection of hemodynamic significance of coronary stenosis can be improved by integrating of quantitative assessment of MBF and CFR. Thus, stress-PET/CT with quantification of MBF in absolute terms and CFR is a promising direction in the non-invasive assessment of the hemodynamic significance of coronary stenosis [1-3].

Due to the fact that dynamic PET/CT can be performed with various radiopharmaceuticals, scan and reconstruction protocols, software packages for calculating indices the results often differ.

The present study is our first experience in this direction.

2. Materials and methods

63 patients with known coronary artery disease (CAD) (mean age 64±9 years) underwent ^{13}N-ammonia stress-PET/CT and invasive coronary angiography (ICA). Exclusion criteria were coronary artery bypass graft surgery and presence of scar tissue defined by echocardiography or perfusion ^{13}N-ammonia stress-PET/CT. We also analyzed control group with low likelihood of CAD (11 patients, mean age 55,7±10,5 years). None of the control subjects had a clinical history or evidence of CAD or other cardiac disease, they had normal invasive coronary arteriograms (stenoses didn't exceed 30%).

^{13}N-ammonia PET with dynamic protocol enables to determine MBF in absolute units (mL/min/g). CFR was defined as the ratio of MBF at pharmacological stress with adenosine triphosphate (ATP) infusion to myocardial blood flow at rest. All patients received 700-800 MBq injection of ^{13}N-ammonia into a peripheral vein as a slow bolus of 15 s both at stress and at rest. Image acquisition was started right after the end of ^{13}N-ammonia injection. Images were acquired on 64-slice PET/CT scanner (Biograph; Siemens) in 3-dimensional list mode. Dynamic acquisitions of the scans were performed using a standard 10-min protocol consisting of 12 frames: 6 x 10s, 4 x 30s, 1 x 60s and 1 x 360s. Quantitative MBF and CFR were determined using the Carimas 2.9 software package developed at the Turku PET Centre, Finland [4].

3. Results

We compared two groups of patients with CAD with one or more coronary arteries stenoses confirmed by invasive coronary angiography: the first group with ≥75% stenoses (n = 36) and the second group with <75% stenoses (n = 27); and group of healthy patients (n = 11).

CFR >2,0 was considered as normal like in the most of the world's clinics [5, 6].

To compare the values of stress and rest MBF and CFR we considered only one coronary artery with the most severe stenosis in each patient.

When the groups of healthy patients and patients with CAD were compared, reliable difference on MBF at rest was not revealed (p = NS), (Fig. 1). Whereas MBF at stress was significantly lower in group with ≥75% diameter stenoses (median 1,44 [1,21; 1,85] mL/min per g) compared with group <75% diameter stenoses (2,42 [1,75; 2,89] mL/min/g) and the normal group (2,54 [2,31; 2,86] mL/min/g), (p <0,001). MBF at stress in patients with <75% diameter stenoses was similar to that in healthy patients (p = NS), (Table 1, Fig. 2).

CFR was significantly lower in the group of patients with severe ≥75% stenoses (1,85 [1,54; 2,31]) in comparison with patients group with coronary stenoses of intermediate <75% severity (2,73 [2,19; 3,21]), and also in comparison with the normal group (3,12 [2,75; 3,23]), (p <0,001). The results are summarized in Table 1 and Fig. 3. It should be noted that none of the patients in normal group had a decrease in CFR less than 2,0 either global or in single segments.

Table 1: Quantitative characteristics of patients groups.

	Coronary stenosis ≥75% (n = 36)	Coronary stenosis <75% (n = 27)	p value	Healthy patients (n = 11)	p value
MBF at stress (mL/min/g)	1,44 [1,21; 1,85]	2,42 [1,75; 2,89]	p<0,001	2,54 [2,31; 2,86]	*p<0,001 **p = NS
MBF at rest (mL/min/g)	0,78 [0,61; 0,91]	0,90 [0,70; 1,02]	p = NS	0,85 [0,70; 0,92]	*p = NS **p = NS
CFR	1,85 [1,54; 2,31]	2,73 [2,19; 3,21]	p<0,001	3,12 [2,75; 3,23]	*p<0,001 **p = NS
CA – coronary artery; MBF – myocardial blood flow; CFR – coronary flow reserve.					
* Comparison of patients group with coronary stenoses ≥75% and healthy patients.					
** Comparison of patients group with coronary stenosis <75% and healthy patients.					

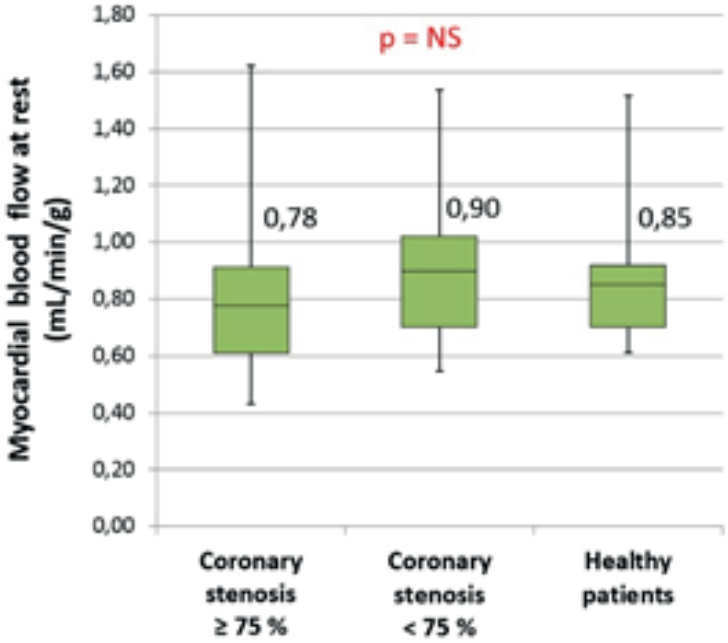

Figure 1: Myocardial blood flow (MBF) at rest. There is no significant difference in rest MBF between patients with coronary artery disease and healthy patients.

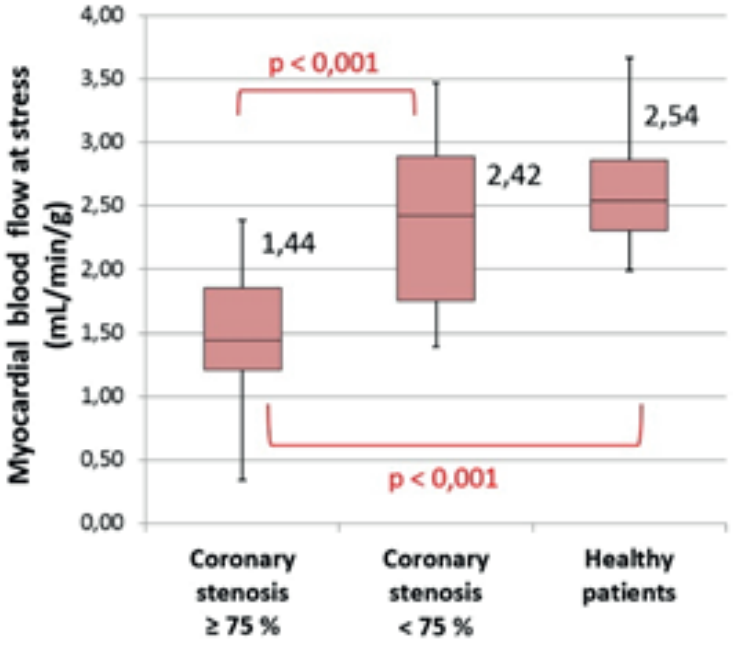

Figure 2: Myocardial blood flow (MBF) at stress. Stress MBF is significantly lower in patients with coronary stenoses ≥75% comparing with the group of patients with stenoses <75% and the healthy patients group.

4. Discussion

In the present study the values of MBF at stress and CFR are significantly lower in patients with severe coronary arteries stenoses compared with the group of patients

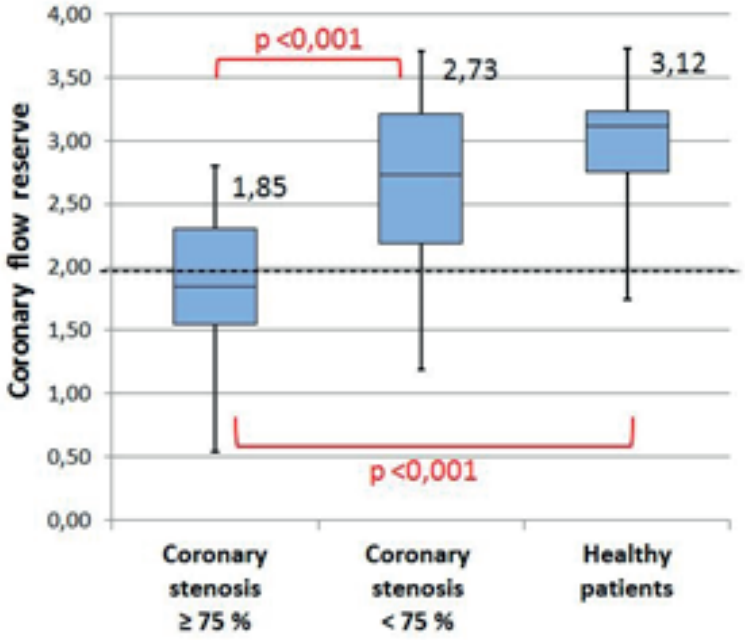

Figure 3: Coronary flow reserve (CFR). CFR is significantly lower in patients with severe coronary arteries stenoses (≥75%) comparing with the group of patients with mild and moderate stenoses (<75%) and the healthy patients group.

with mild and moderate stenoses. The value of MBF at rest used independently has no diagnostic utility for detection of functional significance of coronary artery stenoses.

Beanlands R.S.B. et al. [3] presented in their study comparable results: CFR was significantly lower in group with coronary stenoses of 95-100%, whereas significant difference between CFR in groups with mild and moderate stenoses (50-69% and 70-94%) was not revealed (2,09±0,47 and 2,02±0,51, respectively, p = NS). Lee J.M. et al. [7] compared the quantitative ^{13}NH3-PET measures between lesions with low and high fractional flow reserve (FFR). The lesions with FFR ≤0,80 showed significantly lower stress MBF than those with high >0,80 FFR (1,71±0,05 versus 2,24±0,05 mL/min/g; p<0,001).

Thus, the data of our study are comparable with the results of other researchers and demonstrate the dependence of PET/CT quantitative indices on the severity of coronary artery stenosis confirmed by ICA. As for the absence of significant differences in CFR between the patients group with stenoses of intermediate severity and a group without a pathology of coronary arteries, this is obviously due to the fact that not all stenoses are functionally significant, and for mild stenoses the probability of malfunction is expected to be lower.

5. Disclosure

The authors have no conflict of interest and nothing to disclose.

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