Coronary micorvascular dysfunction

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The link between myocardial ischemia and obstructive atherosclerosis of the epicardial coronary arteries is well established, and coronary angiography has demonstrated a relationship between the severity and extent of coronary artery disease(CAD) and survival. However, about 20-25 % of the patients undergoing coronary angiogram for signs and symptoms of myocardial ischemia show "normal" epicardial coronary arteries. This phenomenon is most frequently found in patients with hypertension and/or hypertrophic cardiomyopathy. Coronary microvascular dysfunction may be sustained by several pathogenetic mechanisms, as summarized in Table[1)]

Alterations	**Causes**
Structural	
Luminal obstruction	Microembolization in acute coronary syndromes, or after recanalization
Vascular-wall infiltration	Infiltrative heart disease
Vascular remodeling	Hypertrophic cardiomyopathy, arterial hypertension
Vascular rarefaction	Aortic stenosis, arterial hypertension
Perivascular fibrosis	Aortic stenosis, arterial hypertension
Functional	
Endothelial dysfunction	Smoking, hyperlipidemia, diabetes
Dysfunction of smooth muscle cell	Hypertrophic cardiomyopathy, arterial hypertension
Autonomic dysfunction	Autonomic dysfunction
Extravascular	
Extramural compression	Aortic stenosis, hypertrophic cardiomyopathy, arterial hypertension
Reduction in diastolic perfusion time	Aortic stenosis

We hypothesized that the flow reserve capacity(CFR) of penetrating intramyocardial coronary arteries (PICA) in these patients may be related to myocardial ischemia.

The present studies were designed to compare the hemodynamic and morphologic differences of PICA between normal and hypertrophied myocardium and to elucidate the relation between PICA-CFR and biochemical marker of myocardial fibrosis in hypertensives.

Study 1: PICA-CFR in Apical Hypertrophic Cardiomyopathy [2)]

Subjects and Methods: In 65 subjects with normal coronary angiogram [mean age 56±10 yrs ; M:F=33:32; 30 normotensive subjects without hypertrophy (Control group), 24 hypertension subjects without hypertrophy (HTN group), 11 subjects with apical hypertrophic cardiomyopathy (AH group)], we examined the myocardium just beneath the apical impulse window at a depth of 3 to 5 cm by using TTE (6- or 7-MHz centerline frequency transducer). After obtaining the linear color signals using a special preset coronary program with low Nyquist limit (12 to 20 cm), the width and peak diastolic pulsed Doppler velocities(PDV) were measured. PICA-CFR was calculated as the ratio of hyperemic PDV after the intravenous infusion of adenosine (140 μg/kg/min) to baseline PDV. PICA-width ratio was calculated as the ratio of hyperemic to baseline width of color Doppler signal of PICA.

Results: PICA-CFR was 1.65±0.49 in AH group, 2.50±0.77 in HTN group and 2.42 ± 0.73 in control group($p<0.005$ versus HTN and Control). PICA-width ratio was 1.44±0.42 in AH group, 2.14±0.72 in HTN group, and 1.81 ± 0.55 in control group ($p=0.025$ versus HTN and Control). PICA-CFR was closely related to width-ratio of PICA ($r= 0.448$, $p= 0.002$).

Study2: Relation between PICA-CFR and Myocardial Fibrosis in Hypertensives [3)]

Subjects and Methods: In fifty-eight subjects (M:F= 31:27, mean age 47±9 years) with chest pain and normal coronary angiogram, PICA-CFR and PICA-width ratio were measured as the ratio of hyperemic to baseline PDV and as the ratio of hyperemic to baseline width after the adenosine infusion (140 μg/kg/min), respectively. Serum PIP (carboxy-terminal propeptide of procollagen type I), as a biochemical marker, was measured and all subjects were divided into 3 groups: 19 hypertensives with PICA-CFR< 2.0(group A), 23 hypertensives with PICA-CFR ≥ 2.0 (group B), and 16 normotensives with PICA-CFR ≥ 2.0(group C).

Results*:* Baseline PDV in group A was higher than the other two groups ($p<0.005$ versus group B and group C). PICA-width ratio was higher than the other two groups ($p<0.005$ versus group B and group C). Serum PIP was 137.1±16.6 ng/ml in group A, 96.2± 13.7 ng/ml in group B, and 78.8± 11.2 ng/ml in group C ($p<0.0001$ versus group B and group C). PICA-CFR was closely related serum PIP ($p<0.001$, $r=-0.723$).

Conclusions: PICA in hypertrophic cardiomyopathy has higher resting diastolic velocity, wider diameter, and impaired CFR than those of normal myocardium. The impaired PICA-CFR is related to myocardial fibrosis in hypertensive patients with chest pain and normal coronary angiogram. Coronary microvascular dysfunction in the absence of obstructive CAD is the functional counterpart of traditional coronary risk factors. Since this type of dysfunction is at least partly reversible, its assessment might be used to guide interventions aimed at reducing the burden of risk factors. Coronary microvascular dysfunction caused by traditional coronary risk factors or by yet unknown mechanisms is severe enough to cause myocardial ischemia.[4)]

References

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