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Assessment of Coronary Hemodynamics and Vascular Function

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ARTICLE INFO

Keywords:
Coronary resistance vessels
Coronary blood flow
Coronary pressure
Coronarography

ABSTRACT

Coronary blood flow closely matches to metabolic demands of heart and myocardial oxygen consumption and is conditioned by function of coronary resistance vessels. The microvascular endothelium of coronary resistance vessels is exposed to a spatially and temporally regulated input from cardiomyocytes and the haemodynamic forces of the cardiac cycle. Functional measurements of coronary pressure and flow are important approaches that provide complementary information on the function of coronary vessel function that could not be assessed by the methods utilized for the anatomic characterization of coronary disease, such as coronary angiography. The goal of this paper is to review the methodologies for assessment of coronary vascular function and haemodynamics which are utilized in research and to discuss their potential applicability in the clinical settings.

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Coronary blood flow closely matches to metabolic demands of the heart and myocardial oxygen consumption. Coronary circulation (CC) is made of conduit arteries – two coronary arteries (left, which branches to the left anterior descending and circumflex artery) and right coronary artery, that lie on the epicardial surface of the heart. After penetrating the myocardium, they branch to resistant vessels- small arteries and arterioles (75–200 micrometers in diameter), which are the primary sights of coronary vascular resistance. From arterioles, a dense network of capillaries arises, running parallel with the myocardiocytes (ratio of capillaries to cardiomyocytes is app 0.91–1.12). Beside the aforementioned small arteries and arterioles, the coronary microcirculation includes capillaries and postcapilarry venules. The microvascular endothelium of coronary resistance vessels is exposed to a spatially and temporally regulated input from cardiomyocytes, and haemodynamic forces due to cardiac cycle. Local regulation of coronary blood flow (CBF) is responsive to metabolic factors, changes in blood flow velocity/volume and changes in intramural pressure. Epicardial arteries as well as the intramyocardial capillary system may have a modest contribution to overall CBF regulation during the normal physiological condition, however, these arteries become crucial in the regulation of CBF during conditions leading to increased metabolic demand and to ischemia. There are a number of

Statement of Conflict of Interest: see page 428.

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http://dx.doi.org/10.1016/j.pcad.2014.11.006
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Abbreviations and Acronyms

CA = coronary angiography

CAD = coronary artery disease

CBF = coronary blood flow

CC = coronary circulation

CCTA = coronary computed tomography angiography

CDPe = pressure-drop coefficient

CFR = coronary flow reserve

CV = cardiovascular

CT = multi-detector computed tomography

FFR = fractional flow reserve

HMR = hyperemic microvascular resistance

ICA = invasive CA

LV = left ventricle

MRI = magnetic resonance imaging

PET = positron emission tomography

PMVA = primary microvascular angina

PSS = physiological salt solution

ROS = reactive oxygen species

SR = synchrotron radiation imaging

TIMI frame count = the corrected Thrombolysis in Myocardial Infarction frame count

collateral vessels that interconnect and present structural and functional salvage pathways of potentially ischemic areas of the myocardium.[1] Increases in oxygen demand results in increases of CBF from resting levels to maximal flow and is termed coronary flow reserve (CFR).[1,2] A normal CFR implies that both the epicardial and minimally achievable microvascular bed resistances are low and normal. However, when abnormal, CFR cannot dissociate which component is affected, thus limiting the clinical applicability of this measurement.

A recent Scientific Statement from the American Heart Association Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology emphasizes that functional measurements of coronary pressure and flow are important approaches that provide complementary information on coronary vessel function that is otherwise not assessed by the standard methods currently utilized for the anatomic characterization of coronary artery disease (CAD). Due to discrepancies between observed changes in arterial structure by coronary angiography (CA) and functional symptoms of the patients, using coronary physiological measurement may help to overcome the limitations of CA and provide as objective as possible indicator of clinically relevant lesion significance.[1]

The current clinical diagnostic approach primarily utilizes coronarography (or CA) of coronary epicardial blood vessels, together with symptoms and other laboratory (blood) samples analysis. Coronarography does not allow for assessment of coronary microcirculation structure and functional relationship.[1,3] Since primary microvascular angina (PMVA; or cardiac syndrome X) becomes a very important entity in cardiac health, particularly in women with no significant structural changes of epicardial artery, it is of utmost importance to have reliable, reproducible, cost-effective, low-risk methods for assessment of coronary microcirculation. Diagnosis of PMVA relies primarily on epicardial vessel changes on CA, clinical findings and objective evidence. For the assessment of the structure of coronary microcirculation, present methods are available: myocardial blush grade, myocardial contrast echocardiography, positron emission tomography (PET), multi-detector computed tomography (CT). Functional method options are TIMI frame count. The corrected Thrombolysis in Myocardial Infarction frame count is a semiquantitative assessment of epicardial coronary blood flow),[4] transthoracal doppler echocardiography, intracoronary Doppler, quantitative CA/intravascular ultrasound, temperature and pressure sensors, and single photon emission tomography. The best prospects for a complete structural-functional display has magnetic resonance imaging (MRI).[5,6] However, the majority of these diagnostic methods do not satisfy conditions to be simple, low risk and objective enough for regular clinical practice.[5] The goal of this paper is to review the novel, mainly experimental methodologies for the assessment of coronary vascular function and haemodynamics which are utilized in research and to discuss the respective applicability in the clinical settings. Table 1 summarizes the advantages of methodology while Table 2 summarizes the limitations of each methodology to assess coronary structure/function in clinical settings.[3,5,6]

Functional in vivo assessment of CC

Pre-clinical, animal studies

Indexes obtained from CA

CA remains a widely used technique for the assessment of CC due to its availability in clinical care, despite its invasive nature. Since the 1990's, intracoronary pressure and flow velocity measured with sensor-tip guide-wires have been introduced as a novel approach for assessment of coronary hemodynamics. However, so far this powerful tool has not been implemented as a functional end-point in large animal models of CAD and in particular those designed to validate new angiogenic therapies such as growth factors/cytokines, stem cell therapy or gene therapy. Several intracoronary pressure- and flow velocity-derived indicators have been studied for the ability to reach conclusions on the health or diseased status of the CC.[7]

Additionally, CFR is an indicator which describes the effects of various physiologic conditions and disease states of the CC. There are three different indices derived from CFR testing including absolute flow reserve, relative flow reserve, and fractional flow reserve.[1,8] Absolute CFR describes the ratio of blood flow during maximal hyperemia in a stenotic artery to blood flow in the same artery under resting conditions. Unfortunately, absolute CFR varies between and within subjects as it depends on several parameters, such as metabolic demand, the diastolic time fraction, blood pressure and microvascular disease. Changes in CBF (or myocardial) can be used as a surrogate parameter for microvascular function.[9] Also, CFR can be determined as the ratio of maximal

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