Evaluation of Microvascular Disease and Clinical Outcomes

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KEYWORDS

• Microvasculature • Intravascular • Physiology • Outcomes

KEY POINTS

- Myocardial blood supply is controlled through an interplay of metabolic, myogenic, endothelial, and neural factors; all of which may be involved in its dysfunction.
- Intravascular physiology allows the exploration of the microvascular domain in heart disease and has the potential to obtain information with prognostic relevance.
- Because interrogation of the microvasculature using intravascular techniques allows real-time assessment, it can potentially guide intracoronary adjuvant therapy, particularly during acute coronary syndromes.
- Most intravascular microcirculatory assessment tools are based on measures of coronary flow, either alone (resting flow profile) or in combination with pressure during rest (wave intensity analysis) or hyperemia to provide downstream information.
- The selection of a method to interrogate the coronary microcirculation should be based on the suspected dominant cause of dysfunction.

INTRODUCTION

Unlike the large capacitance vessels of the epicardium, the microcirculation has a highly dynamic role in coronary blood flow and is regulated through metabolic, myogenic, endothelial, and neural influences to provide the dominant component of coronary resistance.[1,2] Microcirculatory abnormalities can arise through any of these pathways, either alone or in combination, and may convey an adverse prognosis equivalent to frank obstructive epicardial vessel disease. In addition to such marked complexity in its physiologic organization and pathophysiologic potential, it anatomically consists of vessels that are less than 300 μm in diameter that escape the spatial resolution available at coronary angiography. Therefore, although assessment of the microcirculation is essential for modern cardiologic practice, it requires tools that are both sophisticated and dynamic even though they are unable to operate with direct visualization.

At present, the most widely used intravascular investigative technique is fractional flow reserve (FFR). Although this is an excellent tool for the assessment of epicardial stenosis, it is unable to provide information on the microcirculation and, therefore, cannot offer a complete cardiac assessment of the patient in the catheter laboratory. If concomitant microvascular disease could also be quantified, a more satisfactory clinical picture could be established, which would not only aid with diagnoses but also guide immediate changes in treatment and provide an individually tailored approach.

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Additionally, although in stable patients it is possible to gain some of this additional information through other investigative modalities performed at a separate time, situations in which time is a determinant of prognosis implementation of ad hoc therapy (eg, intracoronary pharmacotherapy or thrombus aspiration during ST-elevation myocardial infarction [STEMI]) requires immediate microcirculatory quantification. A periprocedural intravascular assessment technique is optimal in this setting because results can be acted on during this short therapeutic window.

Important in the treatment of microvascular dysfunction is that this may result from several potential mechanisms, including endothelial abnormalities, arteriolar or capillary remodeling, and extravascular compression. At present, there are several methods that allow such intravascular quantification of the microvasculature, each with specific advantages for exploring these respective domains (Fig. 1). This article highlights these techniques along with the prognostic information provided by these modalities.

DIRECT ANGIOGRAPHIC ASSESSMENT

The first attempts to obtain information on the microvasculature at the time of angiography began with quantification of the radiographic density of dye as it passed through the coronary system using digital extraction technology to map its timing. This predicted the resting flow rate reasonably well and recognized an impairment of coronary flow reserve (CFR) in patients with significant coronary stenosis[3] (Fig. 2).

The investigators of the Thrombolysis in Myocardial Infarction (TIMI) trials introduced several methods to objectively stratify coronary blood flow and thus assess microvascular health. The thrombolysis in myocardial infarction (TIMI)-flow grade is a qualitative assessment that uses contrast injected into the artery of interest and correlating it with resting flow rates from Doppler-flow wires.[4] It is relatively specific, with only TIMI-flow grade 3 displaying a normal underlying blood velocity. As such, the TIMI-flow grade after a treated myocardial infarction is correlated with outcome[5] and TIMI grade 2 has been associated with an outcome similar to that of an occluded artery.[6]

TIMI 0: Absence of complete antegrade flow

TIMI 1: Faint antegrade flow beyond the occlusion, incomplete filling of the distal coronary bed

TIMI 2: Partial reperfusion, delayed antegrade flow but with complete filling of the distal territory

TIMI 3: Normal flow, the distal coronary bed is completely filled

A more quantitative assessment is provided by the TIMI frame count (TFC), defined as the number of cine frames required for radiographic

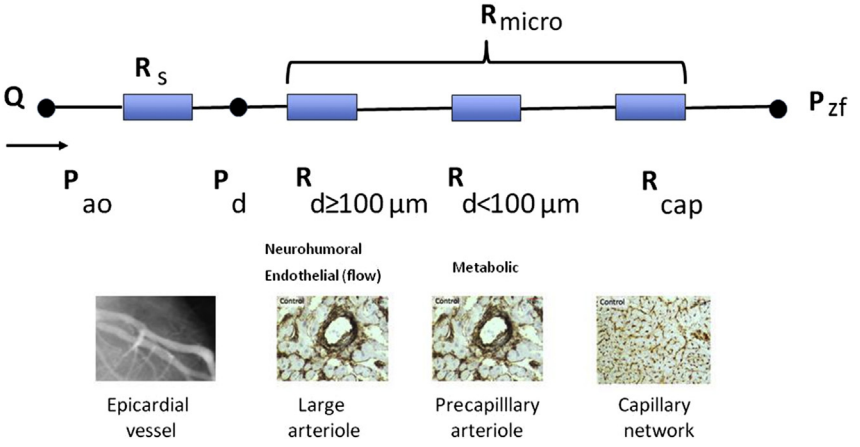

Fig. 1. Schematic representation of the coronary circulation as a resistive system. In the absence of a coronary stenosis, arteriolar tone constitutes the main seat of coronary resistance and is controlled by metabollic, myogenic, llow-dependent (enothelial) and neurogenic mechanisms. Microcirculatory dysfuntion may result from structural remodelling of arterioles or capillaries (rarefaction), dysregulation (paradoxical arteriolar vasoconstriction), hypersensitivity to vasoactive factor or adrenergic stimulation, and extravascular compression of collapsable vascular elements (capillaries). Pao, aortic pressure; Pd, pressure distal to the stenosis; Pzf, zero flow pressure; Q, coronary flow; Rcap, capillary resistance; Rmicro, microcirculatory resistance; Rd≥100mcm and Rd<100mcm, resistance of arterioles with diameters above and below 100mcm, respectively; Rs, stenosis resistance.