Chapter 3
Coronary Microvascular Dysfunction (CMD)

Keywords Coronary microcirculation system · Coronary microvascular dysfunction · Coronary blood flow · Angina · Myocardial ischemia

Coronary microvascular dysfunction (CMD) has emerged as an important mechanism of myocardial ischemia in the past two decades. CMD can result from functional and/or structural alterations to the vessel and it results in varying degrees of disruption to the normal coronary physiology as described in Table 3.1.

The intramyocardial arterioles with diameters below 500 μm are actively involved in myocardial perfusion, which is responsible for coronary microcirculation. The epicardial arteries and major arteries are only one segment of the arterial coronary circulation. They are connected to smaller arteries and arterioles that feed the capillaries and cumulatively they are referred to as the coronary microcirculation. This coronary microcirculation system is the main site that regulates the myocardial blood flow, as shown in Fig. 3.1 [47].

The coronary circulation provides the oxygen required by the cardiac pump in order to generate enough adenosine triphosphate (ATP) necessary for systolic contraction. The coronary arterial system, as shown in Fig. 3.1, is composed of three compartments fused together, namely, the proximal compartment of the large epicardial coronary arteries or conductance vessels with diameters ranging from 500 μm up to 2–5 mm, the intermediate compartment of prearteriolar vessels or small arteries with diameters ranging from 100 to 500 μm, and the distal compartment of the arterioles with diameters less than 100 μm. The large epicardial coronary arteries have thick walls and three well-defined layers, as shown in Fig. 2.1. They provide the least resistance to coronary blood flow (CBF) and are further classified into three types: Type I, II and III, based on the number of initial branches

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Table 3.1 Pathogenic mechanisms of coronary microvascular dysfunction (CMD) [56]

Alteration	Causes
Structural	
Luminal obstruction	Microembolization in acute coronary syndrome (ACS) or after recanalization
Vascular-wall infiltration	Infiltrative heart disease (e.g. Anderson–Fabry cardiomyopathy)
Vascular remodelling	Hypertrophic cardiomyopathy (HCM), arterial hypertension
Vascular rarefaction	Aortic stenosis, arterial hypertension
Perivascular fibrosis	Aortic stenosis, arterial hypertension
Functional	
Endothelial dysfunction	Smoking, hyperlipidaemia, diabetes
Dysfunction of smooth muscle cell	HCM, arterial hypertension
Autonomic dysfunction	Coronary recanalization
Extravascular	
Extramural compression	Aortic stenosis, HCM, arterial hypertension
Reduction in diastolic perfusion time	Aortic stenosis

and the area of tissue to be supplied with blood as seen in Fig. 3.1. Small arteries and large arterioles are more responsive to flow-dependent dilatation and to changes in intravascular pressure respectively. Large arterioles are responsible for the autoregulation of the coronary blood flow (CBF) [47, 52–54].

Coronary microvascular dysfunction (CMD) can be caused by various pathogenic conditions and mechanisms, so they are classified clinically as CMD in the presence or absence of myocardial disease, or obstructive CAD, or iatrogenic CMD. This last example could be due to percutaneous coronary intervention (PCI) caused primarily by vasoconstriction or distal embolization. CMD can lead either to impaired dilatation or increased vasoconstriction of the coronary microvessels as a result of these pathogenic conditions [40]. The difference in myocardial ischemia caused by coronary artery stenosis and coronary microvascular dysfunction is depicted in Fig. 3.2 [55]. The pathogenic mechanisms of CMD are described in Table 3.1 [56].

In the case of an epicardial stenosis, the ischemia involves the myocardial territory distal to the stenotic vessel and is more severe in the subendocardium. This is the red area resulting in impairment of contractile function over an extensive zone. In the case of microvascular dysfunction, the ischemia is localized in small myocardial areas that are distributed throughout the myocardial wall (small circles). This does not usually result in detectable impairment of contractile function due to the presence of normal contractile myocardial cells in the same zone [55].

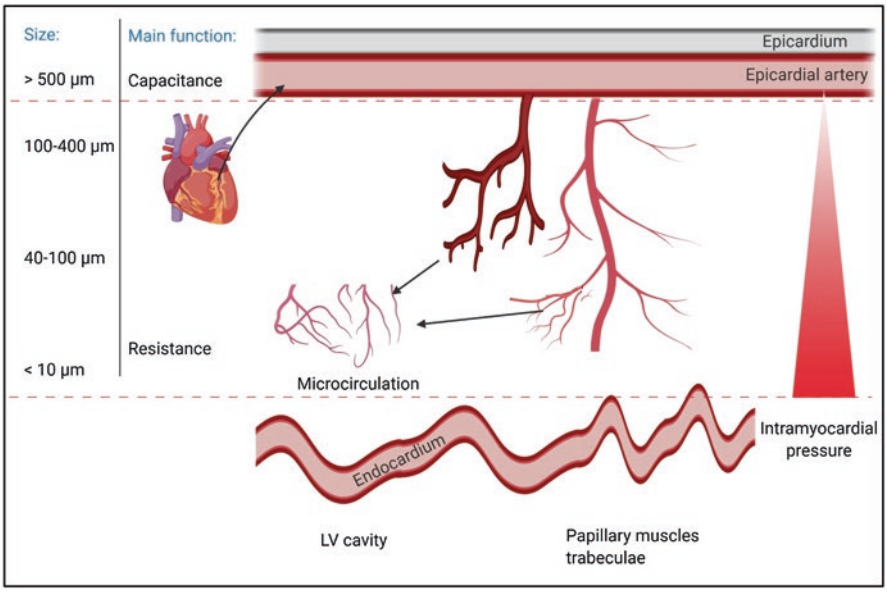

Fig. 3.1 Coronary arterial system. (Diameter: Epicardial arteries >500 µm, main stimulus for vasomotion – flow, Main function – transport; small arteries <500–150 µm, main stimulus for vasomotion – pressure, Main function – regulation; large arterioles <150–100 µm, Arterioles <100 µm, main stimulus for vasomotion – metabolites, Main function – regulation; capillaries <10 µm, exchange as a main function; *LV* Left ventricular) [47–51]. (Created with BioRender.com)

Understanding the cause of CMD is important to understand the abnormal microvascular constriction in patients with normal coronary arteries but who present with chest pain or with symptoms of chronic stable angina. This type of microvascular constriction is an important pathogenetic component of microvascular obstruction (MVO) observed in a high fraction of patients who undergo primary percutaneous coronary intervention (PCI) due to ST-elevated myocardial infarction (STEMI) [57].

Patients who undergo PCI have a high probability for intravascular plugging caused by atherosclerotic debris, micro-emboli and thrombus material typically released during PCI. It also explains why there are ≈20–50% of patients with a prevalence for angina despite successful revascularization surgery [58]. The current goal of PCI or any other revascularization method is to relieve the symptoms rather than improve the pathology, which will require new research in this area if an improvement in CMD pathology is to be achieved [59–62].

In conclusion, among patients with stable or unstable angina, both the symptoms and the myocardial ischemia are caused by a combination of epicardial artery stenosis and CMD. However, the contribution of these two conditions will vary depending on the clinical status of each patient.

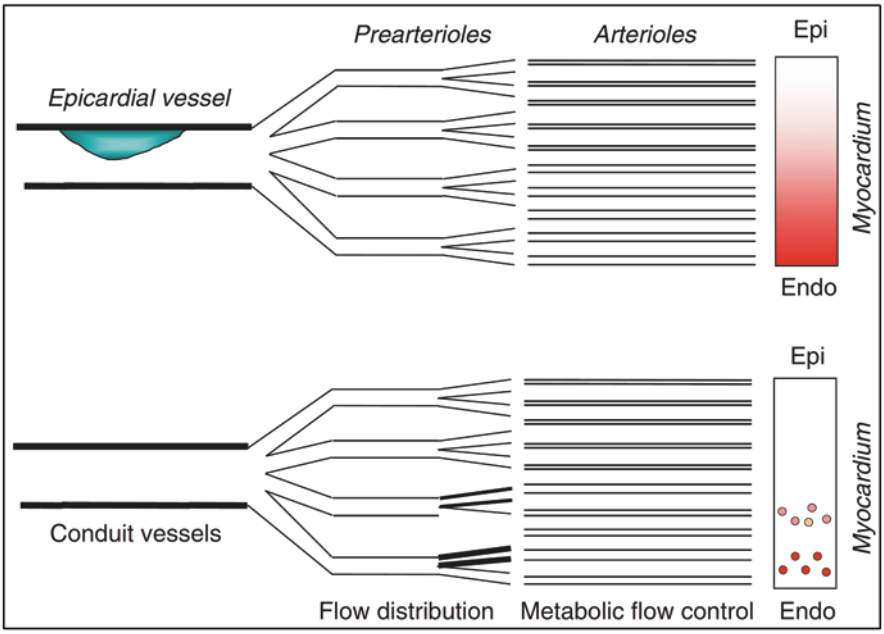

Fig. 3.2 Differences in myocardial ischemia caused by a coronary artery stenosis (upper drawing) or coronary microvascular abnormalities (bottom drawing) [55]