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*Editor*

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# Preface

Interventional cardiology is a very exciting and fast-developing area in modern medicine. Since percutaneous coronary angioplasty was introduced in 1977, the inventions of novel devices, such as the balloon catheter, bare metal stent, and drug-eluting stent, have steadily improved clinical outcomes of percutaneous coronary intervention. These advances were undoubtedly based on insights derived from intracoronary imaging or physiologic evaluations.

Intravascular ultrasound is the "gold standard" among intravascular imaging modalities and provides various information about lesional characteristics and interventional therapy. Optical coherence tomography enables visualization of intravascular morphologies clearly based on high resolution. The assessment of fractional flow reserve, as known, guides whether the stenotic lesion needs revascularization. Because these examinations have their own advantages and disadvantages, it is important to know their characteristics and applications. The comprehensive understanding of intravascular imaging and physiology eventually might help to treat patients with coronary artery diseases in daily practice.

It is my honor to provide a state-of-the-art update on the most relevant topics of *coronary imaging and physiology* written by an expert group of Imaging and Physiology on Patients with Cardiovascular Disease (IPOP) in Korea. I appreciate the authors' dedication to this work despite their busy practices. I hope that this book helps clinicians to provide the optimal treatment for patients with coronary artery diseases.

Seoul, South Korea — Myeong-Ki Hong, MD

# Introduction: Coronary Anatomy and Circulation

## Coronary Anatomy

The coronary artery is the first branch of the aorta and is divided into the left and right coronary arteries. The left main coronary artery is derived from the left coronary cusp and is divided into the left anterior descending artery (LAD) and left circumflex artery (LCX). The LAD is located in the anterior interventricular groove and supplies the anterior wall, septum, and apex. The branches of the LAD are septal perforating arteries and diagonal branches. The septal perforating arteries supply most of the septum, and the diagonal branches supply the lateral wall of the left ventricle. The LCX passes through the atrioventricular groove and supplies the left atrium, as well as most of the lateral and posterior walls of the left ventricle. The branches of the LCX are obtuse marginal branches, and approximately 30–40% of the sinoatrial nodal branch is derived from the LCX [1, 2].

The right coronary artery (RCA) is derived from the right coronary cusp; it runs along the right atriventricular groove and continues to the posterior interventricular sulcus. The RCA supplies the right atrium, right ventricle, sinoatrial node, and atrioventricular node via several branches (conus, right ventricular wall, sinoatrial nodal, atrioventricular nodal branch). At the distal portion of the RCA (i.e., the crux), it divides into two branches: the posterolateral and posterior descending arteries, which supply the inferior portion of the interventricular septum and apex. In more than 80% of cases, the RCA has posterior descending and posterolateral branches. The others are left-dominant systems, in which the LCX gives rise to posterolateral and posterior descending branches, or codominant systems, in which both arteries provide an equal supply (Fig. 1).

The incidence of coronary anomaly is approximately 1%. Common anomalies are separate origin of the LAD and LCX (0.4%), high takeoff (0.25%), single coronary artery (atresia), origin from opposite coronary sinus, and anomalous termination (fistula) [1, 2]. Myocardial bridge is a specific congenital condition in which the epicardial coronary artery travels the intramuscular course, usually in the middle portion of the LAD. Approximately 5–80% of autopsy, 25% of CT scan, and 0.15–25% of cases were detected during coronary angiography as systolic compression of the coronary artery. The myocardial bridge is usually benign, but sometimes it causes chest pain, acute coronary syndrome, left ventricular dysfunction, and arrhythmias [3, 4].

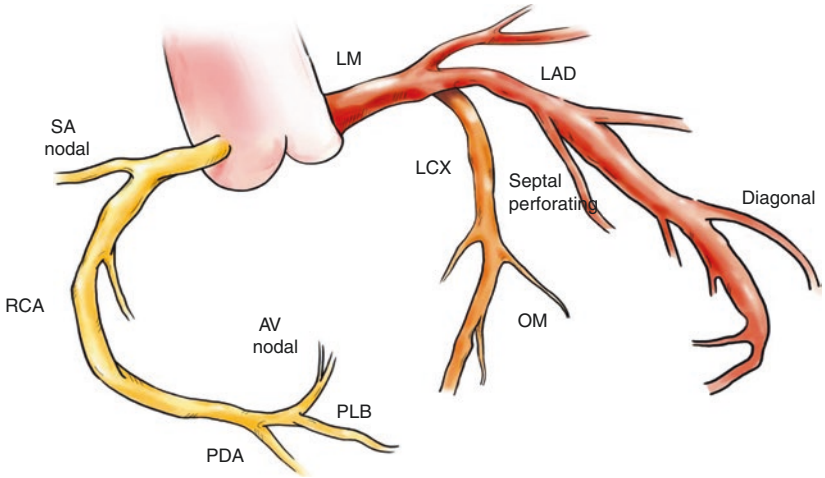


**Fig. 1** Anatomy of coronary artery. *LM* left main, *LAD* left anterior descending artery, *LCX* left circumflex artery, *OM* obtuse marginal, *RCA* right coronary artery, *SA nodal* sinoatrial nodal, *AV* atrioventricular, *PDA* posterior descending, *PLB* posterolateral branch

## Coronary Circulation

Coronary blood flow is a phasic pattern; main arterial flow in the coronary artery occurs in diastole. During systole, contraction of the myocardium compresses the coronary microvessels, impedes arterial blood flow, and increases venous outflow. Coronary flow is determined by myocardial demand and blood supply. Major determinants of myocardial blood flow are heart rate, myocardial contractility, and myocardial wall stress (preload, afterload). Because coronary blood flow passes from the epicardium to the endocardium, the subendocardial area is susceptible myocardial ischemia. The pressure difference between the epicardial coronary artery and the left ventricle is important to maintain myocardial perfusion. The "potential" for coronary flow to the subendocardium is the difference between diastolic aortic and left ventricular pressures multiplied by the diastolic period. A low aortic pressure or a brief diastolic period (tachycardia) may compromise subendocardial blood flow [5, 6].

The epicardial coronary artery is the conduit to transfer blood to the arteriole, capillary, and myocardium and consists of less than 10% of coronary resistance unless severe stenosis develops. The precapillary arteriole (100–500 μm) connect epicardial conduit to myocardial capillaries; it covers less than 30% of coronary resistance. In a normal state, it gives little contribution to resistance. Distal precapillary arteriolar vessels (<100 μm) are mainly responsible for resistance and flow.

## Regulation of Coronary Blood Flow

Coronary blood flow is reasonably constant despite changes in coronary artery pressure to keep myocardial perfusion, although blood pressure changed within certain range, usually between 40–150 mmHg. Below the

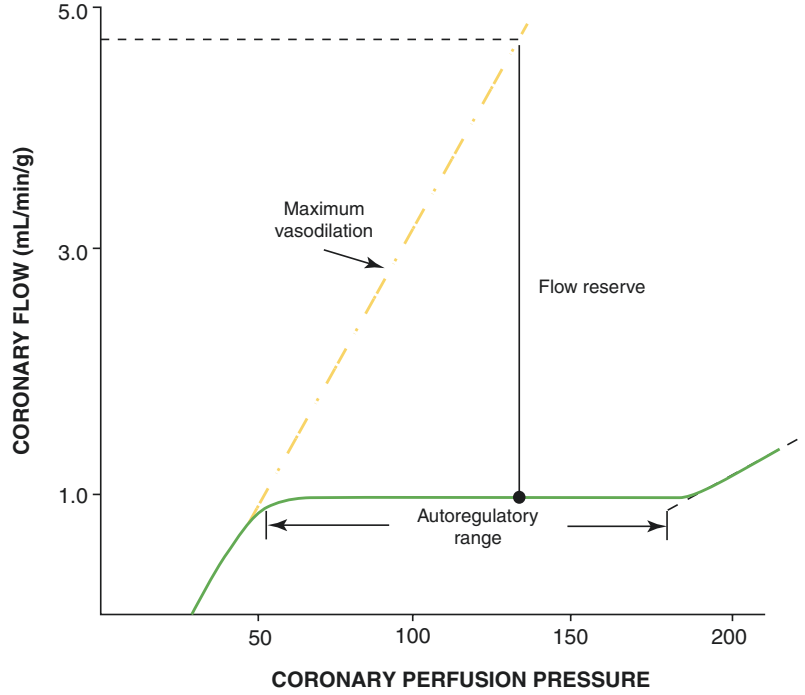


**Fig. 2** Coronary autoregulation

autoregulatory range (approximately 60 mmHg), flow is strongly pressure-dependent. Vasodilator reserve is the increase in flow between the prevailing flow and a specified "maximum" vasodilator stimulus. Below the autoregulatory range, vasodilator reserve is exhausted. In a normal coronary artery, blood flow of maximally dilated coronary increases fourfold to sixfold of resting state [7–9] (Fig. 2).

## Endothelial-Dependent Regulation

Endothelium-dependent regulation is mediated by nitic oxide (NO). NO is made by NO synthase in endothelial cell. It diffuses into smooth muscle in media, which in turn vasodilate by decreasing intracellular $Ca^{++}$. Shear stress and paracrine mediators (endothelial-dependent hyperpolarizing factor, endothelin) can influence endothelial function via NO. In a normal coronary artery, acetylcholine dilates coronary artery via increasing NO; however, in case of endothelial denudation, acetylcholine causes vasoconstriction due to decreased NO production [5, 10].

## Myogenic Regulation

Myogenic regulation is controlled by coronary smooth muscle, which can change coronary vessel diameter in response to pressure. In normal conditions, smooth muscle of the coronary artery maintains vessel diameter below

maximal vasodilation level. According to Laplace law, to decrease wall tension, resistance is inversely related with pressure (Laplace law). If coronary artery pressure increase, it influences smooth tone and results in vasoconstriction via increasing resistance to decrease wall stress. Myogenic regulation is primarily observed in the arteriole (<100 μm) [11].

### Metabolic Regulation

Adenosine mainly dilates small coronary arterioles by binding A2 receptor on vascular smooth muscle. It increases cAMP followed by increasing intracellular $Ca^{++}$ mainly small arteriole. Endothelin and hypoxia cause vasoconstriction [5].

### Neural Regulation

Increased sympathetic tone stimulates beta-2 receptor followed by coronary vasodilation; however, alpha-1 stimulation leads to vasoconstriction. Although flow-mediated vasodilation is the main mechanism after sympathetic activation in a normal artery, alpha-1-mediated vasoconstriction is developed in case of impaired NO-mediated vasodilation. For cholinergic nervous system, acetylcholine dilates the coronary artery via NO-mediated vasodilation [12, 13].

### Extravascular Compression

During systole, coronary blood flow is limited due to the effect of increased resistance as a consequence of coronary artery compression and higher left ventricular pressure than coronary pressure due to myocardial contraction.

## Reference Values of Normal Coronary Flow Measurements in Clinical Setting

The characterization of normal coronary blood flow dynamics could provide crucial guidelines for the physiologic assessment of diseased coronary artery. Spectral flow velocity parameters, including average peak velocity (APV), average diastolic peak velocity (ADPV), average systolic peak velocity (ASPV), and diastolic-to-systolic velocity ratio (DSVR), were measured using Doppler wire at baseline and intracoronary adenosine-induced maximal hyperemic state. Coronary flow reserve (CFR) was calculated from the ratio of hyperemia to baseline APV [14–16] (Figs. 3 and 4).

Summary of characteristics of normal coronary flow patterns are as follows:

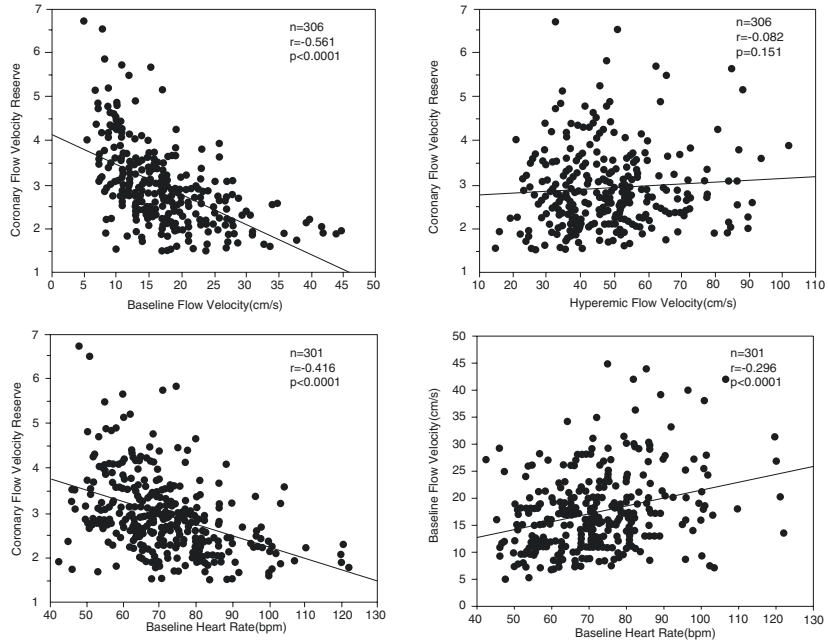


**Fig. 3** Correlations between coronary flow velocity and coronary flow reserve (**a**), and between baseline heart rate and coronary flow reserve or baseline coronary flow (**b**). (**a**) CFR had no significant correlation with hyperemic flow velocity, and showed significant inverse correlation with baseline flow velocity. (**b**) Baseline heart rate significantly correlated with baseline flow velocity

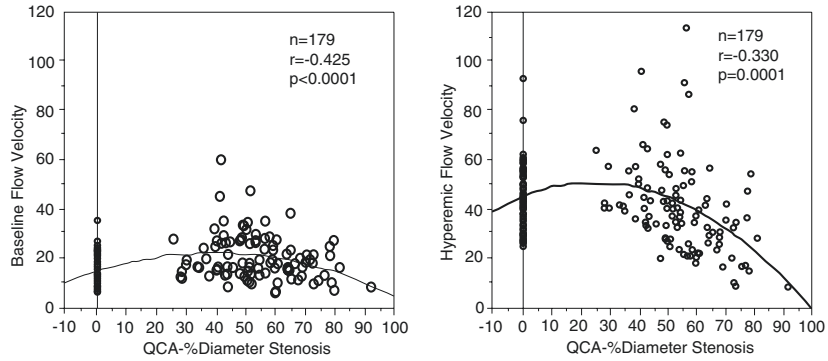


**Fig. 4** Correlations between coronary flow and stenosis severity on quantitative coronary angiography at baseline and hyperemia

1. Intracoronary flow velocity was relatively well preserved from proximal to distal segment, especially in the left coronary system (tapered branching model).
2. CFR was preserved from the proximal to distal segments.
3. There was a significant difference in CFR between left and right arteries. CFR of the right artery is significantly higher.

4. CFR has a wide range of individual variation: from 1.6 to 6.7. Incidence of low CFR (<2.0) was 13%.
5. CFR was adversely affected by the level of baseline flow and heart rate at the time of measurement rather than the level of hyperemic flow.
6. In physiologic evaluation of diseased coronary arteries in a real clinical setting, significant regional differences of coronary flow patterns and factors affecting flow pattern, especially baseline hemodynamic status of patients, should be considered.

## Coronary Blood Flow Under Coronary Stenosis

When a given coronary artery stenosis is present, pressure drop across a stenosis is influenced by viscous loss and post-stenosis flow separation. According to Poiseuille's Law, $\Delta P$ (pressure difference) is inversely related to radius and positively related to stenosis length and flow, so viscous losses are related to stenosis diameter and length. For separation losses, pressure gradient is related to flow, and the relationship is nonlinear.

Under normal coronary autoregulation, coronary blood flow is maintained despite presence of stenosis. In the relationship between pressure drop across a stenosis and coronary blood flow, the pressure drop is that which might be seen across an 80–85% diameter stenosis of a coronary artery. If the aortic pressure is 100 mmHg and the flow is 1.0 ml/min/g myocardium, then the pressure distal to the stenosis will be below the lower limit of autoregulation (approximately 60 mmHg). The patient will probably experience angina, even though flow is greater than an initial resting value of approximately 0.5 ml/min/g myocardium. The pressure-flow relationship curve showed that the pressure drop across the lesion was more prominent as the degree of stenosis was more severe. Because of the nonlinear resistance characteristics of stenoses, the critical narrowing is approximately 80–85% at resting flows but approximately 45% during hyperemia. To prevent myocardial ischemia, the coronary microvasculature dilates to decrease pressure difference across a lesion [14–17].

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