Journal of Molecular and Cellular Cardiology 52 (2012) 786–793

Contents lists available at ScienceDirect

Journal of Molecular and Cellular Cardiology

journal homepage: www.elsevier.com/locate/yjmcc

Review article

Coronary pressure-flow relations as basis for the understanding of coronary physiology

Tim P. van de Hoef [a,b], Froukje Nolte [a], M. Cristina Rolandi [a], Jan J. Piek [b], Jeroen P.H.M. van den Wijngaard [a], Jos A.E. Spaan [a], Maria Siebes [a,*]

[a] Department of Biomedical Engineering and Physics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[b] Department of Cardiology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 8 June 2011
Received in revised form 27 July 2011
Accepted 28 July 2011
Available online 10 August 2011

Keywords:
Coronary blood flow
Coronary flow reserve
Fractional flow reserve
Functional stenosis severity
Microvascular resistance
Myocardial perfusion
Pressure–flow relation

ABSTRACT

Recent technological advancements in the area of intracoronary physiology, as well as non-invasive contrast perfusion imaging, allow to make clinical decisions with respect to percutaneous coronary interventions and to identify microcirculatory coronary pathophysiology. The basic characteristics of coronary hemodynamics, as described by pressure–flow relations in the normal and diseased heart, need to be understood for a proper interpretation of these physiological measurements. Especially the hyperemic coronary pressure–flow relation, as well as the influence of cardiac function on it, bears great clinical significance. The interaction of a coronary stenosis with the coronary pressure–flow relation can be understood from the stenosis pressure drop–flow velocity relationship. Based on these relationships the clinically applied concepts of coronary flow velocity reserve, fractional flow reserve, stenosis resistance and microvascular resistance are discussed. Attention is further paid to the heterogeneous nature of myocardial perfusion, the vulnerability of the subendocardium and the role of collateral flow on hyperemic coronary pressure–flow relations. This article is part of a Special Issue entitled "Coronary Blood Flow".

Contents

* Corresponding author at: Dept. of Biomedical Engineering and Physics, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. Tel.: +31 20 566 7240/5200 (sec); fax: +31 20 691 5233.
E-mail address: m.siebes@amc.uva.nl (M. Siebes).

0022-2828/$ – see front matter
doi:10.1016/j.yjmcc.2011.07.025

1. Introduction

The oxygen extraction from the coronary circulation is high and even at baseline conditions approximates 75%, while the overall oxygen extraction in the systemic circulation amounts to 25–30% [1]. In extreme exercise in dogs, coronary venous saturation may be reduced further from 25% to approximately 10% [2], but this increased extraction is much too small to account for the 4 to 5 times increase in oxygen demand that may occur and consequently necessitates an increase in coronary blood flow [1]. Normally, coronary blood flow is well controlled and matched to the oxygen needs of the heart by adapting the caliber of the coronary resistance arteries, including arterioles, via inter-related processes involving mechanisms intrinsic to the vascular wall, as well as metabolic and neurohumoral factors [3,4].

One of the first observations on coronary physiology several centuries ago was that coronary arterial flow is pulsatile, high in diastole and low in systole [5]. This is opposite to the flow pattern in arteries feeding other organs where flow is high in systole. The particular coronary bi-phasic flow pattern is the result of compressive forces that are exerted by the contracting heart muscle on the embedded microvessels. Hence, the heart impedes its own perfusion by the contraction that is needed to fulfill its principal function.

Many of the physiological phenomena underlying coronary flow regulation have been studied in conscious and unconscious animal preparations where there is great freedom in instrumentation and interventions. More recently, investigation of human coronary physiology has become possible in clinical studies owing to the miniaturization of pressure and flow sensors at the tip of coronary guide wires used during cardiac catheterization and by myocardial perfusion imaging via magnetic resonance imaging, positron emission tomography and contrast echocardiography [6,7].

The purpose of this paper is to provide a brief overview of some principles of coronary physiology, and how these principles translate to diagnostic applications in clinical practice.

2. Characteristics and limits of coronary blood flow control

In functional terms, the two major determinants of coronary flow are coronary arterial pressure and myocardial oxygen consumption. It was found very early on that, at constant oxygen consumption, coronary flow is relatively independent of arterial pressure which is referred to as coronary autoregulation [8]. Similarly, at a given coronary arterial pressure, coronary flow increases with oxygen consumption, which is defined as metabolic adaptation. These two mechanisms are interrelated and may even be due to the same control mechanism designed to maintain the controlled variable at a desired level. The controlled variable may be tissue oxygen pressure or a different factor related to metabolism. Since in the intact circulation coronary pressure equates to aortic pressure and aortic pressure is a main determinant of myocardial oxygen consumption, it is difficult to study metabolic flow adaptation and autoregulation independently in an intact preparation. This can best be studied in a system where the coronary blood supply is controlled independently, e.g. by an extracorporeal system.

Conceptually, it is important to have a clear picture of the two manifestations of coronary flow control as illustrated in Fig. 1. The left panel schematically depicts coronary pressure–flow relations at rest and during maximal vasodilation. The steepest line (hyperemia) represents the situation where flow control is abolished. Hyperemic flow increases with pressure, but not proportional, since this relation does not pass through the origin. The hyperemic pressure–flow relation bears great clinical significance as will be discussed below. The autoregulatory action of the coronary system is indicated by the lines with a smaller slope at two different levels of constant oxygen consumption, demonstrating the characteristic parallel shift with oxygen consumption. Coronary flow is kept fairly constant over a large range of perfusion pressure by adjusting coronary microvascular resistance to changing perfusion pressures. Note that coronary autoregulation is not perfect, which would correspond to horizontal plateaus in the autoregulation range. The right panel in Fig. 1 depicts results from an experiment where oxygen consumption of the heart was altered at two different coronary pressures [9]. Coronary flow increases with oxygen consumption, but also not in a proportional manner and oxygen extraction becomes less efficient at higher coronary pressure. Clearly, metabolic adaptation is not perfect either, since at the same oxygen consumption, flow rate is higher for a higher coronary pressure. Obviously, the pressure dependence of metabolic adaptation corresponds to the slope of the autoregulation curve.

In a conceptual model, control of coronary blood flow can best be understood as a system designed to maintain tissue oxygen pressure (P_{O2}) at a constant level. In such a model, factors causing a decrease of tissue P_{O2} will lower coronary resistance by inducing vasodilatation [10,11]. Similarly, vasoconstriction will result via factors inducing an increase in tissue P_{O2}. This does not imply that tissue P_{O2} is the controlled variable in real life, since such model behavior can be realized in several ways. However, the concept of tissue P_{O2} control has guided the design of experiments to unravel the specific role of mechanisms involved in blood flow control using coronary venous P_{O2} as a surrogate for myocardial tissue P_{O2} [1,12,13]. In this way a direct vasoactive effect of a drug may be distinguished from an indirect effect via alterations in oxygen consumption [14].

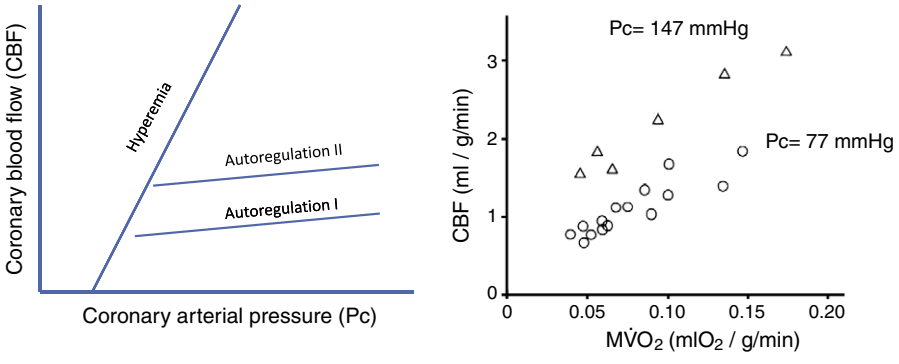

Fig. 1. Left panel: Schematic pressure–flow relations illustrating autoregulation and maximal vasodilatation (hyperemia). The hyperemic relationship is incremental-linear with a non-zero intercept. Autoregulation is shown at two levels of constant oxygen consumption, which induces a parallel shift. Right panel: Coronary blood flow, CBF, as a function of oxygen consumption, MV̇O2, for two different coronary arterial pressures.
Data from [9].