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International Journal of Cardiology 107 (2006) 382 – 388

International Journal of Cardiology

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Transmural distribution of myocardial blood perfusion and phasic coronary blood flow pattern in a canine model of acute ischemia[B]

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Received 26 January 2005; received in revised form 15 March 2005; accepted 26 March 2005
Available online 10 May 2005

Abstract

Background: Although several investigators have analyzed coronary artery blood flow under various conditions, almost all these studies have measured only some branches of the left anterior descending (LAD), left circumflex (LCX), or right coronary (RCA) artery.
Methods: In a canine model of acute ischemia ($n=5$), we simultaneously assessed (a) regional myocardial blood perfusion using microspheres and (b) phasic coronary blood flow patterns as measured by three epicardial flow probes placed around the LAD, LCX, and RCA.
Results: The results from this study indicated that the LAD supplies blood to the epicardial ($r=0.687$, $p<0.0001$), midwall ($r=0.556$, $p=0.0021$), and endocardial layers ($r=0.666$, $p=0.0001$) of the LAD area; the LCX supplies the midwall ($r=0.514$, $p=0.0051$) and endocardial layer ($r=0.621$, $p=0.0004$) of the LCX area, antero-lateral papillary muscle ($r=0.548$, $p=0.0025$), and postero-medial papillary muscle ($r=0.641$, $p=0.0002$), especially during the diastolic phase; and the RCA supplies the right ventricular apex ($r=0.559$, $p=0.0020$), left atrium ($r=0.618$, $p=0.0005$), right atrium ($r=0.471$, $p=0.0114$), and postero-medial papillary muscle ($r=0.486$, $p=0.0088$), especially during the systolic phase.
Conclusions: These results are potentially relevant to understanding the physiology of myocardial blood perfusion and to improving treatment of acute myocardial ischemia and infarction.

Keywords: Transmural distribution; Coronary blood flow; Cardiovascular physiology; Coronary microcirculation

1. Introduction

Coronary reperfusion therapy (often a combination of thrombolytic therapy and/or percutaneous transluminal coronary angioplasty of epicardial lesions) improves the clinical outcomes of patients presenting with acute myocardial infarction. However, the impact of lesion revascularization on myocardial reperfusion is difficult to predict, secondary to the complex phasic flow patterns and regional flow variability. Measurement of coronary blood flow using flow probes is a standard technique, and several studies have been conducted to analyze coronary blood flow under various conditions [1–10]. Hoffman and associates reported that the epicardial region of the left ventricle was primarily perfused during the systolic phase, the endocardial region was primarily perfused during the diastolic phase [8,9], and the right ventricle was mainly perfused during the systolic phase [10]. However, these studies analyzed regional coronary blood flow using a Gregg cannula placed into the left main coronary artery or right coronary artery (RCA), a method that resulted in nonphysiological extracorporeal circulation. Furthermore, all of these studies measured flow in only one or two branches of the left anterior descending

☆ This study was financially supported by NeoMed Inc., Cleveland, OH.
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0167-5273/$ - see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijcard.2005.03.056

coronary artery (LAD), left circumflex coronary artery (LCX), and RCA. None of the studies simultaneously analyzed the phasic coronary blood flow patterns of all three coronary arteries. The effects of the sum of the three coronary artery flows and any collateral flow to jeopardized myocardium are also still unclear.

Microsphere techniques have been used extensively in animals for quantifying not only systemic blood flows but also regional organ blood perfusion [11–17]. However, radiolabeled and optically labeled microspheres have infrequently been used because of their cost and the need for complicated measuring methods [18]. Recently, the development of the neutron activation assay technique using stable isotopically labeled microspheres (BioPhysics Assay Laboratory [BioPAL], Worcester, MA) has enabled the measurement of up to 10 different conditions in a relatively straightforward way [18].

The hypothesis of this study was that the simultaneous measurement of all three major coronary blood flows using ultrasonic flow probes should show a significant correlation with the transmural distribution of myocardial blood perfusion as measured by microspheres. Therefore, the purpose of this study was to measure and analyze phasic coronary blood flow patterns in three major coronary arteries simultaneously and correlate the findings with the transmural distribution of myocardial blood perfusion. These serial measurements might contribute to understanding the physiology of myocardial perfusion and to improving the treatment (e.g., intraaortic balloon pumping or coronary arterial interventions for multiple atherosclerotic coronary arteries) of acute myocardial ischemia and infarction.

2. Materials and methods

2.1. In vivo experiments

This study was performed using dogs under authorization by the Institutional Animal Care and Use Committee of the Cleveland Clinic Foundation. The animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press, revised 1996.

Five adult mongrel dogs, weighing from 20.8 to 28.0 kg (24.8±3.2 kg), were anesthetized with intravenous thiopental (20 mg/kg), intubated, and mechanically ventilated with a mixture of isoflurane (0.5–2.5%) and oxygen. A venous catheter was placed in a peripheral vein to administer fluids. During the surgical procedure, performed using non-sterile techniques, electrocardiography was monitored continuously. With the animal in the supine position, the right femoral artery was cannulated for blood sampling and arterial pressure monitoring. Arterial pH, partial pressure of carbon dioxide (PCO_2), and partial pressure of oxygen (PO_2) were measured serially, and the ventilator was adjusted to maintain these parameters within the physiologic range.

A median sternotomy was performed, and the heart was suspended in a pericardial cradle. A catheter was placed in the left atrium for injection of microspheres. The pulmonary artery, proximal LAD, LCX, and RCA were isolated for placement of flow probes (16A for pulmonary artery, SB-3.0 mm for LAD and LCX, SS-2.5 mm for RCA; Transonic Systems Inc., Ithaca, NY). The flow probes measured the cardiac output, LAD flow (LADF), LCX flow (LCXF), and RCA flow (RCAF). We obtained the total coronary blood flow (TCBF) by summing the three coronary flow values. Hydraulic occluders (model OC3, In Vivo Metric, Healdsburg, CA), vascular occluders (GB-3, Braintree Scientific Inc., Braintree, MA), or tourniquets were also placed distal to the flow probes of the LAD and LCX.

Hemodynamic data was obtained continuously. After baseline measurements, TCBF was reduced in a stepwise fashion to yield 5–30% reductions resulting from a partial stenosis of the LAD or LCX by adjusting the occluder. If a 30% reduction was not obtained by occluding one coronary artery, we regulated both LAD and LCX flows. After 10 min of hemodynamic stabilization, hemodynamic data were measured in each condition. Immediately after recording hemodynamic data and the phasic coronary blood flow pattern in each condition, microspheres were administered and reference blood samples were taken.

2.2. Phasic coronary blood flow pattern

Systolic coronary blood flow was defined as the flow occurring in the period between the onsets of rapid acceleration of TCBF associated with ventricular contraction and the onset of rapid acceleration of TCBF associated with ventricular relaxation. From the time–domain flow signal, the peak flow of the systolic and diastolic flow components was obtained. The time–flow integrals of the systolic and the diastolic flow components were also measured by the time–domain flow signal. The proportion of blood flow that occurs during diastole (diastolic fraction) was determined. The diastolic/systolic peak velocity ratios were calculated. Values for each parameter were obtained by averaging measurements from 7 to 10 consecutive cardiac cycles.

2.3. Measurement of transmural distribution of myocardial blood perfusion

Transmural distribution of myocardial blood perfusion was measured with stable neutron-activated microspheres (BioPAL). A 2.4 mL bolus containing six million microspheres (mean diameter, 15 μm) was injected into the left atrium at the end of the baseline data and during each stenosis condition immediately after recording hemodynamic data and the phasic coronary blood flow pattern. A different type of microsphere (samarium, lanthanum,