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Ventral cardiac denervation increased right coronary arterial blood flow

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Abstract

Background: Cardiac denervation accompanied with coronary artery bypass surgery has been widely performed for the treatment of vasospastic angina associated with atherosclerotic coronary artery disease. However, the effect of cardiac denervation on phasic coronary blood flow patterns of the left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA) remains unknown. This study aimed to investigate the effect of cardiac denervation on phasic coronary blood flow patterns of the LAD, LCX and RCA.
Methods: Phasic coronary blood flow patterns were analyzed using three flow probes placed around the LAD, LCX and RCA with and without LAD stenosis. Ventral cardiac denervation (VCD) was performed in 8 pigs, and 16 pigs were used as control subjects. Autonomic activities before and after the VCD were quantified by wavelet analysis of heart rate variability.
Results: The mean LAD flow (34.4 ± 9.4 to 32.6 ± 7.1 ml/min, $p = 0.638$) and mean LCX flow (26.3 ± 10.2 to 27.2 ± 6.0 ml/min, $p = 0.825$) showed no significant change after VCD, while the mean RCA flow (31.3 ± 9.0 to 38.2 ± 11.2 ml/min, $p = 0.003$) significantly increased. The hemodynamic variables in the VCD group were well maintained after creation of LAD stenosis, while they deteriorated in the control group. The low-frequency components, high-frequency components and their ratio did not change after VCD.
Conclusions: VCD prevented the deterioration of cardiac function after creation of an LAD stenosis and resulted in an increase of the mean RCA flow. VCD did not affect autonomic nervous system activity.

Keywords: Cardiac denervation; Coronary blood flow; Vasospastic angina

1. Introduction

Cardiac denervation combined with coronary artery bypass surgery [1–4] has been widely performed for the treatment of vasospastic angina associated with atherosclerotic coronary artery disease since Prinzmetal et al. [5] reported variant angina in 1959. Although cardiac denervation went out of use for patients with Prinzmetal's angina due to the effectiveness of calcium antagonists, the ventral cardiac denervation (VCD) technique recently has been modified to prevent postoperative atrial fibrillation after coronary bypass grafting [6–8]. Cardiac denervation has also contributed to the postoperative clinical improvement following transmyocardial laser revascularization [9,10]. These studies revealed the effectiveness of cardiac denervation from the standpoint of the postoperative symptoms; however, its mechanism and its effects on the coronary blood flows and autonomic nervous activity are still unclear.

Amano et al. [11] reported that a significant increase in the saphenous vein graft flow to the left anterior descending coronary artery (LAD) was observed after a combination of coronary artery bypass grafting and cardiac denervation in those patients with organic coronary artery disease. However, the effects of VCD on phasic coronary blood flow patterns of the LAD, left circumflex coronary artery (LCX) and right coronary artery (RCA) have not been assessed. The autonomic nervous system response to VCD remains

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unknown. The hypothesis of this study was that the simultaneous measurement of all three major coronary blood flows should show a significant change after VCD. Therefore, the objective of this study was to investigate the effects of VCD on coronary circulation and autonomic nervous system activity.

2. Materials and method

2.1. Animal model

Twenty-four pigs weighing 42.9 to 61.7 kg (50.1 ± 5.4 kg) were used in this study. This study was approved by the Cleveland Clinic's Institutional Animal Care and Use Committees, and all animals received humane care in accordance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (National Institutes of Health publication 85-23, revised 1985).

2.2. Anesthesia and surgical preparation

The animal was anesthetized with an intramuscular injection of ketamine (20 mg/kg), and after intubation, the animal was ventilated through an endotracheal tube with a respirator. Anesthesia was maintained with isoflurane (0.5–2.5%) until the end of the study. A venous catheter was placed in a peripheral vein to administer fluids. ECG leads were attached to the extremities to monitor cardiac vital signs. The settings of the respirator were adjusted as required based on the results of the arterial blood gas.

The animal was placed on the surgical table in the supine position. A continuous infusion of lidocaine was started at the rate of 1 mg/kg/hr before neck incision. A right lateral neck incision was made to isolate the right carotid artery and the jugular vein. An arterial pressure monitoring line was inserted into the right carotid artery, and a venous infusion line and a right atrial pressure monitoring line were inserted through the right jugular vein. A median sternotomy was performed and the infusion rate of lidocaine was increased to 2 mg/kg/hr when the pericardium was opened. A left atrial pressure monitoring line was inserted from the left atrial appendage into the left atrium. The pulmonary artery was isolated for placement of a flow probe (16 mm, Transonic Systems Inc., Ithaca NY) to assess the cardiac output. The RCA, LAD and LCX were also isolated for placement of flow probes (SB-3.0 mm for LAD and LCX, SS-2.5 mm for RCA, Transonic Systems Inc.) in order to assess the coronary blood flow pattern throughout the experiment. 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. A vascular tourniquet was placed distal to the flow probe of the LAD.

2.3. Ventral cardiac denervation

The animals were non-randomly divided into two groups. VCD was performed in 8 pigs (VCD group), and 16 pigs were used as control subjects (control group). VCD consisted of a circumferential incision in the adventitia around the ascending aorta and the main pulmonary artery. All fatty tissues within the aorta-pulmonary groove were also incised.

2.4. Intraoperative hemodynamic assessment

Hemodynamic data were taken at baseline and after creation of LAD stenosis in the control group. Hemodynamic data were taken at baseline, after VCD and after creation of LAD stenosis in the VCD group. The LAD stenosis condition was induced by adjusting the tourniquet placed around the LAD distal to the flow probe to produce approximately a 50% reduction in the LADF. Heart rate, right atrial pressure, left atrial pressure, arterial pressure, coronary blood flows, and cardiac output were recorded.

2.5. Phasic coronary blood flow pattern

Systolic coronary flow was defined as the flow occurring in the period between the onset 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 diastolic/systolic peak velocity ratios were calculated. Values for each parameter were obtained by averaging measurements from 7 to 10 consecutive cardiac cycles during temporary cessation of ventilation (Fig. 1).

2.6. Analysis of heart rate variability

Ten minutes of autonomic activity before and after the VCD were quantified by wavelet analysis of heart rate variability as other investigators reported elsewhere [12,13]. In brief, time-domain analysis and spectral analysis of heart rate variability were performed using the MemCalc system (MemCalc Version 2.5, Suwa Trust CO, Tokyo, Japan) in each condition [14]. High frequency components (HF: 0.15 to 0.40 Hz) were defined as a marker of parasympathetic nervous activity, and low frequency components (LF: 0.04 to 0.15 Hz) related to a combination of parasympathetic and sympathetic nervous activities. The ratio of LF to HF (LF/HF) was defined as an indicator of sympathetic nerve activity.

2.7. Statistical analysis

The hemodynamic variables and ECG data were obtained using a PowerLab data acquisition system (AD