Coronary active perfusion system can maintain myocardial blood flow and tissue oxygenation

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Abstract

Objectives: To avoid myocardial ischemia in off-pump coronary artery bypass, we developed a coronary active perfusion system (CAPS). The purposes of this study were to investigate the changes in myocardial blood flow and tissue oxygenation during CAPS perfusion, and to validate the ventricular arrhythmias and hemodynamic deterioration preventing the effect. Methods: Sixteen pigs were divided into a CAPS perfusion group (group C) and a simple coronary occlusion group (group O). The left anterior descending coronary artery was snared in both groups and 30 min of CAPS perfusion was performed in group C. Results: Ventricular arrhythmias were not observed in group C, but occurred in seven out of eight pigs in group O ($P = 0.003$). None of the hemodynamic variables changed in group C, but they deteriorated in group O. Myocardial blood flow, saturation, and hemoglobin plus myoglobin concentration were maintained with a baseline level in group C, but decreased significantly in group O ($P < 0.001$). Conclusion: CAPS is a reliable method to avoid myocardial ischemia during coronary occlusion and it may be useful for off-pump coronary artery bypass © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Off-pump coronary artery bypass; Coronary active perfusion system; Myocardial blood flow; Myocardial oxygenation

1. Introduction

Off-pump coronary artery bypass grafting (OPCAB) usually requires a temporary coronary occlusion during anastomosis of the vascular graft to the target vessel. In general, the temporary occlusion of a totally or subtotally occluded branch is well tolerated in the presence of sufficient collateral circulation. However, if the stenosis of the target vessel is moderate, temporary occlusion can cause myocardial ischemia, and subsequent arrhythmias and hemodynamic instability may occur, although such cases may be unusual. Several methods, including intracoronary shunt, aorto-coronary shunt, and ischemic preconditioning, have been devised to attenuate myocardial damage during OPCAB [1–5]. However, the myocardial protective effects of these methods are uncertain if a prolonged anastomosis time is required. To avoid myocardial ischemia completely during anastomosis in OPCAB in any situation, we developed coronary active perfusion system (CAPS), which perfuses arterial blood to the coronary artery at the diastolic phase of the cardiac cycle, similar to native coronary flow.

The purposes of this study were to examine the changes in myocardial blood flow and tissue oxygenation during the period of CAPS perfusion, and to validate the ventricular arrhythmias and hemodynamic deterioration preventing the effect of CAPS. For evaluation of real-time myocardial blood flow, a thermal diffusion tissue blood flowmeter was used [6–8]. Real-time continuous tissue blood flow measurement has been made possible in other organs such as the liver and the brain using the thermal diffusion method [6–8], and we applied it to myocardial blood flow monitoring in a preliminary study [8]. For the measurement of myocardial oxygenation, three-wavelength near-infrared spectroscopy (NIRS) was used [9,10]. This apparatus allows real-time monitoring of the changes in myocardial tissue oxygenation within the beating heart.

2. Materials and methods

All animals received human care in compliance with the ‘Principles of Laboratory Animals Care’ formulated by the
National Society for Medical Research and the ‘Guide for the Care and Use of Laboratory Animals’ prepared by the Institute of Laboratory Animal Resources and published by the National Institute of Health (NIH Publication no. 86-23, revised 1985). Sixteen pigs with a body weight of 48.4 ± 4.2 kg were studied. Anesthesia was induced with an intramuscular administration of ketamine hydrochloride (20 mg/kg). After tracheotomy, a cuffed endotracheal tube was inserted and ventilation was performed with a volume-regulated ventilator (KMA-1300IIIS, Acoma, USA). Then, muscle relaxation was achieved with 0.1 mg/kg pancuronium via peripheral intravenous access. Anesthesia was maintained with 1% halothane. A catheter was inserted into the ascending aorta through the right carotid artery for continuous aortic pressure monitoring, and a catheter was also inserted into the right femoral artery to remove arterial blood for CAPS. A Swan–Ganz catheter (Baxter Healthcare Corp., Edwards Division, Santa Ana, CA) was inserted into the pulmonary artery through the right internal jugular vein for pressure monitoring and continuous cardiac output measurements (SAT-II, Baxter). Following a median sternotomy, a thermal diffusion probe (TGD-8, Biomedical Science Co. Ltd., Kanazawa, Japan) for myocardial blood flow (MBF) monitoring and an NIR probe (PSP-15R; Biomedical Science) were attached to the anterior surface of the left ventricle distal to the left anterior descending coronary artery, avoiding the epicardial fat tissue. Systemic heparinization (200 U/kg) was performed in all the pigs. The pigs were divided into two groups: a CAPS perfusion group (group C) and a simple coronary occlusion group (group O). In group C, the CAPS circuit was connected to the catheter inserted into the right femoral artery. After the measurement of baseline data, the left anterior descending coronary artery was snared at a point just proximal from the first diagonal branch, a coronary arteriotomy was performed and a CAPS cannula was inserted, and 30 min of CAPS coronary perfusion was performed. In group O, after the measurement of baseline data, the coronary artery was occluded at the same point as in group C for 30 min. The endpoints of this study were 30 min observation without ventricular arrhythmias or the occurrence of ventricular arrhythmias.

The CAPS is a device that perfuses arterial blood to the coronary artery at the diastolic phase of the cardiac cycle, similar to native coronary flow during anastomosis (Fig. 1). Blood injection is controlled to provide pulsatile flow synchronized with an electrocardiogram. The arterial blood removed from femoral artery is perfused to the coronary artery through a fine flexible cannula during anastomosis. Although the proximal site of anastomosis is snared, myocardial ischemia does not occur during anastomosis due to CAPS. According to our preliminary study, the CAPS perfusion setting was adjusted to 0.1 ml/stroke, the early diastolic perfusion timing in this study (data not shown).

Continuous myocardial blood flow was measured using a thermal diffusion tissue blood flowmeter (BTG-221, Biomedical Science). This method is based on the linear relationship between blood flow and the heat conductivity increment in tissues [6–8]. The probe consists of a Peltier stack with gold plates arranged so that the voltage output is proportional to the temperature difference between the plates. Activation of the stack creates a temperature gradient between the plates which includes the ambient heart temperature. Blood flow increments the temperature gradients, cools the heated plate, warms the cold plate, and causes a decrease in the thermocouple voltage output. Tissue blood flow approximately 3 mm beneath the probe is calculated as being inversely proportional to the thermocouple voltage output.

Myocardial tissue oxygenation was measured using a three-wavelength NIRS apparatus (PSA-IIIN; Biomedical Science). Near-infrared light from the NIRS passes through tissue with relative ease and is significantly absorbed by

![Fig. 1. Left: schematic presentation of CAPS. Right: the usage of CAPS in clinical off-pump coronary artery bypass.](image-url)
oxygenated and deoxygenated hemoglobin, which have distinctly different absorption spectra in the near-infrared region. On the basis of this difference, changes in the tissue concentration of hemoglobin can be measured by NIRS. As the oxygenated hemoglobin and oxygenated myoglobin have essentially identical near-infrared spectra, hemoglobin plus myoglobin (Hb) were added. The optical information from a myocardial tissue of depth 2.5–5.0 mm was obtained. The near-infrared signal was analyzed using a set of algorithms that solved oxygenated and deoxygenated Hb. Oxygenated Hb divided by the sum of oxygenated and deoxygenated Hb corresponded to the tissue oxygen saturation (SO2). The method used in this study has been described in detail previously [9,10].

Cumulative data are expressed as the mean ± the standard deviation. The χ² test was done for analysis of the occurrence of ventricular arrhythmias between groups. The paired t test was done for analysis of hemodynamics before and after the experiments, and repeated analysis of variance (ANOVA) was done for analysis of changes in the myocardial blood flow, myocardial SO2, and myocardial Hb concentrations in each group.

3. Results

In group C, ventricular arrhythmias were not observed in any of the eight pigs (0%). However, five ventricular fibrillation and two ventricular tachycardia were observed among eight pigs in group O (88%). There was a significant difference in the occurrence rate of ventricular arrhythmias between the groups (P=0.003).

The hemodynamic changes in groups C and O are shown in Table 1. In group C, none of the hemodynamic variables (heart rate, mean aortic pressure, systolic pulmonary artery pressure, and cardiac output) changed during the experiments. In group O, increasing heart rate and decreasing mean aortic pressure, systolic pulmonary artery pressure, and cardiac output were observed in pigs with and without ventricular arrhythmias. These hemodynamic deteriorations were significant in pigs with ventricular arrhythmias (P value; Table 1).

The baseline value of regional myocardial blood flow was 115.4 ± 5.4 ml/100 g/min in all groups (Fig. 2). In group C, the regional MBF decreased rapidly at coronary occlusion to 80.6 ± 5.5 ml/100 g/min, and increased rapidly after the establishment of CAPS perfusion to 140.1 ± 8.4 ml/100 g/min. Then, it decreased slightly and maintained a stable level of 118.2 ± 5.2 ml/100 g/min during CAPS perfusion. In group O, the regional MBF decreased rapidly at coronary occlusion to 72.5 ± 6.9 ml/100 g/min, which was similar to that in group C. However, these decreases continued down to 36.1 ± 13.3 ml/100 g/min just before the occurrence of ventricular arrhythmias and 58 ml/100 g/min in a pig without ventricular arrhythmias. Repeated ANOVA showed that the level of regional MBF in group C was significantly higher than that in group C (P<0.001).

The baseline value of myocardial SO2 was 75.3 ± 2.1% in all groups (Fig. 3). In group C, the regional SO2 decreased rapidly at coronary occlusion to 65.3 ± 2.1%, and increased rapidly after the establishment of CAPS perfusion to 83.3 ± 2.2%. Then, it decreased slightly and maintained a stable level of 79.3 ± 3% during CAPS perfusion. In group O, the regional SO2 decreased rapidly at coronary occlusion to 63.4 ± 2.9% which was similar to that in group C. However, these decreases continued down to 49.7 ± 1.4% just before the occurrence of ventricular arrhythmias and 53% in a pig without ventricular arrhythmias. Repeated ANOVA showed that the level of regional SO2 in group C was significantly higher than that in group O (P<0.001).

The change in myocardial Hb concentration was similar to that of the regional MBF and myocardial SO2 (Fig. 3). The baseline value of myocardial tissue Hb was 586 ± 19 g/L mm in all groups. In group C, the regional Hb decreased

![Fig. 2. Changes in the myocardial blood flow of pigs. MBF, myocardial blood flow; VT, ventricular tachycardia; VF, ventricular fibrillation.](image-url)
rapidly at coronary occlusion to 425 ± 48 g/L mm, and increased rapidly after the establishment of CAPS perfusion to 704 ± 44 g/L mm. Then, it decreased slightly and maintained a stable level of 601 ± 35 g/L mm during CAPS perfusion. In group O, the regional Hb decreased rapidly at coronary occlusion to 395 ± 31 g/L mm, similar to that in group C. However, these decreases continued down to 297 ± 25 g/L mm just before the occurrence of ventricular arrhythmias and 350 g/L mm in a pig without ventricular arrhythmias. Repeated ANOVA showed that the level of myocardial Hb in group C was significantly higher than that in group O (P < 0.001).

4. Discussion

The major findings of this study were as follows. (1) Using CAPS, hemodynamic deterioration and occurrence of ventricular arrhythmias were prevented during coronary occlusion. (2) The cardioprotective effect of CAPS could be confirmed regarding regional MBF using a thermal diffusion tissue blood flowmeter and myocardial oxygenation using NIRS.

The CAPS ejects arterial blood using a computer-controlled syringe pump system. CAPS supplies coronary perfusion up to approximately 50 ml/min by changing the stroke setting under any condition, including heart rate and systemic blood pressure. The blood transmission tube of the CAPS circuit has elasticity similar to human arterial walls, making it possible to obtain physiologic blood flow and to absorb extremely high pressure. The CAPS cannula has flexibility, to prevent direct coronary artery endothelial injury due to insertion, to prevent backbleeding from the arteriotomy site, and to support anastomosis handling. The tip of the CAPS cannula can be selected from 1.25 to 2.0 mm, and backbleeding can be almost completely prevented by selecting a suitable size of the tip when the CAPS is driven at 0.1 ml/stroke and at the early diastolic perfusion timing setting applied in this study. The blood removal cannula is inserted into the femoral artery, and not into the aorta, to avoid the manipulation of the aorta with the aim of decreasing the risk of stroke, which may occur due to dislodgment of aortic debris. Thus, the CAPS was designed to perform OPCAB safely, and the CAPS was already used in over 150 cases of clinical OPCAB and no complications resulting from CAPS have been observed in Kanazawa University Hospital.

Guyton et al. emphasized the unreliability of passive flow systems such as aorto-graft shunt [11]. They described passive flow systems which necessarily deliver blood at pressures below systemic levels, and if the heart begins to fail, these passive flow systems will participate in a vicious spiral of progressive perfusion failure and progressive pump failure. They developed the perfusion-assisted direct coronary artery bypass (PADCAB) to achieve active coronary perfusion in OPCAB [11]. They also demonstrated excellent results from clinical OPCAB using the PADCAB system: however, it perfused arterial blood through anastomosed grafts, and could not solve the problem of myocardial ischemia during anastomosis. The CAPS is the first apparatus to achieve active coronary perfusion during anastomosis in OPCAB.

In this study, regional MBF could be evaluated continuously during CAPS perfusion and simple coronary occlusion using a thermal diffusion tissue blood flowmeter. Earlier, there was no method to measure real-time MBF, and we demonstrated the validity of the thermal diffusion method for measuring real-time MBF in a previous study [8]. This simple method is not a new technique, and it has been applied to the brain and many organs [6,7]. However, it has not been applied to the myocardium and the previous study is the first report on the thermal diffusion method applied for MBF measurement [8].
The regional MBF in group C showed a temporary decrease just after coronary occlusion, followed by a subsequent increase just after the establishment of CAPS perfusion, and reached a stable level as the baseline value. The ejected blood from CAPS was approximately 15 ml/min under 0.1 ml stroke as used in this study. It seemed to be a small amount of blood compared with other similar investigations with non-pulsatile coronary perfusion models [12,13], although the hemodynamics and regional MBF were maintained under CAPS perfusion. This result may be due to the characteristic of the CAPS in that it perfused blood to the coronary artery only in the diastolic phase. Essentially, the coronary blood flow pattern is dominant in the diastolic phase because cardiac contraction squeezes the myocardial vessels [14], and the blood perfused in the systolic phase is probably not perfused effectively. We believed that the selective perfusion in the diastolic phase required a lesser amount of blood than non-pulsatile perfusion to maintain the regional MBF and hemodynamics.

The present study demonstrated that ventricular arrhythmias occurred in 88% of pigs with simple occlusion of the left anterior descending coronary artery. Gross described that the right coronary artery and left anterior descending artery are almost equal and the left circumflex plays a minor role in pigs [15]. When the blood supply to one of the major arteries is interrupted acutely in pigs, the collateral anastomosis systems are generally not adequate in preventing necrosis or/and focal ventricular arrhythmias. Thus, a pig heart may easily suffer ventricular arrhythmias by coronary occlusion. However, the CAPS prevents ventricular arrhythmias and hemodynamic deterioration in left anterior descending coronary artery occluded pigs.

NIRS is a sensitive and valuable method for monitoring tissue oxygen metabolism. Parsons et al. investigated myocardial oxygenation in dogs during coronary artery occlusion using NIRS in detail [10]. They demonstrated that complete occlusion of the left anterior descending coronary artery produced an approximately 21% decrease in tissue \( \text{O}_2 \) levels and approximately 25% decrease in myocardial blood flow. This result corresponded with the present study wherein the deterioration in myocardial oxygen metabolism could be sensitively detected by NIRS. Myocardial \( \text{SO}_2 \) and myocardial \( \text{Hb} \) in group C were well maintained, similar to the regional MBF in this study. It suggested that both myocardial oxygen metabolism and tissue blood flow could be well maintained during coronary occlusion using CAPS.

In conclusion, hemodynamic deterioration and the occurrence of ventricular arrhythmias during coronary occlusion were prevented using CAPS. Continuous monitoring of the regional MBF using a thermal diffusion tissue blood flow-meter and myocardial oxygenation using NIRS were applied in this study, and these were well maintained during coronary occlusion using CAPS. CAPS is a reliable method to avoid myocardial ischemia during coronary occlusion and it may be a useful cardioprotective method in OPCAB. However, clinical advantages of the CAPS should be studied in further investigations.

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References