Comparison of active and passive coronary perfusion in off-pump coronary artery bypass grafting

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Received 14 April 2008; received in revised form 25 August 2008; accepted 27 August 2008

1. Introduction

To prevent regional myocardial ischemia during distal anastomosis of off-pump coronary artery bypass grafting (CABG) internal and external shunt tubes have been developed [1, 2]. However, the perfusion volume is subject to systemic blood pressure, characteristics of the perfusion tubes, and coronary vascular resistance. The perfusion volume of an internal shunt tube strongly depends on the degree of proximal coronary stenosis and is reduced at low blood pressure [3].

To overcome this disadvantage, active coronary perfusion has been proposed, since it is independent of systemic blood pressure, provides sufficient distal coronary perfusion and has myocardial protective effects [3–9].

Nevertheless, in the real world some surgeons achieved the distal anastomosis during only simple clamp with excellent result, where others used the passive coronary perfusion such as an internal shunt tube. A few cardiac surgeons utilized the active coronary perfusion [6–9]. It is unproven which perfusion is the most preferable maneuver for off-pump CABG and a direct comparison of myocardial protection using active and passive coronary perfusion in a coronary stenosis model has not been performed. Therefore, we produced coronary stenosis model and compared the performance of passive and active perfusion with regard to prevention of regional myocardial ischemia.

2. Materials and methods

Adult dogs (mean body weight: 19.7 ± 1.7 kg) were used in the study. After intravenous induction of anesthesia with pentobarbital sodium (20 ml/kg), anesthesia was maintained with continuous infusion of pentobarbital sodium (6.0 µg/kg/min) and suxamethonium chloride (3.0 µg/kg/min). Animals were mechanically ventilated to maintain PaO$_2$ of ≥100 mmHg, PaCO$_2$ of 30–40 mmHg, and pH of 7.35–7.45. An arterial pressure line was inserted into the femoral artery (FA) and a 12-Fr cannula (Fem-Flex II, Edwards Lifesciences Research Medical, Midvale, UT, USA) was indwelled in the contralateral FA of animals receiving active perfusion to establish an inflow for the active coronary perfusion circuit. A thoracotomy was performed via the fifth intercostal space and heparin (150 U/kg) was administered intravenously; active clotting time was maintained at ≥300 s. A pressure transducer (SPC-320, Millar Instruments, Houston, TX) was positioned from the left...
ventricular apex to the left ventricle to measure the left ventricular pressure continuously.

To prepare a left anterior descending (LAD) coronary artery stenosis model, the LAD was temporarily blocked at the proximal site by a snare and arteriotomy was performed. To confirm that the LAD inner diameter was ≥2.0 mm, a 2.0-mm coronary metal probe was inserted into the LAD, and then an internal shunt tube with a 0.5-mm inner diameter (IVS1512; Edwards Lifesciences Research Medical, Midvale, UT, USA) was positioned to produce a 75% coronary stenosis model. Next, to make a pseudo-anastomosis on the distal side, two silicon tapes (Vesseloops, Argon Medical Devices, TX, USA) for snaring were placed around the LAD between the first and second diagonal branches. To collect venous blood selectively from the LAD perfusion area, a 24-G catheter (Peripheral Intra-vascular Catheter, Terumo, Tokyo, Japan) was positioned in the anterior interventricular vein (AIV). To determine regional myocardial blood flow (RMBF) continuously in the LAD perfusion area using a thermal gradient blood flow-meter (BTG-221; Biomedical Science Ltd., Kanazawa, Japan), a monitor probe was directly sutured and fixed on the myocardial surface. Animals were treated in accordance with the ‘Principles for Care of Laboratory Animals’ of 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 Institutes of Health (NIH Publication No. 86-23, revised 1985).

An outline of the experiments is shown in Fig. 1. LAD stenosis models were prepared in 10 adult dogs, as described above. Animals were randomly assigned to one of two groups: passive to active perfusion and active to passive perfusion groups. Distal coronary perfusion was conducted for 10 min under conditions of normal and low blood pressure. The low blood pressure was maintained as 50% of normal blood pressure by inferior vena cava (IVC) snaring. Passive perfusion was conducted by LAD incision at the anastomosis site and insertion of an internal shunt tube with a 2.0-mm outer diameter (IVS2012; Edwards Lifesciences Research Medical, Midvale, UT, USA). Active perfusion was conducted by insertion of an external shunt tube with a tip of 1.7 mm in outer diameter (Coronary perfusion catheter; Sumitomo Bakelite Co., Ltd., Tokyo, Japan). Bleeding during tube placement was prevented with a rubber snare. Active perfusion was performed continuously using a computer-controlled servo pump (Myocardial Protection System; Quest Medical Inc, Allen, TX, USA) with the FA used for inflow. Perfusion pressure can be specified using this pump and we chose a value corresponding to normal systolic blood pressure. The volume of active perfusion was measured continuously using an electromagnetic blood flowmeter (MFV-3100; Nihon Kohden, Tokyo, Japan).

Data were collected during active and passive perfusion at normal and low blood pressure. These data included hemodynamic indices (systemic blood pressure, left ventricular pressure, heart rate and first derivative of the left ventricular pressure (dP/dt)) and RMBF in the LAD perfusion area. Blood was sampled from the FA and AIV, and arterial and venous oxygen saturation (SaO2) and blood lactate concentrations were determined. Hemodynamic data were digitized using a videographics program (LEG 1000; Nihon Kohden, Tokyo, Japan), processed by a computer algorithm, and analogized. Regional myocardial lactate extraction was calculated by dividing the difference between the arterial and venous lactate concentrations by the arterial lactate concentration. Similarly, regional oxygen extraction was calculated by dividing the difference between arterial and venous SaO2 by arterial SaO2.

Data are expressed as means ± standard error. Continuous data were compared by t-test and ANOVA between active and passive perfusion, at a significance level of P < 0.01.

3. Results

In the model of proximal LAD stenosis, regional myocardial blood flow in the perfusion area after stenosis decreased to 44.7% of that before generation of stenosis (Table 1). Data measured after stenosis were regarded as baseline values and were compared between passive and active perfusion.

Hemodynamic data are shown in Table 2. With passive perfusion at normal blood pressure, heart rate significantly increased, and dP/dt significantly decreased. At low blood pressure, heart rate increased further, dP/dt decreased further, and left ventricular systolic pressure (LVSP) and left ventricular end-diastolic pressure (LVEDP) decreased. In contrast, with active perfusion all indices showed no significant changes at normal blood pressure, except for a significant decrease in heart rate. At low blood pressure, LVSP, LVEDP and dP/dt decreased significantly and heart rate increased significantly.

RMBF values for each group are shown in Table 3. With passive perfusion, RMBF decreased to 60% of the baseline value at normal and to 43% at low blood pressure. In contrast, with active perfusion, RMBF was significantly higher than the baseline value regardless of the systemic
75% coronary stenosis

Table 1
RMBF in the model with 75% coronary stenosis

<table>
<thead>
<tr>
<th></th>
<th>No coronary stenosis (n=10)</th>
<th>75% coronary stenosis (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMBF (ml/min/100 g)</td>
<td>125.3 ± 7.5</td>
<td>53.6 ± 5.8</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

RMBF, regional myocardial blood flow.

Table 2
Hemodynamic data

<table>
<thead>
<tr>
<th></th>
<th>75% Stenosis model</th>
<th>Group P</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotension</td>
<td>Hypotension</td>
<td>Normotension</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>119.5 ± 8.0</td>
<td>132 ± 11.0</td>
<td>155 ± 9.0</td>
</tr>
<tr>
<td></td>
<td>(P=0.03)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>LVSP (mmHg)</td>
<td>103.9 ± 4.3</td>
<td>93.6 ± 3.7</td>
<td>51.7 ± 1.8</td>
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<tr>
<td></td>
<td>(P=0.014)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>LVEDP (mmHg)</td>
<td>5.4 ± 0.8</td>
<td>5.4 ± 1.2</td>
<td>2.0 ± 0.7</td>
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<tr>
<td></td>
<td>(P=0.42)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
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<td>DBP (mmHg)</td>
<td>72.9 ± 4.3</td>
<td>63.1 ± 4.6</td>
<td>24.2 ± 1.7</td>
</tr>
<tr>
<td></td>
<td>(P=0.11)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>dP/dt (mmHg/s)</td>
<td>1297.2 ± 85.0</td>
<td>949.2 ± 64.1</td>
<td>597.8 ± 47.4</td>
</tr>
<tr>
<td></td>
<td>(P&lt;0.01)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
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<tr>
<td>dP/dt (−mmHg/s)</td>
<td>−1184.6 ± 78.2</td>
<td>−934.4 ± 72.6</td>
<td>−469.3 ± 40.1</td>
</tr>
<tr>
<td></td>
<td>(P&lt;0.01)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
</tr>
</tbody>
</table>

HR, heart rate; LVSP, left ventricular systolic pressure; LVEDP, left ventricular end-diastolic pressure; DBP, diastolic blood pressure; dP/dt, first derivative of left ventricular pressure.

*P-value vs. 75% stenosis model.

*P-value vs. normotension in the same series.

Table 3
RMBF, O₂ extraction and lactate extraction

<table>
<thead>
<tr>
<th></th>
<th>75% Stenosis model</th>
<th>Group P</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotension</td>
<td>Hypotension</td>
<td>Normotension</td>
</tr>
<tr>
<td>RMBF (ml/min/100 g)</td>
<td>53.6 ± 5.8</td>
<td>33.4 ± 3.9</td>
<td>20.9 ± 4.1</td>
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<tr>
<td></td>
<td>(P&lt;0.01)</td>
<td>(P&lt;0.01, P&lt;0.02)</td>
<td>(P&lt;0.01)</td>
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<tr>
<td>O₂ extraction (%)</td>
<td>51.3 ± 2.1</td>
<td>67.0 ± 2.5</td>
<td>72.1 ± 4.1</td>
</tr>
<tr>
<td></td>
<td>(P&lt;0.01)</td>
<td>(P&lt;0.01, P&lt;0.01)</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>Lactate extraction (%)</td>
<td>17.1 ± 8.8</td>
<td>−21.7 ± 16.6</td>
<td>−23.6 ± 10.5</td>
</tr>
<tr>
<td></td>
<td>(P&lt;0.02)</td>
<td>(P&lt;0.04, P&lt;0.01)</td>
<td>(P&lt;0.12)</td>
</tr>
</tbody>
</table>

RMBF, regional myocardial blood flow.

*P-value vs. 75% stenosis model.

*P-value vs. normotension in the same series.

blood pressure, indicating equivalent blood flow to that before LAD stenosis.

Myocardial oxygen and lactate extraction in the perfusion area are shown in Table 3. With passive perfusion, oxygen extraction significantly increased at normal and low blood pressure, with no significant difference between the two conditions. Lactate extraction was significantly lower at normal and low blood pressure and had a negative value. However, no difference in systemic blood pressure was observed. With active perfusion, oxygen extraction decreased significantly regardless of the blood pressure and there was no change in systemic blood pressure. There was also no significant change in lactate extraction between normal and low blood pressure and positive values were obtained.

4. Discussion

The results of the present study showed that an internal shunt tube placed in a moderate (75% and more) stenosis model at normal systemic blood pressure induced regional myocardial ischemia, which further aggravated at low blood pressure.

Kamiya et al. [10, 11] reported that real-time RMBF can be measured by application of a thermal gradient technique: in a study in pigs the RMBF decreased to approximately 30% with placement of an internal shunt tube at normal blood pressure. Muraki et al. [3] reported similar results using a microsphere method. In the present study, RMBF in the 75% coronary stenosis model decreased to approximately 40% of that of an animal without coronary stenosis, showing good agreement with previous reports.

Muraki et al. also indicated that insertion of an internal shunt tube induced regional myocardial ischemia only at low blood pressure in an animal model with a normal coronary artery. However, in the current study, coronary blood flow with a moderate stenosis at a proximal site was further reduced due to insertion of an internal shunt tube, even at normal blood pressure, and resulted in myocardial...
ischemia. Our data supported that regional myocardial ischemia cannot be excluded completely even when systemic blood pressure is within normal limit and internal shunt tube is used.

We note that a decrease in coronary blood flow does not indicate myocardial ischemia directly, since this condition is defined by a failure to meet the oxygen requirement and should be evaluated by indices including lactate generation.

In the current study, passive perfusion caused RMBF (regional oxygen supply) to decrease to approximately 62% of baseline in the LAD stenosis model at normal blood pressure. The oxygen requirement was reduced by decreases in dP/dt and left ventricular systolic performance, but phenomena inducing an increase in oxygen requirement (including an accelerated heart rate) occurred simultaneously. Therefore, in total, oxygen extraction showed a relative increase (oxygen extraction has a high correlation with myocardial oxygen consumption) and the oxygen requirement exceeded oxygen supply. This resulted in myocardial ischemia, which was confirmed by lactate production.

At low blood pressure, RMBF decreased further to approximately 25% of the baseline level, but there was no significant difference in lactate production between normal and low blood pressure. The decrease in blood pressure due to preload reduction by IVC snaring, with a concurrent decrease in myocardial workload, caused a decreased requirement for myocardial oxygen and smaller changes in lactate and oxygen extraction.

Active coronary perfusion was not involved in left ventricular preload or postload and showed no correlation with an increase in oxygen extraction or lactate production. With the perfusion pressure maintained at a level equal to normal systolic blood pressure, blood flow was between approximately 15 and 30 ml/min. Coronary active perfusion system produced by Kamiya et al. [12] prevented ischemia at a relatively low perfusion volume of approximately 15 ml/min. Further studies are required to establish the optimal perfusion pressure and volume for clinical prevention of myocardial ischemia.

The limitation in the current study is that the acute myocardial ischemia model was prepared in normal heart, and this model is different from chronic angina that is common in practice. Collateral blood flow often develops in patients with chronic angina accompanied by severe coronary artery stenosis lesion, and therefore the imbalance of oxygen supply and demand observed in our model may not be induced by blockage of the coronary artery.

We do not insist that the active coronary perfusion is required for all OPCAB cases. In the current period, marked improvements in techniques and devices have made most off-pump CABG extremely safe. However, although there is few numbers of conversions from off-pump to on-pump CABG, the major reason is still related to hypotension and ischemia [13, 14]. Active perfusion eliminate this, and might be useful in resuscitating patients whose hemodynamic are unstable due to ischemia.

Moreover, one of the unsolved problems of current OPCAB is that techniques to predict the myocardial ischemia in real time are not available. The only measure to detect the regional ischemia is to collect blood sample directly from the vessels of heart to measure lactate concentration. The active coronary perfusion should be limited when the perfusion pressure decreased to low levels. However, we cannot determine in real time whether the regional myocardial ischemia occurs in the target myocardium or how is the extent of ischemia during the distal anastomosis. We believe that it is necessary to take a measure like the active coronary perfusion in selective patients to accomplish OPCAB as safely as possible.

References


