Coronary Vascular Reserve and Regional Myocardial Contractile force

With Special Reference to Myocardial Metabolism

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SUMMARY

The relations among coronary vascular reserve, regional myocardial contractile force and myocardial metabolism were investigated in anesthetized dogs under open-chest condition. The reactive hyperemia response was examined during stepwise occlusion of circumflex artery. A change in percent repayment was used as an index of the coronary vascular reserve. Contractile force was measured with strain gauge arches sutured to ischemic and nonischemic areas of the left ventricle. The nonischemic muscle contractile force (NIMCF) increased or showed no significant change with the reduction of repayment by stepwise constriction of circumflex artery. The ischemic muscle contractile force (IMCF) began to decrease markedly following reduction of repayment below 50%. NIMCF was found to be slightly decreased by the severe reduction of coronary blood flow (CBF) in ischemic region. Thus there was a low ($r=0.39$) correlation between NIMCF and CBF in ischemic region. However, the correlation between IMCF and CBF in ischemic region was relatively high ($r=0.68$).

The arterial and coronary sinus blood samples were obtained for the determination of oxygen content, lactate and potassium concentrations. In the range of constriction without reduction of CBF, IMCF decreased significantly following reduction of repayment below 50%, but O_2 , lactate and potassium extraction ratios were not significantly different. Application of further constriction revealed significant reductions of CBF, stroke volume, aortic pressure, IMCF and lactate extraction ratios, and it also revealed significant elevation of O_2 extraction ratio.

The above observation suggests that a reduction of coronary vascular reserve might affect regional contractile force without change in CBF, and reduction of CBF could decrease regional and global left ventricular performance with changes in myocardial metabolism.

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IN recent years much effort has been directed toward defining the mechanical and metabolic consequences of myocardial ischemia. It was already reported in the experimental study with the heart in situ that reductions in coronary blood flow resulted in decreases in the contractile force of the ischemic muscle.^{1),2)} Resting coronary blood flow does not decrease until coronary arterial diameter is reduced by 85%. However, maximal coronary blood flow or coronary vascular reserve begins to decrease with stenosis of 30 to 45% of arterial diameter.³⁾ At present somewhat less is known about relation between coronary vascular reserve and regional myocardial contractile force. This study was designed to investigate the effect of reduction of coronary vascular reserve in several grades of stenosis with or without reduction of coronary blood flow upon the ischemic and non-ischemic myocardial contractile force with special reference to the myocardial metabolism.

METHODS

Twelve mongrel dogs of either sex were anesthetized intravenously with sodium pentobarbital (30 mg/Kg). After endotracheal intubation, respiration was controlled with a Harvard pump respirator supplying mixture of room air and 100% O₂ at 1 L/min. The chest was opened in the fifth left interspace and the heart was exposed. The left circumflex coronary artery was dissected and a silk suture was passed under the artery, and its end was loosely retained for subsequent constriction of the artery (Fig. 1). For intermittent occlusions, another snare was placed loosely around circumflex artery proximal to the suture. A square wave electromagnetic flowmeter (Nihon Kohden) was used for measurement of circumflex and aortic blood flows. Ascending aortic pressure was measured by a catheter advanced through the femoral artery. The coronary sinus was catheterized through the jugular vein to obtain coronary sinus blood. Contractile force was measured with strain gauge arches sutured to the apex (non-ischemic area) and the lateral wall (ischemic area) of the left ventricle. Great care was taken to fix the arch in the direction of superficial muscle fasciculi with the segment of myocardium beneath the arch stretched by 20 to 30% of its resting length. Contractile force was calculated by subtracting the resting tension from the peak systolic tension and expressed as a percent change of control value. Left atrial pressure was maintained constant by connecting the reservoir to the left atrium. The arterial and coronary sinus blood samples were obtained for determination of oxygen content, lactate and potassium (K) concentrations. The measurement of oxygen content was done by a fuel cell analyser (The 'Lex-O₂-Con').⁴⁾ Lactate was analysed with the use of spectrophotometer (Hitachi Perkin-Elmer UV-VIS 102) by the method of Horst.⁵⁾ Potassium was analysed with the use of atomic absorption spectrophotometer (Perkin-Elmer).⁶⁾ Oxygen, lactate and potassium extraction ratios were cal-

Fig. 1. Diagram of the preparation.

Fig. 2. Tracing obtained from a dog in the control state. P_{AO} =aortic pressure; AO.F.=aortic blood flow; C.B.F.=circumflex coronary blood flow; P_{LA} =left atrial pressure; IMCF=ischemic myocardial contractile force; NIMCF=nonischemic myocardial contractile force; occl.=10 sec occlusion of circumflex artery.

culated as the ratio of the arteriovenous difference to the arterial concentration of each substance.

After the dog's heart rate and aortic pressure became stable, hemodynamic data were recorded on a multi-channel pen-writing recorder (Fig. 2), and blood for chemical analysis was obtained. A continuous hemodynamic recording was obtained before and during coronary occlusion for 10 sec, and after the release of occlusion in each degree of coronary obstruction. At a minimum of 3 min after the coronary occlusion for 10 sec, when the coronary flow returned to the preocclusion level, the degree of coronary constriction was increased. Percent repayment of the flow debt was calculated as described by Coffman and Gregg⁷⁾ and used as an index of the coronary vascular reserve.

RESULTS

Fig. 3 showed a representative experiment in which reactive hyperemia

Fig. 3. Representative experiment showing effects of stepwise constriction of circumflex artery upon various parameters including myocardial metabolism. O₂ Extr. R.=oxygen extraction ratio; Lac. Extr. R.=lactate extraction ratio; K Extr. R.=potassium extraction ratio.

was examined in 4 degrees of coronary stenosis including control state. There was a progressive reduction in percent repayment from 113 in the first occlusion to 89 in the second, to 71 in the third and to zero in the fourth run. There were no significant changes in preocclusion coronary blood flow (CBF), aortic (Ao), and left atrial (LA) pressures and Ao flow. Ao pressure decreased slightly during the occlusion, but it increased immediately after the release of occlusion and rose above preocclusion levels, then gradually returned to control levels. LA pressure was maintained at constant levels. Coronary occlusion for 10 sec caused reduction in the ischemic muscle contractile force (IMCF). Prior to production of severe coronary stenosis, IMCF increased above preocclusion levels for a while after release of occlusion and then returned to preocclusion levels. But the time from the release of occlusion to maximum contractile force was prolonged at severe coronary stenosis. After coronary occlusion for 10 sec the non-ischemic muscle contractile force (NIMCF) increased immediately. When the occlusion was released, there was an immediate decrease in NIMCF. In this dog the coronary sinus oxygen content ($CS\ O_2$) was already reduced before stepwise coronary constriction, and O_2 extraction ratio (O_2 Extr. R.) was at the maximum before stepwise constriction. Lactate extraction ratio (Lac. Extr. R.) was reduced after production of severe coronary stenosis. The progressive reduction in K extraction ratio (K Extr. R.) was showed during stepwise constriction.

1) Relationship among coronary vascular reserve, coronary blood flow and regional myocardial contractile force.

NIMCF and IMCF were plotted against percent repayment in Fig. 4. Data of NIMCF were obtained from 6 dogs and that of IMCF from 8 out of 12 dogs. The other cases were eliminated in this Figure because tracings available for further analysis could not be obtained from them. NIMCF increased or showed no significant change with the reduction of repayment by stepwise constriction of circumflex coronary artery. IMCF began to decrease following reduction of repayment below 100% in some cases and it decreased significantly following reduction of repayment below 50% in all but 2 cases.

Fig. 5 illustrated the relationship between NIMCF and circumflex coronary blood flow and the relationship between IMCF and circumflex coronary blood flow. Circumflex coronary blood flow (CBF in ischemic region) was expressed as a percent change to control which was taken as 100%, because there was an individual difference in CBF. NIMCF was slightly decreased by the severe reduction of CBF in ischemic region, but Ao pressure, that was coronary perfusion pressure to the non-ischemic region, was also lowered in such cases. The correlation between NIMCF and CBF in ischemic region was low ($r=0.39$, $p<0.02$). Stepwise reduction in CBF in ischemic region

Fig. 4. Relationship between percent repayment and regional myocardial contractile force. Contractile force was expressed as a percent change from control which was taken as 100%. Open circles represented control data.

Fig. 5. Relationship between coronary blood flow in ischemic region and regional myocardial contractile force. Regression line was plotted by least square method.

caused IMCF to diminish gradually in a similar direction. A regression analysis revealed that the correlation between these 2 parameters was relatively high ($r=0.68$, $p<0.001$).

Recognizing the limitation of applying coronary sinus blood as being representative of the coronary venous blood which perfused only ischemic area, we used the product of circumflex coronary blood flow and the corresponding arteriovenous oxygen difference as a substitute for myocardial oxygen consumption of the ischemic region ($M\dot{V}O_2$). The correlation between IMCF and $M\dot{V}O_2$ was not high ($n=45$, $r=0.45$, $p<0.01$).

2) Effect of reduction of coronary vascular reserve upon coronary blood flow, myocardial contractile force, and metabolism.

The coronary vascular reserve consumption was divided into 3 grades. Grade I: percent repayment $\geq 50\%$, CBF unchanged. Grade II: percent repayment $< 50\%$, CBF unchanged. Grade III: percent repayment $= 0$, CBF decreased. Grade II was subdivided into 2. Grade IIa: percent repayment > 0 , Grade IIb: percent repayment $= 0$.

In 4 dogs, several grades of stenosis produced both Grade I and II consumption in each case, and the effects of consumption of coronary vascular reserve without decrease in CBF upon myocardial contractile force and metabolism were compared between these 2 grades (Fig. 6). There was no significant difference in CBF between Grade I and II, 66.1 and 65.8 ml/min, in average, respectively. IMCF in Grade II (87.3% in average) was sig-

Fig. 6. Effect of reduction of coronary vascular reserve upon coronary blood flow, IMCF and myocardial metabolism. Grade I vs. II.

Fig. 7. Effect of reduction of coronary vascular reserve upon coronary blood flow, IMCF, and myocardial metabolism. Grade IIa vs. IIb and III.

nificantly lower than that in Grade I (97.2% in average). Concerning the myocardial metabolism, O₂, lactate and K Extr. R. were not significantly different between these 2 grades.

In 6 dogs, Grade IIa and IIb and/or III were produced in each case. Grade IIa was compared to Grade IIb and III (Fig. 7). There was a significant difference in CBF between Grade IIa and Grade IIb and III, 63.0 and 25.8 ml/min, in average, respectively. IMCF in Grade IIb and III (62.3% in average) was significantly lower than those in Grade IIa (96.0% in average). O₂ Extr. R. in Grade IIb and III (90.1% in average) was significantly higher than that in Grade IIa (76.5% in average). However, lactate and K Extr. R. were not significantly different between these 2 grades.

As shown in Fig. 3, time to maximum contractile force was often prolonged at severe coronary stenosis. It was significantly ($p < 0.05$) prolonged in Grade II and III (34.4 ± 34.7 sec) than that in Grade I (13.5 ± 8.3 sec).

3) The changes in myocardial metabolism vs. regional myocardial contractile force.

The effect of change in myocardial metabolism upon IMCF was examined (Table I). IMCF in those with O₂ Extr. R. more than 85% was significantly lower than those below 85%. IMCF in those with Lac. Extr. R. less than 20% was also significantly lower than those above 20%. However, there was no significant difference in IMCF between those with and without K extraction.

Table I. Effect of the Changes in Myocardial Metabolism upon Ischemic Myocardial Contractile Force

Group				IMCF (%)
A	O ₂	Extr. R.	<85%	99.8+9.1
B			≧85%	81.7±28.8
C	Lac.	Extr. R.	<20%	83.6±24.2
D			≧20%	97.5±19.8
E	K	Extr. R.	≧ 0%	83.7±29.9
F			> 0%	94.2±16.3
P				<0.01
C : D				<0.05
E : F				N.S.

A significant, but not so high correlation was found between Lac. and K Extr. R. ($n=49$, $r=0.47$, $p<0.001$). No significant correlation was found between O₂ and Lac. Extr. R. as well as O₂ and K Extr. R.

DISCUSSION

Myocardial contractility and myocardial metabolism have been evaluated independently in the range of severe reduction of coronary blood flow. But correlation between those 2 with reference to coronary blood flow was not well known.

Regional myocardial function would be more labile than global left ventricular function in the cases with ischemic heart disease. In this study, we used strain gauge arch to get a parameter of regional myocardial function. The contractile characteristics of non-ischemic myocardium during regional coronary obstruction is controversial. Increased circulating catecholamines⁸⁾ or ischemic myocardial catechol release⁹⁾ could increase in NIMCF. Nakano¹⁰⁾ showed an increase in NIMCF by total ligation of coronary artery. Banka¹¹⁾ and Heikkila¹²⁾ reported NIMCF was not altered by coronary occlusion. Tatoes¹³⁾ and Wyatt¹⁴⁾ showed a decrease in NIMCF by the same procedure. In this experiment, we minimized the change of left ventricular diastolic volume by which measurement of isometric developed tension was affected. The force measured by strain gauge arch could represent myocardial contractility when left atrial pressure was maintained constant.¹⁵⁾

Our observation that IMCF decreased following a reduction of repayment below 50% in the range of coronary constriction without reduction of CBF could be explained from the viewpoint of intramyocardial inhomogeneity of blood flow and functional change introduced by coronary occlusion. These

assumption, however, should be tested in further investigation.

The correlation between IMCF and CBF in ischemic region was relatively high in this study. Downey,¹⁾ Daniell,²⁾ Fisher¹⁶⁾ demonstrated that contractile force was highly dependent on the coronary blood flow. However, Opie¹⁷⁾ and Bacaner¹⁸⁾ concluded that it was the rate of oxygen delivery rather than changes in coronary blood flow per se which was primarily responsible for the alteration in the contractile state. Coronary sinus blood was not the representative of the coronary venous blood which perfused only ischemic area, but it was the blood draining from areas of ischemic and non-ischemic myocardium. The correlation between IMCF and the product of circumflex CBF and the difference of corresponding arteriovenous oxygen was not so high. Possible explanation is that a decrease in the relative contribution of circumflex drainage during left circumflex artery obstruction make it difficult to interpret the correlation between these 2 parameters¹⁹⁾ or metabolic changes may be very minute for detection from the arterial and coronary sinus samplings.

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