Coronary perfusion related changes in myocardial contractile force and systolic ventricular stiffness

Toshihiro Iwamoto, Xiao-Juan Bai, and H Fred Downey

Objective: The mechanism by which changes in coronary perfusion alter myocardial oxygen consumption (MVO₂; Gregg phenomenon) is controversial. This study examined the effect of coronary perfusion on myocardial contractile force and systolic ventricular stiffness in the intact, ejecting heart. Methods: During selective perfusion of the left anterior descending coronary artery, coronary blood flow was changed with or without concurrent changes in coronary perfusion pressure in 19 α chloralose anaesthetised dogs. Regional myocardial segment length (end diastolic length; end systolic length) and developed force were measured with piezoelectric crystals and with a miniature force transducer, respectively. MVO₂ was calculated from coronary flow and arteriovenous O₂ difference. The slope of the force-length curve during ejection period (ΔF/ΔSL) was used as an index of systolic myocardial stiffness. Results: When coronary perfusion pressure was varied from 60 to 180 mm Hg (protocol 1, n = 11), maximum developed force (Fₘₐₓ), ΔF/ΔSL, and MVO₂ increased with perfusion pressure while end diastolic length, segmental shortening, and other haemodynamic variables stayed constant. When coronary blood flow was increased at constant perfusion pressure by infusion of either a low dose or a high dose adenosine (protocol 2, n = 8), Fₘₐₓ, ΔF/ΔSL, and MVO₂ increased while end diastolic length, segmental shortening, and other haemodynamic variables stayed constant. MVO₂ and ΔF/ΔSL increased more steeply with flow in protocol 1. Conclusions: (1) Increased coronary blood flow enhances myocardial contractile force, systolic ventricular stiffness, and MVO₂ in the intact, ejecting heart. (2) Coronary blood flow induced changes in myocardial contractile force and systolic ventricular stiffness, but not end diastolic length, are probably responsible for coronary blood flow related changes in MVO₂.

Cardiovascular Research 1994;28:1331-1336

Since Gregg reported coronary perfusion related changes in myocardial performance and myocardial oxygen consumption (MVO₂) in 1958,1 controversy continues about this "Gregg phenomenon" and its mechanism.2-4 The phenomenon has been observed in both working hearts5-12 and non-working hearts13-14 of different species. A possible explanation for the Gregg phenomenon is the "garden hose effect"15: increased coronary perfusion pressure distends the coronary vessels, increases myocardial fibre length, and therefore increases myocardial performance and MVO₂ by a Frank-Starling effect.16 In contrast to the original report about the garden hose hypothesis, other laboratories reported that increased coronary flow, rather than coronary perfusion pressure, is responsible for the Gregg phenomenon.5-8-12

Increased coronary perfusion (increase in flow with or without increase in pressure) has been reported to enhance ventricular performance in isovolumetric, non-ejecting preparations when peak left ventricular pressure or left ventricular dP/dt max was used as an index of contractility.6-8-10-16 However, increased coronary perfusion fails to cause increases in segmental shortening or segmental thickening in intact, ejecting hearts.17-23 Such observations led Miller et al.22 to propose that the garden hose effect is, in part, a model dependent phenomenon, evident only in the non-ejecting heart.

Increases in coronary perfusion have been shown to increase diastolic myocardial stiffness by its "erecile effect" on the coronary circulation.16-17 23-29 However, the effect of coronary perfusion on systolic ventricular stiffness remains unknown. If increased coronary perfusion pressure increases internal resistance to shortening, which would vary with systolic ventricular stiffness, this could explain why an increase in coronary perfusion would increase MVO₂, although other determinants of myocardial oxygen demand remain constant.

In the present study, we tested the effects of increased coronary blood flow with or without increased coronary perfusion pressure on myocardial mechanical properties (segment length and developed force) in intact, ejecting canine hearts. We estimated changes in systolic ventricular stiffness, and then related these observations to pressure-related changes in MVO₂.

Methods

Surgical preparation

All surgical procedures for this study were approved by the institutional animal care and use committee. Nineteen adult mongrel dogs of either sex (16.5-26.8 kg), free of clinically evident disease, were used in this study. Dogs were anaesthetised with intravenous thiamylal sodium (10 mg·kg⁻¹) and α chloralose (100 mg·kg⁻¹), a tracheostomy was performed, and the animals were mechanically ventilated with room air supplemented with oxygen. Supplemental α chloralose was given as needed to maintain stable anaesthesia. A vinyl catheter was inserted into the right femoral artery to monitor aortic pressure, and a polyethylene catheter into the right femoral vein for infusion of supplemental blood and anaesthetic. The arterial catheter was connected to a pressure transducer. A polyethylene catheter was inserted into the right femoral artery to withdraw blood to supply an extracorporeal coronary perfusion circuit. A left thoracotomy was performed in the fifth intercostal space, and the heart was suspended in a pericardial cradle. A catheter tipped manometer was placed in the left ventricle through the left atrial appendage to measure left ventricular pressure and dP/dt. A Tygon catheter was inserted into the left atrium to monitor left atrial pressure.

After piezoelectric crystals and a miniature force transducer were positioned (see below), the left anterior descending coronary artery was isolated distal to its first large diagonal branch, and a silk snare was passed around it. After administration of heparin (500 U·kg⁻¹ by guest on 25 September 2017)
A typical example of the force-length relationship. Muscle contraction occurred at point A, and the line from A to B reflects isovolumetric contraction. The line from B to C reflects ejection. The slope of line B-C ($\Delta F/\Delta SL$) was used as an index of systolic ventricular stiffness.

intravenously the coronary artery was cannulated with a stainless steel cannula (2.9 mm outside diameter, 2.2 mm inside diameter) and perfused with arterial blood from a pressurized reservoir, which was supplied with blood from the left femoral artery. To monitor coronary perfusion pressure, a saline filled PE-50 catheter was advanced to the orifice of the cannula and connected to a pressure transducer. Coronary blood flow was measured with an electromagnetic flowmeter and an inline flow transducer. Blood temperature was kept at 37-38°C by a thermostatically controlled water jacket. A PE-50 catheter was inserted into a vein draining the area perfused by the left anterior descending coronary artery for determination of regional M VO$_2$. Venous blood was allowed to drain freely into a thermostatically controlled water jacket. Blood temperature of these samples were measured with an automated blood gas analysis system. Blood oxygen content (ml O$_2$.dl$^{-1}$) was calculated as the sum of the haemoglobin bound and the dissolved oxygen. The former was measured directly by a CO oximeter and the latter was calculated as $0.003 \times P_{5O_2}$(mm Hg). M VO$_2$ of the area perfused by the left anterior descending coronary artery was calculated from the product of coronary blood flow times the regional arteriovenous oxygen difference.

Assessment of regional myocardial mechanics

Segment length and developed force were measured to assess the force-length relationship, as reported in recent studies. To measure segment length, a pair of piezoelectric crystals were implanted in the midmyocardium of the left anterior descending artery territory. They were orientated parallel to the minor axis of the heart and separated by about 10 mm. Systolic shortening ($\%$) equalled (EDL - ESL)/EDL $\times 100$, where EDL = end diastolic length and ESL = end systolic length. End diastole and end systole were defined as the beginning of the positive upstroke of the left ventricular dP/dt tracing and a point 20 ms before peak negative dP/dt, respectively.

A miniature force transducer was sutured approximately 10 mm toward the base of the heart relative to position of the crystals on the left anterior descending artery territory to record developed force. It also was orientated parallel to the minor axis, and held in place with approximately 5 mm deep 3-0 silk sutures. To maintain constant fibre length throughout the cardiac cycle, the feet of the transducer were anchored so that underlying fibres were stretched by about 38% of their resting length. Removing the transducer from the heart surface at the end of the experiment caused no change in the phasic record of segment length. This confirmed that the measurement of isometric force did not affect the measurement of segment length.

The force-length curve obtained from segment length and isometric developed force measurements was used to calculate regional internal resistance. A typical force-length loop was illustrated in the figure. Muscle contraction occurred at point A, and the line from A to B reflects isovolumetric contraction. The line from B to C reflects ejection. $\Delta F$ is the force the ventricular muscle is able to produce during the ejection period if the muscle contracts isometrically. $\Delta SL$ is the shortening of ventricular muscle during ejection. The slope of line B-C ($\Delta F/\Delta SL$) was used as an index of internal resistance, and calculated from $\Delta F$ divided by the change in segment length ($\Delta SL$) during ejection. At constant afterload, the changes in $\Delta F/\Delta SL$ reflect alterations in systolic ventricular stiffness. Although actual force generation during ejection in the shortening segment would be lower than $\Delta F$, that value would be a linear function of $\Delta F$, since the isochronal force-length relationship throughout systole for various conditions is linear. Point B was determined as a point of largest decrease in the slope of the A-C portion of the loop. Point C was defined as the point of maximum developed force. In 18 out of 19 experiments, the timing of the point C coincided with end systole, which was defined at 20 ms before peak negative dP/dt. Data at every 10 ms were plotted to construct the force-length relationship. At least three stable beats at end expiration were analysed. Variables were calculated for each beat and averaged, and $\Delta F/\Delta SL$ values were calculated from averaged $\Delta F$ and $\Delta SL$.

Experimental protocols

Protocol 1 – Pressures, coronary flow, segment length, and developed force were recorded at coronary perfusion pressures of 60, 100, 140, and 180 mm Hg. The order for recordings was randomly chosen, and at least 2 min were allowed for coronary blood flow to stabilise. Coronary arterial and venous samples were taken at the completion of each recording, and pressure was immediately changed after each recording and arteriovenous sampling.

Protocol 2 – This protocol was conducted to determine if an increase in coronary blood flow independent of an increase in coronary perfusion pressure would increase systolic stiffness. Baseline values were recorded at a perfusion pressure of 100 mm Hg (condition 1). Adenosine (0.2 mg ml$^{-1}$) was infused into the coronary perfusion line to double coronary blood flow (condition 2), and then to dilate the coronary circulation maximally (condition 3).

Statistics

Values are expressed as mean(SEM). Differences in the data between conditions were evaluated by repeated measures analysis of variance (ANOVA). The linear polynomials contrast (linear trend) was tested if a significant treatment difference was found by repeated measures ANOVA. Linear regression analysis was used to determine if the mean effects of CBF on M VO$_2$(tables II and V) and $\Delta F/\Delta SL$(tables III and VI) differed between the two protocols. Probability ($p$) values $<0.05$ were taken to indicate statistically significant differences.

Results

Protocol 1

Eleven dogs contributed to protocol 1. Systemic haemodynamic variables are summarised in table I. Heart rate, systolic and diastolic blood pressures, rate-pressure products, mean left atrial pressure and left ventricular dP/dt$_{max}$ were not affected by changes in coronary perfusion pressure in the left anterior descending artery region. These

| Table 1 Summary of systemic haemodynamic variables in protocol 1. Values are mean(SEM). |
|-------------------------------------|-----|-----|-----|-----|-----|
| Coronary perfusion pressure (mm Hg) | 60  | 100 | 140 | 180 |
| HR (beats min$^{-1}$)               | 154(9) | 154(8) | 157(8) | 156(8) |
| SBP (mm Hg)                        | 111(4) | 111(5) | 111(4) | 111(5) |
| DBP (mm Hg)                        | 90(4) | 90(5) | 91(4) | 90(5) |
| RPP (mm Hg/beat min$^{-1}$ $\times 10^{2}$) | 172(12) | 172(13) | 176(13) | 176(14) |
| LAP (mm Hg)                        | 2.70(0.4) | 2.90(0.3) | 2.80(0.4) | 2.70(0.4) |
| LV dP/dt$_{max}$ (mm Hg s$^{-1}$)   | 273(306) | 277(313) | 278(301) | 276(314) |

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; RPP = rate-pressure product; LAP = mean left atrial pressure; LV dP/dt$_{max}$ = maximum rate of left ventricular pressure development.
Coronary perfusion-related changes in myocardial oxygen consumption

Table II Summary of coronary blood flow and myocardial oxygen consumption in protocol 1. Values are mean(SEM).

<table>
<thead>
<tr>
<th>Coronary perfusion pressure (mm Hg)</th>
<th>60</th>
<th>100</th>
<th>140</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF (ml·min⁻¹·g⁻¹)</td>
<td>0.73(0.10)</td>
<td>1.07(0.15)</td>
<td>1.60(0.29)</td>
<td>2.39(0.45)</td>
</tr>
<tr>
<td>MVO₂ (ml O₂·min⁻¹·g⁻¹·× 10⁻²)</td>
<td>10.4(1.6)</td>
<td>12.2(1.7)</td>
<td>13.8(2.0)</td>
<td>16.1(2.4)</td>
</tr>
</tbody>
</table>

ANOVA Trend

- p < 0.05
- p < 0.05
- p < 0.05
- p < 0.05

CBF = coronary blood flow; MVO₂ = myocardial oxygen consumption.

Table III Summary of regional myocardial function variables in protocol 1. Values are mean(SEM).

<table>
<thead>
<tr>
<th>Coronary perfusion pressure (mm Hg)</th>
<th>60</th>
<th>100</th>
<th>140</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDL (mm)</td>
<td>9.72(0.31)</td>
<td>9.72(0.31)</td>
<td>9.71(0.29)</td>
<td>9.67(0.31)</td>
</tr>
<tr>
<td>ELS (mm)</td>
<td>8.23(0.34)</td>
<td>8.23(0.32)</td>
<td>8.17(0.33)</td>
<td>8.19(0.32)</td>
</tr>
<tr>
<td>SS (%)</td>
<td>15.5(1.5)</td>
<td>15.5(1.5)</td>
<td>16.1(1.6)</td>
<td>15.4(1.7)</td>
</tr>
<tr>
<td>ΔASL (mm)</td>
<td>0.94(0.15)</td>
<td>0.88(0.14)</td>
<td>0.89(0.14)</td>
<td>0.84(0.14)</td>
</tr>
<tr>
<td>Fₘₐₓ (g)</td>
<td>36.4(3.1)</td>
<td>43.4(4.5)</td>
<td>47.5(4.9)</td>
<td>52.0(5.2)</td>
</tr>
<tr>
<td>ΔF (g)</td>
<td>8.8(1.7)</td>
<td>12.4(2.2)</td>
<td>14.7(2.6)</td>
<td>17.4(2.9)</td>
</tr>
<tr>
<td>ΔP/ΔASL (g·mm⁻¹)</td>
<td>10.0(1.7)</td>
<td>17.0(2.4)</td>
<td>20.4(4.7)</td>
<td>27.0(6.9)</td>
</tr>
</tbody>
</table>

ANOVA Trend

- p < 0.05
- p < 0.05
- p < 0.05
- p < 0.05

EDL = end diastolic length; ELS = end systolic length; SS = segmental shortening; ΔASL = changes in segment length during ejection period; Fₘₐₓ = maximum developed force; ΔF = changes in developed during ejection period; ΔP/ΔASL = index of internal resistance.

Table IV Summary of systemic haemodynamic variables in protocol 2. Values are mean(SEM).

<table>
<thead>
<tr>
<th>Condition</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats·min⁻¹)</td>
<td>163(11)</td>
<td>163(10)</td>
<td>164(10)</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>113(7)</td>
<td>113(6)</td>
<td>114(6)</td>
<td>NS</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>91(8)</td>
<td>90(7)</td>
<td>91(7)</td>
<td>NS</td>
</tr>
<tr>
<td>RPP (mm Hg·beats·min⁻¹×10⁶)</td>
<td>188(22)</td>
<td>186(20)</td>
<td>189(19)</td>
<td>NS</td>
</tr>
<tr>
<td>LAP (mm Hg)</td>
<td>2.0(0.5)</td>
<td>2.0(0.5)</td>
<td>1.9(0.5)</td>
<td>NS</td>
</tr>
<tr>
<td>LV dP/dtₘₐₓ (mm Hg·s⁻¹)</td>
<td>250(359)</td>
<td>255(313)</td>
<td>260(325)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conditions: 1 = baseline; 2 = coronary flow was doubled by low dose adenosine; 3 = coronary flow was maximally increased by high dose adenosine.

Findings indicate that the changes in regional coronary perfusion pressure did not affect global heart function or left ventricular preload and afterload conditions.

Coronary blood flow and MVO₂ are shown in table II. There were significant differences in coronary flow by ANOVA, and a significantly increasing trend was found by the test for linear polynomial contrast. MVO₂ also increased significantly with increasing coronary perfusion pressure, reflecting the Gregg phenomenon.

Regional myocardial variables were summarised in table III. There were no significant differences in end diastolic length, end systolic length, segment shortening, and ΔASL. When coronary perfusion pressure was changed from 60 to 180 mm Hg, Fₘₐₓ increased by 43% from 36.4 to 52.0 g (p < 0.05). Similarly, ΔF was significantly increased from 8.8 to 17.4 g as perfusion pressure was raised. ΔF/ΔASL increased 2.7 times from 10.0 to 27.3 g·mm⁻¹ as perfusion pressure was changed from 60 to 180 mm Hg (p < 0.05).

Table V Summary of coronary blood flow and myocardial oxygen consumption in protocol 2. Values are mean(SEM).

<table>
<thead>
<tr>
<th>Condition</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF (ml·min⁻¹·g⁻¹)</td>
<td>0.86(0.13)</td>
<td>1.74(0.26)</td>
<td>4.17(0.72)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>MVO₂ (ml O₂·min⁻¹·g⁻¹·× 10⁻²)</td>
<td>10.5(1.9)</td>
<td>12.9(2.2)</td>
<td>16.3(3.0)</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

Conditions: 1 = baseline; 2 = coronary flow was doubled by low dose adenosine; 3 = coronary flow was maximally increased by high dose adenosine.

Protocol 2

Eight dogs contributed to protocol 2. Systemic haemodynamic variables are summarised in table IV. Heart rate, systolic blood pressure, diastolic blood pressure, rate-pressure product, mean left atrial pressure and left ventricular dP/dtₘₐₓ were not different between the conditions.

Coronary blood flow and MVO₂ are shown in table V. In conditions 2 and 3, coronary blood flow was increased twofold and fivefold, respectively, by graded infusion of adenosine, while perfusion pressure was held at 100 mm Hg. MVO₂ was increased significantly by adenosine.

Regional myocardial variables are summarised in table VI. There were no significant differences in end diastolic length, end systolic length, systolic shortening, and ΔASL. Fₘₐₓ increased from 52.3 to 56.6 g with low dose adenosine infusion, and to 61.6 g with high dose adenosine infusion. This increase in Fₘₐₓ produced by adenosine was statistically significant. ΔF was increased from 20.0 to 26.0 g by adenosine infusion (p < 0.05). ΔF/ΔASL was increased from 21.2 to 25.6 g·mm⁻¹ by low dose adenosine infusion and was further increased to 29.1 g·mm⁻¹ by high dose adenosine infusion. This increase in systolic stiffness produced by adenosine was also significant.

Both MVO₂ and ΔF/ΔASL increased significantly more steeply with coronary blood flow when flow was altered by perfusion pressure in protocol 1 than when flow was altered by adenosine infusion in protocol 2.

Discussion

In this study, we found that increases in left anterior descending coronary artery flow, with or without increases in perfusion pressure, increased regional myocardial...
Coronary hyperperfusion has been shown by a number of investigators to enhance ventricular function. Many studies reported that an increase in coronary blood flow, rather than perfusion pressure, is responsible for the Gregg phenomenon. Our findings are consistent with those reports. In the protocol 2 of the present study, we found that the increases in coronary blood flow without changes in perfusion pressure (condition 2 and 3) increased regional myocardial contractile force, systolic ventricular stiffness, and MVO<sub>2</sub>. Our laboratory recently found that increases in coronary vascular volume and MVO<sub>2</sub> induced changes in coronary perfusion pressure were greater when coronary autoregulation was poor or absent, indicating that a change in flow rather than a change in pressure is the more important factor in producing the Gregg phenomenon.

The mechanism by which contractile force increases with coronary perfusion remains to be elucidated. Kitakaze and Marban found that there were coronary perfusion induced changes in intracellular calcium transients in isolated ferret hearts, and concluded that coronary perfusion (pressure or flow) modulates intracellular calcium and consequently contractile force. In their study, perfusion-induced changes in developed pressure were found even in hearts stretched to the peak of the Frank-Starling relation, so changes in sarcomere length could not explain the observed changes in myocardial performance. Schouten et al also reported perfusion induced changes in contractile force without changes in segment length in a rat papillary muscle preparation. In the present study, changes in end diastolic and end systolic length were not detected. Furthermore, muscle length under the isometric force transducer was constant throughout the cardiac cycle. These findings support the earlier observations described above, that coronary perfusion enhances muscle contractile force independent of a Frank-Starling effect. A recent report indicated that myocardial contractility is affected by an endothelium derived upregulating factor, which is sensitive to increased coronary venous oxygen tension, and by an endothelium derived downregulating factor, which is sensitive to decreased coronary blood flow. The change in contractile force seen in the Gregg phenomenon could be explained by these endothelium derived factors, since increasing coronary flow increases venous oxygen tension.

Regarding ventricular stiffness, Salisbury et al first demonstrated increased diastolic stiffness of the left ventricular wall with increased coronary perfusion. They speculated that increased coronary perfusion increased coronary vascular volume, and this engorgement of the coronary vascular bed decreased compliance of the ventricular wall. A coronary perfusion induced increase in diastolic stiffness has been confirmed by many but not all reports. The present study showed that increases in coronary perfusion increased ventricular stiffness during systole, though we have no data about diastolic stiffness. The erectile effect of a distended coronary vasculature, as proposed by Salisbury et al, would also explain the perfusion related increase in systolic ventricular stiffness. A stiffer left ventricular wall would increase myocardial oxygen demand, since more energy must be expended to deform the ventricular wall during ejection. In addition, the heart muscle performs work on blood within the coronary circulation as blood is displaced from the microcirculation and veins during each contraction. As ventricular stiffness increases, the load on this "intramyocardial pump" would increase.

Engorgement of the coronary circulation could result from raised coronary perfusion pressure as in protocol 1, and by

<p>| Table VI Summary of regional myocardial function variables in protocol 2. Values are mean(SEM). |</p>
<table>
<thead>
<tr>
<th>Condition</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>p trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDL (mm)</td>
<td>9.5(10.50)</td>
<td>9.51(0.54)</td>
<td>9.53(0.56)</td>
<td>NS</td>
</tr>
<tr>
<td>ESL (mm)</td>
<td>8.06(0.52)</td>
<td>8.09(0.55)</td>
<td>8.13(0.58)</td>
<td>NS</td>
</tr>
<tr>
<td>SS (%)</td>
<td>15.3(2.3)</td>
<td>15.2(2.9)</td>
<td>15.0(3.9)</td>
<td>NS</td>
</tr>
<tr>
<td>ΔSL (mm)</td>
<td>1.14(0.18)</td>
<td>1.03(0.15)</td>
<td>1.02(0.15)</td>
<td>NS</td>
</tr>
<tr>
<td>F&lt;sub&gt;max&lt;/sub&gt; (g)</td>
<td>52.3(35.1)</td>
<td>56.6(5.6)</td>
<td>61.6(5.2)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ΔF (g)</td>
<td>20.0(3.2)</td>
<td>23.0(3.6)</td>
<td>26.0(3.4)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ΔF/ΔSL (g/mm)</td>
<td>21.2(5.9)</td>
<td>25.6(6.2)</td>
<td>29.1(6.1)</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

Conditions: 1 = baseline; 2 = coronary flow was doubled by low dose adenosine; 3 = coronary flow was maximally increased by high dose adenosine. EDL = end diastolic length; ESL = end systolic length; SS = segmental shortening; ΔSL = changes in segment length during ejection period; F<sub>max</sub> = maximum developed force; ΔF = changes in developed force during ejection period.
vasodilation as in protocol 2, but raised perfusion pressure would be likely to cause greater distension of the coronary vasculature than would dilatation of resistance vessels. This notion is consistent with our findings that MVo₂ and ventricular systolic stiffness increased more steeply with flow when coronary blood flow was increased by raised perfusion pressure than when it was increased by adenosine infusion. Any pressure difference between the cannulated left anterior descending coronary artery and the other arteries would induce coronary collateral flow, and inclusion of collateral flow into the measurements could lead to errors in calculation of MVo₂. Therefore, the actual increases in coronary blood flow and MVo₂ induced by coronary perfusion pressure could have been lower than the observed values in protocol 1. However, it is reasonable that the observed increases in myocardial contractile force and systolic ventricular stiffness, which increase the area of the force-length loop, would increase myocardial oxygen demand. Furthermore, significant increases in MVo₂ were also increased in protocol 2, where pressure differences producing collateral flow were negligible. Thus while an influence of collateral on values of MVo₂ reported for protocol 1 cannot be ruled out it appears that such influence would have been slight.

In conclusion, the present study showed (1) that increased coronary blood flow increases myocardial contractile force, systolic ventricular stiffness and MVo₂ in intact, ejecting hearts; (2) that changes in myocardial contractile force and systolic ventricular stiffness induced by coronary blood flow are probably responsible for coronary perfusion related changes in MVo₂; and (3) that the positive effect of flow on MVo₂ and ventricular systolic stiffness was greater when flow was increased by coronary perfusion pressure than when flow increased by adenosine mediated coronary vasodilatation.

This work was supported by National Heart, Lung, and Blood Institute grant HL 35027. The expert technical assistance of Arthur G Williams Jr and Chong-Hong He is gratefully acknowledged.

Key terms: coronary blood flow; coronary perfusion pressure; Gregg phenomenon; myocardial function; myocardial stiffness; oxygen consumption.

Received 23 December 1993; accepted 20 April 1994. Time for primary review 35 days.


