Relation Between Coronary Blood Flow and Myocardial Oxygen Consumption


A variety of factors have been considered to be of importance in influencing the oxygen consumption of the heart. Among these have been the amount of work done by the heart,\(^1\)\(^2\) the end diastolic volume or fiber length,\(^3\)\(^5\) the heart rate,\(^6\)\(^10\) the developed myocardial tension,\(^11\) and the heart rate times the mean arterial pressure.\(^12\) More recently, it has been suggested that coronary blood flow may influence myocardial oxygen consumption independently of changes in the activity of the heart.\(^13\)\(^17\) The objective of the investigation described below was to ascertain whether or not this occurs in the isolated, metabolically supported heart preparation and, if so, under which experimental circumstances.

Methods

Experiments were performed on mongrel dogs of both sexes ranging in weight from 20.0 to 27.0 kg. The animals were anesthetized with a warmed mixture of chloralose (60 mg/kg) and urethane (600 mg/kg) given intravenously. The experimental preparation employed was a modification of the isolated supported heart.\(^18\) This is shown in figure 1. A large-bore cannula was inserted into the left atrium through the appendage and then connected to a blood reservoir (RES) by way of an electrically operated inflow resistance (IR). Atrial inflow was continuously recorded using a Potter electroturbinometer (PET).\(^19\) The lower thoracic aorta was ligated and a cannula inserted proximally. Outflow from the aorta was led to the blood reservoir (RES) through a second, electrically operated, outflow resistance (OR). A cannula previously placed in the left main pulmonary artery was connected through a recording rotameter (TR) to a reservoir (TCR) supplying blood to the support dog’s (SD) jugular veins. Previously placed ligatures around the subclavian and brachiocephalic arteries, superior and inferior venae cavae, the azygos vein, the hilum of the right lung and left pulmonary veins were then rapidly ligated and the left lung removed. Following ligation of the lungs, the rotameter (TR) connected to the pulmonary artery recorded total coronary venous flow (other than left ventricular Thebesian flow). The femoral arteries of the support dog (SD) were connected to the blood reservoir (RES) through a solenoid (SOL) which was activated by a microswitch (M) connected to a float (F) in the blood reservoir so as to keep the reservoir blood level constant. An external heating coil around the blood reservoir (RES) was set to maintain blood temperature at 37 ± 0.5°C.

A Gregg coronary cannula was inserted through the left subclavian artery and aorta into the previously exposed left main coronary artery and tied securely in place. This was connected through a rotameter (LR) to another blood reservoir (LCR). This reservoir received blood from the aortic line distal to the outflow resistance (OR) by the use of a modified Dale-Schuster pump (P). The blood level in the coronary reservoir was kept constant by means of an overflow tube (OT). Left coronary perfusion pressure and flow were varied by changing the height of the coronary reservoir (LCR) or by adjusting a screw-clamp (R) between the reservoir and the cannulated left main coronary artery.

Blood was pumped by means of a roller pump (RP) from the left arterial and total coronary venous flow lines. Coronary arterial and mixed venous pH were recorded with a Beckman pH electrode (pH); coronary arteriovenous O\(_2\) difference was continuously measured by a Guyton recorder (G).\(^20\) The calibration curve for the Guyton recorder was established during each experiment by the analysis of simultaneously drawn arterial and venous samples (S\(_a\) and S\(_v\)) over the full range of observed arteriovenous O\(_2\) difference. Hematocrits ranged from 35 to 46 (avg 44).

Left ventricular pressure was measured through a short, wide-bore, Y-shaped metal cannula inserted through the apical dimple. A Statham strain gauge (Tr) was connected directly to each arm of the cannula. One transducer (Tr) recorded the full left ventricular pulse; the other recorded left ventricular pressures from 0 to 40 cm H\(_2\)O for higher resolution of ventricular end diastolic pressures. Aortic pressure was recorded through a

From the Laboratory of Cardiovascular Physiology, National Heart Institute, Bethesda, Maryland.

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cannula introduced through the right common carotid artery into the aortic arch and connected directly to a Statham strain gauge transducer. The heart was paced by a Grass impulse generator with an electrode sutured to the right atrium. Clotting was prevented by an initial dose of 5 mg/kg of heparin with an hourly dose thereafter of 10 mg to the support dog and the main blood reservoir. Whenever it was desired to obtain a determination of \( MV_{\text{O}_2} \), the total coronary flow was ascertained by timed collection into a graduated cylinder as a check on the recording rotameter (TR). Great care was taken to be certain that the recordings both of total coronary flow and the arteriovenous \( O_2 \) difference were unvarying for a minimum of two and generally three to five minutes before establishing an \( MV_{\text{O}_2} \) for that point or drawing samples for analysis. Left ventricular stroke work in gram-meters was calculated as the stroke volume in ml times mean aortic pressure in mm Hg minus LVEDP in cm Hg divided by 100. The tension time index (TTI) in mm Hg sec/min was calculated as previously described. This preparation permitted the independent control of cardiac output, mean aortic pressure, heart rate, and left main coronary flow.

The experiments described in this report were performed in the following manner. 1) Cardiac output, mean aortic pressure, and heart rate were held constant and total coronary flow was varied either by adjusting the height of the left coronary reservoir (LCR) or varying the resistance of the left coronary inflow line. 2) Aortic pressure alone was varied by changing the outflow resistance (OR). 3) Left ventricular work was varied by reciprocal adjustments of stroke volume and aortic pressure. 4) Heart rate was varied with the pacemaker.

Results

In the earlier experiments an attempt was made to examine a wide range of coronary blood flow above that level which produced grossly observable deterioration of myocardial function. The results of the nine such experiments in four isolated supported hearts are shown in figure 2. Aortic pressure, heart rate and stroke volume were constant in each experiment. In the experiment of figure 2A, coronary flow was reduced in five steps from 516 to 156 ml/min and then re-elevated in four steps to 460 ml/min. Figure 2B shows the results of three experiments in the third heart. Different combinations of aortic pressure, stroke volume, and heart rate were used but each was held constant in the course of the individual experiment. Figure 2D shows the results of varying coronary flow over a comparable range at each of two different heart rates.

The possibility was examined that if the change in coronary flow imposed was an abrupt large change instead of stepwise smaller ones, this might influence the result. Four experiments of this type were done in three preparations. Aortic pressure, stroke volume, and heart rate were held constant. In these four experiments, coronary blood flow was changed from 246 to 154, 240 to 100,
Effect of changing coronary blood flow on myocardial oxygen consumption; $AP = aortic pressure; SV = stroke volume; HR = heart rate. See text.

216 to 94, and 425 to 197; the average change in coronary flow was a decrease of 51.5%. In three experiments $O_2$ consumption ($MV_{O_2}$) fell slightly and in the fourth it rose slightly. The average change was a decrease in $MV_{O_2}$ of 4.6% after going from the high to the low flow.

The above experiments indicated that in a given heart working at a constant aortic pressure, stroke volume and heart rate, above a certain level of coronary blood flow $MV_{O_2}$ is not systematically influenced by changes in coronary blood flow.

Since it was obvious that at zero coronary blood flow, $MV_{O_2}$ would also be zero, it was at least theoretically possible that a range of coronary flow could be found within which a change in $MV_{O_2}$ would occur. Fourteen experiments in nine preparations were devoted to an examination of this possibility. The procedure used was to restrict coronary blood flow in a stepwise manner to that level which produced a rise in LVEDP. An attempt was made to produce the greatest possible restriction of coronary flow which would not result in a continuing and self-perpetuating rise in LVEDP. An attempt was made to produce the greatest possible restriction of coronary flow which would not result in a continuing and self-perpetuating rise in LVEDP. An attempt was made to produce the greatest possible restriction of coronary flow which would not result in a continuing and self-perpetuating rise in LVEDP.

In three of the fourteen such experiments attempted, when coronary flow was lowered in the manner described and LVEDP rose, the heart could not maintain the control level of aortic pressure. A fall of $MV_{O_2}$ occurred in these experiments but, since it was not possible to know whether the observed fall in $MV_{O_2}$ was a consequence of the lower aortic pressure, the decreased coronary flow, or both, these data were not considered satisfactory for analysis. In the remaining eleven experiments aortic pressure was maintained. In seven of these eleven experiments a diminution of $MV_{O_2}$ of 10% to 19% (average 14%) below the control level was observed at the lowest coronary flows. Figure 3A shows the data from one such experiment. In the remaining four experiments a decrease in $MV_{O_2}$ was not observed even though a substantial rise in LVEDP occurred when coronary flow was restricted. Figure 3B shows the data from one such experiment.

In two preparations inflow to the left atrium was stopped in order to examine the effects of changing coronary flow in a non-pumping heart. These experiments were performed more easily since a runaway rise of
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Myocardial oxygen consumption was measured using the method described by TCF = total coronary flow; A-V O₂ Diff. = coronary arteriovenous oxygen difference; myocardial qO₂ = myocardial oxygen consumption; LVEDP = left ventricular end diastolic pressure. Aortic pressure was 106/48 mm Hg; stroke volume was 4.6 ml and heart rate was 200 throughout.

LVEDP and mitral regurgitation were not complications to be feared when coronary flow was restricted. In these two hearts coronary flow was reduced in a stepwise manner from 233 ml to 82 ml and from 366 ml to 77 ml. MVO₂ was decreased by 32% and 36% respectively at the lowest coronary flows. Although the usual methods of evaluating ventricular contractility could not be used in these studies, a decrease in peak developed pressure in both, and pulsus alternans in one, were noted at the lowest coronary flow; the decrease in developed tension may have contributed to the observed decrease of MVO₂ in these experiments. These observations in the nonworking heart were consistent with the impression gained from the experiments with pumping ventricles, i.e., when coronary blood flow is reduced, a fall in MVO₂ is accompanied or preceded by evidence of deteriorating ventricular performance.

The objective of the experiments described thus far was to ascertain whether varying coronary flow influences MVO₂ when the activity of the heart remains constant. Seven experiments were then carried out in four preparations in which total coronary flow was held relatively constant (coronary reservoir at constant height) and the effect observed on MVO₂ of changing the activity of the heart by raising aortic pressure. Table 1 shows the elevations of aortic pressure and the accompanying values for total coronary flow (TCF), left coronary artery flow (LCAF), and MVO₂. Figure 4 illustrates the relation between the tension time index (TTI) and MVO₂ when aortic pressure was at each of four different levels in the same heart (experiment 2, table 1). These data indicate that when the activity of the pumping heart is increased in such a manner as to elevate the TTI, the consequent increase in MVO₂ is not contingent upon a simultaneous coronary flow increase.

In two experiments in two preparations the activity of the heart was changed radically by simultaneously lowering aortic pressure slightly and increasing cardiac output markedly in such a way as to maintain TTI relatively constant while the external work produced was markedly increased. Results from the first of these are shown in the slow speed tracing of figure 5, upper. At the low cardiac output stroke volume was 9.5 ml, stroke work 13.9 gram-meters, TTI 2000 mm Hg sec/min, and MVO₂ was 16.1 ml/min. At the high cardiac output, stroke volume was 44.1 ml, stroke work was 36.5 gram-meters, TTI 2190 mm Hg sec/min and MVO₂ was 15.8 ml/
min. High speed tracings from the second such experiment are shown in figure 5, lower. At the low cardiac output (left side of fig. 5) mean aortic pressure was 162 mm Hg, stroke volume was 6.9 ml, stroke work 14.2 gram-meters, TTI 3200 mm Hg see/min and MVₒ was 18.7 ml/min. At the high cardiac output (right side of fig. 5), mean aortic pressure was 100 mm Hg, stroke volume 33.4 ml, stroke work 39.1 gram-meters, TTI 3500 mm Hg see/min and MVₒ was 19.6 ml/min. The impression gained from these experiments was such as to confirm previous data¹¹ indicating that MVₒ is not primarily influenced by the amount of external work, per se, produced by the heart but rather by the type of work done and its influence on the amount of tension developed by the myocardium. These data also suggest that LVEDP is not the dominant factor influencing MVₒ. If it be assumed that a change in ventricular distensibility did not occur, then the further conclusion is also admissible, namely that LVED fiber length is not, of itself, the major determinant of MVₒ.

**Discussion**

The experiments described above indicate that the following generalities obtain in the isolated supported heart preparation. First, there is a wide range of coronary blood flows within which variations in flow do not systematically influence MVₒ (fig. 2). These observations were made at coronary flows above that level which produced a grossly observable deterioration of ventricular performance. Secondly, by carefully reducing coronary flow in a stepwise manner in the lower ranges, a certain reduction in MVₒ can be achieved.

**TABLE 1**

<table>
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<th>Expt.</th>
<th>AP (mmHg)</th>
<th>TCF (ml/min)</th>
<th>LCF (ml/min)</th>
<th>MVₒ (ml/min)</th>
<th>Δ%</th>
<th>Δ%</th>
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<tr>
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<td>266</td>
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<td>Average change</td>
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<td>+61.7</td>
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while the heart continues to beat at a constant rate and continues to maintain a constant aortic pressure and stroke volume (fig. 3A). This is accompanied by a deterioration of ventricular performance as evidenced by a substantial elevation of LVVEDP. A slight further reduction in coronary flow below this point results in a self-perpetuating rise in LVVEDP, grossly observable mitral regurgitation and a condition which, if not promptly corrected by an increased coronary flow, is likely to result in ventricular fibrillation.

These experiments were conducted in that manner which was thought most likely to enable the heart to achieve the maximal reduction in MVo2 obtainable in this preparation. It may be that the observed reductions of MVo2 reflect the maximal level of anaerobic metabolism achievable in this preparation but whether it was actually taking place and the extent of it will require further investigation. Lastly, it is clear that a rise in LVVEDP can be induced by restricting coronary flow in the absence of any diminution in MVo2 (fig. 3B). This is presumably due either to the diminished supply of a substrate or of substrates other than O2 or to the diminished rate of removal of metabolites. No data were obtained which would be helpful with regard to this question.

In sharp contrast to the effect on MVo2 of varying coronary flow were those experiments in which the activity of the heart was markedly varied while permitting total coronary blood flow to change only slightly. This was done in two ways. The first was to increase the amount of tension developed per minute by the left ventricle as a result of elevating aortic pressure (table 1). In each instance the MVo2 increased substantially; in the one experiment (table 1, experiment 2) in which there were four different levels of aortic pressure, TTI and MVo2, the previously observed correlation between TTI and MVo2 was found.11 Of further interest with regard to these experiments was the observation that, even though total coronary blood flow was permitted to increase slightly on the average,
left coronary artery flow did not change. It seems reasonable to assume that the right ventricular \( O_2 \) consumption did not change and thus that the observed increases of total \( MV_o \) took place as the result of the altered activity of the left ventricle. When the heart rate was increased, an intervention known to increase the TTI, a constant increase of \( MV_o \) was also observed over the entire range of coronary blood flows examined (fig. 2).

The second way in which the activity of the heart was altered was to increase greatly the amount of external work the heart produced but to make this change in such a manner that TTI did not change substantially. \( MV_o \) also changed only slightly (fig. 5).

It has been suggested that, when \( MV_o \) is observed to increase after elevating aortic pressure, this \( MV_o \) increase is attributable to the marked increase in coronary flow which normally occurs under such circumstances. The above data are not consonant with such a position because, if the TTI be increased while holding coronary flow constant, \( MV_o \) increases. If those factors known to influence TTI are held constant and coronary flow is markedly varied, \( MV_o \) does not change except under circumstances in which grossly observable deterioration of ventricular function occurs.

In the absence of coronary insufficiency, the amount of tension developed by the myocardium per minute, as reflected in the tension-time index, appears to be the most relevant, presently known variable influencing the \( O_2 \) consumption in the isolated, metabolically supported heart.

**Summary**

Experiments were done in the isolated supported heart preparation to ascertain whether a change in coronary blood flow would induce a change in myocardial \( O_2 \) consumption if the activity of the heart (aortic pressure, heart rate and stroke volume) was controlled. Over a wide range of coronary blood flows, the \( O_2 \) consumption did not vary under such circumstances. If the coronary flow was restricted to levels which produced an unequivocal deterioration of ventricular performance, a modest decrease in \( O_2 \) consumption was sometimes observed.

Reciprocal type experiments were also performed. In these, coronary flow was held constant or nearly so while varying the activity of the heart markedly. Under these circumstances the myocardial \( O_2 \) consumption did vary directionally with the amount of ventricular myocardial tension developed insofar as this was indicated by the tension-time index.

Data were also obtained suggesting that ventricular end diastolic fiber length is not of itself a major determinant of myocardial \( O_2 \) consumption.

**References**

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