Influence of Coronary Flow upon Oxygen Consumption and Cardiac Performance

By Howard Weisberg, Ph.D., Louis N. Katz, M.D., and Eugene Boyd

Work of our department and of others has shown that the magnitude of coronary flow (CF) is determined primarily by the oxygen consumption of the heart (O2C) in such a manner that oxygen availability alters in a parallel fashion with O2C while oxygen extraction (O2E), within limits, remains constant. Two kinds of factors cause deviation of this relationship:

(A) Factors which independently change the caliber of the coronary vessels in the sense that they are specific coronary vasodilators. These include hypoxemia, hypercapnia, acidemia, catecholamines, calcium, ouabain, as well as the spontaneous change occurring during periods of excessive stress.

(B) Changes in the mechanical factors controlling the perfusion pressure to the coronaries and in the duration of the phases of the cardiac cycle. All our work suggests that the metabolic factor determined by O2C is predominant. This has been illustrated by the influence of progressive hypoxemia where, until the hypoxemia becomes extreme, the CF rises to the extent, seemingly, of keeping oxygen availability commensurate with O2C.

The foregoing considerations are based on the presumption that it is O2C which determines CF, and not vice versa. Work by Gregg has suggested that the reverse may occur, i.e., augmentation of CF may also give rise to increase in O2C. The CF rises to the extent, seemingly, of keeping oxygen availability commensurate with O2C.

The possibility that it was mediated by an elevation of coronary pressure was not excluded. Since then we have had occasion to review some 11 experiments with this isovolumic preparation, some with and some without exhibition of ouabain. The results of our later findings are summarized in the present report.

Methods

Mongrel dogs (13 to 18 kg), anesthetized with 30 mg/kg sodium pentobarbital, were used in the eleven isovolumic preparations, a preparation in which the left ventricle ejects no blood. Each ventricle is bypassed by its own auxiliary pump. The azygos vein is tied off and the systemic venous return, through cannulae in the venae cavae, is pumped to a reservoir and then to the lungs of a donor-oxygenator dog (fig. 1) which receives a 95% O2 and 5% CO2 gas mixture from a demand valve positive pressure system. The oxygenated blood is returned to another reservoir, via a cannula in the left atrium of the donor dog, and then to the experimental animal by retrograde aortic perfusion, using a second pump of adjustable output. The volume of retrograde flow (cc/min) is adjusted to give a mean aortic pressure of 100 to 120 mm Hg at the start. This pressure range is sufficient to close the aortic valves, at the same time providing nourishment for the whole body including the myocardium. In this preparation CF is determined by the pressure, as influenced by the rate of input infusion, on the one hand, and by the vascular resistance existing employed with end diastolic volume and pressure, and in some instances heart rate, maintained constant. It was found that under these circumstances augmentation of CF, by raising the input into the aorta from the perfusion pump (and with it the aortic pressure), results in an increase in O2C. Since the elevated aortic pressure, per se, did not increase the effort of the isolated isovolumic left ventricle in this preparation, it was presumed that the augmented O2C was altered by means of an elevation in perfusion rate through the coronaries. The possibility that it was mediated by an elevation of coronary pressure was not excluded.

From the Cardiovascular Institute, Michael Reese Hospital and Medical Center, Chicago, Illinois. These studies were supported by the Chicago Heart Association, American Heart Association, and Grants HE-06375 and HTS-5252 from the National Heart Institute.

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Schematic diagram of the isovolumic left heart preparation, modified slightly from previously employed preparations.15,25 R.V. and L.V., right and left ventricle; I.V.C. and S.V.C., inferior and superior venae cavae, showing placement of catheters to drain systemic venous return; R.A., right atrium; C.S., coronary sinus; M.P.A., main pulmonary artery used as outflow tract for Thebesian, coronary sinus and accessory coronary vein drainage, the sum of which is C.F., coronary flow (except for that small portion draining into left heart—this latter is drained out via the left atrium-L.A.); A.P.P., aortic perfusion pressure monitor; C.O., coronary ostium; V.en., venous; Art., arterial; Balloon, showing position in left ventricle, with catheter leading to pressure transducer. Discussed in text.

In the systemic circuit and in the coronary bed, on the other; the latter depending upon changes in the durations of the phases of systole and upon direct actions on the smooth muscle tone (vasomotion) of the coronary vessels.

After complete heart bypass is established, a latex balloon attached to a polyethylene catheter is passed through the left atrium into the left ventricle. Bulging of the balloon into the atrium is prevented by passing ligatures behind the chordae tendineae of the mitral valve leaflets and closing the valve orifice around the neck of the balloon. The valve closure is slightly incomplete to permit exit of left ventricular Thebesian accumulation. The balloon is then filled with a measured volume of fluid while the pressures are monitored in the aorta and the balloon (left ventricle) circuit (fig. 1). The final volume in the balloon (7 to 20 cc), an amount which is below threshold for extrusion through the aortic valves, is kept constant during each experiment.

In this preparation the right atrium and ventricle are kept practically empty and therefore pump hypodynamically. They receive only coronary venous blood which is siphoned out through a cannula in the main pulmonary artery into the venous reservoir. The coronary venous flow is measured periodically (for 30 seconds) from the pulmonary artery outflow in a graduated cylinder.

The parameters observed in this series were: mean aortic blood pressure (BP), peak left ventricular pressure (PLVP), left ventricular pressure area (LVPA), coronary blood flow (CF), myocardial oxygen consumption (\( O_2C \)), and oxygen extraction (\( O_2E \)). Heart rate was used to calculate some of the above parameters per stroke. Hematocrits ranged from 39 to 46 (avg 43).

The average prevailing heart rate during these experiments was 125 beats/min (range 90 to 160).
FIGURE 2
Relationship of oxygen consumption (O$_2$C) to coronary flow (CF) observed in nine isovolumic experiments, in each of which coronary flow was altered and heart size kept constant. T.W. is heart weight.

Blood pressure and peak left ventricular pressure were measured simultaneously using Statham transducers and Sanborn recorders. Left ventricular pressure area was obtained by planimeter measurements of the left ventricular pressure curve; in one case the pressure area during systole (from the beginning to the peak of pressure) was also measured. Blood gas analyses were done according to the method of Van Slyke and Neill. Drugs were introduced through the aortic perfusion system and aortic input (AI) as well as aortic pressure changes were accomplished by adjusting the output of the aortic perfusion pump.

Results
In 9 of 11 experiments regression lines could be drawn relating O$_2$C and CF (fig. 2). In most of these (six out of nine), O$_2$C went up as CF was augmented. In two experiments, 11y and 16I, it was found that increase of O$_2$C with augmentation of CF occurred only in the lower and not in the higher range of coronary flow. In one experiment, 19I, we found that O$_2$C did not change with CF during the first one-half hour but that when the experiment was repeated, after an interval of one-half hour, O$_2$C showed a rise with elevation of CF, even though the CF was in a higher range than in the previous experimental period. This unexpected result is attributed to deterioration of the preparation. It is our contention that when O$_2$C does not change with CF alteration then O$_2$C is CF independent. However, when O$_2$C varies with CF as the latter is changed, O$_2$C is CF dependent. The latter relationship is further revealed by the observation that O$_2$E remained constant, within narrow limits, in those instances where O$_2$C varied with CF change. On the other hand, O$_2$E declined as CF increased in those parts of the three experiments during which O$_2$C was CF independent.

Figure 2 shows a composite of experiments for which a reasonable single regression line, or pair of regression lines, could be constructed from the data. This figure shows that the curves of individual experiments are not superimposable even though adjusted for heart weight. This is understandable because, among other things, the ventricular end diastolic pressure and volume were not identical in the different experiments; because the part of the O$_2$C attributable to deterioration of the preparation was variable between preparations, and its rate of progress was also not the same; and because the velocity of heart muscle contraction also differed from one preparation to another.

The next question we attempted to answer was whether or not this O$_2$C variation with CF change, when O$_2$C was CF dependent, was paralleled by a similar effect on the performance of the isovolumic left ventricle. This was first analyzed by determining the effect of CF/stroke upon the two indices of left ventricular pressure development (peak pressure and pressure area/stroke). By and large it was found that peak pressure gave as good results as pressure area.

In 5 of 11 experiments analyzed, no correlation between these two indices of performance of the heart and O$_2$C could be determined. These included the three experiments in which a pair of regression lines depicted the O$_2$C-CF relationship and one experiment, in which such a pair of regression lines depicted the relationship of CF/stroke to the performance parameter of peak left ventricular pressure (see below). However, when O$_2$C was CF dependent throughout an experiment, a good correlation was seen be-
Relationship of peak left ventricular pressure to \( O_2C \) observed in six experiments, in each of which coronary flow was altered and heart size kept constant. In five of them \( O_2C \) was CF dependent throughout (fig. 2). Between \( O_2C \) and a left ventricular performance parameter (figs. 2 and 3). This suggests that left ventricular performance exhibits a CF dependency when \( O_2C \) is similarly dependent, and further that good correlation between CF and \( O_2C \) is simply a measure of change in left ventricular performance caused by the induced variation in CF.

Because other factors besides the level of cardiac performance (as measured) affect \( O_2C \), we have compared CF/stroke vs. either peak left ventricular pressure or left ventricular pressure area. This is illustrated in figures 4 to 6. As expected, in a given experiment this correlation did not always coincide with that between \( O_2C \) and CF. In some experiments a regression line could be established between CF and \( O_2C \) but not between the parameters of left ventricular performance and CF, and vice versa. In others, the regression lines with CF could be identified both for \( O_2C \) and for the parameter of left ventricular performance and yet the regression lines were different. Attention is drawn especially to experiments 11Y and 16I in which left ventricular performance was CF independent throughout while \( O_2C \) was CF dependent at lower coronary flows and independent at higher coronary flows.

In figure 6 not only is there a straight line relationship of CF/stroke with total pressure area but also with the pressure area during systole, the two curves being parallel with the latter lower than the former, as expected. Because of the result in this experiment we have not computed the systolic portion of the area of the ventricular pressure curves in the other experiments.

Finally, the fact that only in a few instances was there a difference between the relation of CF to left ventricular peak pressure as compared to its relation to pressure area shows that the contour of the left ventricular pressure curve was not strikingly altered as CF was changed and that the duration of pressure development paralleled the change in peak pressure.

**Discussion**

It must be borne in mind that in these experiments with this isovolumic left ventricular preparation CF was the only planned variable introduced, and that the end diastolic volume and pressure of the isovolumic left ventricle were kept constant during any single experiment. Under these circumstances, and depending upon the conditions of the experiment and the levels of CF induced, \( O_2C \) was found to be either CF dependent or CF independent. In a few instances both phases, i.e., a CF dependent and a CF independent phase, could be demonstrated in a single preparation. The level of \( O_2C/100 \) g heart wt and the rate of change with CF was variable from experiment to experiment, as was
also the turning point at which a change from CF dependency to CF independency occurred.

When \( O_2C \) is CF dependent, the \( O_2C \) change is associated with a like change in the development of pressure and therefore with a change in the performance of the heart. This occurred despite the constancy of the end diastolic pressure and volume of the ventricle. That such parallelism between cardiac performance and \( O_2C \) did not occur in every experiment is not surprising because \( O_2C \) is determined not only by the level of cardiac performance as measured, but by other factors also: a) The heart may obtain some of the energy for its performance from substrates passing to it from the blood and this may modify \( O_2C \) independently of its performance, to varying degrees. b) The need for \( O_2C \) to maintain the architecture of the heart is variable. c) It is possible that a degree of \( O_2 \) debt, having developed in a deteriorating preparation, can be dissipated to varying extent by improvement of the coronary flow. d) There is an \( O_2C \) difference with disparities in the rate of pressure development during systole. However, whenever coronary resistance is changed by a direct alteration of the caliber of the coronary vessels or by changes in the duration of the phases of systole, \( O_2E \) deviates from its usual level. In this preparation we found that \( O_2E \) remained constant within narrow limits as CF was altered only in the CF dependent stage. Contrariwise in the CF independent phase, in which \( O_2C \) remained constant as CF changed, \( O_2E \) changed in the direction opposite to CF.

In previous work we have found that \( O_2E \) remains constant, within limits, when the metabolic factor controlling CF is predominant. However, whenever coronary resistance is changed by a direct alteration of the caliber of the coronary vessels or by changes in the duration of the phases of systole, \( O_2E \) deviates from its usual level. In this preparation we found that \( O_2E \) remained constant within narrow limits as CF was altered only in the CF dependent stage. Contrariwise in the CF independent phase, in which \( O_2E \) remained constant as CF changed, \( O_2E \) changed in the direction opposite to CF.

Extrapolating our results to the intact animal (and man), it is our tentative conclusion that under ordinary circumstances in the intact animal the presence of a fixed relationship between CF and \( O_2C \) is due to the fact that CF is predominantly controlled by the metabolic activity of the heart, as indicated by its \( O_2C \). Only when CF becomes sufficiently inadequate for the energy needs of the heart, as determined by the level of performance or by factors which independently restrict CF, does one obtain the reverse situation in which it is CF which determines \( O_2C \) and not vice versa.

Several obvious conditions in abnormal

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physiology which can be encountered at the bedside come to mind, in which $O_2C$ and cardiac performance would become $CF$ dependent. One is excessive hypoxemia in which $O_2$ availability becomes very limited. Another is anatomical narrowing or obstruction of the coronary channels, as is found in ischemic heart disease. Here the ischemia to local regions of the heart, or to the entire heart, may make $O_2C$ and performance of the heart $CF$ dependent. The corollary to this is that any procedure which improves coronary flow, whether mechanical or pharmacological, and hopefully in the future corrective coronary vascular surgery, obviously will permit, per se, the heart to increase its performance and its $O_2C$. When the performance of the heart is not $CF$ dependent, these procedures would seemingly have no utility unless considered as prophylactic measures to prevent the heart from getting into that range of $CF$ where its performance would become $CF$ dependent. Our recent experience reported here shows that the physiological facts and the relation between $O_2C$ and $CF$ are more complex than our previous work had indicated. In conclusion, it appears that $CF$ under certain circumstances can affect the performance of the heart and its $O_2C$.

Summary

The influence of induced changes in coronary flow upon oxygen consumption and cardiac performance were observed in the in situ isovolumic left ventricle. This preparation was established with auxiliary pumps which bypass the dog's right and left heart and by inserting a balloon into the left ventricle so that the latter ejected no blood. Coronary flow was set or varied by a retrograde aortic perfusion pump. Oxygen consumption of the heart was found to be coronary flow dependent or independent, according to the conditions of the experiment. When it is coronary flow dependent there is usually a similar relationship between coronary flow and cardiac performance. In a single preparation, it was sometimes found that cardiac oxygen consumption was coronary flow dependent at lower rates of coronary flow and independent at higher flow rates. Possible explanations and clinical applications are given.

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References


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