Influence of Coronary Flow upon Oxygen Consumption and Cardiac Performance

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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)\(^1\)–\(^8\) in such a manner that oxygen availability alters in a parallel fashion with O₂C while oxygen extraction (O₂E), within limits, remains constant.\(^8\)–\(^10\) Two kinds of factors cause deviation of this relationship:\(^9\)

(A) Factors which independently change the caliber of the coronary vessels in the sense that they are specific coronary vasodilators. These include hypoxemia,\(^4\) hypercapnia,\(^5\) acidemia,\(^6\) catecholamines\(^11,\)\(^12\) calcium,\(^13\) ouabain,\(^14\) as well as the spontaneous change occurring during periods of excessive stress.\(^8\)–\(^15\)–\(^17\)

(B) Changes in the mechanical factors controlling the perfusion pressure to the coronaries and in the duration of the phases of the cardiac cycle.\(^20\)–\(^22\) All our work suggests that the metabolic factor determined by O₂C is predominant. This has been illustrated by the influence of progressive hypoxemia\(^4\) where, until the hypoxemia becomes extreme, the CF rises to the extent, seemingly, of keeping oxygen availability commensurate with O₂C.\(^8\)

The foregoing considerations are based on the presumption that it is O₂C which determines CF, and not vice versa. Work by Gregg\(^23\) has suggested that the reverse may occur, i.e., augmentation of CF may also give rise to increase in O₂C.\(^8\)

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...
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 (O₂C), and oxygen extraction (O₂E). 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).
Relationship of oxygen consumption \((O_2C)\) to coronary flow \((CF)\) observed in nine isovolumic experiments, in each of which coronary flow was altered and heart size kept constant. TJ.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 \(O_2C\) and CF (fig. 2). In most of these (six out of nine), \(O_2C\) went up as CF was augmented. In two experiments, 11Y and 16I, it was found that increase of \(O_2C\) 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 \(O_2C\) 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, \(O_2C\) 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 \(O_2C\) does not change with CF alteration then \(O_2C\) is CF independent. However, when \(O_2C\) varies with CF as the latter is changed, \(O_2C\) is CF dependent. The latter relationship is further revealed by the observation that \(O_2E\) remained constant, within narrow limits, in those instances where \(O_2C\) varied with CF change. On the other hand, \(O_2E\) declined as CF increased in those parts of the three experiments during which \(O_2C\) 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 \(O_2C\) 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 \(O_2C\) variation with CF change, when \(O_2C\) 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 \(O_2C\) could be determined. These included the three experiments in which a pair of regression lines depicted the \(O_2C\)-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 \(O_2C\) 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 ven-
tricular pressure area. This is illustrated in 
figures 4 to 6. As expected, in a given ex-
periment this correlation did not always co-
incide with that between $O_2C$ and CF. In 
some experiments a regression line could be 
established between CF and $O_2C$ but not be-
tween the parameters of left ventricular perfor-
ance and CF, and vice versa. In others, 
the regression lines with CF could be identi-
fied both for $O_2C$ and for the parameter of 
left ventricular performance and yet the re-
gression 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 in-
stances was there a difference between the 
relation of CF to left ventricular peak pres-
sure as compared to its relation to pressure 
area shows that the contour of the left ven-
tricular pressure curve was not strikingly 
altered as CF was changed and that the dura-
tion of pressure development paralleled the 
change in peak pressure.

Discussion

It must be borne in mind that in these ex-
periments 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 experi-
ment. Under these circumstances, and de-
pending upon the conditions of the experi-
ment and the levels of CF induced, $O_2C$ was 
found to be either CF dependent or CF in-
dependent. 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 vari-
able from experiment to experiment, as was
Relationship of area beneath left ventricular pressure curve to coronary flow (CF/stroke) observed in six isovolumic experiments, in each of which coronary flow was altered and heart size kept constant.

Experiment 161 illustrating that in this case the left ventricular pressure area is independent of coronary flow (CF/stroke) throughout. The area of the systolic portion of the left ventricular pressure curve is also plotted (TTI). It is the pressure created during systole. In a heart contracting isovolumically, this pressure would give a measure of the tension created in the heart wall during this time simply by multiplying the area obtained by a constant. Cavity pressure in the isovolumically contracting ventricle is a truer index of tension-time than in the case of a ventricle which is emptying its contents.

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 $O_2C$ 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 \( O_2 \)C 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 \( O_2 \)C 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 \( O_2 \)C. 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 \( O_2 \)C 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 \( O_2 \)C.

**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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