Counterpulsation Effects of Coronary Blood Flow and Cardiac Oxygen Utilization

By L. J. Hirsch, Ph.D., S. Lluch, M.D., and L. N. Katz, M.D.

With the Assistance of A. Ellis, B.S.

ABSTRACT

Counterpulsation in dogs with normal systemic arterial blood pressure produced a reduction in myocardial oxygen consumption without a significant concomitant change in total coronary flow. In dogs with a deteriorating heart and low systemic arterial blood pressure, myocardial oxygen consumption became dependent on coronary flow. Under these circumstances, counterpulsation produced an increase in coronary flow, and with it a secondary augmentation of cardiac oxygen consumption. Counterpulsation reduced the mean systemic arterial blood pressure during ventricular ejection to a greater degree when the control level of this pressure was normal than when it was hypotensive. This lessened effect may also occur when the heart has deteriorated. The mechanisms involved in causing the several effects of counterpulsation are discussed.

ADDITIONAL KEY WORDS aortic blood flow and pressure pulses right heart by-pass dp/dt mean ejection pressure phasic coronary flow pump effect cardiac oxygen consumption alteration in pump phasing dogs

The use of assisted circulation has been proposed for a variety of conditions which produce circulatory collapse, e.g., hemorrhagic, cardiogenic and septicemic shock. There are three possible methods which may support the heart under such circumstances: (1) to put a pump in series with the heart, (2) to place a pump in parallel with the heart or to by-pass one of the ventricles, and (3) to replace the heart with an artificial one. We are concerned with a pump in series with the heart. Harken's group (1) introduced the concept of counterpulsation by placing a reciprocating pump in series with the heart. The way counterpulsation supports the heart can be briefly stated. The pump is synchronized with the electrocardiogram (ECG) so that the pump removes blood from the aorta during ventricular systole, reducing the afterload against which the heart contracts and thereby the cardiac work load. During ventricular diastole, the pump returns the blood to the aorta under pressure, thereby raising the diastolic pressure in the aorta, and in this way, presumably also providing a greater flow of blood through the coronary arteries during this phase of the cycle. Since this is the phase during which most of the coronary flow occurs, it should lead, all other things being equal, to an increase in over-all coronary flow. Jacobey et al. (2, 3) observed an increased collateral circulation in the hearts of animals which had been treated by counterpulsation. However, since they did not present quantitative data, it is difficult to evaluate the significance of their results.

Thus, the concept of counterpulsation is twofold. It is designed, on the one hand, to decrease the oxygen consumption of the heart...
by reducing its work load during systole and, on the other hand, to increase the coronary perfusion pressure during diastole. It has been assumed that by lowering the myocardial work load and, thus, its oxygen consumption, the heart would be placed in a more suitable condition to recover its ability to pump.

It would appear that counterpulsation might be employed for an incompetent heart but would be most aptly used when the patient has both an impaired myocardium and hypotension that results in a lower coronary perfusion pressure. Under these circumstances, not only would the work load decrease but a greater coronary flow would lead to an increased availability of oxygen to the myocardial cells. Weisberg, Katz and Boyd (4) have shown that in the isovolumic heart preparation, in which the heart does no external work and so has no afterload, the cardiac oxygen consumption and performance increased as the coronary flow was elevated. Opie (5), using a modification of the Langendorff technique in the rat heart, also observed that left ventricular contractility and total cardiac oxygen uptake became greater at higher coronary perfusion pressures and flow rates.

For these reasons, therefore, it is not enough to determine the effects of counterpulsation upon cardiac output, the work of the heart, or its coronary flow. It is equally important to measure the oxygen required and consumed by the heart (6, 7). Therefore, it is advantageous to use the right heart by-pass preparation (8), in which the input can be maintained fixed so that the analysis of cardiac oxygen consumption is, in reality, that obtained with constant input.

**Methods**

A modification of the right heart by-pass-coronary flow preparation (8) was used in 15 dogs. In 4 others, the circulation was intact and the chest opened.

In the by-pass preparation, a Kay-Cross disc oxygenator was used to maintain an arterial oxygen content of at least 17 vol%. A pneumatic counterpulsation pump (Flow Corporation, Cambridge, Massachusetts) working under 60 psi and activated by the R wave of the ECG was attached to the femoral arteries by cannulas 5 mm in diameter and 8.5 cm long that faced upstream. The artificial ventricle of the pump produced its best results when a stroke volume of about 10 ml was used. Coronary flow was measured in a graduate cylinder as it flowed out of the cannulated by-passed right ventricle. Myocardial oxygen consumption was determined from the product of coronary flow and the AV oxygen difference across the coronary bed. Blood oxygen samples were analyzed by the manometric technique (9). The blood samples were taken from the carotid artery and from the coronary venous blood. Aortic and left ventricular pressures, ECG, and aortic flow were recorded on a Sanborn multichannel polygraph. Aortic flow was measured using a Medicon multichannel electromagnetic flowmeter, with the probe placed on the ascending aorta. In some instances, the rate of rise of the isovolumic phase of the left ventricular pressure curve (dp/dt) was measured electronically and in others computed directly from the aortic and left ventricular pressure curves, using the former to mark the onset of ejection. Pressures were obtained with Statham transducers (P 23AA) connected to the ventricle and aorta by polyethylene tubing.

In the by-pass experiments, an extracorporeal electromagnetic flow probe (4 mm) was connected to the coronary flow outlet tube from the by-passed right ventricle to continuously monitor coronary flow. In dogs with circulation intact, coronary flow probes (2 mm) were placed around the circumflex or the anterior descending coronary arteries or both to study phasic changes in coronary flow produced by counterpulsation. Analyses were made of aortic and left ventricular pressures, aortic flow, and dp/dt by methods similar to those used in the by-pass preparation.

Each dog was allowed a period of stabilization before beginning counterpulsation. Blood samples were taken and pressures and flows measured at 5-min intervals. Counterpulsation was maintained for at least 15 min and as long as 30 min, to observe any later hemodynamic alterations which might have been attributable to a longer period of counterpulsation.

The extracorporeal probe was initially calibrated by pumping blood through it at a known rate. In addition, flow measured by the probe was periodically checked during the experiments against the coronary blood flow measured at the outlet tube. The aortic flow probe was initially calibrated by perfusion with saline or blood and checked for stability periodically during the experiments by clamping the aorta and obtaining zero flow during occlusion. The flow probes around the coronary arteries were similarly...
checked for stability by short periods of occlusion (0.5 sec).

In the dogs with intact circulation, myocardial oxygen consumption per gram of perfused left ventricle was estimated by multiplying the AV oxygen difference across the coronary bed by the mean coronary flow obtained with the coronary probes. Venous oxygen was measured from the cannulated coronary sinus.

**Results**

Analysis of the results indicated that there was no difference between the results obtained at 15 min and at 30 min of counterpulsation. Therefore, the results of all counterpulsation periods are treated similarly.

We separated the by-pass experiments into two categories on the basis of the cardiac oxygen consumption. In group A (11 dogs), it decreased and in group B (4 dogs), it did not change or increased.

**Changes in Pressure, Work and External Efficiency**

Figure 1 shows a typical experiment from group A. The record shows the dip in aortic and ventricular systolic pressures with slight recovery, but with a final stabilized systolic pressure of about 25 mm Hg below control values. The aortic pulse pressure was widened and a rapid speed trace from another dog, Figure 2A, shows this was the case. However, the aortic pulse pressure increase was due entirely to the changed configuration of the diastolic portion of the pressure curve. The top of the aortic curve occurred during the compression phase of counterpulsation in diastole. It was higher than the systolic pressure during the control period. The aortic end-systolic pressure (just before the arrowhead) during counterpulsation was lower than in the control. The mean aortic pressure decreased approximately 15 mm Hg (Fig. 1), dp/dt also decreased (Figs. 1 and 2A).

Figure 2B shows a rapid speed record from a typical experiment from group B in which only a slight decrease (10 mm Hg) in peak systolic pressure was observed. The systemic arterial pressures in this group initially were lower than those seen in group A. The negative phase in the aortic flow curve was produced by the rapid retrograde movement of blood into the aorta during compression by the counterpulsation pump, since the probes are able to measure movement of blood in either direction.

The effect of counterpulsation on several variables when plotted against the product of mean ejection pressure (MEP) times heart rate (HR) is shown in Figures 3 and 4.
Cardiac minute-work was decreased by counterpulsation in both groups, but to a greater degree in group A. The effect of counterpulsation on cardiac external efficiency was variable in group A and resulted in a decrease in group B. The alteration with counterpulsation which results in the MEP × HR decrease was primarily due to the change in mean ejection pressure.

The greater fall in cardiac minute-work with counterpulsation in group A is ascribed to the larger drop in aortic ejection pressure. This is seen clearly in the greater decrease in the MEP × HR index in group A as compared to that in group B (Figs. 3 and 4). This is also shown quite clearly in Figure 5; this figure is from a dog in group A in which counterpulsation was used at two control pressure levels. In panel A, the starting peak aortic pressure before counterpulsation is 100 mm Hg; in panel B, after the animal had been allowed to return to its previous state, the cardiac output was increased, thereby raising the starting peak aortic pressure before counterpulsation to 150 mm Hg. In panel A, counterpulsation caused the left ventricular peak pressure to drop by 10 to 15 mm Hg, while in panel B the drop with counterpulsation was 30 to 40 mm Hg. Thus, initial peak systolic pressure was higher, and the effect of counterpulsation

**FIGURE 2**

A Recording from dog with intact circulation from group A. Panel at left before, one at right during CP. Onset of compression phase of pump shown by the arrowhead. The widening of the aortic pressure pulse with CP (Fig. 1) is due mostly to the altered configuration of the diastolic pressure phase produced by the compression phase of the CP pump. The mean aortic pressure during ventricular ejection drops during CP. The widened coronary flow tracing is due to an increased diastolic flow and a decreased systolic flow, resulting in no change in recorded mean flow; the negative flow in systole is due to the actual suction of blood from coronary arteries by the CP pump. Symbols as in Figure 1.

B Recording from a dog with intact circulation from group B arranged as in Figure 2A. The mean aortic pressure during ventricular ejection in this animal decreased much less when CP was used than in group A (Fig. 2A). During CP mean recorded coronary flow increased in contrast to a lack of change in group A (Fig. 2A). Symbols as in Figure 2A.
COUNTERPULSATION AND MYOCARDIAL OXYGEN CONSUMPTION

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15

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GROUP A

9

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12

13

14

15

MEP

HR

FIGURE 3

Group A. Relationship of MEP x HR (mean ejection pressure x heart rate) to the several variables measured or computed in right heart bypass dogs. Control points are indicated by X's, points during CP by circles. Arrows show direction of changes during CP.

upon it was greater. In addition, this figure shows that the counterpulsation pump raised the peak diastolic pressure approximately 60 mm Hg in panel B compared to 40 mm Hg in panel A even though the stroke input into the aorta by the counterpulsation pump was the same in both cases.

When all the data from the 15 right heart bypass dogs were used in a plot relating the ΔMEP (the change in mean ejection pressure induced by counterpulsation) against the initial mean ejection pressure before counterpulsation (Fig. 6), a regression coefficient value of 0.87 was obtained indicating clearly that the mean ejection pressure during counterpulsation is a function of the initial mean ejection pressure. Since the cardiac input was fixed in these experiments, it is apparent that the lower the control systemic pressure, the smaller the decrease in cardiac minute-work when counterpulsation is instituted.

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MYOCARDIAL OXYGEN CONSUMPTION AND CORONARY FLOW

Figures 3 and 4 show the relation of myocardial oxygen consumption and coronary flow to mean ejection pressure times heart rate. There was a definite reduction of myocardial oxygen consumption in all dogs in group A, as might be expected, while in group B, 3 of the 4 dogs showed an increase and the fourth showed no change. Thus, in group A, myocardial oxygen consumption decreased as the minute-work of the heart decreased, but this unexpectedly did not occur in group B.

Coronary flow changes did not parallel myocardial oxygen consumption alterations (Figs. 3 and 4). In group A, despite the high peak aortic diastolic pressure, coronary flow was essentially unaltered, with some dogs showing slight increases and others slight decreases. But in group B, coronary flow increased noticeably in 3 dogs and was unchanged in the other. Figure 5 shows a typical example from group A, coronary flow did not change from the preceding control value in either instance during counterpulsation. On the other hand, an increase in aortic pressure induced between A and B by raising minute cardiac output increased the level of coronary flow. A typical example from group...
B is shown in Figure 2B, the increase in coronary flow occurred during the diastolic compression phase of counterpulsation. In group B, myocardial oxygen consumption followed closely the alterations in coronary flow; this did not occur in group A (Figs. 3 and 4). This difference in relation between coronary flow and myocardial oxygen consumption closely the alterations in coronary flow; this did not occur in group A (Figs. 3 and 4). This difference in relation between coronary flow and myocardial oxygen consumption followed closely the alterations in coronary flow; this did not occur in group A (Figs. 3 and 4). This difference in relation between coronary flow and myocardial oxygen consumption followed closely the alterations in coronary flow; this did not occur in group A (Figs. 3 and 4).

**FIGURE 5**
Recording from group A animal with right heart by-pass in which minute cardiac output was increased in the control period from 1500 ml to 2000 ml between panel A and panel B. In each pair of panels, the one on the left is before, and the one on the right during, CP. CF = total coronary flow measured with extracorporeal flow probe on the outlet tube from the by-passed right ventricle. Arrows in aortic pressure curve indicate onset of compression phase of CP pump. Note that the aortic flow stylus hits the top and bottom of the record during CP in panel B and the bottom in panel A.

**FIGURE 6**
The relationship of ΔMEP (the change in MEP induced by CP) to control MEP found in all experiments with right heart by-pass dogs of groups A and B. The significant r value suggests that decrease in MEP during CP is directly related to the level of the initial MEP.
gen consumption between groups A and B reinforces the idea that in the latter group myocardial oxygen consumption becomes coronary flow-dependent, as discussed below.

PHASIC CORONARY FLOW CHANGES

Coronary flow probes were placed around the anterior descending or circumflex branch of the left coronary artery or both in 4 dogs with intact circulation without by-pass; 3 of these were in group A and 1 in group B. Figure 2A is a typical recording from 1 of the group A animals. Although the mean coronary flow did not change when counterpulsation was used, counterpulsation caused the systolic flow to decrease (below zero) and the diastolic flow to increase. These changes paralleled the direction of the alterations caused by counterpulsation in the aortic pressure trace. The counterpulsation pump sucked blood out of the aorta during ventricular ejection and ejected blood into the aorta during diastole. Thus, the phasic coronary flow characteristics are considerably different during counterpulsation even though the total flow rate does not change. Figure 2B shows this effect in a dog in group B. Here the mean coronary flow increased with counterpulsation but the direction of phasic flow changes is the same as in Figure 2A.

PUMP PHASING

If the counterpulsation pump is not properly phased, the pump itself can alter cardiac work, myocardial oxygen consumption and coronary flow by imposing an increase in afterload during ejection. The effects of proper and improper phasing of counterpulsation in one of the experiments are shown in Table 1.

When the counterpulsation pump was partially out of phase so that the compression of the pump began before the end of ventricular ejection, a definite increase in myocardial oxygen consumption and coronary flow was observed with oxygen extraction essentially unchanged, when compared with counterpulsation properly phased. There was also an increase in left ventricular systolic pressure. These observations demonstrate the importance of proper counterpulsation pump phasing previously noted by others (10,11).

Discussion

Counterpulsation was designed to reduce pressure work of the heart during periods when continued high afterload (relative or absolute) would operate to the disadvantage of the myocardium. This is particularly true in cases of acute myocardial infarction, where the compromised myocardium attempts to maintain systemic arterial pressure at approximately normal levels. If systemic hypotension or shock supervenes, the reduction in blood pressure to low levels produces a cycle of events frequently terminating in ventricular fibrillation and death. The simple reduction of blood pressure in shock may serve, in part, as a means of lowering the work load of the heart. However, there is an accompanying disadvantage in that blood flow to the other organs is reduced and the drop in pressure leads to a decline in coronary flow itself. In instances of hypotension, therefore, the action

| Table 1: Alteration of Cardiac Hemodynamics during Improper Phasing of the Counterpulsation (CP) Pump in Dog with Right Heart By-pass |
|-------------------------------|-----------------|-----------------|
| Unit                          | CP properly phased | CP out of phase |
| Coronary flow ml/min/100 g whole heart wt | 60                | 70              |
| MVO2* ml/min/100 g whole heart wt | 5.41             | 5.99            |
| MEP mm Hg                      | 90               | 100             |
| LVFP* mm Hg                   | 105              | 115             |
| Stroke work g-m/stroke         | 8.0              | 9.0             |
| Oxygen extraction %            | 57               | 58              |

*Cardiac oxygen consumption.
†Mean ejection pressure.
‡Left ventricular peak pressure.
of counterpulsation to reduce cardiac oxygen needs is not as important as the maintenance of an adequate coronary perfusion pressure; in other words, it is not the systolic suction but the diastolic compression of the counterpulsation pump which is of prime importance.

Other investigators working with counterpulsation on dogs have noted that coronary sinus flow increases or shows no change. Thus, Soroff (12) has reported an increase in coronary flow of almost 50 ml/min with no change in over-all cardiac oxygen consumption, while Harken et al. (11) reported essentially no change in coronary flow with a reduction of about 25% in myocardial oxygen consumption. The reason for the difference in results is not clear. Watkins et al. (13) have also used a similar but more elaborate pump to reduce systolic work load, but they did not present any data for coronary flow or myocardial oxygen consumption. All of the animals used in these reports were essentially normotensive without obvious evidence of cardiac incompetence.

It has been definitely established that there is a clear relationship of myocardial oxygen consumption to the blood pressure and heart rate. The most commonly used indices are BP X HR (the product of mean arterial blood pressure and heart rate) (6) and TTI (Tension Time Index, the area under the systolic portion of the ventricular or aortic pressure curve times heart rate) (7). These indices have a similar relationship to cardiac performance. From the rate of rise of the left ventricular pressure (dp/dt), one can, under normal conditions, predict the direction of change in myocardial oxygen consumption (14). In the normal animal and group A of our experiments, counterpulsation leads to a reduction of HR X MEP, TTI and dp/dt, and on this basis a reduction of cardiac oxygen consumption is expected. The index BP X HR was not used because during counterpulsation the compression effect of the pump makes the mean blood pressure during the entire cycle deviate from its usual relationship to the mean ejection pressure seen in the absence of counterpulsation.

The results presented here suggest that cardiac oxygen consumption decreases during counterpulsation only in those instances in which the heart maintains a reasonably normal cardiac output and systemic arterial blood pressure. A decrease in cardiac oxygen consumption during counterpulsation is not surprising in such animals since it produces a drop in pressure during ventricular ejection as well as in cardiac work.

Coronary flow did not follow the changes in oxygen utilization by the heart when counterpulsation caused a reduction in cardiac oxygen consumption. Instead, coronary flow was found to remain relatively constant or changed only slightly in either direction during counterpulsation. It has been previously pointed out by us and others (4, 13, 15) that a close relationship ordinarily exists between changes in coronary flow and myocardial oxygen consumption. This was found to be true in the present experiments only when the control data were considered (x's in Fig. 7; r = 0.86). This close correlation did not appear in our experiments during counterpulsation, as shown by the circles in this figure (r = 0.61); this indicates the operation of factors acting upon coronary flow independently of the normal metabolically induced autoregulation of the coronary vasculature. These independent factors are attributable to the mechanical action of the counterpulsation pump during its compression phase.

It is seen, therefore, that a heart which is capable of adequately adjusting to its needs will predictably have a reduction in cardiac work and oxygen consumption during properly phased counterpulsation. However, coronary flow does not show an absolute increase, but only a relative increase with respect to the reduced work load present. This is due to the somewhat equal but opposite influence of the metabolic autoregulation of coronary flow and that of the direct mechanical effect of the counterpulse pump on this flow.

In normotensive animals with the heart in good condition, our results are essentially similar to those reported by Harken's group (9), but our evaluation has offered a
Alteration in the relationship of CF to myocardial oxygen consumption (MVO₂) produced by CP in the right heart by-pass dogs. When CP was instituted the value changed from 0.86 to 0.61. X's and solid regression line are from controls; circles and dash line, during CP.

reasonableness explanation for them. On the other hand, when systemic blood pressure cannot be maintained at its normal level and, as a result, coronary perfusion pressure is presumably reduced, the myocardium begins to deteriorate. In such a deteriorating heart, or in the presence of severe hypotension, it can be assumed that a relative myocardial hypoxia is taking place. The oxygen lack acts either directly or through some intermediate chemical substance (16) to increase the caliber of the coronary vessels, thereby increasing the coronary flow in an attempt to maintain the performance of the heart. Counterpulsation under these abnormal circumstances has an additive effect in enhancing coronary flow by raising the aortic diastolic pressure. Under such circumstances, cardiac oxygen consumption can become coronary flow dependent (4) and, hence, as the flow increases so does the oxygen consumption of the heart and also its performance. As a result, the peak systolic pressure is only slightly reduced unlike the sharp reduction when the heart and blood pressure are normal. Therefore, if counterpulsation has any salutory effects on the performance of the heart in circulatory collapse, it is not due to the reduction in cardiac work, but presumably to the increase in myocardial oxygen consumption induced by the better coronary perfusion, which permits an augmentation in cardiac performance.

If the principle of counterpulsation is to be applied to man, several additional factors must be considered. One must bear in mind that the character of the compression phase of the counterpulse may have certain actions. The sudden pressure rise at the beginning of the compression phase of the pump may facilitate the expansion of existing collaterals and, perhaps, the development of new collaterals (3). But there is also the hazard that this abrupt rise in pressure, acting like a water hammer, may lead to intramural hemorrhages and even rupture of vessels. In our early experiments, when we were less experienced with the use of the pump, counterpulsation led to hemorrhages in the dog's heart. While this may be attributed to improper phasing, the hazard may still exist even with the best phasing, especially in the case of severely sclerotic blood vessels, or when an improperly constructed counterpulsation pump is used. This factor requires careful checking in controlled human studies.

Furthermore, in accordance with the observations of Burton (17) on the critical closing pressure of blood vessels, it is possible that the suction phase may bring about collapse of the arteries and thus interfere with the proper function of the pump particularly when circulating blood volume or intravascular pressures are low.

Finally, consideration must be given to the effects of counterpulsation on other vascular beds since the suction and compression phases of the pump affect the hemodynamics of other areas of the body as well as that of the heart.

It is quite apparent that counterpulsation is not a simple tool. It has multiple effects each of which can vary independently under different circumstances. Before this method can
be regarded as a safe therapeutic tool, further studies not only in animals, but ultimately in man, are needed to clarify the precise role of counterpulsation under the several hemodynamic conditions in which it might be considered for use.

References
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