Comparison of Two Types of Mechanical Assistance in Experimental Heart Failure

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Various forms of mechanical assistance are now being used clinically in attempts to alleviate acute heart failure. However, the physiologic effects of each type of assisted circulation upon the various decompensation syndromes are not well known and the results of their application in human patients have not been evaluated. The multiple measurements needed and the critical condition of the patients usually preclude adequate monitoring of physiologic variables during these therapeutic procedures. The influence of mechanical assistance procedures on cardiac failure states should therefore be investigated under conditions which permit continuous observations of all important indices of cardiac function. Data reported here describe experiments in which 7 different types of cardiac failure were produced in dogs and where each type of decompensation was treated with 2 forms of mechanical assistance.

Methods

Fifteen mongrel dogs under pentobarbital sodium (25 mg./Kg.) underwent a sternum-splitting thoracotomy in the fourth or fifth intercostal space while ventilated under positive pressure through a cuffed endotracheal tube. Careful hemostatic technics were applied in order to minimize variations of the dog's blood volume during the experiments. Pressures were registered with polyethylene tubing (i.d. 2.1 mm.; o.d. 3.2 mm.) in the femoral artery, the right ventricle (via the atrial appendage), a femoral artery, and the left subclavian artery. This permitted the following procedures of assisted circulation: (1) pumping of blood by a calibrated, occlusive pump ("veno-arterial pumping") or by a heart-lung machine ("partial heart-lung bypass"—not used here) from the inferior vena cava into a femoral artery; (2) pumping of blood (calibrated roller pump or Davol calibrated pump*) from the left atrium into a femoral artery ("partial left ventricular bypass"); (3) withdrawal and administration of blood (Davol pump) from and to the ascending aorta via the subclavian artery, synchronized with the electrical and mechanical systole of the heart ("synchronized arterio-arterial assistance"). Because of technical difficulties, the data reported here do not include synchronized arterio-arterial assistance. All cannulations were made and all extracorporeal circuits were fully primed with blood before failure was produced experimentally. All dogs were heparinized (1.5 mg./Kg.).

Decompenation of 1 or both main cardiac chambers was characterized by elevation of the end-diastolic pressure in the failing chamber from 10 mm./Hg or less to 15 mm./Hg or more. This was often accompanied by systemic hypotension and by elevated left atrial pressure. The following methods were used for the production of various types of heart failure: (a) The main pulmonary artery was gradually constricted with a screw clamp. When a certain degree of constriction was reached, failure of the right ventricle and systemic hypotension supervened, while the left ventricle remained compensated. (b) Overtransfusion of blood, up to 45 ml./Kg., when used alone, caused only transient failure of the heart; compensation was usually restored within 5 minutes. However, when any degree of failure in either cardiac chamber had been produced by any other method, even slight...

* Davol Rubber Company, Providence, R. I.
expansion of the blood volume (5 ml./Kg.) intensified the pre-existing failure. (e) The ascending aorta was gradually constricted with a screw clamp. This resulted in marked systolic hypertension in both ventricles, systemic hypotension, and mild increase of the left ventricular diastolic pressure. (d) A plastic tube with multiple perforations, fitted with an obturator, previously described by Braunwald et al.,4 was inserted through the apex of the left ventricle (purse string) so that its distal portion was positioned in the ascending aorta and the proximal end protruded through the apex of the left ventricle. Withdrawal of the obturator invariably produced aortic insufficiency and failure of the left ventricle. Replacement of the obturator reversed the aortic insufficiency and the failure. (e) Distention of a balloon in the left ventricle (introduced via the apex) caused cardiac failure when the balloon exceeded a certain critical volume (10 to 15 ml. of air in most instances) which depended upon the size of the heart. When distended, the balloon was drawn against the apex so that it would not obstruct the inflow or outflow tracts. Distention of the balloon produced failure of the left ventricle of any desired degree. (f) The anterior descending coronary artery was either ligated, or else cannulated and perfused with arterial blood by a separate pump. Arrest of the coronary flow per se did not cause failure of the left ventricle; however, when the flow was arrested, minimal distention of the balloon, minimal aortic insufficiency or constriction, or slight expansion of the blood volume each caused pronounced left ventricular failure, although each of these auxiliary maneuvers did not result in frank decompensation when applied alone. (g) "Myocardial failure" of the left ventricle could not be produced deliberately, but appeared spontaneously after prolonged experimentation when the heart had been repeatedly exposed to multiple insults. Here, the highest observed left ventricular diastolic pressure was 25 mm. Hg.

Evaluation of the various forms of assisted circulation followed a general pattern. First, a severe state of cardiac failure was produced. During this control period of decomposition there either existed abnormal, but stable pressures, or else continued intensification of heart failure was evident (rising ventricular diastolic pressure). Following this control period, mechanical assistance was begun and was continued until its influence on cardiac decompensation was clearly established. At this time, the pumps were either turned off or the other form of mechanical assistance was started. In many instances, both modes of circulatory assistance were successively employed during the same observation, allowing comparison of their effectiveness. Whenever possible, flow rates and other characteristics of the mechanical circuits were varied over a wide range. In all experiments, the degrees of failure before and after periods of assisted circulation were compared in order to detect any "compensating" effect.

Results

Right Heart Failure (12 Observations)

After control periods of acute failure of the right ventricle, left ventricular bypass yielded only small flow rates because the left atrium would collapse easily. Bypass was without effect upon the failure or upon systemic hypotension (table 1a). Veno-arterial pumping usually resulted in an improvement of the contractile strength of the ventricles, decreased diastolic pressure in the right ventricle, and improvement of the systemic hypotension (table 2a). The "therapeutic" effect of veno-arterial pumping in this particular situation depended upon the volume of extracorporeal flow, which was limited by the flow capacity of the venous cannula.

Heart Failure Caused by Sudden Expansion of the Blood Volume (37 Observations)

Here, left ventricular bypass always caused immediate return towards compensation. When left ventricular bypass was arrested, compensation often remained (table 1b); however, in combined aortic insufficiency and overtransfusion, the hemodynamic conditions reverted to the state before transfusion (table 1c). Veno-arterial pumping usually returned the abnormal pressures to the levels which existed before the expansion of the blood volume (table 2b); sometimes in slight failure veno-arterial pumping achieved full compensation (fig. 1). When the blood volume was expanded during aortic insufficiency, veno-arterial pumping always intensified the failure to a point where the experimental preparation had to be rescued by left ventricular bypass (table 2c).

Left Heart Failure Caused by Constriction of the Ascending Aorta (23 Observations)

Full compensation returned in this type of left ventricular failure when the flow from the
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Table 1
Effects of Left Ventricular Bypass (LVB) in Heart Failure

<table>
<thead>
<tr>
<th>Group</th>
<th>RVP (mm Hg)</th>
<th>LAP (mm Hg)</th>
<th>LVP (mm Hg)</th>
<th>SA (mm Hg)</th>
<th>AV flow rate (ml Kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Right heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>112/5</td>
<td>7</td>
<td>88/3</td>
<td>60/35</td>
<td>0</td>
</tr>
<tr>
<td>LVB on</td>
<td>115/5</td>
<td>6</td>
<td>85/3</td>
<td>70/50</td>
<td>22</td>
</tr>
<tr>
<td>LVB off</td>
<td>115/5</td>
<td>6</td>
<td>80/2</td>
<td>55/38</td>
<td>0</td>
</tr>
<tr>
<td>b. Overtransfusion in heart failure, except aortic insufficiency</td>
<td>38/3</td>
<td>30</td>
<td>108/18</td>
<td>60/35</td>
<td>0</td>
</tr>
<tr>
<td>Control</td>
<td>109/3</td>
<td>5</td>
<td>112/2</td>
<td>63/37</td>
<td>0</td>
</tr>
<tr>
<td>V-A on</td>
<td>109/0</td>
<td>5</td>
<td>130/0</td>
<td>105/38</td>
<td>0</td>
</tr>
<tr>
<td>V-A off</td>
<td>109/0</td>
<td>5</td>
<td>110/3</td>
<td>75/55</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2
Effects of Veno-Arterial Pumping (V-A) in Heart Failure

<table>
<thead>
<tr>
<th>Group</th>
<th>RVP (mm Hg)</th>
<th>LAP (mm Hg)</th>
<th>LVP (mm Hg)</th>
<th>SA (mm Hg)</th>
<th>AV flow rate (ml Kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Right heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>40/2</td>
<td>31</td>
<td>115/20</td>
<td>62/34</td>
<td>0</td>
</tr>
<tr>
<td>V-A on</td>
<td>35/0</td>
<td>8</td>
<td>95/4</td>
<td>85/70</td>
<td>28</td>
</tr>
<tr>
<td>V-A off</td>
<td>35/0</td>
<td>12</td>
<td>100/4</td>
<td>75/58</td>
<td>0</td>
</tr>
<tr>
<td>b. Overtransfusion in heart failure, except aortic insufficiency</td>
<td>40/2</td>
<td>31</td>
<td>117/15</td>
<td>110/32</td>
<td>0</td>
</tr>
<tr>
<td>Control</td>
<td>52/0</td>
<td>9</td>
<td>240/9</td>
<td>67/59</td>
<td>0</td>
</tr>
<tr>
<td>V-A on</td>
<td>36/0</td>
<td>6</td>
<td>170/7</td>
<td>96/71</td>
<td>33</td>
</tr>
<tr>
<td>V-A off</td>
<td>50/0</td>
<td>8</td>
<td>205/7</td>
<td>70/50</td>
<td>0</td>
</tr>
</tbody>
</table>

left atrium to the femoral artery was in the range of 25 to 45 ml./Kg./min. Veno-arterial pumping (40 to 50 ml./Kg./min.) also improved the state of the circulation. At identical flow rates left ventricular bypass would reduce the left ventricular diastolic pressure to normal, while veno-arterial pumping would halve the elevation of the diastolic pressure (fig. 2). Both forms of assisted circulation increased the systemic arterial pressure and
diminished the elevated pressures in the left atrium and the right ventricle (tables 1d and 2d).

**Left Heart Failure Caused by Controlled, Reversible Aortic Insufficiency (46 Observations)**

Aortic insufficiency produced with the “Braunwald tube” was apparent from the shape of the systemic pulse, which exhibited abnormally high systolic and low diastolic pressures (Corrigan’s pulse). Partial bypass of the left ventricle invariably resulted in rapid and complete compensation in all chambers of the heart. In the most severe types of insufficiency, about 70 to 90 ml./Kg./min. had to be pumped in order to restore compensation. When pumping was discontinued the left heart failure returned. In the less severe instances, compensation was restored with a flow of 40 to 60 ml./Kg./min. pumped from the left atrium to the arterial tree; in some of these observations, compensation of the heart remained after the mechanical assistance was discontinued (table 1e).

**Veno-arterial pumping** always aggravated the existing left heart failure when this was caused by aortic insufficiency (table 2e). The intensification of failure by veno-arterial pumping was in direct proportion to the rate of flow. In most instances where veno-arterial pumping was used, the preparation had to be rescued by emergency left ventricular bypass (fig. 3), by reversal of the aortic insufficiency, or by both.

**Left Heart Failure Caused by Balloon in Left Ventricle (35 Observations)**

Bypass of the left ventricle in this type of failure always resulted in complete compensation of the left heart; 60 to 70 ml./Kg./min. had to be pumped from the left atrium to the femoral artery in order to reverse left heart failure of the most severe degree. When the degree of failure was not severe in the control period, compensation often remained after arrest of the left ventricular bypass, even though the balloon was still distended (table 1f).

**Veno-arterial pumping** had paradoxical results in this situation (table 2f). In 12 of 17 observation where veno-arterial pumping (20 to 75 ml./Kg./min.) was used, the left ventricular diastolic pressure increased, indicating severe, rapid intensification of the cardiac failure, even as pressures in the left atrium and the right ventricle decreased and systemic
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Figure 3
A. Left ventricular failure caused by aortic insufficiency.
B. Start of veno-arterial pumping, 40 ml./Kg./min. Marked intensification of failure.
C. Start of left ventricular bypass, 62 ml./Kg./min. Return of compensation.

arterial pressure rose. The preparation usually had to be rescued by left ventricular bypass, as illustrated in figure 4, or by deflation of the balloon. In 5 of the 17 observations, the control decompensation was not severe; veno-arterial pumping caused improvement, but full compensation was not restored. In the instances of veno-arterial pumping, the improvement of decompensation occurring during the mechanical assistance was maintained after arresting the veno-arterial pump; for this reason we suspect that compensation might have occurred spontaneously.

Left Heart Failure Produced by Arresting the Flow in a Coronary Artery in Conjunction with Other Insults (53 Observations)

This "coronary" heart failure was characterized by a fall of the systemic arterial pressure, increases of the left ventricular diastolic, the left atrial, and right ventricular systolic pressures.

Left ventricular bypass invariably changed the abnormal pressures in the direction of compensation (fig. 5), but the degree of compensation achieved was dependent upon the bypass flow, 50 to 70 ml./Kg./min., producing complete compensation of even the most severe failure states. When the left ventricular bypass was arrested and when the left ventricular diastolic pressure had been above 10 mm.

Hg before the bypass, severe failure reappeared as soon as the bypass was stopped. In lesser degrees of failure, compensation sometimes remained after the bypass was discontinued (table 1g).

When veno-arterial pumping of any magnitude was started after severe "coronary" failure had supervened, decompensation of the left ventricle was always intensified. In this situation, the pressure in the systemic arterial system was increased, the left ventricular diastolic and the left atrial pressures rose, with concomitant decreases of the systolic peak pressures in both ventricles (table 2g). After veno-arterial pumping, the preparation usually had to be rescued by left ventricular bypass (fig. 5). When the control decompensation was relatively modest (5 to 10 mm. Hg left ventricular diastolic pressure), veno-arterial pumping had no effect on the left ventricular diastolic pressure, although it caused decreases of the left atrial and the right ventricular pressures.

Whenever overtransfusion was combined with coronary occlusion, failure of both chambers was initially observed, but the heart would usually regain compensation spontaneously over a period of 5 to 10 minutes. In this experimental situation, both types of assisted circulation caused rapid return of compensation.
Spontaneous Failure of the Left Ventricle (22 Observations)

In this type of failure, left ventricular bypass increased the systemic arterial pressure and restored compensation of the left ventricle (table 1b, fig. 6). In several instances, compensation continued after arrest of the bypass procedure.

In spontaneous failure, veno-arterial pumping had no influence on the abnormal pressure in the left atrium or on the systemic arterial pressure. It usually decreased the pressures in the left atrium and the right ventricle (table 2h, fig. 6).

Discussion

The effects of various types of assisted circulation on compensated hearts have been reported before. Galletti et al.5,7 have shown that closed-chest dogs can tolerate partial heart-lung bypass for prolonged periods and that the pulmonary blood flow, the heart rate, and the right ventricular and systemic arterial pressures can be markedly reduced in such animals when their intracorporeal blood volume is decreased. It is now known that mean left ventricular pressure (strongly influenced by heart rate and by systemic arterial pressure) is a determinant of the oxygen requirement of compensated hearts.8 The experiments of the above authors demonstrated therefore that partial heart-lung bypass can decrease the cardiac oxygen need. Their data also show that prolonged decreases of the intracorporeal blood volume can be tolerated by normal dogs in the presence of a heart-lung bypass of sufficient magnitude without the development of shock or acidosis. It is likely that similar decreases of the blood volume without the bypass pumping would also have reduced cardiac oxygen need. Normal dogs can tolerate prolonged veno-arterial pumping which reduces the blood flow through the lungs,9,10 but veno-arterial pumping can also cause systemic hypotension and acidosis.5,11 In carefully monitored open-chest experiments with drainage of the right ventricle, it was shown that partial left heart bypass lowered the pressure in the left atrium but did not necessarily result in changes of the left ventricular pressure or of the cardiac oxygen requirements.8,12,13

In earlier experiments8 concerning the effects of bypass on the heart, we made observations on compensated hearts and also during failure of the left ventricle, which was due to atrial tachycardia or admixture of aconitine to the systemic circulation. Graphical analysis of our pooled data (unpublished experiments) showed that abnormally high left ventricular diastolic pressure could become a major determinant of cardiac oxygen need and would then outweigh the parameter determining oxygen consumption in compensated hearts (mean left ventricular pressure). It was also evident that diastolic pressure in the left ventricle was not always closely related to left atrial pressure8 (fig. 6). The effect of mechanical assistance was therefore reinvestigated as reported here, since it had become apparent that the influence of assisted circulation upon the failing heart could not be predicted from experiments with uncompensated hearts or from any experimental design which did not measure left ventricular diastolic pressure with a reliable method.

All investigators who compare experimental procedures with clinical situations must realize that many features of disease in human patients cannot be reproduced in the labora-
Acute experimental cardiac decompensation is not comparable in every respect with clinical heart failure because of species differences, and also because the dog heart—unlike its human counterpart—possesses an intact, fully reactive coronary system and usually has no scars or excess connective tissue. In spite of these reservations, we believe that several types of experimental heart failure reported here reproduce essential features of comparable clinical situations and may therefore help to evaluate therapeutic maneuvers.

In our experiments, each type of interference with the blood flow, blood volume, or the contractile mechanism of the heart produced a distinct pattern of heart failure. It has long been appreciated that constriction of the pulmonary artery can cause decompensation of the right ventricle and a pattern of flows and pressures comparable with the acute cor pulmonale seen after massive pulmonary embolism in human patients. As reported here, a slight increase of the blood volume aggravated pre-existing decompensation of any type, an observation which mimics many clinical situations. Coarctation of the aorta often causes left ventricular failure in humans when it has existed for prolonged periods; we could not consistently produce heart failure in dogs by constricting the ascending aorta, but combination with coronary occlusion caused failure of the left ventricle, a finding which is somewhat analogous to a similar clinical situation. Aortic insufficiency usually develops in patients over a period of years; the experiments reported here produced this abnormality within seconds and exhibited all hemodynamic features of the clinical picture. The balloon in the left ventricle can be compared with the rarely seen ventricular myxoma or clot; it is not strictly comparable with any other common clinical situation. The balloon resulted in distention and overloading of the left ventricle, manifested by the typical signs of left ventricular failure. The failure produced in dogs by a combination of coronary occlusion and other insults exhibited hemodynamic characteristics resembling the clinical picture seen in human patients when left heart failure and shock has been caused by coronary occlusion. The spontaneous heart failure observed in some of our experiments resembled the pattern of cardiac failure in humans when this was caused by diseases which weaken the myocardium.

The effects of veno-arterial pumping and of left ventricular bypass were studied in all types of experimental heart failure described here (table 3). Since the extracorporeal circuit was ready for operation, start or termination of mechanical assistance did not cause changes of the intracorporeal blood volume or disturbances to the heart due to mechanical manipulation. Veno-arterial pumping was not used for periods exceeding 15 minutes; we did not measure chemical parameters, but believe that such brief periods of pumping essentially reproduce the hemodynamic effects of partial heart-lung bypass (using a heart-lung machine).

Veno-arterial pumping always relieved failure of the right ventricle, where it also increased the systemic arterial pressure. It also ameliorated failure states when these were aggravated by expansion of the blood volume (except in aortic insufficiency). In occasional instances of other types of heart failure, veno-arterial pumping would decrease right ventricular and left atrial pressures, even though it did not influence the pressure in the left ventricle. However, a surprising and unexpected effect in the great majority of left ventricular
Table 3

Comparison of Two Types of Mechanical Assistance in Experimental Failure of Left Ventricle*

<table>
<thead>
<tr>
<th>Cause of failure</th>
<th>Left ventricular bypass</th>
<th>Veno-arterial pumping</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LAP [cm. H2O]</td>
<td>LVP [mm. Hg]</td>
</tr>
<tr>
<td>1. Overtransfusion (18 obs.) alone or together with other insults, except aortic insuff.</td>
<td>30</td>
<td>108/18</td>
</tr>
<tr>
<td>2. Overtransfusion (19 obs.) together with aortic insuff.</td>
<td>43</td>
<td>105/30</td>
</tr>
<tr>
<td>3. Aortic constriction alone (23 obs.)</td>
<td>12</td>
<td>235/10</td>
</tr>
<tr>
<td>4. Aortic insufficiency alone (46 obs.)</td>
<td>34</td>
<td>110/24</td>
</tr>
<tr>
<td>5. Balloon in left ventricle alone (35 obs.)</td>
<td>36</td>
<td>148/18</td>
</tr>
<tr>
<td>6. Coronary occlusion plus other insults (3, 4, 5 above) (53 obs.)</td>
<td>27</td>
<td>140/15</td>
</tr>
<tr>
<td>7. &quot;Spontaneous&quot; failure (22 obs.)</td>
<td>21</td>
<td>108/14</td>
</tr>
</tbody>
</table>

*Pressures and flows given here are arithmetical means of data from number of observations stated.

failure experiments was the marked intensification of failure resulting from veno-arterial pumping. The procedure would usually increase the cardiac failure to a point which would have been catastrophic in comparable human situations. Vein-to-artery pumping was deleterious, or had no effect on left ventricular failure in 83 per cent of 93 observations. Although we have shown here that veno-arterial pumping is harmful or useless in most cases of normovolemic left ventricular failure, we do not imply that the procedure cannot improve conditions caused by abnormal left atrial pressure when this is due to other causes. It has already been demonstrated in dogs and man* that veno-arterial pumping or partial heart-lung bypass can diminish elevated left atrial pressures caused by malfunction of the mitral valve.

Left ventricular bypass (pumping of blood from the left atrium to the arterial tree) always ameliorated or relieved all forms of experimental heart failure, with the exception of the cor pulmonale produced by pulmonary artery constriction. The beneficial effect of left ventricular bypass was apparent immediately. In left heart failure, the amount of blood which could be pumped from the left atrium varied directly with the severity and type of decompensation. Adverse effects of left ventricular bypass were not observed. The striking reproducibility of the "compensating" effect of bypass of the left ventricle suggests its application in human patients with refractory, acute left heart failure, even though thoracotomy and positive pressure ventilation are necessary in order to gain access to the left atrium.

We do not attempt analysis of our findings at this time because normal cardiac function is presently not completely understood and even less is known about the failing heart.

Summary

In open-chest dog experiments, 7 different types of cardiac failure were produced. In each type of failure, the effect of veno-arterial

*Salamon, F.: Department of Surgery, University of Virginia Medical College, Charlottesville, Va.: Personal communication, October 22, 1959.
pumping and of left ventricular bypass (blood pumped from the left atrium to femoral artery) was investigated. Pressures were recorded in the left ventricle, the left atrium, the right ventricle, and the femoral artery.

Veno-arterial pumping reversed failure of the right ventricle. It also was beneficial when overtransfusion had aggravated failure of the right or left ventricles, except in pre-existing aortic insufficiency. Veno-arterial pumping markedly increased decompensation of the left heart in the majority of observations, even though it occasionally reduced pressures in the left atrium and the right ventricle. The experiments suggest the use of veno-arterial pumping or of partial bypass with a heart-lung machine in acute cor pulmonale and in pulmonary congestion caused by abnormalities of the mitral valve where the left ventricle remains compensated. Veno-arterial pumping appears contraindicated in true failure of the left ventricle.

Left ventricular bypass always restored compensation in all types of heart failure except cor pulmonale. The experiments suggest the clinical use of left ventricular bypass in left heart failure.

Interlingua translation will be found on page 445.

References

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