Hemodynamic Effects of Extracorporeal Circulation

In Closed-Chest Normal Animals and in Those with Myocardial Infarction with Shock

By LESLIE A. KUHN, M.D., FRANK L. GRUBER, M.D., ALBERT FRANKEL, M.D., AND SHERMAN KUPFER, M.D.

The hemodynamic effects of closed-chest extracorporeal circulation were investigated in normal dogs and in dogs subjected to coronary embolization. In both groups, despite delivery of large volumes of blood into the abdominal aorta through peripheral routes, a rise in proximal aortic pressure could not be achieved; to accomplish this it was necessary to increase vascular resistance by balloon obstruction of the lower abdominal aorta, the distal aorta being supplied with superior vena cava blood. The resulting rise in proximal aortic pressure was accompanied by a diminution in calculated left ventricular work.

A LTHOUGH the use of vasopressor agents has reduced mortality in myocardial infarction with shock, about 50 to 60 per cent of these patients fail to respond to presently available therapy.1,2 In such patients, extracorporeal circulatory support might prove useful in maintaining the circulation to vital areas until adequate homeostatic mechanisms or responsiveness to drug therapy have been restored. The use of such extracorporeal circulation requires that a suitable apparatus can be rapidly assembled and operated for relatively prolonged periods with the chest closed. The major objective in using this apparatus is to produce a sustained increase in aortic pressure, and hence an increase in perfusion of the coronary, cerebral, and other important regional circulations. It would also be desirable if such extracorporeal support of the circulation were not accompanied by an increase in left ventricular work of sufficient magnitude to result in further deterioration of an already damaged left ventricle. With these considerations, the hemodynamic effects of extracorporeal circulation have been investigated in closed-chest dogs with normal circulation, with ventricular fibrillation and with shock following coronary embolization.

Methods

Pentobarbital, 30 mg/Kg, was injected intravenously for anesthesia. Arterial and intracardiac pressures were measured with cardiac catheters or needles attached to Statham strain gages and suitable recording equipment. Teflon plastic, or Bar- dex latex catheters, 12-16 French, were utilized for venous drainage and arterial delivery. Appropriate fittings connected these catheters with the Tygon® plastic tubing (0.64 cm. I.D.) used in the extracorporeal circulation. Heparin, 2 mg/Kg, was employed as the anticoagulant. The arterial flow rate delivered by the apparatus was determined at the conclusion of each experiment by measuring the rate of collection of blood pumped through the arterial delivery catheter at each pump setting used during the procedure. Plasma hemoglobin was measured spectrophotometrically at hourly intervals.

Group I. Closed-Chest Animals with Total Circulatory Support from Pump-Oxygogenator

This group was studied to determine the degree of extracorporeal circulatory support which could be achieved in a closed-chest animal with peripheral cannulations. Ventricular fibrillation was induced in 5 dogs by a suitable tetanic current delivered through needle electrodes placed percutane-
Figure 1
Diagrammatic representation of a closed-chest animal with circulation "compartmentalized" by balloon obstruction of the abdominal aorta. Blood from the superior vena cava drains by gravity into a reservoir from where it is pumped via a femoral artery into the distal aorta below the site of obstruction (See text for further detail).

Mid-thoracic aortic pressure was measured at 5-minute intervals via a catheter inserted into a femoral artery. At the conclusion of 3 hours of ventricular fibrillation, defibrillation was carried out in each case by means of an Electrodyne external defibrillator (0.15 second impulses delivering 250 to 550 volts).

Group III. Closed-Chest Animals with Balloon Obstruction of the Abdominal Aorta and Superior Vena Caval-Distal Aortic Shunting (fig. 1)

Because it was apparent that shunting of large quantities of blood into the abdominal aorta could not effect a rise in proximal aortic pressure in normal animals or in those with shock following coronary embolization, it was decided to increase vascular resistance by obstructing the abdominal aorta with a balloon catheter. In this manner, the circulation was "compartmentalized," leading to a rise in proximal aortic pressure with increased perfusion of the heart and the brain. Blood from the superior vena cava supplied the abdominal aorta below the site of obstruction, as described in Group II. Since the oxygenator was eliminated a small priming volume of about 150 ml. of either blood or saline was adequate.

Obstruction of the abdominal aorta was effected by means of a triple-lumen cardiac catheter inserted via a femoral artery. The distention of the balloon was controlled via the middle lumen of this catheter while the other lumens were used for periodic pressure recording and sampling on either side of the obstruction. The catheter was placed at the lowest point in the abdominal aorta at which inflation of the balloon produced a proximal aortic pressure rise. Preliminary experimentation with the abdomen open revealed this to be usually at a point corresponding to vertebral level L2 to L4. It was always possible to achieve a rise in proximal aortic pressure by obstructing the aorta just above the renal arteries, between the superior mesenteric artery and the renal arteries. Occasionally, it was possible to raise the proximal aortic pressure by obstruction of the aorta below the renal arteries, between the renal and inferior mesenteric arteries.

In 8 animals, cardiac outputs were determined by the indicator-dilution method of Stewart4 and Hamilton5 as conventionally employed, utilizing the carotid artery as the sampling site. Left ventricular work was calculated as the product of cardiac output and mean proximal aortic pressure, measured during each output determination. Cardiac output and ventricular work were measured during the control period (after the catheters had been positioned) and at hourly intervals during the 4-hour procedures. In order to maintain a constant blood volume, a quantity of blood equivalent to that removed was replaced following each cardiac output determination.

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Right atrial pressure was measured in 5 animals by means of a cardiac catheter inserted via a femoral vein and positioned fluoroscopically. Oxygen contents of blood drawn from the shunt line (superior vena cava), inferior vena cava and aorta, proximal and distal to the obstruction, were determined at hourly intervals by the method of Van Slyke and Neill. In one animal with suprapelvic aortic obstruction the changes in glomerular filtration rate were determined periodically by the standard creatinine clearance technic. Twelve of the 19 animals in the group were observed for intervals from 1 week to several months following the procedure.

In 2 open-chest animals, left ventricular pressure was recorded through 20-gauge needles inserted directly into the ventricular cavity.

Group IV. Abdominal Aortic Obstruction with Superior Vena Caval-Distal Aortic Shunting in Closed-Chest Animals with Hypotension Following Coronary Embolization

The arrangement of the extracorporeal circulation in this group of 6 animals was the same as that described for Group III. After the appropriate catheters had been placed, coronary embolization was performed by a modification of the method of Agress and his associates. Instead of a metal cannula, however, as used by Agress, a no. 10 to 12 nylon-plastic cardiac catheter was inserted via a femoral or carotid artery and positioned fluoroscopically just above the aortic valve. Mixed plastic spheres (2 to 3 mg./Kg.) suspended in a 15 per cent solution of acacia in normal saline were injected by means of a hand-operated pressure injector into the catheter during transient balloon occlusion of the ascending aorta. In some, another departure from Agress' method was utilized. The spheres were injected into the coronary circulation during transient cardiac arrest with 0.4 mg./Kg. of acetylcholine injected intravenously. Following coronary embolization, the extracorporeal circulation was started. The duration of the shock-like state averaged 2 hours, although longer periods could be produced by repeating the injections of the plastic spheres.

Results

Group I. Closed-Chest Animals with Ventricular Fibrillation and Total Circulatory Support from Pump-Oxygenator

The results in this group are illustrated in table 1. Average flows of 60 ml./Kg./min. were maintained. The average aortic pressure was 94 mm. Hg and external defibrillation was successfully performed in each case after 3 hours of ventricular fibrillation.

<table>
<thead>
<tr>
<th>Control mm. Hg</th>
<th>During V.F. with extracorporeal circulation mm. Hg</th>
<th>Flow ml./Kg./min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>70</td>
<td>61</td>
</tr>
<tr>
<td>130</td>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td>140</td>
<td>110</td>
<td>50</td>
</tr>
<tr>
<td>120</td>
<td>120</td>
<td>65</td>
</tr>
<tr>
<td>140</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>Av. 126</td>
<td>94</td>
<td>60</td>
</tr>
</tbody>
</table>

Group II. Closed-Chest Animals with Superior Vena Caval-Abdominal Aortic Shunting

As can be seen from the data recorded in table 2, there was no significant rise in thoracic aortic pressure during superior vena caval to abdominal aortic shunting in either normal animals or in those with arterial hypotension following coronary embolization. As might be expected, even when a reduced cardiac output was present, pressor effects could not be induced in the aorta despite the delivery of relatively large amounts of blood into the abdominal aorta inasmuch as the volume reaching the circulation through the left heart is reduced.

Group III. Closed-Chest Animals with Balloon Obstruction of the Abdominal Aorta and Superior Vena Caval-Distal Aortic Shunting (fig. 1)

Table 1, a summary of data from 19 normal animals, demonstrates that a proximal aortic
Hemodynamic alterations in dogs with balloon obstruction of the abdominal aorta and superior vena caval-distal aortic shunting, as diagrammed in Figure 1. Despite a rise in proximal aortic pressure produced by mechanical increase in vascular resistance, there is diminution in calculated left ventricular work owing to shunting of a portion of the venous return into the distal aorta. Although average figures are presented for graphic purposes, similar directional changes were noted in each animal.

A pressure rise could be obtained and sustained throughout the course of the 4-hour experiment with this method. The average flow shunted into the distal aorta was 44 ml./Kg./min., which was sufficient to maintain the distal aortic mean pressure at 80 to 92 mm Hg. The rise in proximal aortic pressure was unassociated with alterations in right atrial mean pressure or left ventricular diastolic pressure.

Figure 2 indicates that, despite a rise in proximal aortic pressure, the calculated left ventricular work was diminished. This appears to be a result of reduction in cardiac output due to shunting of a portion of the venous return into the distal aorta. Average values are presented for graphic purposes, but similar directional changes were noted in each animal.

Table 4 demonstrates the diminution in renal function when the aorta was obstructed above the renal arteries. As could be expected, glomerular filtration rate was considerably reduced. After releasing the balloon, the glomerular filtration rate returned towards normal. There was no post-operative azotemia either in this animal or in the 4 other animals tested. In the 4 animals autopsied, there was no gross or microscopic abnormality in the kidneys.

The oxygen concentration of the blood shunted into the distal aorta (table 5) remained at about 50 per cent that in the proximal aorta. The oxygen content of the blood in the distal aorta varied between this level and that of the proximal aorta. This was thought to be due to a variable mixture of...
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superior vena caval blood with proximal aortic blood, the latter entering the distal aorta either through collaterals or because of incomplete aortic obstruction. The arteriovenous oxygen difference showed no change in the upper portion of the body as measured by the proximal aorta-superior caval difference, although the data are sparse. The oxygen difference between blood from the distal aorta and from the inferior cava remained at control levels in 2 dogs, whereas in the third animal, there was a considerable increase. More data are required to assess adequately this factor. Transient hind limb weakness was noted in 4 of the animals with the lowest distal aortic pressures.

Plasma hemoglobin (table 6) showed a progressive increase during the procedure. However, less hemolysis was noted when saline was used for priming.

Group IV. Abdominal Aortic Obstruction with Superior Vena Caval-Distal Aortic Shunting in Closed-Chest Animals with Coronary Embolization

Aortic pressures are recorded in table 7. Considerable increases in proximal aortic pressure and hence coronary perfusion, were obtained in these hypotensive animals, the pressor effect lasting throughout the 2-hour duration of the experiments.

Discussion

There is evidence from these experiments that substantial quantities of blood can be delivered by mechanical means through accessible peripheral routes in a closed-chest animal. In animals with ventricular fibrillation, the amount of blood delivered to the abdominal aorta by this means can maintain a coronary circulation sufficient to permit defibrillation after a prolonged period.

A more pertinent question from the standpoint of potential usefulness in myocardial infarction with shock, however, is whether delivery of even these quantities of blood into the abdominal aorta can substantially increase proximal aortic pressure and hence, coronary perfusion, when cardiac performance is not interrupted. The use of a pump-oxygenator with delivery of blood into a peripheral artery has been advocated as a treatment for patients with acute myocardial infarction in shock.

The protocols in 2 of the 3 cases so treated do not record arterial pressure levels. In the third case there was an initial associated supraventricular tachycardia, subsequent control of which may have been instrumental in raising arterial pressure. The data obtained in the present experiments suggest that a significant proximal aortic pressor response cannot be induced when even relatively large rates of blood flow are delivered into the abdominal aorta in either normal animals or in those with arterial hypotension following coronary embolization. Therefore, it would seem that the use of extracorporeal circulation, as conventionally employed, may be in-

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Table 5

<table>
<thead>
<tr>
<th>A-V O₂ Difference (Vol. %)</th>
<th>Distal aorta</th>
<th>Shunt line % O₂ saturation (SVC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal aorta SVC</td>
<td>Primalière</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4.22</td>
<td>4.89</td>
</tr>
<tr>
<td>1 Hr.</td>
<td>4.58</td>
<td>49.5</td>
</tr>
<tr>
<td>2 Hrs.</td>
<td>5.92</td>
<td>55.8</td>
</tr>
<tr>
<td>3 Hrs.</td>
<td>4.40</td>
<td>53.4</td>
</tr>
<tr>
<td>4 Hrs.</td>
<td>4.52 (2 dogs)</td>
<td>6.49 (3 dogs)</td>
</tr>
</tbody>
</table>

Table 6

<table>
<thead>
<tr>
<th>Plasma Hemoglobin Levels during Abdominal Aortic Obstruction and Superior Vena Caval-Distal Aortic Shunting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primed with dog blood (1-7 days old) (Av. of 7 dogs)</td>
</tr>
<tr>
<td>1 Hr. 2 Hrs. 3 Hrs. 4 Hrs.</td>
</tr>
<tr>
<td>191 212</td>
</tr>
<tr>
<td>Primed with Saline (Av. of 5 dogs)</td>
</tr>
<tr>
<td>28 81 127 160</td>
</tr>
<tr>
<td>Initial donor blood level (Av. of 3 dogs)</td>
</tr>
<tr>
<td>290</td>
</tr>
</tbody>
</table>

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Table 7

Arterial Pressures following Coronary Embolization and the Effects of Abdominal Aortic Obstruction and Superior Vena Cava-Distal Aortic Shunting

<table>
<thead>
<tr>
<th>Coronary Embolization</th>
<th>Pressure (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>After</td>
</tr>
<tr>
<td>Arterial Pressure (S/D (mean))</td>
<td>embolization</td>
</tr>
<tr>
<td>Average of</td>
<td>143/98 (113)</td>
</tr>
<tr>
<td>6 dogs</td>
<td>(S.D. 21)</td>
</tr>
</tbody>
</table>

adequate to increase aortic pressure and hence, coronary perfusion, when shock is present. While simple veno-arterial shunting, with or without oxygenation, may be a useful mechanical method of treating acute, severe congestive heart failure,6,8 this situation is not necessarily or usually associated with clinical9 or experimental10 myocardial infarction with shock.

However, a proximal aortic pressure rise with consequent increase in coronary and cerebral perfusion was achieved by obstructing the abdominal aorta. Since the cardiac output diminishes following coronary embolization,10 the pressor effect in the proximal aorta is attributable to the mechanical increase in vascular resistance produced by aortic obstruction. Although there was a rise in proximal aortic pressure, the calculated work of the left ventricle was measurably reduced. The reduction was mainly associated with the diminished cardiac output. This reduction in cardiac output may not necessarily be accompanied by a diminished total myocardial oxygen utilization.11,12 The significance of this observation has not been completely evaluated since clinical experience indicates that a rise in aortic pressure is associated with increased survival in patients with myocardial infarction in shock despite the associated increase in oxygen utilization by the myocardium.

The only late complication observed in these animals was transient hind limb weakness. This was attributed to spinal cord ischemia. Obstruction of the aorta at appropriate levels in man may be less troublesome since the human cord ends at a higher level than the canine cord.

Although the diminution in glomerular filtration rate associated with aortic occlusion above the renal arteries is of concern, there was no apparent residual renal damage under these experimental conditions. The distal aortic flows and pressures obtained were well above those required for maintenance of renal viability, as judged from the work of Moyer and his associates13 on dogs with supra-renal aortic occlusion, and exceeded the figure of 35 ml./Kg./min. determined by Morris and his associates14 as adequate to maintain renal function in human subjects during extracorporeal circulation.

It is difficult to translate the effects of prolonged pumping on the elements of the blood of the dog to man. Blood typing and cross-matching were not attempted and incompatibility of dog blood may add a detrimental factor.15 That it is possible to pump blood for prolonged periods with little observable damage to its elements has been demonstrated by Hamer and his associates.7 Studies on a human subject after 16 hours of pumping blood from the superior vena cava into the unobstructed aorta, utilizing a different pump, revealed a negligible degree of hemolysis.

Summary

To determine the degree of extracorporeal circulatory support which could be maintained in closed-chest dogs with peripheral cannulations, the cardiac outputs in 5 dogs were reduced to zero by ventricular fibrilla-
tion and the circulation was maintained by a pump-oxygenator. Flows averaging 60 ml./Kg./min. were maintained. Average mean arterial pressure was 94 mm. Hg and a sufficient coronary circulation was attained to permit external defibrillation after 3 hours of ventricular fibrillation.

However, in normal animals and in those with hypotension following coronary embolization, a rise in proximal aortic pressure could not be achieved by transferring large quantities of blood from the veins to the abdominal aorta.

To increase proximal aortic pressure, and hence coronary perfusion, it was necessary to increase vascular resistance. This was accomplished by "compartmentalizing" the circulation with balloon obstruction of the lower abdominal aorta. The distal aorta, below the site of obstruction, was supplied with blood from the superior vena cava. In 19 closed-chest normal animals studied for 4 hours, and in 6 with hypotension following plastic sphere coronary embolization, combined abdominal aortic obstruction and superior vena cava-distal aortic shunting achieved a rise in proximal aortic pressure. There was a diminution in calculated left ventricular work which is attributable to shunting of a portion of the venous return into the distal aorta.

Summario in Interlingua

Pro determinar le grado del extracorporeo supporto circulatorio mantenibile in cases a thoraco claudite con cannulaciones peripherie, le resultados cardiace de 5 cases essva reducida a zero per fibrillatio et le circulation essva mantenita per medio de un pumpe-oxygenator. Fluxos de un valor medio de 60 ml per kg de peso corporce per minuta essva manteniti. Le valor medio del tension arterial essva 94 mm de Hg, e un sufficiente circulation coronari essva obteinte pro permitter defibrillation ex- terne post 3 horas de fibrillation ventricular.

Tamen, in animales normal e in animales con hypotension post embolismo, un augmento del tension aortic proximal non poter esser effectuate per transferer grande quantitates de sanguine ab le venas al norta abdominal.

Pro augmentar le proximal tension aortic e ergo le perfusion coronari, il essva necessari augmentar le resistentia vascular. Isto essva effectuate per "compartmentaliser" le circulation per medio del obstruction a balloon del aorta infero-abdominal. Le aorta distal, infra le sito del obstruction, essva provisionate de sanguine ab le vena cave superior. In 19 animales normal a thoraco claudite studiate durante 4 hora e in 6 animales con hypotension post embolismo coronari a spherico de plastico, le combination de obstruction aortic con shunting ab vena cave a aorta distal resultare in un augmento del tension in le aorta proximal. Essva constatate un diminution del calculate labor sinistro-ventricular que es attribuibile al shunting de un portion del retour venose a in le norta distal.

References


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