Tissue Blood Flow to the Heart

INFLUENCE OF CORONARY OCCLUSION AND SURGICAL MEASURES

By Lloyd D. MacLean, M.D., Ph.D., Paul H. Hedenstrom, M.D., and Ralph R. Rayner, M.D.

Many surgical procedures designed to increase the total blood flow to the heart or to distribute the existing flow more equitably have been proposed.1-3 The assessment of these operations has been hampered in the past by: (1) difficulty in obtaining objective data from clinical patients, (2) lack of a method to measure capillary (tissue) blood flow to specific areas of myocardium, and (3) lack of a method to measure quantitatively and selectively the functional blood flow to the heart before and after coronary occlusion and after attempts at revascularization.

In the present study, tissue blood flow to specific regions of the canine heart was measured utilizing the deuterium oxide method.4-6 The influence of coronary occlusion and of two operative procedures on regional blood flow was quantitated.

Methods

All experiments were performed on healthy, adult mongrel dogs of either sex, anesthetized with sodium pentobarbital (30 mg./Kg.). Perfusion of coronary vessels was performed in situ via a catheter placed in the ascending aorta advanced from the right carotid and brachiocephalic arteries. Tapes were placed about the superior and inferior venae cavae and about the brachiocephalic artery. Occlusion of the aorta immediately distal to the brachiocephalic artery was provided by a surgical clamp. A collecting catheter was placed in the ostium of the coronary sinus and fixed in place with a purse-string suture. At the beginning of the experiment, inflow occlusion was established by occluding the venae cavae; following this, coronary perfusion was started using oxygenated blood at 37 C. from a pressure flask (135 mm. Hg). The tape about the brachiocephalic artery was drawn up and the clamp placed about the aorta immediately beyond the brachiocephalic artery, thereby limiting perfusion to the coronary system. Following an initial period of equilibration of the isolated beating heart with nonlabeled perfusion fluid (blood), the inflow was changed to blood containing 2 per cent deuterium oxide.7 The perfusion with blood-D2O mixture was discontinued after 20 to 30 seconds. The heart was removed, and the blood was allowed to drain from the cut vessels and was blotted dry and weighed. Seven tissue pieces weighing 2 to 3 Gm. were taken from the right ventricle and the left ventricle in the distribution of the left anterior descending and the circumflex coronary arteries. The tissues and samples of the perfusing blood were prepared for D2O analysis by distilling in vacuo to dryness. The distillate was equilibrated with hydrogen gas at atmospheric pressure in the presence of a platinum oxide catalyst. The tissue and fluid D2O concentrations were determined in the mass spectrometer with an average difference between duplicates of less than 1 per cent. Knowing the concentration of D2O in the arterial perfusion fluid and in the heart tissue, it is possible to calculate tissue blood flow from the following formula:6

$$F = \frac{1}{V_T} \ln \frac{C_A}{C_T}$$

where $$F$$ = flow in milliliters blood/min.; $$V_T$$ = volume of water in the tissue in milliliters; $$t$$ = perfusion time; $$C_A$$ = concentration of D2O in arterial blood; $$C_T$$ = concentration of D2O in tissue. This formula is applicable to any test substance; the rate of uptake of this substance by the tissue is limited by the blood flow through the tissue. This relationship would be obtained if exchange of the material between blood and the extravascular space in the organ were instantaneous relative to its rate of delivery to the organ by the blood. That this relationship obtains for D2O in heart muscle has been documented by Johnson et al.4 and by Thompson et al.5 A detailed discussion of this method has appeared in a previous publication from this laboratory.6

Since the water content of heart muscle, scarred heart muscle, and blood were all approximately 80 per cent, and since the specific gravity of blood...
was nearly one, the perfusion ratios (blood water/min.-ml. of tissue water) for these tissues closely approximate the blood flow through the tissue in milliliters of blood/min.-Gm. of tissue. Results are expressed in the latter more familiar form. Six experiments were performed: (1) normals—the entire coronary system of the dog heart was perfused; (2) acute coronary occlusion—the perfusion was carried out as in (1), however, the left anterior descending coronary artery was ligated immediately prior to perfusion; (3) chronic coronary occlusion—the left anterior descending coronary artery was ligated four to six months prior to perfusion; (4) pulmonary artery to left atrial shunt—this procedure, designed to increase intercoronary anastomoses, was performed six weeks to six months prior to perfusion, and immediately prior to perfusion, the left anterior descending coronary artery was ligated; (5) poudrage with coronary sinus narrowing (Beck I operation)—this procedure was performed four to six months prior to perfusion, and immediately prior to perfusion, the left anterior descending coronary artery was ligated; (6) Beck I operation and left anterior descending coronary occlusion were both performed four to six months prior to perfusion.

Left anterior descending coronary occlusion was performed immediately distal to the circumflex branch of the left coronary artery and did not include the septal artery in any experiments herein reported. The pulmonary artery-left atrial anastomosis was made between the main pulmonary artery and the left atrium within the pericardial sac. In all animals perfused with D₂O, the shunt was functioning prior to perfusion, and oxygen saturation of these animals ranged between 75 per cent and 88 per cent for several weeks prior to perfusion.

Results and Discussion

In the control group of normals, blood flow to the heart ranged from 0.4 to 1.6 ml./Gm./min., which is within limits described using other techniques (1). The present method permits measurement of regional tissue blood flow, which has an advantage over methods which measure total coronary blood flow (e.g., nitrous oxide method) for the type of investigation herein reported. The blood flow per gram did not vary significantly between right ventricle and various parts of the left ventricle in any given animal. This remarkably uniform distribution of blood was seen in all control animals and was useful when considering later experiments which showed a marked alteration in flow from one area to another in the same animal.
CORONARY OCCLUSION AND SURGERY

TABLE 3
Chronic Left Anterior Descending Coronary Occlusion (Blood Flow ml./Gm./min.)

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Right ventricle</th>
<th>Anterior descending distribution</th>
<th>Circumflex distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3-4</td>
<td>5-6</td>
</tr>
<tr>
<td>E 44</td>
<td>0.38 0.33</td>
<td>0.22 0.50</td>
<td>0.59 0.58 0.32</td>
</tr>
<tr>
<td>E 45</td>
<td>0.89 0.65</td>
<td>0.53 0.34</td>
<td>0.35 0.36 0.36</td>
</tr>
<tr>
<td>E 47</td>
<td>0.35 0.19</td>
<td>0.55 0.42</td>
<td>0.45 0.43 0.42</td>
</tr>
</tbody>
</table>

With acute occlusion of the anterior descending branch of the left coronary artery, there was a marked decrease in flow to the sample or samples of myocardium removed from this area (table 2). There appeared to be also a decrease in flow to areas immediately adjacent to the most ischemic area. The flow to the muscle supplied by the left anterior descending coronary artery dropped to 0.1 ml./Gm./min., or less, in at least one of the muscle samples from this area. This degree of ischemia was obvious grossly at the time of the experiment in that there was paradoxical movement and a cyanotic hue to the area in question. There was little chance for the development of collaterals under the conditions of this experiment in that perfusion with D2O was done within minutes of the time of coronary occlusion.

In experiment 3, occlusion of the anterior descending branch of the left coronary artery was performed four to six months prior to the determination of tissue blood flow to the heart. The results appear in table 3. There is a much greater blood flow to the region of the myocardium supplied by the anterior descending artery (areas 5 and 6) than existed immediately after occlusion. Scar tissue representing a healed infarct was present in all hearts at this later date. While collateral flow undoubtedly developed, this did not appear soon enough to prevent infarction. May,11 in anatomical studies of coronary collaterals, has been able to differentiate these vessels from intercoronary anastomoses. It is believed by May11 that the vessels found coursing throughout a scarred area are newly developed, are not enlargements of previously existing vessels, and are the result of the stimulus of necrosis. These collaterals obviously are of little value in preventing the infarct but may account for the return of normal blood pressures in the peripheral coronary system after coronary occlusion as described by Garamella et al.12

The results of experiment 4 appear in table 4. Pulmonary artery to left atrial shunt was performed to increase intercoronary anastomoses, thereby increasing the blood flow to areas of myocardium most apt to become ischemic after acute coronary occlusion. There was a marked reduction in blood flow to the myocardium supplied by the anterior descending artery after occlusion of this vessel, even though a previous and functioning shunt was present. This flow did not vary from controls in which coronary occlusion alone was performed. Poudrage with coronary sinus nar
TABLE 5
Poudrage with Coronary Sinus Narrowing Followed by Acute Left Anterior Descending Coronary Occlusion (Blood Flow ml./Gm./min.)

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Right ventricle</th>
<th>Anterior descending distribution</th>
<th>Circumflex distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>E 5</td>
<td>0.09</td>
<td>0.39</td>
<td>0.03</td>
</tr>
<tr>
<td>E 7</td>
<td>0.67</td>
<td>0.26</td>
<td>0.06</td>
</tr>
<tr>
<td>E 9</td>
<td>0.39</td>
<td>0.09</td>
<td>0.03</td>
</tr>
<tr>
<td>E 15</td>
<td>0.60</td>
<td>0.26</td>
<td>0.02</td>
</tr>
<tr>
<td>E 16</td>
<td>0.34</td>
<td>0.16</td>
<td>0.29</td>
</tr>
</tbody>
</table>

TABLE 6
Poudrage with Coronary Sinus Narrowing and Chronic Left Anterior Descending Coronary Occlusion (Blood Flow ml./Gm./min.)

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Right ventricle</th>
<th>Anterior descending distribution</th>
<th>Circumflex distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>E 6</td>
<td>0.37</td>
<td>0.20</td>
<td>0.09</td>
</tr>
<tr>
<td>E 13</td>
<td>0.45</td>
<td>0.37</td>
<td>0.45</td>
</tr>
<tr>
<td>E 17</td>
<td>1.21</td>
<td>1.21</td>
<td>1.04</td>
</tr>
<tr>
<td>E 18</td>
<td>0.94</td>
<td>0.72</td>
<td>0.45</td>
</tr>
</tbody>
</table>

rowing likewise was ineffective in increasing blood flow to the ischemic area (table 5). When this operation and coronary occlusion were done together and preceded the measurement of blood flow by four to six months, there was evidence of collateral blood flow to the area of myocardium supplied by the occluded vessel (table 6). However, the development of collateral flow did not vary from those obtained in experiment 3 in which coronary occlusion alone was done four to five months previously, again suggesting tissue necrosis as one important stimulus for development of collateral blood flow. The deuterium oxide method was used in the present investigation to measure blood flow because it enables one to quantitate that component of total flow that actually reaches the tissue cells. It provides a direct measurement of the "effective" flow which at least potentially serves the nutritive demands of the organ. This method would appear to be superior to the injection of plastic substances or other masses that do not allow precise quantitation of intercoronary anastomoses or provide any evidence of that portion of the flow, via potential anastomoses, which actually reaches the capillary bed. Furthermore, measurements using D₂O can be made under physiological conditions in the beating heart. This investigation indicates that after ligation of the anterior descending coronary artery, intercoronary anastomoses in the dog heart, although present, are inadequate to maintain functional blood flow to the myocardium in the distribution of this vessel. There does appear to be a regular loss of muscle with fibrous tissue replacement as a sequel to this maneuver. There is no detectable improvement when this ligation has been preceded by a functioning pulmonary artery-left atrial shunt or poudrage with coronary sinus narrowing.

The reports of increased survival after coronary occlusion of animals protected by a myocardial revascularization procedure may be unrelated to blood flow to the ischemic area. It is possible that removal of the epicardium or other procedure may render the heart less vulnerable to ventricular fibrillation. The cause of death after coronary occlusion in the dog is predominantly ventricu-
Coronary occlusion and surgery

Ventricular fibrillation. Studies of the influence of various myocardial revascularization procedures on the vulnerability of the dog heart to ventricular fibrillation have been reported. These investigations indicate that the vulnerability of the dog heart to fibrillation after coronary occlusion is not altered by previous pulmonary artery to left atrial shunt or by poudrage with coronary sinus narrowing. Implantation of the internal mammary artery into the myocardium did afford considerable protection from ventricular fibrillation if this vessel remained patent, but no protection if thrombosed. These separate investigations support the concept, clearly stated by Beck, that normal cardiac function is related to equal distribution of blood throughout the myocardium. However, these studies further suggest that, while bringing a new blood supply to the heart may be effective, two methods currently in use to redistribute the blood are not effective either in increasing tissue blood flow in an ischemic area nor in returning the ventricular fibrillation threshold to normal. Figure 1 is a summary of all results of the present investigation. In each animal, the flow to affected areas of the myocardium is expressed as a percentage of the "normal" areas, regions not influenced by coronary occlusion. Normals (●); chronic left anterior descending artery ligation (●); chronic left anterior descending artery ligation with poudrage and coronary sinus narrowing (∆); acute left anterior descending artery ligation (×); acute left anterior descending artery ligation with previous pulmonary artery to left atrial shunt (◇); acute left anterior descending artery ligation with previous pulmonary artery to left atrial shunt (◇). Acute coronary artery ligation causes a drop in blood flow to less than 10 per cent of normal in the affected area of myocardium regardless of the performance of two operations designed to redistribute blood more equitably by the creation of intercoronary anastomoses. The blood flow to areas of myocardium supplied by an artery which was ligated four to six months previously approximates 50 per cent of normal in those dogs which survive. One myocardial revascularization procedure did not influence this result. The previously mentioned operative procedures are performed, indicating no additional collateral development as a result of these operations. Previous work would suggest that the collateral flow which develops from the stimulus of infarction is not sufficient to favorably influence the depressed and dangerous ventricular fibrillation threshold in this area.

Further investigation, using the method herein described, would be useful to determine the influence of slow gradual coronary occlusion on the development of collateral blood flow.
Summary

Regional tissue blood flow to the heart was measured in the dog using deuterium oxide as a tracer substance. The method assumes that the rate of uptake of the tracer by a tissue is limited by the blood flow through the tissue and that the exchange of the tracer between blood and the extravascular space in the organ is instantaneous by comparison. This assumption has had previous confirmation. Six groups of animals were studied and the results revealed: (1) a uniform distribution of blood flow per unit of weight of tissue between the right ventricle and various parts of the left ventricle; (2) a decrease in tissue blood flow to (0.1 ml./Gm./min., or less), approximately 7 per cent of normal in the area supplied by the left anterior descending coronary artery after acute occlusion of this vessel; (3) a failure of two operative procedures designed to increase intercoronary anastomoses to influence this greatly decreased flow, when these procedures were performed six weeks to six months prior to testing; (4) an increase in tissue blood flow to an ischemic area of myocardium to 50 per cent of normal four to six months after coronary occlusion; (5) a failure of operative procedures to increase significantly the blood flow to the ischemic area over that which developed naturally, indicating no additional collateral vessel development due to the operations. The results of this investigation were discussed in relation to experiments which deal with myocardial function and vulnerability to ventricular fibrillation after coronary occlusion.

References

Tissue Blood Flow to the Heart: INFLUENCE OF CORONARY OCCLUSION AND SURGICAL MEASURES
Lloyd D. MacLean, Paul H. Hedenstrom and Ralph R. Rayner

Circ Res. 1962;10:45-50
doi: 10.1161/01.RES.10.1.45

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1962 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/10/1/45

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/