Further Studies on the Effect of Arteriovenous Fistulas and Elevations of Sinus Pressure on Mortality Rates Following Acute Coronary Occlusions

By George Smith, F.R.C.S., James Demming, Morton Eleff, and Richard W. Eckstein, M.D.

Observations were made on the mortality rates within the first hour following acute ligation of the circumflex artery. The experiments were divided into the following groups: (1) those with arteriovenous fistulas, (2) those with elevation of coronary sinus pressure, (3) those with complete coronary sinus occlusion, and (4) those with arterialization of the coronary sinus. There was a mortality of 70 per cent in the first group, 30 per cent in the second group, 40 per cent in the third group, and no deaths in the fourth group. The results indicate that arterialization of the coronary sinus provides the greatest protection against ventricular fibrillation and that such arterialization provides the only practical means of chronically elevating coronary sinus pressures to effective levels.

Previous investigations have shown that acute arterialization of the coronary sinus in dogs leads to remarkable protection against acute ventricular fibrillation during the first hour following acute coronary artery ligation. Although no attempts were made to analyze the exact mechanism of the protective nature of this procedure certain questions were raised at that time. It is the purpose of this report to repeat some of our previous experiments and to present the results of studies to determine whether there are beneficial effects from: (1) arteriovenous fistulas as close as possible to the heart, (2) simple elevation of coronary sinus pressure without arterialization of the sinus, and finally (3) complete coronary sinus occlusion without arterialization of the sinus. This study deals with comparisons of acute mortality rates within one hour in dogs following circumflex artery ligation with each of the above named variables. It is hoped that through these studies facts may be obtained which will lead to an understanding of the exact physiologic processes operating to protect the heart after the coronary sinus anastomosis of Beck and his associates.

Methods and Results

Mongrel dogs varying in weight from 8 to 21.5 Kg. were anesthetized with morphine and pentobarbital. Under artificial respiration the left chest was opened between the fourth and fifth ribs. The pericardium was slit and the circumflex artery was dissected free at its origin and a loose ligature was placed beneath it. The left subclavian artery was treated likewise. The coronary sinus was isolated. The animal was heparinized and a long, glass cannula was passed to the level of the right auricle through the left jugular vein. A cannula was also placed in the aorta by way of the left common carotid artery for optical recordings of blood pressure. Electrocardiograms were taken and usually lead aVR was used. At this point the procedure was varied so as to divide the experiments into four groups.

Group 1. Arteriovenous Fistulas

This group consisted of 10 dogs whose average weight was 12.7 Kg. An arteriovenous fistula was created by an appropriate connection between the left subclavian artery and the right auricle through the left jugular
cannula. In an effort to handle these hearts exactly as in the other groups a cannula was passed through the tip of the right auricle into the coronary sinus where it was secured with a ligature. The sinus blood entered the right auricle through a wide side opening in the cannula. The external end of the cannula remained closed. After the electrocardiograms and optical aortic pressures were recorded the arteriovenous fistula was opened. Its magnitude was estimated by measuring the fistula flow into a graduate held at the level of the jugular vein. A further set of records were taken.

QRS complex, with a deep inversion of the T wave and a marked depression of the S-T segment. These changes occurred in all dogs whether they died with ventricular fibrillation or survived for one hour. The blood flow through the fistulas ranged from 240 cc. per minute to 420 cc. per minute with an average of 344 cc. per minute. (See table 1.)

**Group 2. Elevation of Coronary Sinus Pressure**

This group also consisted of 10 dogs whose average weight was 12.6 Kg. The coronary sinus was cannulated through the tip of the right auricle. The cannula was made secure with a ligature and the sinus pressure was optically recorded. The sinus blood was led into the left jugular vein. The left subclavian artery was ligated. In an effort to maintain a high mean sinus pressure of about 50 mm. Hg and to reduce the high levels of sinus systolic pressure, an air chamber was placed in the tubing between the sinus and the jugular vein (fig. 1). After control records were obtained a clamp was placed near the jugular cannula distal to the air chamber to elevate sinus pressure. To produce mean pressures of 50

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**Table 1.—Average Data for Each Group**

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.V. Fistulas</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dog weights (Kg.)</td>
<td>12.7</td>
<td>12.6</td>
<td>13.9</td>
<td>13.7</td>
</tr>
<tr>
<td>Percentage of total heart weight made ischemic by circumflex ligation</td>
<td>37</td>
<td>43</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>Mean aortic pressure prior to opening of A.V. fistulas, elevation of sinus pressure, arteriolarization of sinus or sinus occlusion (mm. Hg)</td>
<td>79</td>
<td>88</td>
<td>103</td>
<td>112</td>
</tr>
<tr>
<td>Mean aortic pressure after manipulation as above but prior to circumflex ligation (mm. Hg)</td>
<td>75</td>
<td>87</td>
<td>89</td>
<td>109</td>
</tr>
<tr>
<td>Mean aortic pressure one hour after circumflex ligation (mm. Hg) (surviving dogs)</td>
<td>79</td>
<td>75</td>
<td>69</td>
<td>84</td>
</tr>
<tr>
<td>Mean coronary sinus pressure prior to circumflex ligation (mm. Hg)</td>
<td>40</td>
<td>45</td>
<td>39</td>
<td>48</td>
</tr>
<tr>
<td>Mean coronary sinus pressure 30 seconds after circumflex ligation (mm. Hg)</td>
<td>37</td>
<td>43</td>
<td>35</td>
<td>38</td>
</tr>
<tr>
<td>Survival time (all dogs) (minutes)</td>
<td>27</td>
<td>50</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>Survival time for dogs dying in less than one hour (minutes)</td>
<td>13</td>
<td>39</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Per cent surviving for one hour</td>
<td>30</td>
<td>60</td>
<td>100</td>
<td>80</td>
</tr>
</tbody>
</table>

After changes ceased to occur the circumflex artery was ligated at its origin and the animal was observed for one hour. At the close of the experiment the ischemic area was injected with India ink, cut out and weighed. This was done also in all the experiments described below.

In this group of 10 dogs with arteriovenous fistula three dogs survived for one hour following circumflex ligation. Seven dogs died in from 1½ to 58 minutes, with an average survival time of 13 minutes. All dogs showed the usual rapid cardiographic changes in aVR, consisting of an increased amplitude of the
mm. Hg to compare with previous sinus arteriovenous experiments it was often necessary to completely occlude the sinus outflow. After records were obtained and a steady state was reached, the circumflex artery was ligated as before and the animal was observed.

![Diagram](image)

Fig. 1. Showing experimental method for simple elevation of coronary sinus pressure. (A) Cannula through left common carotid artery to aorta for aortic pressure; (B) ligation about left subclavian artery; (C) coronary sinus cannula introduced through right auricle; (D) outlet to record coronary sinus pressure; (E) air chamber of 25 cc. capacity; (F) cannula through left external jugular vein to level of right auricle; (G) ligature about tip of cannula in coronary sinus; (X) point of constriction for elevation of sinus pressure.

There were 10 dogs in this group whose mean coronary sinus pressure averaged 40 mm. Hg at the time of circumflex ligation. There was an average drop of 3 mm. Hg in mean sinus pressure 30 seconds after circumflex ligation. In this series, six dogs survived for one hour and four died in ventricular fibrillation in an average time of 39 minutes. The average mean aortic pressure in the six surviving dogs was 75 mm. Hg one hour after circumflex ligation. Electrocardiographic changes were as described above (table 1, group 2).

**Group 3. Arterialization of the Coronary Sinus Alternating with Elevation of Sinus Pressure**

In this group there were 20 dogs which were divided into two groups of 10 each.

A. Arterialization of the Coronary Sinus.

This group of 10 dogs had an average weight of 13.9 Kg. The sinus was cannulated with the cannula described previously. After the control records were obtained the sinus was arterialized at a mean pressure of 50 mm. Hg and the circumflex ligated. Arterialization of the sinus produced a fall in average mean aortic pressure from 103 to 89 mm. Hg. The average mean coronary sinus pressure before circumflex ligation was 45 mm. Hg, and immediately after artery ligation the average mean sinus pressure was 43 mm. Hg. One hour after circumflex artery ligation there were 100 percent surviving dogs whose average mean aortic pressure was 69 mm. Hg. Previously described electrocardiographic changes were present (table 1).

B. Elevation of Sinus Pressure. Alternating with the 10 dogs in A were the 10 dogs in this group whose weights averaged 13.7 Kg. These dogs were prepared and handled exactly as in group 2 above with simple elevation of sinus pressure. This was done so as to study more adequately the effects of sinus pressure elevation and to control the possible variations in technic.

The average initial mean aortic pressure was 112 mm. Hg. This pressure fell to an average of 109 mm. Hg when the mean pressure in the sinus was raised to an average of 39 mm. Hg. The sinus pressure fell an average of 4 mm. Hg when the circumflex artery was ligated. At the end of one hour there were eight surviving dogs whose mean aortic pressure was 84 mm. Hg. The two deaths occurred in an average of 28 minutes (table 1, group 3B).

**Group 4. Complete Sinus Occlusion**

The 10 dogs in this group had an average weight of 14.1 Kg. The coronary sinus was cannulated with a rigid cannula with connections
for optically recording sinus pressure and for diverting the sinus blood into the jugular cannula prior to sinus occlusion. After control records were obtained closure of a stopcock served completely to occlude the sinus. When stable conditions were reached the circumflex artery was ligated and the fate of the animal was awaited.

These 10 dogs had an initial mean aortic pressure of 111 mm. Hg which fell to 100 mm. Hg when the sinus was completely occluded. Such sinus occlusion resulted in a mean coronary sinus pressure of 48 mm. Hg. Circumflex artery ligation resulted in an average decline in the mean sinus pressure of 10 mm. Hg. Six of these dogs lived one hour at which time the average mean aortic pressure was 70 mm. Hg. Death occurred in the remaining four dogs in an average of 39 minutes (table 1). The electrocardiographic changes following circumflex ligation were as described above.

**DISCUSSION**

It was previously found that, in our hands, ligation of the circumflex artery at its origin is attended by a mortality of 70 per cent within one hour.1 In these present studies the presence of an arteriovenous fistula which emptied into the right auricle did not modify the mortality resulting from circumflex artery ligation. Therefore, we believe that the arteriovenous fistula itself is of no significance in providing the remarkable protection to the heart which results from arterialization of the coronary sinus.

The 10 dogs reported here which survived circumflex ligation after arterialization of the sinus together with the 10 previously reported1 give considerable support to the view that this procedure is protective against ventricular fibrillation. The questions naturally arise whether the benefits from this procedure are due to arterialization of the sinus and whether identical benefits can be expected by simple elevation of sinus pressure.

The 70 per cent survival rate in 20 experiments described here with simple elevation of sinus pressure gives substantial proof that this procedure is also decidedly protective. It must be pointed out, however, that in many dogs a mean sinus pressure of 50 mm. Hg is impossible to attain by simple restriction of sinus outflow. It is believed that the anatomic arrangement of veins may explain the low sinus pressure in certain dogs. Usually a large posterior vein drains into the ostium of the coronary sinus and therefore it does not share in the elevation of venous pressure. Since there are frequently large communications at the cardiac apex between branches of anterior veins and this posterior vein there exists a large low-pressure drainage channel which may make the maintenance of high sinus pressure impossible.

Likewise the studies of Thornton and Gregg4 revealed the impossibility of chronic marked elevation of coronary sinus pressure by simple sinus ligation since in their experiments even after one month of chronic sinus ligation the acute high pressure had been replaced by pressures only slightly higher than control pressures. It is noteworthy, however, that in a small series all of their dogs survived combined arterial and venous ligation. Gross2 was likewise able to reduce his mortality rates by partial elevation of coronary sinus pressure induced by partial occlusion. Our own studies showing 30 per cent mortality with sinus pressure elevation and 40 per cent mortality with complete sinus occlusion are not significantly different from each other. However, when compared with the 20 dogs with sinus arterialization reported here and elsewhere1 there is a significant difference, since the p values are .02 for the group with sinus pressure elevation and .015 for the group with complete sinus occlusion.

By means of the expansion chamber it was hoped to approximate the mean sinus pressures induced by arterialization and to prevent the attainment of deleterious high systolic pressures. However, an inspection of table 1 reveals that exact duplication of mean sinus pressures was not obtained. Therefore, one cannot, from these experiments, separate the effects of arterialization from those of pressure elevation. The fact remains though, that only by arterialization can suitable chronic elevations in sinus pressure be realized.

It is believed that these studies offer con-
vincing proof that arterialization of the coronary sinus at a mean pressure of about 50 mm. Hg offers the greatest degree of protection against ventricular fibrillation when compared with other methods of raising the sinus pressure. The attainment and maintenance of effective pressures by other means would require the use of pumps and therefore is impractical.

Although much speculation is possible, the true factors which provide protection for the heart are unknown. Physiologic studies have been begun to test whether this procedure creates pressure relationships likely to supply blood to ischemic capillaries from the arterialized sinus during the critical period following occlusion of a coronary artery, or establishes conditions which enable existing but nonfunctioning collaterals to become functional. Although the value of arterialization of the coronary sinus following acute coronary occlusion in dogs is unquestionable, it is the conviction of the authors that these studies neither confirm nor deny the question of the effectiveness of this procedure in the treatment of human angina pectoris.

Summary

Mortality rates due to acute ligation of the circumflex artery have been determined. Comparisons are made of the value of various procedures in protecting the heart against ventricular fibrillation. It has been found that there is a mortality of 70 per cent within one hour following artery ligation in the presence of an arteriovenous fistula. This mortality is reduced to 30 per cent when coronary sinus pressure is elevated and to 40 per cent when the sinus is completely occluded. There were no deaths from circumflex artery ligation in the presence of sinus arterialization. It is concluded that arterialization of the sinus provides not only superior protection but is also the only practical means for chronic maintenance of effective sinus pressure.

Acknowledgment

We wish to express our appreciation to Dr. George F. Badger for the statistical analysis of this data.

REFERENCES

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Circulation. 1952;6:262-266
doi: 10.1161/01.CIR.6.2.262

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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