Experimental Studies on the Coronary Insufficiency and the Coronary Occlusion

II. The Relation of the Coronary Blood Flow to the Arterial Blood Pressure, and the Effect of the Vagus Nerves upon It

By

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In the previous report1) we used the hypotonics such as C₈, Rauwolfia, etc. in order to diminish the coronary flow. As seen in our experiments the coronary flow diminishes when the arterial pressure falls. According to the literature, however, the relation between them is not so simple. Various opinions were published regarding this problem.

Relatively large numbers of the authors have the opinion that the coronary blood flow diminishes accompanying with the fall in the arterial blood pressure. Already in 1913 Markwalder and Starling2) and Mora- witz and Zahn3) introduced such an opinion. From that time, Hochrein and Keller4), Schmidt and Engelhorn5), Klisiecki and Flecks, and others7)8)9) pointed out the dependence of the coronary flow on the arterial blood pressure, although it is, of course, not considered as a sole factor. Rein10), however, claimed that the factor to change the coronary flow is the oxygen requirement of the heart muscle, but not the blood pressure. According to him, the coronary blood flow is dependent on the arterial blood pressure only in the enfeebled, dilated hearts, or under the intravenous barbiturate anesthesia. Gollwitzer-Meier and Kroetz11), Foltz, et al.12), Eckstein, et al.13), and others14) also stated that the coronary blood flow changes rather in the response to the myocardial oxygen consumption.

On the one hand, the function of the vagus and sympathetic nerves must be taken into account concerning this problem, because, as widely known, the coronary vessels are distinctly influenced by them. But some of the authors, especially who thought the role of the myocardial oxygen consumption as most important, denied the effect of the nerves on this relation.
In this respect we have analyzed our data obtained in the experiments reported in the preceding paper, in which the vagus nerves were intact in some cases and cut off in others.

**Experimental**

**Methods**

All the procedures were same as in the previous paper. The blood flow in the left coronary artery was measured by the bubble flowmeter and the blood pressure in the femoral artery was recorded by the mercury manometer. The employed hypotonic were C₉, Rauwolfia serpentina, or histamine, etc., and as the hypertonics, neosynephrine and nor-epinephrine were chosen. Both vagal trunks were cut in the cervical region.

**Results**

The observations were classified in three groups: 1) in the cases of the spontaneous fall in the arterial blood pressure, 2) in the cases of the blood pressure fall caused by the hypotonic, and 3) in the cases of the blood pressure rise caused by the hypertonics injected in the hypotonic states resulted from above two conditions. The results were summarized in Figs. 1, 2, 3, 4, 5 and 6, in which the values of the coronary flow were plotted against the arterial blood pressure.

It was observed that in the cases of the spontaneous blood pressure fall the coronary flow diminished in general with the lowering of the pressure, as seen in Figs. 1 and 2. This finding was seen whether the vagus nerves were intact or not.

On the other hand in the cases in which the hypotonic was used such a relation was hard to be observed, as shown in Fig. 3. But after cutting both cervical vagi it seemed to be present (Fig. 4). In order to investigate these relations exactly, we have calculated the correlation rates between the arterial blood pressure and the coronary flow. The results were summarized in Table I.

The significant correlation were observed in the cases of the spontaneous blood pressure fall, though it was not so high, while in the cases of the hypotension introduced by the hypotonic it was not present when the vagus nerves were intact. After cutting vagi, however, the correlation rate became somewhat higher. Similar results were obtained in the cases in which the hypertonics were injected in the hypotonic states. The rate was very low in the intact vagal cases, while considerably high in the severed vagal cases.

**Discussion**

We have two subjects to study on the relation between the arterial
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Fig. 1. The relation of the coronary blood flow to the arterial blood pressure. (1) Spontaneous blood pressure fall in intact vagal cases.

Blood pressure and the coronary flow: One is the change in the coronary flow when the arterial blood pressure is primarily changed, and the other is the change in the arterial blood pressure when the coronary flow is primarily changed. These two situations, however, may be not regarded as the same. The main purpose in this paper is to study the former problem.

As already mentioned, there is a disagreement between the authors regarding the relation of the coronary flow to the arterial pressure. Some authors observed the presence of the direct dependence of the former on the latter, while others denied it. We believe, our data will make some contributions to compromise this disagreement of the opinions.

Our experimental observations disclosed that the vagus nerves have a role on this relation in some measure. The correlation rates were higher, as a rule, in the severed vagal cases than in the intact vagal cases. The vagus nerves are frequently compared to a safeguard equipment against the derangement in the living body. It is supposed, in this viewpoint, that the vagus nerves play role on the maintenance of the coronary flow when the arterial pressure falls critically.

In the cases of the spontaneous blood pressure fall the correlation was
significant even when the vagi were not cut. This is explained by the idea that in such cases the function of the vagi was poor as a result of "weakening" of the heart. From these considerations, Rein's view that the coronary blood flow is influenced by the arterial blood pressure only in the enfeebled heart can be explained by the lowering of the function of the vagi.

Some authors pointed out that the coronary flow is ruled by the cardiac oxygen consumption. Their conclusion, however, were obtained in the cases of the intact vagi for the most part. Nevertheless, already in the old literatures the effects of cutting vagi were examined. More than about twenty years ago, Anrep and Segall\cite{15} reported that the arterial pressure has effect on the coronary flow only in the vagus-cut cases. Gollwitzer-Meier, et al.,\cite{11} observed similar findings. Probably because of some reason, this finding was neglected and in the recent papers the role of the vagus nerves has come again into question.
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Fig. 3. The relation of the coronary blood flow to the arterial blood pressure. (3) When hypotonics were used in intact vagal cases.

Fig. 4. The relation of the coronary blood flow to the arterial blood pressure. (4) When hypotonics were used in vagi-cut cases.

**Table I**
Correlation Rates between the Coronary Blood Flow and Arterial Blood Pressure

<table>
<thead>
<tr>
<th>Spontaneous blood pressure fall</th>
<th>Vagi intact</th>
<th>Vagi cut</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=78</td>
<td>N=43</td>
<td>N=121</td>
<td></td>
</tr>
<tr>
<td>r=0.50</td>
<td>r=0.69</td>
<td>r=0.61</td>
<td></td>
</tr>
<tr>
<td>Fs=25.33</td>
<td>Fs=37.25</td>
<td>Fs=69.89</td>
<td></td>
</tr>
<tr>
<td>F (0.01)=6.96</td>
<td>F (0.01)=7.30</td>
<td>F (0.01)=6.84</td>
<td></td>
</tr>
<tr>
<td>When hypotonics were used</td>
<td>N=15</td>
<td>N=15</td>
<td>N=30</td>
</tr>
<tr>
<td>N=15</td>
<td>N=15</td>
<td>N=30</td>
<td></td>
</tr>
<tr>
<td>r=0.49</td>
<td>r=0.21</td>
<td>r=0.21</td>
<td></td>
</tr>
<tr>
<td>Fs=0</td>
<td>Fs=1.29</td>
<td>Fs=1.29</td>
<td></td>
</tr>
<tr>
<td>F (0.05)=4.69</td>
<td>F (0.05)=4.67</td>
<td>F (0.05)=4.20</td>
<td></td>
</tr>
<tr>
<td>When hypertonics were used</td>
<td>N=10</td>
<td>N=12</td>
<td>N=22</td>
</tr>
<tr>
<td>N=10</td>
<td>N=12</td>
<td>N=22</td>
<td></td>
</tr>
<tr>
<td>r=−0.19</td>
<td>r=0.68</td>
<td>r=0.58</td>
<td></td>
</tr>
<tr>
<td>Fs=0.30</td>
<td>Fs=8.52</td>
<td>Fs=10.13</td>
<td></td>
</tr>
<tr>
<td>F (0.05)=5.32</td>
<td>F (0.05)=4.96</td>
<td>F (0.01)=8.10</td>
<td></td>
</tr>
</tbody>
</table>

Our analysis of the correlation showed that the pressure-flow relation-
Fig. 5. The relation of the coronary blood flow to the arterial blood pressure. (5) When hypertonics were injected in the hypotonic states in intact vagal cases.

Coronary blood flow, cc/100 g. of left ventricle/min.

Fig. 6. The relation of the coronary blood flow to the arterial blood pressure. (6) When hypertonics were injected in the hypotonic states in vagi-cut cases.
ship approached to the linear one to some extent when the vagi were cut. Osher pointed out that this relation is rather logarithmic, that is, log-pressure to flow relation is linear. Such a relation, however, was not obtained in our data. The reason for the difference may be attributed to the difference in the experimental procedures. Osher used the preparations of donor and recipient dogs, and the perfusion pressure of the flow from the former's heart were variously changed. In our opinion, Osher's observations may be more suitable in the biological sense, but ours also has some significances, because it means that the arterial pressure tends to influence directly on the coronary flow if the vagal function is abolished.

Whether the sympathetic nerves play part on this relation or not, is also a problem. But we have not studied on it. At the start of our experiments reported in the preceding paper, we had no special purposes to study the role of the vagus nerves, and the vagi were cut merely for the elevation or maintenance of the arterial pressure. Analyzing the data the results shown in Table I was obtained. It is, therefore, no more than a by-product, and the role of the sympathetic nerves did not come into our considerations.

The problem discussed in above section is the change in the coronary flow caused by the primary change in the arterial pressure. There is another problem, as already mentioned, how is the behavior of the arterial pressure when the coronary flow is changed primarily. We have also carried out some experiments on it; the changes in the arterial pressure was examined when the coronary flow was reduced by compressing the rubber or vinyl tube connecting the flowmeter to the brachiocephalic artery. But as shown in Fig. 7, it showed no changes either in the intact vagal or in the severed vagal cases.

![Fig. 7. Records of the arterial pressure when the coronary blood flow was primarily changed. (a) Before and (b) after section of the vagi. At (A) the tube was compressed, and at (B) released. The numbers above the records indicate the coronary blood flow.](image-url)
There are few reports on the experimental reduction of the coronary flow. We can find only the works of Wégria, Katz, et al., Rein, and others. Wégria's work was concerned the ST-depression as referred in our preceding paper. The experiments of Katz, et al. were to study the reactive hyperemia after the temporary reduction of the coronary flow in the fibrillating heart. Only the experiments of Rein, who published the data that the arterial pressure fluctuates in parallel with the change in the coronary artery flow when the heart became enfeebled, have the relation to the problem discussed here. But we have never observed such a situation even in the cases with markedly low pressure and reduced coronary flow. Fig. 8 shows one of our observations.

Fig. 8. Records of the arterial pressure when the coronary blood flow was primarily changed. The left is the case which shows the lower initial pressure, and the right the higher initial pressure. Both show little changes in the arterial pressure in spite of the marked changes in the coronary blood flow.

It is a confused problem to answer why no changes in the arterial pressure are observed when the coronary flow is primarily reduced. But it is at least sure that the mechanism to maintain the arterial pressure when the coronary flow reduces is not related to the vagus nerves, because its severing has no effect. Presumably, the reduction of the coronary flow does not directly or immediately result in the weakening of the myocardial contraction. Of course, however, if the excessive reduction are continued too long, the ventricular fibrillation occurs. Nevertheless, its occurrence is usually abrupt and the blood pressure shows little change until that time.

SUMMARY

1. The relation of the coronary blood flow to the arterial blood pressure was analyzed using the experimental data reported in the preceding paper. In general, the fall of the blood pressure was accompanied by the diminution of the coronary flow.

2. As a rule, the correlation rates were higher in the severed vagal cases than in the intact vagal cases.
3. In the spontaneous blood pressure fall the correlation was significant even in the intact vagal cases, though it is not so high. This may be attributed to the lowered function of the vagi as a result of “weakening” of the heart.

4. From above observations it was supposed that the vagus nerves act to maintain the coronary flow when the arterial pressure falls critically; that is to say, they act as a safeguard equipment.

5. On the other hand, the arterial pressure showed no changes when the coronary flow primarily reduced. The vagus nerves played no part on it.

References

2) Markwalder & Starling, J. Physiol., 1913, 47, 275.
8) Eckenhoff, Hafkenschiel & Landmesser, ibid., 1947, 148, 582.
10) Rein, Arch. ges. Physiol., 1951, 253, 205.
14) Eckenhoff, Hafkenschiel, Landmesser & Harmel, ibid., 1947, 149, 634.
15) Anrep & Segall, Heart., 1926, 13, 239.