EXPERIMENTAL STUDY ON CIRRHOSIS OF THE LIVER: WITH PARTICULAR REFERENCE TO THE INFLUENCE OF THE LIGATION OF THE HEPATIC ARTERY UPON THE PORTAL BLOOD FLOW IN THE DOG WHOSE HEPATIC VEIN HAD BEEN CONSTRICTED

Author(s)
HOSONO, KOGO

Citation
日本外科宝函 28(4): 1127-1146

Issue Date
1959-05-01

URL
http://hdl.handle.net/2433/206853

Type
Departmental Bulletin Paper

Textversion
publisher

Kyoto University
EXPERIMENTAL STUDY ON CIRRHOSIS OF THE LIVER
WITH PARTICULAR REFERENCE TO THE INFLUENCE
OF THE LIGATION OF THE HEPATIC ARTERY UPON
THE PORTAL BLOOD FLOW IN THE DOG WHOSE
HEPATIC VEIN HAD BEEN CONstricted

By

KOGO HOSONO

From the lst Surgical Division, Kyoto University Medical School
(Director: Prof. Dr. Chisato Araki)
(Received for publication Mar. 6, 1959)

Index

I. Introduction
II. Method and Material
1) Constriction of the hepatic vein in dogs
2) Determination of the rate of blood flow in the portal vein
   i) High frequency current generator
   ii) Galvanometer and lampscale
   iii) Trough type thermo-couple
   iv) "Thermostromuhr"
3) Determination of the volume of blood flow in the portal vein
4) Determination of the systemic arterial blood pressure

III. Results
1) Changes in the rate of the portal blood flow after the ligation of the hepatic artery
   i) In dogs of the control group
   ii) In dogs in which the constriction of the hepatic vein was not followed by the development of ascites
   iii) In dogs in which the marked ascites developed after the constriction of the hepatic vein
   iv) Comments
2) Changes in the volume of the portal blood flow per 100g of liver after the ligation of the hepatic artery
3) Balance of the increase and decrease in the volume of the portal blood flow at 30 minutes after the ligation of the hepatic artery in various dog groups
4) Changes in the systemic arterial blood pressure after the ligation of the hepatic artery
5) Long-term observation of the changes in the portal blood flow after the ligation of the hepatic artery in the normal dogs

IV. Study with Bubble-Flowmeter
1) Method
2) Results

V. Discussion

VI. Summary

VII. References

I. INTRODUCTION

Since RIENHOFF, BERMAN and others recently advocated that the ligation of the
hepatic artery was effective for the treatment of cirrhosis of the liver, many investigators reexamined this problem from various angles. They are, however, of a diversity of opinions about this procedure.

Author intended to investigate the effects of the ligation of the hepatic artery upon the blood flow in the portal vein in cases of the liver cirrhosis associated with or without ascites. By constriction of the hepatic veins in dogs, we succeeded to produce the conditions quite similar to those of the liver cirrhosis in human beings. In these dogs, the hepatic artery was ligated and changes in the portal blood flow were studied.

Herrick in 1907, through his perfusion test of the liver, suggested there was a interrelation between the blood pressure of the hepatic artery and that of the portal vein. Later McIndoe (1926), Dock (1942) and Taylor & Rosenbaum (1953) also performed the perfusion test of the liver in cases of the portal hypertension particularly of the liver cirrhosis and found an interrelation between the blood pressure of the hepatic artery and that of the portal vein. Also they studied the correlation between the volume of blood flow of the hepatic artery, portal vein and that of the hepatic vein. We, instead of perfusion on the removed liver, carried out similar kind of experiment, in vivo, with the use of “Thermostromuhr”.

II. METHOD AND MATERIAL

Mongrel dogs of 7.6-15.0kg body weight were used. These were divided into three groups, i.e. 1) dogs in normal control group, 2) dogs in which the constriction of the hepatic vein was not followed by the development of ascites and 3) dogs in which the marked ascites developed after the constriction of the hepatic vein. Both in group 2) and 3), the animals underwent a reoperation for the determination of the rate of blood flow in the portal vein on the 14th day after the constriction of the hepatic vein.

1) Constriction of the hepatic vein in dogs

Prior to the procedure the animal was kept away from food for 24 hours. Under general anesthesia with an intravenous injection of thiopental sodium in dose of 0.04g/kg, laparotomy was carried out with r-subcostal incision. Ligation or constriction of the individual hepatic vein was carried out according to the Tsuchiya’s method. In the present experiment, however, manipulation for the right hepatic veins was slightly simplified, i.e. the right hepatic veins were divided into two groups, superior and inferior, and veins in each group were ligated en masse.

During these procedures a particular care was taken not to constrict the abdominal inferior vena cava. For the middle and left hepatic veins, constriction or ligation of a individual vein was made following the Tsuchiya’s original method.

2) Determination of the rate of blood flow in the portal vein (shown in photograph)

“Thermostromuhr” was used for the determination of the rate of blood flow in the portal vein. “Thermostromuhr” consists of high frequency current generator, galvanometer and lampscale and trough type thermo-couple.
i) High frequency current generator (Fig. 1, 2)
This apparatus was made under the guidance of Mr. Yoshifumi Sunahara who is an assistant in the institute of applied physics, faculty of technical engg.

ii) Galvanometer and Lamp scale
The galvanometer used in the present study was: resistance of wiring line 803 ohms, critical resistance 66,000 ohms, sensitivity $2.4 \times 10^{-10}$ amperes, $160 \times 10^{-7}$ volts, period 7.3 sec.

iii) Trough type thermo-couple
In Fig. 3, the trough type thermo-couple which was used by Herrick et al., was shown. In our experiment, instead of the electric heater, a diathermy electrode was used and this was connected with the diathermy generator which is believed to be ideal for warming the blood. Also 110V A.C. was used instead of the battery, and the rubber plate was used in place of the bakelite plate in order to provide a better approximation to the wall of the blood vessel.

---

1. High frequency current generator
2. Scale
3. Lamp
4. Lead wire to A.C. 110V
5. Lead wires to Diathermy terminals
6. Galvanometer
7. Copper wire (connect with constantan wire)
8. Lead wire to A.C. 110V

---

Fig. 1 High frequency current generator
iv) Use of the "Thermostromuhr"

The dog was anesthetized with thiopental-sodium and laparotomy was carried out with upper midline incision. The portal vein was dissected from the surrounding tissue. Distally from the bifurcation with the splenic vein and as close as possible to the liver, the trough type thermo-couple was applied to the wall of the portal vein, thus the rate of blood flow in the portal vein was measured. To minimize the errors in measurement by the manipulation of ligating the artery as much as possible, silk thread was wrapped previously around the artery as shown in Fig. 4. Then, blood through the portal vein was warmed with the use of diathermy. Scale of the galvanometer at a time when the blood through the portal vein was thus warmed and before the hepatic artery was ligated, was set at 0 point. Change in scale after the quick-ligation of the hepatic artery by the silk thread previously wrapped around the artery, was read and recorded.

3) Determination of the volume of blood flow in the portal vein

Fig. 2 B-Source of H.F.C. generator with stabilizer.

Fig. 3 Thermostromuhr used by BAlDeS and HerrrK.
A piece of the portal vein with a considerable length was taken out from the experimental dogs in order to determine the volume of blood flow through the portal vein. The trough type thermocouple was applied to this piece of removed portal vein. Two canules were inserted into the both ends of the vein and one of which was connected with a graduated irrigator filled with the heparinized blood in it. Blood volume which dropped from the irrigator was measured and at the same time change in scale of the “Thermostromuhr” was read. Thus, from these two measured values, the volume of blood flow was determined. This experiment was performed at the room temperature.

4) Determination of the systemic arterial blood pressure
Systemic blood pressure was determined with the mercury manometer at the femoral artery.

III. RESULTS
1) Changes in the rate of the portal blood flow after the ligation of the hepatic artery

Since it was difficult from various reasons to observe the animals for long period after the ligation of the hepatic artery, the experiments were limited within a period of 30 minutes. The interruption of the blood flow through the hepatic artery was carried out either by the ligation of common hepatic artery alone or the ligation of the three major arteries (common hepatic, gastroduodenal, and right gastric artery) in one time.

ii) In dogs of the control group

As illustrated in Figs 5 & 6, right after the ligation of the common hepatic artery or ligations of three major arteries, the rate of blood flow in the portal vein increased markedly. Within 5 to 20 minutes, however, it returned to the pre-ligation level, then gradually decreased. It was found that the time required the rate of blood flow to return to the pre-ligation level was longer, in the case of the ligation of three major arteries than that of the common hepatic artery alone. Converting these values into the volume of blood flow, as shown in Tab. 1, similar increase or decrease in the volume of blood flow in the portal vein were noticed. The average value of the volume of blood flow through the portal vein in the normal dogs was 208cc minute.

ii) In dogs in which the constriction of the hepatic vein was not followed by the development of ascites
Table 1. Portal blood flow (cc per minute)

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Body weight (kg)</th>
<th>before Ligation</th>
<th>1min</th>
<th>5min</th>
<th>10min</th>
<th>15min</th>
<th>20min</th>
<th>25min</th>
<th>30min</th>
<th>35min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>after Ligation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ms.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the common</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hepatic artery on normal dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the three major arteries on normal dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of the common hepatic artery on non ascitic dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of the three major arteries on non ascitic dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of the common hepatic artery on asitic dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligation of the three major arteries on asitic dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 7 Changes before and after ligation of the common hepatic artery on non ascitic dogs.
As illustrated in Figs 7 & 8, in some cases, it took longer time the increased rate of blood flow after the hepatic artery ligation to return to the pre-ligation level, compared with that in control animals, or in other cases, after the rate of blood flow decreased beyond the pre-ligation level, it increased again, so the curve directed upwards. These results were equally obtained either in case of the ligation of the three major arteries on non ascitic dogs.
of the common hepatic artery alone or that of three major arteries. In dogs of this group, the average volume of blood flow through the portal vein before the ligation of the hepatic artery was 210cc/minute (Tab. 1).

iii) In dogs in which the marked ascites developed after the constriction of the hepatic vein

As shown in Figs 9 & 10, the increased rate in blood flow after the hepatic artery ligation, though there was slight fluctuation, did not return to the pre-ligation level and this increase in the rate of blood flow through the portal vein was kept continued. This tendency was especially marked in dogs whose three major arteries were ligated. Average value of the volume of blood flow through the portal vein in dogs of this group was 168cc/minute (Tab. 1).

iv) Comments

As shown in Fig. 11, the increase in the rate of blood flow was most obvious in dogs in which the constriction of the hepatic vein had been followed by the development of the marked ascites, and was the second in dogs in which ascites did not develop after the hepatic vein constriction and was the least obvious in dogs of the control group. In the latter two groups, once increased rate of the blood flow dropped beyond the pre-ligation level as the time elapsed. In the former, on the other hand, the increase in the rate of blood flow continued and never returned to the pre-ligation level.

2) Changes in the volume of the portal blood flow per 100g of the liver after the ligation of the hepatic artery

Results were shown in Fig. 12 and Tab. 2.

In the normal dogs average value of the blood flow volume through the portal vein before the ligation was 72cc per minute per 100g of liver. Whilst, in dogs
Fig 11 Average value of each group.

Fig. 12 Average value of each group.
which had the hepatic veins constricted and without ascites it was 68 cc/m/100g of liver, and in dogs with ascites after the hepatic vein constriction it was 49 cc/m/100g of liver. As previously mentioned, the volume of blood flow in the portal vein per minute itself did not show any significant difference between in the normal control dogs and in dogs without ascites after the hepatic vein constriction. But calculating it in volume per minute per 100g of the liver tissue, the volume of the portal blood flow in the dogs without ascites after constriction was smaller than that in the normal dogs. Furthermore, comparing the volume in normal dogs with that in dogs which had the hepatic vein constricted and with a development of ascites, the difference became more significant, i.e. it reached as large as 23 cc/m/100g of liver.

3) Balance of the increase and decrease in the volume of the portal blood flow at 30 minutes after the ligation of the hepatic artery

After the ligation of the hepatic artery, the volume of blood flow in the portal vein was measured at every one minute for 30 minutes. Comparing these values to that of pre-ligation level, the difference between them, i.e. the values of increase or decrease of the volume of blood flow were calculated at every minute after the ligation. Now, these values of difference, either positive or negative, were arithm-

Table 2  Portal blood flow (cc per 100 grams of liver per minute)

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Liver weight</th>
<th>before Ligation</th>
<th>after Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1min.</td>
<td>5min.</td>
</tr>
<tr>
<td>Ligation of the common hepatic artery on normal dogs</td>
<td>2</td>
<td>290</td>
<td>689</td>
</tr>
<tr>
<td>Ligation of the three major arteries on normal dogs</td>
<td>1.5</td>
<td>290</td>
<td>689</td>
</tr>
<tr>
<td>Average</td>
<td>2.7</td>
<td>290</td>
<td>689</td>
</tr>
</tbody>
</table>

After the ligation of the hepatic artery, the volume of blood flow in the portal vein was measured at every one minute for 30 minutes. Comparing these values to that of pre-ligation level, the difference between them, i.e. the values of increase or decrease of the volume of blood flow were calculated at every minute after the ligation. Now, these values of difference, either positive or negative, were arithm-
A resistance upon the blood flow in dogs of the control group and in dogs without ascites after the hepatic veins constriction and in both of which the common hepatic artery alone was ligated. Whilst, it was positive in dogs of the control group and in dogs without ascites after the hepatic veins constriction, and in both of which three major arteries were ligated. It was also positive in dogs with ascites after the hepatic vein constriction, and in which either the common hepatic artery alone or three major arteries were ligated. Among these, however, the positive balance was most markedly observed in dogs which had marked ascites after the hepatic vein constriction and later underwent the ligations of the three major arteries. In these animals an increase in the volume of the portal blood flow for 30 minutes reached as large as 1,000 cc.

This fact, as will be discussed later, may suggest that the blood flow of the hepatic artery is working hemodynamically as a resistance upon the blood flow in the portal vein, especially it is true in dogs with ascites after the hepatic vein constriction. The values of increase and decrease shown in Tab. 3, were average

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Normal dogs</th>
<th>Ascitic dogs</th>
<th>Ascite dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5±1</td>
<td>24.9±13.5</td>
<td>20.9±2.5</td>
</tr>
<tr>
<td>2</td>
<td>4.2±3.6</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>3</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>4</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>5</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>6</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>7</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>8</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>9</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>10</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>11</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>12</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>13</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>14</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>15</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>16</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>17</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>18</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>19</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>20</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>21</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>22</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>23</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>24</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>25</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>26</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>27</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>28</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>29</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
<tr>
<td>30</td>
<td>4.2±4.2</td>
<td>34.2±2.5</td>
<td>24.9±13.5</td>
</tr>
</tbody>
</table>

Total: 5400 2920 1323 1905 2926 1932

Fig. 13 Changes of systemic blood pressure influenced by hepatic artery ligation
values from many animals.

4) Changes in the systemic arterial blood pressure after the ligation of the hepatic artery

Arterial blood pressure was determined at the femoral artery before and after the hepatic artery ligation with the use of mercury manometer. Results were shown

Table 4. Changes of systemic blood pressure influenced by hepatic artery ligation.

<table>
<thead>
<tr>
<th>Dog No</th>
<th>before ligation</th>
<th>1 min</th>
<th>2 min</th>
<th>3 min</th>
<th>4 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 median</td>
<td>120-130</td>
<td>150-160</td>
<td>155-165</td>
<td>160-170</td>
<td>165-180</td>
<td>180-190</td>
<td>190-200</td>
<td>195-205</td>
<td>200-210</td>
</tr>
<tr>
<td>2 median</td>
<td>90-95</td>
<td>110-120</td>
<td>120-130</td>
<td>130-140</td>
<td>140-150</td>
<td>150-160</td>
<td>160-170</td>
<td>170-180</td>
<td>180-190</td>
</tr>
<tr>
<td>3 median</td>
<td>110-115</td>
<td>130-140</td>
<td>140-150</td>
<td>150-160</td>
<td>160-170</td>
<td>170-180</td>
<td>180-190</td>
<td>190-200</td>
<td>200-210</td>
</tr>
</tbody>
</table>

5) Long-term observation of the changes in the portal blood flow after the ligation of the hepatic artery in the normal dogs

As illustrated in Fig. 14, the simultaneous ligation of three major arteries in the normal dogs, was followed by the marked increase in the rate of blood flow within 1-2 minutes. It, however, decreased rapidly, and the rate which was registered at approximately one hour after the ligation did continue for 8 hours, thereafter, it further decreased gradually. This last decrease was considered naturally to be due to the general weakness by the operation, though the particular care was taken for the maintenance of the body temperature or the relaxation of the legs in Fig. 13 and Tab. 4. Actually in all dogs, i.e. in dogs in which either the common hepatic artery alone or three major arteries were ligated, or in dogs either in the control group or those with constricted hepatic vein, the systemic arterial blood pressure rose 10-40mm Hg, within 1-2 minutes after the ligation of the hepatic artery and it continued to rise for approximately 10 minutes. This rise in blood pressure seemed to be due to the neurorefractor mechanism, (Burton, Opitz) and also it quite corresponded in time factor to the transient increase of the portal blood flow soon after the ligation of the hepatic artery. Thus, these two phenomena might have some interrelation with each other.
etc. Exceptionally, as seen in No. 50, very marked decrease in blood flow was observed within an hour.

IV. STUDY WITH BUBBLE-FLOWMETER

For the determination of the volume of blood flow in the peripheral organs, so many different methods have been used. These, however, can be roughly divided into two, i.e. direct and indirect methods. In the present study, in order to confirm the results obtained by the “Thermostromuhr”, the bubble flowmeter which is rather primitive in principle but fairly accurate, was also used. This flowmeter was used for the first time by Soskin et al. in 1934 for the determination of the volume of
We, as shown in Fig. 15, used a vinyl tube with 5 mm of inner diameter, 7 mm of external diameter, and with 15 cc of inner capacity. This tube was again surrounded with vinyl water jacket. At the distal portion of this tube, i.e. close to the liver, a T-tube was set so that the bubble injected could escape through it. The flowmeter we used was the one of spiral type with one circuit which was believed to be of the least resistance. The tube of this flowmeter was placed on the same level as that of the portal vein. In using this flowmeter particular cares were taken for the following matters: use of anticoagulant drugs, cleanness of the apparatus and use of water jackets for warming the irrigated blood etc.

1) Method

The volume of blood flow through the portal vein was measured before and after the ligation of three major arteries in normal dogs. Animals were kept away from food for 24 hours before measurement. Under a general anesthesia with intravenous injection of thiopental-sodium, a laparotomy was carried out with right subcostal incision. The portal vein was dissected from the surrounding tissue and the splenic vein was ligated and cut for convenience of the manipulation. Heparin was injected through the mesenteric vein, the portal vein was interrupted transiently, the vinyl tube was inserted and the portal vein was reopened. From the proximal part of the tube approximately 0.1-0.2 cc of air bubble was injected and the time which was required for the bubble to pass between two points of the tube. These two points were previously marked, so as the inner capacity of the tube between these two points to be 15 cc. Thus, the volume of the portal blood flow was calculated.

2) Results

This method was adopted, as previously mentioned, to re-examine the data obtained by the "Thermostromuhru" from the different angle. By this method, the volume of the portal blood flow was determined before and after the ligation of

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Portal blood flow cc per minute</th>
<th>Liver weight grams</th>
<th>Portal blood flow before ligation cc per 100 grams of liver per min.</th>
<th>Portal blood flow after ligation cc per 100 grams of liver per min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra</td>
<td>13</td>
<td>577</td>
<td>21.0</td>
<td>28</td>
</tr>
<tr>
<td>27</td>
<td>606</td>
<td>215</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>430</td>
<td>250</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>420</td>
<td>350</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>58</td>
<td>170</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>80</td>
<td>255</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>61</td>
<td>80</td>
<td>277</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>54.9</td>
<td>24.5</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Changes of the portal blood flow before and after ligation of the three major arteries, measured by the Bubble Flow Meter
Fig. 16 Changes of the portal blood flow before and after ligation of the three major arteries measured by the Bubble Flow Meter.

three major arteries in the normal dogs. The values of measurement were, as shown in Fig. 16 and Tab. 5, essentially equal to those obtained by "Thermostrom-uhr". That is, within 1-2 minutes after the ligation of three major arteries the volume of blood flow through the portal vein increased (at maximum 10cc/m/100g of liver compared to the pre-ligation value), and returned to pre-ligation level, and continued to decrease gradually thereafter.

V. DISCUSSION

In 1949, RIENHOFF performed the ligation of the hepatic artery to a patient of liver cirrhosis, and concluded that this procedure was worthwhile to try for the treatment of liver cirrhosis particularly with ascites. In 1951, Berman et al. also reported excellent results of this procedure for the treatment of liver cirrhosis with ascites.

Tsuchiya, in our laboratory, performed the constriction of the hepatic vein in dogs and could produce in them the conditions quite similar to those in human cases of liver cirrhosis. In these animals the common hepatic, gastroduodenal and right gastric arteries were ligated. He made it clear that in dogs which tolerated the procedure and survived for long, the blood pressure of the portal vein markedly decreased. From my study, it was confirmed that when the common hepatic, gastroduodenal and right gastric artery were simultaneously ligated in dogs with ascites, a continuous increase in the volume of the portal blood flow resulted. Also in case of the ligation of the hepatic artery alone, similar increase in the volume of
the portal blood flow, though it was less marked, was observed.

Concerning the mechanisms of the development of ascites, there are many different opinions. Among those, a theory that due to the anomalies of the intrhepatic vascular bed the venous congestion may take place, this, in turn, gives rise to the translocation of the liver lymph into the intraabdominal cavity to become ascites, is believed to be most reasonable (RIENHOFF, MADDEN).

In 1873 GAD reported that the blood flow in the hepatic artery slowed down the blood flow in the portal vein, following his experiments on rabbits. In 1907, HERRICK advocated that the hepatic artery worked as a resistance upon the portal vein, through his perfusion test on the human liver. Further, he found this was most markedly seen in the cirrhotic liver. In 1928, MCIINDOE also pointed out that there was a definite relationship between the blood pressure of the hepatic artery and that of the portal vein.

Thus, it can be easily imagined that the ligation of the hepatic artery will be effective in reducing ascites even when we think of only one factor that this procedure can mitigate the congestive state of the liver. In this view point, our experimental data that the hepatic artery ligation resulted in increase in the volume of the portal blood flow, is quite understandable, since in the case of liver cirrhosis with ascites the blood flow of the hepatic artery acts as a more obstacle upon the portal blood flow than in the normal liver.

Thus, we are of the opinion that the increase in the volume of the portal blood flow will serve to improve the liver function of the ascitic dogs with liver cirrhosis.

VI. SUMMARY

In 29 mongrel adult dogs the hepatic veins were constricted and ascites was produced experimentally. In these animals the effects of the ligation of the common hepatic, gastroduodenal and right gastric arteries upon the flow of the portal vein and upon the systemic arterial blood pressure were observed for 30 minutes.

Results obtained were as follows:

1) In dogs whose hepatic vein was constricted and ascites did not develop, the volume of blood flow in the portal vein did not essentially differ from that in normal dogs.

2) In dogs which had ascites after the hepatic vein constriction, on the other hand, the volume of the portal blood flow reduced markedly.

3) The volume of the portal blood flow increased markedly within 1-2 minutes after the hepatic artery ligation either in normal dogs or in dogs which had the hepatic veins ligated.

4) After the hepatic artery ligation in dogs whose hepatic vein had previously been constricted, the most marked and continuous increase of the portal blood flow was obtained in dogs which had ascites and in which the common hepatic, gastroduodenal and right gastric arteries were all ligated, and similar increase was seen, though in the lesser degree, in dogs of same group and in which the common hepatic artery alone was ligated.
5) In dogs of two other groups, i.e. dogs in the control group and those which did not have ascites, the ligation of the hepatic artery was not followed by a significant change in the volume of the portal blood flow.

6) Data obtained with the use of bubble flowmeter were essentially the same as those obtained by "Thermostromuhur".

I do wish to express my deep appreciation to Prof. Dr. Chihiko ARAKI for his guidance and for his correcting paper. Also I am greatly indebted to Assistant Prof. Dr. Ichiro HONNO for his kind and extended directions throughout the period of this experimentation.

REFERENCES

21) MacLeod, J. J. R. and R. G. Pearce: The Outflow of Blood from the Liver as Effected by
STUDY ON CIRRHOSIS OF LIVER


26) T. Misao et al.: Medical Electronics.

27) K. Motokawa: Experimental Electronics. 4th Ed.


和 文 抄 錄

肝 硬 変 症 の 実 験 的 研 究

——特に肝静脈狭窄犬における肝 動 脈
結紮の門脈流に及ぼす影響について——

京都大学医学部外科学教室第1講座 (指導: 荒木千里教授)
細 野 幸 吾

最近, Rienhoff, Berman 等が肝硬変症の治療に肝
静脈結紮が有効であることを提唱して以来, 講家によ
り本法は種々議論をされてきたが, いまだ定説を得
ない現状である. 症者は肝硬変症の場合, 特に腹水
の有無と関連して肝静脈結紮が門脈血流に対して如何
様に働くかを確めるため, 犬の肝静脈を狭帯し肝硬変
類似の状態を作成し, これに肝静脈狭窄犬に肝動脈血
流遮断をおこない, 両脈流に対する影響を "Thermo-
stromuhr" 及び Bubble Flowmeter を使用して検
査した.

実験動物には7.6kg～15.0kgの雛犬を使用し正常犬,肝静脈狭窄犬で腹水の貯留をきたさなかった犬群
及び肝静脈狭窄犬で腹水の貯留をきたした犬群にわ
から, 肝静脈狭窄犬は腹水の有無にかかわらず肝静脈狭
窄後14日目に再開腹し, 門脈血流速度測定を実施し
た. 肝静脈狭窄犬の作成には大略教室の土屋先生行った
方法を採用した.

"Thermostromuhr" 測定装置のうち, 様状熱電対は
Herrick 等の使用したものと大差はないが, ベーグー
ライト板には, よりよく血管に接着させるためゴム板
を, 又血液加熱には高周波発生装置を使用した, 様状
熱電対の門脈管部の挙動は鈴静脈流血部より肝臓側でお
こなった. 門脈血流速度の判明した実験犬について門
脈血流量の測定には犬の剖出門脈管及び同一個体より
t取用したヘパリン加血を使用した. 全身動脈圧測定
には, 便宜上肝動脈管を水銀マノメーターで測定した.

実 験 成 績

1) 肝動脈結紮後の門脈血流速度の変動
肝動脈血流遮断には総肝動脈単独結紮と, 三大動脈
正常犬群

緒肝動脈及び三大動脈結締組織は、緒肝動脈結紮直後、門脈血流量は著明に増加するが5分～20分で結紮前の速度に達し、以後徐々に速度は低下する。門脈血流量を換算しても同様の傾向を認めることは当然で、正常犬の門脈血流量は平均288cc/分である。

肝静脈狭窄犬と腹水の貯留をきたさなかった犬群

正常犬群のそれと比較すると肝動脈結紮直後上昇した血流量は結紮前値に戻る迄の時間が延長し、又一時結紮前値以下の速度に下降した曲線が再び上昇する傾向を示す症例もある。この犬群の肝動脈結紮前後の門脈血流量は平均210cc/分である。

肝静脈狭窄犬と腹水の貯留をきたした犬群

肝動脈結紮後上昇した血流量は多少の増減はあるが結紮前値に至る減少することなく、速度増加を示したままで推移する。この傾向は三大動脈結締組織の場合に特に著明であった。この犬群の門脈血流量は平均168cc/分である。

肝動脈結紮後30分間における各犬群の門脈血流量増減について

各犬群について肝動脈結紮前後門脈血流量に対して緒肝動脈結紮後各分每の増減量を加減した値を30分間で区切って緒肝動脈結紮後と正常犬及び肝静脈狭窄犬で腹水の貯留をきたさなかった犬群の緒肝動脈結紮症例では値の差を示し、他方正常犬及び肝静脈狭窄犬で腹水の貯留をきたさなかった犬群の3大動脈結紮症例、及び肝静脈狭窄犬で腹水の貯留をきたした犬群では緒肝動脈のみの結紮症例でも、3大動脈結紮症例とも共に正の値を示し、特に肝静脈狭窄犬で腹水の貯留をきたした犬群の3大動脈結紮症例では30分間に1000ccの門脈血流量増加を示す。

全身動脈圧の変動

緒肝動脈のみの結紮でも3大動脈の結紮でも、又正常犬でも肝静脈狭窄犬で結紮後1分～2分で10mmHg～40mmHg上昇し10分前後持続する。この動脈結紮後の一時的動脈圧上昇と門脈流の一時的増加は時間的によく一致する。

肝動脈結紮による門脈流変動を長時間観察したが、結紮後大略1時間前後の血流速度を約8時間保つ。その後解剖犬の全身衰弱等により逐次減少した。

空泡流動計による検討

正常犬群について3大動脈結紮前後の門脈血流量を測定した。測定値は "Thermostromuhr" で測定した値と大略同様であることを確かめた。