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# Experimental study on coronary perfusion with selective brain cooling for direct aortic surgery

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**Abstract**

1. Retrograde coronary perfusion in combination with selective brain cooling by irrigation was investigated in dogs, in comparison with direct coronary artery perfusion. 2. High incidence of ventricular fibrillation was seen in both methods in hypothermic state. Operation at the normal temperature using extracorporeal circulation is desirable, 3. In view of the above results optimal perfusion pressure appears 30 mm Hg. in retroperfusion, while 100 mm Hg. in direct coronary artery perfusion. 4. The right ventricle anoxia is an undesirable feature in retroperfusion, while the left ventricle showed a tendency to slight anoxia in both methods.

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# EXPERIMENTAL STUDY ON CORONARY PERFUSION WITH SELECTIVE BRAIN COOLING FOR DIRECT AORTIC SURGERY*

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Open cardiac surgery has developed so rapidly in the past few years since the development of hypothermia and pump-oxygenator provided the possibility of lengthening the periods of circulatory cessation. The direct vision correction of the aortic valve, however, has still two problems remaining to be solved. These are, first, the neccessity of maitaining coronary blood flow to the myocardium during operative procedure and, second, the prevention of coronary air embolism due to free exposure of the coronary ostia. LILLEHEI and his associates[1] have found in their experimental study that the non-working (by-passed) normal canine heart invariably goes into arrest or ventricular fibrillation upon release of the inflow occlusion after only six to eight minutes of total cessation of coronary circulation at the normal temperature. A relatively large amount of air entering the right heart cavity can be tolerated, though serious effects may be produced in some instances. On the contrary, it is well known that a minute amount of air produces a fatal outcome when it enters the left heart[2]. The cause of death, when air is injected into the left heart, is ventricular fibrillation or standstill secondary to coronary air embolism.

The priniple of retrograde coronary perfusion was first suggested by PRATT[3] in 1898 when he stated that the long-contracting, rhythmic heart is not wholly dependent upon the coronary arteries for its blood suppply, but, on the contrary, the heart will beat for hours while its arteries are empty : that there are two ways in which the heart muscle may be nourished — first, through the vessels of Thebesius, which open

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from the ventricles and auricles into a system of fine branches communicating with cardiac capillaries and, second, through the coronary veins, which may convey a backward flow of blood from the auricle into the tissues of the heart. In 1943 Roberts, BROWNE and RODERTS[4] reported experiences on 14 dogs in which an ischemic myocardium may be revascularized by the anastomosis of a large artery with the coronary sinus and coronary veins. Beck[5], in 1948, demonstrated in the dog that anastomosis between a systemic artery or a grafted branch from the aorta and the coronary sinus made it possible to ligate the descending ramus of the left coronary artery at its origin in one stage with no immediate mortality and with little or no damage of heart muscle. The application of this method to one patient who had had severe coronary artery disease over a long time gave rise to successful results. The first application of this principle to the correction of aortic valve was made by BLANCO[6] in 1956 and the successful perfusion of the myocardial capillary bed was carried out through the retroperfusion of the coronary sinus. However, the clinical application was first tried by LILLEHEI[7] in 1956 who operated on seven patients using the above method. Four of them survived the operation. Independently of the above demonstrations, OKADA and his coworkers[8] reported the same method for direct vision aortic valve surgery in dogs.

As another approach to the myocardial blood supply LILLEHEI[1] had perfused the coronary artery via the direct cannulation of the aortic orifices with appropriately sized polyethylene tubes while the aortic valve was exposed. However, they had abondoned this method because, though feasible, it was found to have several undesirable features : technical difficulty of cannulation, intimal damage of the coronary vessels by manipulation, interference of cannulae with the widest exposure of the aortic valve, and a time lag between the incision of the aorta and the completion of cannulations, during which the myocardium was deprived from blood flow and coronary artery air embolism could occur.

On the other hand, retroperfusion has also some disadvantages : the right ventricle cannot be perfused because of occlusion of the vena cordis parva at its orifice to the coronary sinus, insufficient blood supply to the left ventricle due to shunting into the right heart via Thebesian channels, and a tendency to myocardial bleeding even with relativeely low pressure in the catheter placed in the coronary sinus.

The present paper outlines the method of retrograde coronary perfusion and direct coronsry artery perfusion with selective brain cooling by irrigation[9,10,11] and gives the results in dogs, together with some

remarks aboutthe myocardial metabolism. An extensive disussion of this method, from the standpoint of electrocardiography, will be found in the report by IKEDA[12].

## MATERIALS AND METHOD

a) Retrograde coronary perfusion with brain cooling :

Sixteen adult mongrel dogs, varying from 10 to 26 kg. in weight, were employed in this series. Prior to the experiment, cross matching of the blood was performed in order to prevent the vital reaction during coronary perfusion. The animals were anesthetized with Nembutal given intravenously in a dose of 25 mg. per kg. of body weight and a small dose was occasionally added to prevent shivering during brain cooling. An intratracheal tube was inserted into the trachea and connected with an anesthetic machine. Respiration was assisted during the experiment.

The brain cooling system consists of two cannules to be introduced into a unilateral carotid artery, a DeBakey pump, a glass coil cooler dipped in ice-water which has 60 cubic centimeters of capacity, three bubble traps, an arterial irrigator and polyvinyl chloride tubes connecting these parts (Fig. 1). After the intravenous injection of Heparin in a doses of

Brain cooling system

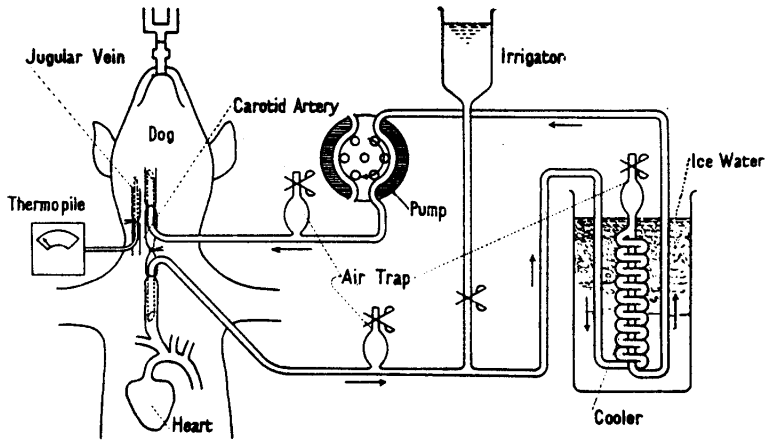


Fig. 1. diagrammatic representation of selective brain cooling by irrigation.

three mg. per Kg. of body weight, the femoral artery is connected to a mercury manometer for measurement of blood pressure. Through a jugu-

lar vein an electrode of copper-constantan thermocouples was inserted cephalad for measurement of brain temperature during the irrigation. Through the carotid artery in the same side, a cannula was placed cephalad and another one caudad which were connected to the inflow and outflow tract of the brain cooling system. The pump was calibrated in advance to deliver seven to nine cubic centimeters of blood per kg. of body weight per minute into the brain via the carotid artery and to remove an equal quantity of blood from the proximal side of the same artery. The body temperature was measured by a long mercury thermometer placed in the rectum.

Two or three dogs whose blood was cross matched were given three mg. per Kg. of body weight of Heparin solution and blood was withdrawn by arteriotomy. The blood collected into the bottle was preserved in a water bath kept at 39～40°C until it was used in order to prevent ventricular fibrillation due to the irrigation of cold blood through coronary vessels.

The thorax was entered through an incision extending in the fourth intercostal space. Placing loops of fine vinyl tube around the both venae cavae, and lung roots, the pericardium was opened longitudinally anterior to the phrenic nerve, both flaps of which were fixed to the thoracic wall to provide better exposure. Fat and adventitial tissues around the ascending aorta were dissected out in order to get a closer view. A cathter was introduced into the right ventricle through the azygos vein for collecting thebesian blood into the right heart. For coronary sinus irrigation a polyvinyl plastic tube four mm. in diameter or silicone rubber tube of the same size was introduced blindly into the coronary sinus through the right auricular appendage, which was anchored in place in the sinus with a silk stitch. During the above procedure the brain was irrigated by operating the pump system and the animals were cooled down to 32°C of rectal temperature. Circulatory cessation was started by the occlusion of the caval veins, both lung roots and ascending aorta, and controlled respiration was discontinued. A longitudinal incision along the anterior surface of the ascending aorta was made immediately after the circulatory cessation. The myocardial circulation was sustained by retrograde coronary perfusion through a catheter connected to a DeBakey pump or pressure bottle[12]. The measurement of inflow pressure and flow rate of coronary vessels was made, and blood samples were withdrawn before and during the perfusion for determination of myocardial metabolism. Ventricular fibrillation developed during experiment was defibrillated by use of a countershock.

Chemical Measurements: In eleven of all the experiment data were compiled on the myocardial extraction and consumption of oxygen, glucose, lactate, pyruvate and electrolyte change in association with the flow study. Blood oxygen was determined by the manometric method of Van SLYKE and NEILL[13], glucose by ferricyanide ferric iron method, lactate by Hydroquinone method, pyruvate by Dinitrophenyl-hydrazine method, and sodium by Flame photometry, calcium by Phosphate method, and potassium by Cobaltonitrite method[14].

Calculations: To calculate blood flow per 100 gm. of the left ventricle, measured blood flow must be multiplied by 100/left ventricle weight in gm. The left ventricle weight can be obtained by the formula of HERRMAN[15], i. e.

Left ventricle weight in gm. = body weight in Kg. x 0.0037.

Myocardial extraction in Vol. % or mg. or mEq. /L

= Coronary sinus catheter level − Coronary artery ostia level

Myocardial consumption in cc. or mg. /100gm. LV. /min.

= Myocardial extraction x left ventricular coronary flow

The control study before circulatory cessation was conducted by following equations :

Coronary sinus flow in cc./100gm. LV/min.

= Measured coronary sinus flow x 100/left ventricle weight in gm.

Myocardial extraction in Vol. % of mg. or mEq./L

= Aorta level − Coronary sinus level

Myocardial consumption in cc. or mg./100gm LV/min.

= Myocardial extraction x Left ventricular coronary flow

b) Direct coronary artery perfusion with brain cooling :

Nineteen adult mongrel dogs, varying in weight from 13 to 19 Kg., were employed in this series. Prior to the experiment, cross matching of the blood was performed as in the previous series. The brain cooling system was connected in the same manner, but there are some differeces between the two methods in the way of coronary perfusion. Perfusion system consists of a pressure bottle, a three-way adapter, and polyethylene tubes measuring two mm. in diameter for coronary artery cannulations. One of the tubes is angulated near its tip for the convenience of introducing into the left anterior descending artery.

After circulatory cessation in the same way the aorta was wide open at its root to get ample exposure of the aortic valve. Through the arotic incision three polyethylene tubes were introduced respectively into the

righ coronary artery, the anterior descending artery and the left circumflex artery. Each of them were fixed with encircling sutures to the aortic wall in order to avoid dislodging. Dissection of fat tissues around the aorta and an incision as close as possible to the aortic ring are essential for easy cannulations. However, any injury of the right coronary artery must be carefully avoided on incision. Too deep cannulations also must be avoided, which may occlude the branches of the coronary artery and lead to circumscribed myocardial anoxia.

Measuremenent of flow and blood sampling were performed, with a study of the relationship between perfusion pressure and myocardial bleeding. The metabolism was studied only in the left ventricle, though both ventricles were irrigated simultaneously in this method. The Fig. 3 shows a diagram of the coronaary artery perfusion.

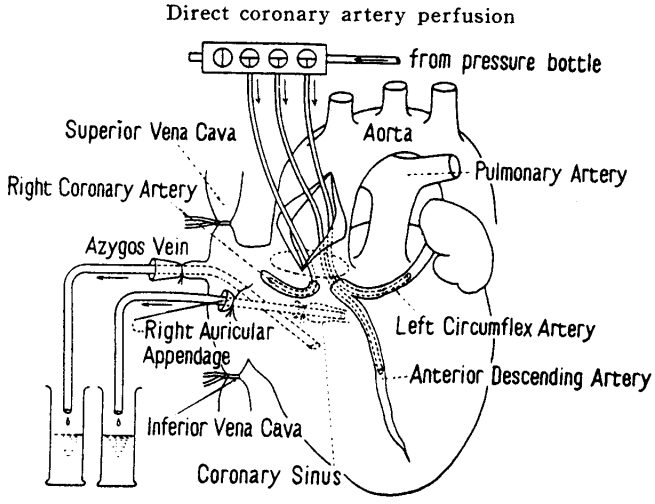


Fig. 3. Diagram illustrating three polyethylene tubes in right ccronary artery, left circumflex artery and anterior descending artery.

## RESULTS

a) Retrograde coronary perfusion:

The results obtained are given in Table 1. Ventricular fibrillation occurred in all cases excepting one (93.8%). Four of the cases got into fibrillation before the circulation was interrupted, of which only one was converted to normal rhythm by countershock and continued to contract for 19 minutes 40 seconds after the inflow occlusion. Blood samples were collected before the appearance of ventricular fibrillation or after the defibrillation

Table 1 Results of operation in retrograde coronary perfusion.

| Dog No. | Wt. in Kg. | Occlusion Time min. | Fibrillation | Rectal temp. C | Mort. |
|---|---|---|---|---|---|
| 1 | 15 | 19'30 | (−) | 32°1 | Killed |
| 2 | 16 | 0 | Occured during brain cooling | 38°1 | Death |
| 3 | 15 | 0 | Occured during brain cooling | 35°5 | Death |
| 4 | 13 | 13'45 | Occured after circul. cessation | 32°0 | Death |
| 5 | 18 | 10'00 | Occured after circul. cessation | 32°8 | Death |
| 6 | 15 | 19'40 | Occured during brain cooling | 33°0 | Death |
| 7 | 16 | 8'00 | Occured after circul. cessation | 32°2 | Death |
| 8 | 19 | 5'12 | Occured after circul. cessation | 31°2 | Death |
| 13 | 20 | 27'00 | Occured after circul. cessation | 33°0 | Death |
| 14 | 16 | 25'00 | Occured after circul. cessation | 32°3 | Death |
| 15 | 18 | 0 | Occured during brain cooling | 34°8 | Death |
| 16 | 15 | 16'41 | Occured after circul. cessation | 32°5 | Death |
| 22 | 17 | 15'00 | Occured after circul. cessation | 32°8 | Death |
| 23 | 17 | 18'00 | Occured after circul. cessation | 33°5 | Killed |
| 27 | 10 | 37'00 | Occured after circul. cessation | 33°5 | Killed |
| 28 | 26 | 30'00 | Occured after circul. cessation | 33°6 | Killed |

by use of a countershock. The effort to restore normal heart beats by the countershock in the fibrillated cases was unsuccessful except three cases. (Dog No. 23, 27, 28). The time for circulatory cessation ranged from minimum five to maximum 37 minutes, but irrigation over about 15 minutes brought about cyanotic discoloration of the right ventricle and myocardial atony. The mean coronary blood flow before circulatory cessation in hypothermic state was 39 cubic centimeters per 100 gm. of the left ventricle per minute varying 31 to 93 cubic contimeters. From our own experience with the coronary perfusion[11] in which the perfusion rate should be kept more than the coronary sinus flow in order to prevent ventricular fibrillation due to myocardial anoxia, these dogs were perfused at the average rate of 50 cubic centimeters per minute. However, for the anatomical distribution of the coronary vessels about 35 % of 50 cubic centimeters flew out from the left coronary artery ostia, the rest of which was shunted into the right heart via Thebesian channels.

It will be seen from Table 2 that the mean myocardial oxygen extraction in retroperfusion is very close to that before circulatory cessation, while myocardial oxygen consumption in retroperfusion are less than the control. It is accordingly conceivable that the myocardium has a deficit in oxygen supply.

It is known that decrease in oxygen supply to the myocardial capil-

Table 2 Myocardial oxygen extraction and consumption in retrograde coronary perfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. vein Vol. % | Lt. cor. a. ostia Vol. % | Extract. Vol. % | Consump. cc/100gm LV/min. |
|---|---|---|---|---|---|---|
| 5 | 18 | 13 | 16.9 | 3.8 | 13.1 | 1.7 |
| 6 | 15 | 14 | 15.1 | 4.8 | 10.3 | 1.4 |
| 7 | 16 | 14 | 17.9 | 2.8 | 15.1 | 2.1 |
| 8 | 19 | 23 | 15.6 | 4.9 | 10.7 | 2.5 |
| 13 | 20 | 8 | 19.2 | 2.6 | 16.3 | 1.3 |
| 14 | 16 | 17 | 14.0 | 3.3 | 10.7 | 1.8 |
| 16 | 15 | 18 | 18.5 | 5.2 | 13.3 | 2.4 |
| 22 | 17 | 25 | 17.6 | 4.4 | 13.2 | 3.3 |
| 23 | 17 | 19 | 20.8 | 5.5 | 15.3 | 2.9 |
| 27 | 10 | 43 | 20.4 | 3.9 | 16.5 | 6.9 |
| 28 | 26 | 16 | 20.8 | 2.0 | 18.8 | 3.0 |
| Average | | 19 | 17.9 | 4.0 | 13.9 | 2.7 |
| Control | | 41 | 16.8 | 3.6 | 13.2 | 5.6 |

lary bed leads to a disturbance of glucose utilization[16]. The Table 3 shows a marked decrease in glucose consumption across the myocardium, but not in glucose extraction.

Although lactate is consumed by myocardium in normal dogs[17, 7],

Table 3 Myocardial glucose metabolism in retroperfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. vein mg. % | Lt. cor. a. ostia mg. % | Extract. mg. % | Consump. mg/100gm LV/min. |
|---|---|---|---|---|---|---|
| 5 | 18 | 13 | 77 | 51 | 26 | 3.4 |
| 6 | 15 | 14 | 126 | 112 | 14 | 2.0 |
| 7 | 16 | 14 | 98 | 68 | 30 | 4.2 |
| 8 | 19 | 23 | 130 | 107 | 23 | 5.3 |
| 13 | 20 | 8 | 117 | 83 | 34 | 2.7 |
| 14 | 16 | 17 | 96 | 90 | 6 | 1.0 |
| 16 | 15 | 18 | 76 | 64 | 11 | 2.0 |
| 22 | 17 | 25 | 35 | 12 | 23 | 5.8 |
| 23 | 17 | 19 | 50 | 42 | 8 | 1.5 |
| 27 | 10 | 43 | 129 | 112 | 17 | 7.3 |
| 28 | 26 | 16 | 121 | 112 | 9 | 1.4 |
| Average | | 19 | 96 | 78 | 19 | 3.3 |
| Control | | 41 | 129 | 110 | 20 | 8.2 |

the metabolic observation in this series revealed negative extraction or consumption in nine dogs of the 11 studied. It is anticipated that the lactate was produced in the myocardium due to anoxic state[16,18] (Table. 4).

Table 4 Myocardial lactate metabolism in retroperfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. vein mg. % | Lt. cor. a. ostia mg. % | Extract. mg. % | Consump. mg./100gm LV/min. |
|---|---|---|---|---|---|---|
| 5 | 18 | 13 | 42 | 57 | −15 | −2.0 |
| 6 | 15 | 14 | 36 | 50 | −14 | −2.0 |
| 7 | 16 | 14 | 52 | 43 | 9 | 1.3 |
| 8 | 19 | 23 | 34 | 51 | −17 | −4.0 |
| 13 | 20 | 8 | 22 | 28 | − 6 | −0.5 |
| 14 | 16 | 17 | 86 | 76 | 10 | 1.7 |
| 16 | 15 | 18 | 41 | 61 | −20 | −3.6 |
| 22 | 17 | 25 | 58 | 62 | − 4 | −1.0 |
| 23 | 17 | 19 | 28 | 29 | − 1 | −0.2 |
| 27 | 10 | 43 | 62 | 71 | − 9 | −3.9 |
| 28 | 26 | 16 | 53 | 56 | − 3 | −0.5 |
| Average | | 19 | 47 | 53 | − 6 | −1.3 |
| Control | | 41 | 37 | 35 | 2 | 1.3 |

Table 5 Myocardial pyruvate metabolism in retroperfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. vein mg. % | Lt. cor. a. ostia mg. % | Extract. mg. % | Consump. mg./100gm LV/min. |
|---|---|---|---|---|---|---|
| 5 | 18 | 13 | 5.10 | 3.30 | 1.80 | 0.23 |
| 6 | 15 | 14 | 2.52 | 3.95 | −1.43 | −0.20 |
| 7 | 16 | 14 | 6.18 | 3.50 | 2.68 | 0.38 |
| 8 | 19 | 23 | 6.20 | 3.72 | 2.48 | 0.57 |
| 13 | 20 | 8 | 1.93 | 1.31 | 0.62 | 0.05 |
| 14 | 16 | 17 | 1.52 | 1.42 | 0.10 | 0.02 |
| 16 | 15 | 18 | 1.62 | 3.50 | −1.88 | −0.31 |
| 22 | 17 | 25 | 4.00 | 2.60 | 1.40 | 0.35 |
| 23 | 17 | 19 | 1.12 | 1.31 | −0.19 | −0.04 |
| 27 | 10 | 43 | 1.88 | 1.73 | 0.15 | 0.06 |
| 28 | 26 | 16 | 2.07 | 1.76 | 0.31 | 0.05 |
| Average | | 19 | 3.10 | 2.55 | 0.55 | 0.10 |
| Control | | 41 | 2.20 | 1.74 | 0.46 | 0.16 |

Table 6 Electrolyte change in retroperfusion utilizing selective brain cooling.

| Dog No. | Wt. in Kg. | Coronary sinus mEq/L | Lt. coronary a. ostia mEq/L | A-V diff. mEq./L |
|---|---|---|---|---|
| Ca | | | | |
| 4 | 13 | 6.3 | 5.8 | 0.5 |
| 5 | 18 | 4.8 | 4.3 | 0.5 |
| 8 | 19 | 4.6 | 3.2 | 1.4 |
| 13 | 20 | 4.3 | 4.5 | 0.2 |
| 14 | 16 | 4.2 | 4.6 | −0.4 |
| Average | | 4.8 | 4.5 | 0.3 |
| Control | | 4.4 | 4.4 | 0 |
| K | | | | |
| 4 | 13 | 5.3 | 6.1 | −0.8 |
| 5 | 18 | 4.8 | 4.7 | 0.1 |
| 6 | 15 | 5.0 | 5.1 | −0.1 |
| 7 | 16 | 6.3 | 7.8 | −1.5 |
| 8 | 19 | 4.7 | 6.2 | −1.5 |
| 13 | 20 | 5.9 | 3.3 | 2.6 |
| 14 | 16 | 5.1 | 5.2 | −0.1 |
| Average | | 5.3 | 5.5 | −0.2 |
| Control | | 4.9 | 5.0 | −0.1 |
| Na | | | | |
| 6 | 15 | 202 | 200 | 2 |
| 7 | 16 | 177 | 177 | 0 |
| 8 | 19 | 157 | 154 | 3 |
| 13 | 20 | 180 | 177 | 3 |
| Average | | 179 | 177 | 2 |
| Control | | 178 | 178 | 0 |

Pyruvate production in the myocardium is, as BING stated[19,16], an important indicator of the metabolic disorder caused by myocardial ischemia. Three of the 11 cases revealed negative extraction and other three showed decrease in extraction. Pyruvate consumption showed the same tendency as in extraction and the mean value was less than that of the control (Table 5).

Electrolyte change remained within the normal range except potassium which was mobilized from the myocardium in five of the seven cases studied. The fact suggests the possibility of myocardial anoxia[20] (Table 6).

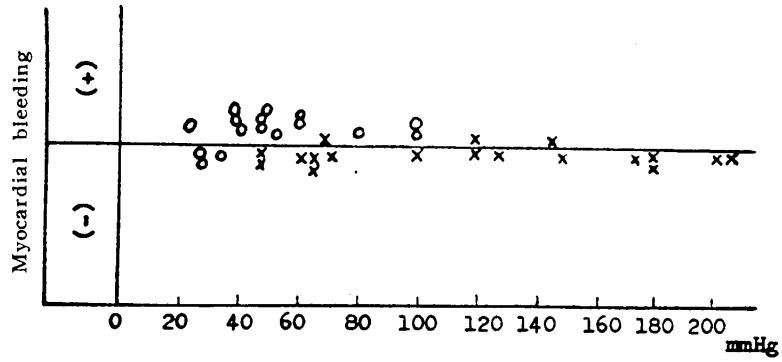


Fig. 2. Relation between perfusion pressure and myocardial bleeding. Small open circles above the middle horizontal line represent myocardial bleeding against different kinds of pressure in retroperfusion. Crosses represent same relation in direct coronary perfusion.

The relation between the perfusion pressure and myocardial bleeding was investigated in 16 cases and shown in Fig. 2, where it may be seen that all the cases perfused at a pressure of over 40 mmHg. developed myocardial bleeding. The results obtained in the analysis of myocardial bleeding were essentially similar to those reported by LILLEHEI[7], and KAL[21].

b) Direct coronary artery perfusion :

Table 7 shows that 15 cases of 19 (78.9%) caused ventricular fibrillation in this series. Although the results obtained here are slightly better than that in the case of retroperfusion. It is our belief that this method with hypothermia is hardly applicable to the correction of aortic valve disease in man.

The time for circulatory cessation ranged six minutes 20 seconds to 45 minutes which is longer than in retroperfusion. Heart beats during the perfusion were more forcible than in retroperfusion, and cyanosis on the right ventricle did not appear until about 18 minutes after circulatory cessation. As mentioned before, localized discoloration of the myocardium developed where the cannulae were inserted deep into the coronary arteries.

Table 8 gives myocardial oxygen extraction and consumption which shows slight decrease as compared to the control before circulatory cessation. Myocardial glucose extraction and consumption vary in relatively wide range as seen in Table 9 the mean values show slight decrease both

Table 7 Results of operation in direct coronary artery perfusion utilizing selective brain cooling.

| Dog No. | Wt. in Kg. | Occlusion Time mins. | Fibrillation | Rectal Temp. C | Mort. |
|---|---|---|---|---|---|
| 9 | 14 | 46′00 | Occured after circul. cessation | 33°5 | Death |
| 10 | 16 | 6′20 | Occured after circul. cessation | 32°7 | Death |
| 11 | 14 | 12′25 | Occured after circul. cessation | 33°0 | Death |
| 12 | 14 | 18′40 | Occured after circul. cessation | 32°8 | Death |
| 17 | 18 | 10′00 | Occured after circul. cessation | 31°8 | Death |
| 18 | 19 | 38′00 | (−) | 33°5 | Killed |
| 19 | 18 | 45′00 | (−) | 31°5 | Killed |
| 20 | 16 | 45′00 | (−) | 32°0 | Death |
| 21 | 15 | 14′30 | Occured during brain cooliog | 32°8 | Death |
| 24 | 15 | 0 | Occured during brain cnoling | | Death |
| 25 | 16 | 0 | A-V block | | Death |
| 26 | 14 | 0 | Occured during brain cooling | | Death |
| 29 | 19 | 34′00 | Occured after circul. cessation | 32°5 | Killed |
| 30 | 19 | 44′00 | Occured after circul. cessation | 33°2 | Death |
| 31 | 16 | 0 | Occured during brain cooling | | Death |
| 32 | 15 | 0 | Occured during brain cooling | | Death |
| 33 | 14 | 0 | Occured during brain cooling | | Death |
| 34 | 14 | 15′00 | Occured after circul. cessation | 30°0 | Death |
| 35 | 13 | 0 | Occured during brain cooling | | Death |

Table 8 Myocardial oxygen extraction and consumption in direct coronary artery perfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. art. Vol. % | Cor. Sinus Vol. % | Extract. Vol. % | Consump. cc/100gm LV/min. |
|---|---|---|---|---|---|---|
| 9 | 14 | 38 | 19.1 | 4.9 | 14.2 | 5.4 |
| 10 | 16 | 13 | 15.9 | 5.3 | 10.6 | 1.4 |
| 11 | 14 | 58 | 17.1 | 7.4 | 13.1 | 6.7 |
| 12 | 14 | 35 | 13.9 | 7.6 | 11.3 | 4.0 |
| 17 | 18 | 42 | 19.5 | 3.8 | 15.7 | 6.6 |
| 18 | 11 | 49 | 16.5 | 7.4 | 9.3 | 4.6 |
| 21 | 18 | 18 | 16.4 | 4.7 | 11.7 | 2.1 |
| 29 | 19 | 31 | 17.3 | 5.5 | 11.8 | 3.7 |
| 30 | 19 | 22 | 13.4 | 4.7 | 8.7 | 1.9 |
| 34 | 14 | 35 | 18.2 | 5.8 | 12.4 | 4.3 |
| Average | | 34 | 17.3 | 5.4 | 11.9 | 4.1 |
| Control | | 41 | 19.8 | 3.6 | 13.2 | 5.6 |

in extraction and consumption.

Lactate was sonsumed in two of 10 cases studied, in the rest of which lactate was produced in the myocardium as given in Table 10.

Myocardial extraction of pyruvate diminished in five cases, the rest

Table 9 Myocardial glucose metabolism in direct coronary artery perfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. art. mg. % | Cor. sinus mg. % | Extract. mg. % | Consump. mg./100gm LV/min. |
|---|---|---|---|---|---|---|
| 9 | 14 | 38 | 135 | 110 | 25 | 9.5 |
| 10 | 16 | 13 | 107 | 98 | 9 | 1.2 |
| 11 | 14 | 58 | 65 | 55 | 10 | 5.8 |
| 12 | 14 | 25 | 78 | 64 | 14 | 5.2 |
| 17 | 18 | 42 | 88 | 81 | 7 | 2.9 |
| 18 | 11 | 49 | 96 | 78 | 18 | 8.8 |
| 21 | 18 | 18 | 78 | 61 | 17 | 3.1 |
| 29 | 19 | 31 | 120 | 115 | 5 | 1.6 |
| 30 | 19 | 22 | 180 | 154 | 26 | 5.7 |
| 34 | 14 | 35 | 105 | 99 | 6 | 2.1 |
| Average | | 34 | 105 | 92 | 14 | 4.6 |
| Control | | 41 | 129 | 110 | 20 | 8.2 |

Table 10 Myocardial lactate metabolism in direct coronary artery metabolism utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. art. mg. % | Cor. sinus mg. % | Extract. mg. % | Consump. mg./100gm LV/min. |
|---|---|---|---|---|---|---|
| 9 | 14 | 38 | 56 | 60 | − 6 | −2.3 |
| 10 | 16 | 13 | 28 | 34 | − 6 | −0.8 |
| 11 | 14 | 58 | 29 | 25 | 4 | 2.3 |
| 12 | 14 | 35 | 30 | 28 | 2 | 0.7 |
| 17 | 18 | 42 | 31 | 32 | − 1 | −0.4 |
| 18 | 11 | 49 | 59 | 62 | − 3 | −1.5 |
| 21 | 18 | 18 | 35 | 43 | − 8 | −1.4 |
| 29 | 19 | 31 | 49 | 53 | − 4 | −1.2 |
| 30 | 19 | 22 | 28 | 39 | −11 | −2.4 |
| 34 | 14 | 35 | 40 | 50 | −10 | −3.5 |
| Average | | 34 | 35 | 39 | − 4 | −1.1 |
| Control | | 41 | 37 | 35 | 2 | 1.3 |

five showed the production of pyruvate as well as consumption (Table 11).

Changes in sodium and calcium remained within normal limits during the coronary perfusion, while potassium were mobilized from the myocardium in two of six cases studied as shown in Table 12.

Perfusion pressure was kept at 45 to 205 mmHg. in this series to set the safe limit of pressure. Most of the cases were tolerated relatively well to high perfusion at 70, 120, and 145 mmHg. caused myocardial bleeding in the right ventricle as shown in Fig. 2.

Table 11 Myocardial pyruvate metabolism in direct coronary artery perfusion utilizing selective brain cooling.

| Dog. No. | Wt. in Kg. | Flow cc/100 gmLV/min. | Cor. art. mg. % | Cor. Sinus mg. % | Extract. mg. % | Consumpt. mg./100gm LV/min. |
|---|---|---|---|---|---|---|
| 9 | 14 | 38 | 7.65 | 9.00 | −1.35 | −0.51 |
| 10 | 16 | 13 | 1.95 | 2.03 | 0.08 | 0.01 |
| 11 | 14 | 58 | 5.24 | 5.11 | 0.13 | 0.08 |
| 12 | 14 | 35 | 2.82 | 2.75 | 0.07 | 0.02 |
| 17 | 18 | 42 | 4.15 | 4.04 | 0.11 | 0.05 |
| 18 | 11 | 49 | 4.48 | 4.57 | −0.09 | −0.04 |
| 21 | 18 | 18 | 4.11 | 4.21 | −0.10 | −0.02 |
| 29 | 19 | 31 | 2.45 | 2.75 | −0.30 | −0.09 |
| 30 | 19 | 22 | 2.53 | 2.55 | −0.02 | 0 |
| 34 | 14 | 35 | 2.01 | 1.98 | 0.03 | 0.01 |
| Average | | 34 | 3.74 | 3.90 | −0.14 | −0.05 |
| Control | | 41 | 2.20 | 1.74 | 0.46 | 0.16 |

## DISCUSSION

We have been studyig experimentally the method to maitain blood supply to the myocardium as a basis for direct vision surgery of aortic valve for these two years, together with the selective brain cooling by irrigation[9, 10, 11]. Time limit of safe circulatory intrruption is generally considered as 15 minutes in hypothermia[11], hence operative procedure with the aorta open must be finished within this limit, so far as the selective brain cooling is used. The central nervous system of the animals in which circulatory interruption was continued over this limit is presumed to have been damaged in our experiments.

Ventricular fibrillation occurred in both retrograde and direct coronary perfusion, especially more common in the former. Of the many

Table 12 Electrolytes change in direct coronary artery perfusion utilizing selective brain cooling.

Ca

| Dog No. | Wt. in Kg. | Coronary a. mEq/L | Ooronary sinus mEq/L | A-V diff. mEq/L |
|---|---|---|---|---|
| 9 | 14 | 3.4 | 4.1 | −0.7 |
| 11 | 14 | 4.6 | 5.6 | −1.0 |
| 12 | 14 | 4.9 | 4.7 | 0.2 |
| 12 | 14 | 4.0 | 3.2 | 0.8 |
| 17 | 18 | 5.4 | 6.1 | −0.7 |
| 18 | 19 | 5.6 | 5.7 | −0.1 |
| Average | | 4.7 | 4.9 | −0.2 |
| Control | | 4.4 | 4.4 | 0 |

K

| | | | | |
|---|---|---|---|---|
| 9 | 14 | 5.3 | 6.8 | −1.5 |
| 11 | 14 | 6.1 | 5.0 | 1.1 |
| 12 | 14 | 4.6 | 2.6 | 2.3 |
| 12 | 14 | 6.0 | 5.4 | 0.6 |
| 17 | 18 | 3.2 | 6.4 | −3.2 |
| 18 | 19 | 8.1 | 5.5 | 2.9 |
| Average | | 5.6 | 5.3 | 0.3 |
| Control | | 4.9 | 5.0 | −0.1 |

Na

| | | | | |
|---|---|---|---|---|
| 9 | 14 | 158 | 163 | − 5 |
| 11 | 14 | 174 | 169 | 5 |
| 17 | 18 | 168 | 160 | 8 |
| 18 | 19 | 176 | 172 | 4 |
| Average | | 169 | 166 | 3 |
| Control | | 178 | 178 | 0 |

etiological factors as hypercapnia, hyperkalemia, anoxia and increased irritability due to hypothermia[9], the last two are most responsible, because ventricular fibrillation which is considered to be caused by myocardial anoxia is difficult to be converted into the normal rhythm or to restore previous forcible contraction even if the countershock was effective[11]. In addition, mechanical irritation by introducing the cannula into the coronary sinus and fixing it by silk stitch very close to the A—V node might cause the irregularity of the heart beats. It is quite possible

that myocardial anoxia is brought about by decrease in blood supply to the heart through the coronary sinus in retroperfusion, while in direct perfusion unskillfulness and unsteadiness of the cannulation are assumed to be responsible for myocardial anoxia.

As for the right ventricle the results obtained here are in agreement with the view of LILLEHEI[7] that retrograde flow from the righ coronary artery was either absent or negligible, because vena cordis parva draining the right ventricle into the coronary sinus is not always present as MORI[22] pointed out in his work. Even if the vein is present, tightening of encircling suture around the catheter might occlude the blood flow through this vein to the right ventricle. This was confirmed by the fact that the pink color of the right ventricle was lost gradually during the retroperfusion. Left coronary flow, although considered better than right ventricle, was much less than that before circulatory cessation. Efforts to increase the left coronary flow by high pressure inevitably lead to myocardial bleeding. Hence, it may be concluded that for such operations, performable within 15 minutes, as simple aortic stenosis, retroperfusion is preferable at a pressure of about 30 mmHg., while more complicated operations as that for aortic regurgitation and highly calcified aortic stenosis needs direct coronary artery perfusion at a pressure of about 100 mmHg.

Difficulty of cannulation in the direct perfusion in dogs will be possibly alleviated because of the better visual field in man. The feasibility of the direct coronary artery perfusion in man was confirmed by KAY[21] in 1958.

## SUMMARY AND CONCLUSION

1. Retrograde coronary perfusion in combination with selective brain cooling by irrigation was investigated in dogs, in comparison with direct coronary artery perfusion.

2. High incidence of ventricular fibrillation was seen in both methods in hypothermic state. Operation at the normal temperature using extracorporeal circulation is desirable,

3. In view of the above results optimal perfusion pressure appears 30 mm Hg. in retroperfusion, while 100 mm Hg. in direct coronary artery perfusion.

4. The right ventricle anoxia is an undesirable feature in retroperfusion, while the left ventricle showed a tendency to slight anoxia in both methods.

## REFERENCES


1. LILLEHEI, C. W., DEWALL, R. A., GOTT, V. L., and VARCO, R. L. : The diredt vision correction of calcified aortic stenosis by means of a pump-oxygenator and retrograde coronary perfusion, *Dis. Chest* **30**, 123, 1956.
2. LEWIS, F. J., SHUMWAY, M. E., NIAZI, S. A., and BENJAMIN, R. B. : Aortic valvulotomy under direct visfon during hypothermia, *J. Thor. Surg.* **32**. 481, 1956.
3. PRATT, F. F: The nutrition of the heart through the vessels of Thebesius and the coronary veins, *Am. J. Phisiol.* **1**, 86, 1898.
4. ROBERTS, I. T., BROWM, R. S., and ROBERTS, G. : Experimental studies on the nourishment of the left ventricle by the luminal (thebesian) vessels. Nourishment of the myocardium by way of the coronary veins, *Fed. Proc. Balt.* **2**, 90, 1943.
5. BECK, C. S., STANTON, E., BATIUCHOCK, W., and LEITER, E. : Revascularization of heart by graft of systemic artery into coronary sinus, *J. A. M. A.* **137**, 436, 1948.
6. BLANCO, G., ADAM, A., and FERNANDEZ, S.: A direct experimental approach to the aortic valve II. Acute retroperfusion of the coronary sinus, *J. Thor. Surg.* **32**, 171, 1956.
7. GOTT, V. L., GONZALEZ, J. L., ZUHDI, M. N., VARCO, R. L., and LILLEHEI, C. W.: Retrograde perfusion of the coronary sinus for direct vision aortic surgery, *Surg. Gynec. & Obst.* **104**, 319, 1957.
8. OKADA, N. et al. : Retrograde coronary perfusion, *The Saishin Igaku* **12**, 91, 1957, (In Japanese).
9. KIMOTO, S. et al. : Extension of indications to operation for congenital heart disease, especially on a new method for direct vision intracardiac surgery, *Nihon Rinsho* **140**, 709, 1955, (In Japanese).
10. PARKINS, W, M., JOHSEN, J. M., and VARS, H. M.: Brain cooling in the prevention of brain damage during periods of circulatory occlusion in dogs, *Ann. Surg.* **140**, 284, 1954.
11. SUNADA, T., TAGUCHI, K. et al.: *Japanese J. Thor. Surg* **10**, 33, 1957.
12. IKEDA, Y.: Personal communications.
13. VAN SLYKE, J. D., and NEILL, J. M.: Determination of gases in blood and other solutions by vacuum extraction and manometric measurement, *J. Biol. Chem.* **61**, 523. 1924.
14. SAITO, M.: Clinical chemical measurements by electrophotometer, 6th ed. Nanzando, Tokyo, 1956.
15. HERRMAN, G. H.: Experimental heart disease; Method of dividing hearts with sectional and proportional weighs and ratios for two hundred normal dog's hearts, *Am. Heart J.* **1**, 213, 1925.
16. HARA, T. et al: Coronary circulation in induced hypothermia, *Clinic All-Round* **5**, 1970, 1956.
17. EVANS, C. A. L.: *J. Physiol.* **45**, 213, 1912-13. cited.
18. KOBAYASHI; T. et al. : Myocardial metabolism. *Clinic All-Round* **5**, 1658, 1956.
19. BING, R. J. : Myocardial metabolism, *Circulation* **12**, 635, 1955.
20. DENNIS, J. and MOORE, R. M.: Potassium changes in the functioning heart uuder conditions of ischemia and congestion, *Am. J. Physiol.* **123**, 443, 1938.
21. KAY, E. B., and HEAD, : Direct coronary perfusion for aortic valve surgery. Report of technique, *J. A. M. A.* **168**, 1767, 1958.
22. Mori, M. : Anatomical considerations on the coronary circulations, *Clinic All-Round* **5**, 1457, 1956.