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# LONG LASTING EXTRACORPOREAL CIRCULATION WITH MEMBRANE OXYGENATOR DURING NORMOTHERMIA AND PROFOUND HYPOTHERMIA

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## INTRODUCTION

The duration of the so-called long term extracorporeal circulation has proven not to be so very long. Galletti[1] and others, using normothermia and partial bypass with low flow rate, could keep dogs alive after ten hours of perfusion with 60% long term survivors. But when using complete bypass or profound hypothermia, two to three hours seems to be the upper limit of viability. This, during hypothermia, is quite close to the possibility of extracorporeal circulation with complete circulatory arrest. This study is concerned with the part played in mortality and morbidity of long term extracorporeal circulation by each of these two factors; in one hand, extracorporeal circulation, and in the other hand, hypothermia.

In this study the least traumatic oxygenator, membrane oxygenator, was used, which was primed without any blood, but with normal saline to avoid homologous blood reaction.

## MATERIALS AND METHODS

Nineteen mongrel dogs whose body weight ranged from 8 kg to 13 kg were used in this series of study.

They were divided in three groups by using the closed method: Group 1; Hypothermic perfusion with 2 hours' cardiac arrest. This includes 30 minutes of cooling and 30 minutes of rewarming by partial perfusion in addition to the time of cardiac arrest at temperature below 10°C. Group 2; Hypothermic perfusion with 3 hours' cardiac arrest. This also includes the same procedures as group 1. Group 3; Normothermic perfusion for 4 hours. This is the partial perfusion as the control of group 2.

Immediately after anesthesia was induced with intravenous administration of 30 mg/kg of thiamylal sodium, an endotracheal tube was inserted and respiraion was assisted with tidal volume 250 ml to 300 ml of room air or pure

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oxygen, by means of Harvard respirator.

Anesthesia was maintained at a minimal level with Halothane 0.4 to 1.0% vapor saturation.

In the extracorporeal circulation system, membrane oxygenator was adopted for the purpose of smaller priming volume and less blood trauma. One square meter of membrane surface area was used every time. Thickness of this membrane was 3/4 mil. When the effiiciency of this oxygenator is expressed by the following formula,

$$\frac{O_2 \text{ delivered (ml/min)}}{\text{membrane area (sq.m.)}} = \frac{\text{A-V diff. (vol.\%)} \times \frac{\text{flow rate (ml/min)}}{100}}{\text{membrane area (sq.m.)}}$$

Average efficiency was 15 ml/min in this experiment. According to the data in Special Instrument Laboratory, maximum efficiency is 25 ml/min[2]. At the proximal portion between the oxygenator and one venous reservoir, a roller pump was put in.

At the distal portion of this oxygenator one Brown-Harrison heatexchanger and one bubble trap were put in this order. Both vena cava superior and inferior were canulated through peripheral veins, the iugular and femoral veins with Badic catheter No. 16 to 20. Venous blood was introduced to venous reservoir by gravity drainage, and this blood was returned to femoral artery by the roller pump through membrane oxygenator, heatexchanger, bubble trap and femoral catheter, made of stainless steel, 3 mm in diameter. This circuit was primed with 450 ml of normal saline and any kind of drug was not put in it except 20 mg of Heparin.

At the beginning of the procedure 2.0 mg/kg of Heparin was given to dogs intravenously. Every hour during perfusion 1.0 mg/kg of Heparin was added. Prior to the perfusion, no quinidine was given to dogs. Whenever blood level in venous reservoir came down during perfusion normal saline was added accordingly. Perfusion was started at 50 ml to 60 ml/kg/min of flow rate which was maintained for 15 min until esophageal temperature reached below 15°C and then flow rate was reduced to 30 ml to 35 ml/kg/min. After 2 hours' cardiac arrsst in group 1 and after 3 hours' cardiac arrest in group 2 rewarming began at the same flow rate as at the beginnig. Within 30 min, the temperatur rose up to normal.

Temperature was monitored in different areas: esophagus, rectum and deep muscles of the thigh. Arterial and venous pressures were recorded by means of the transducer and Sanborn amplifier or Honeywell Isicoder. Blood chemistry; $pCO_2$, $pO_2$ pH, and electrolytes were measured. Buffer base and alkali reserve were read from the nomogram of Singer and Hastings. Hematocrit and oxygen content in arterial and venous blood were investigated by using Wintrobe's method and Van Slyke's technique respectively.

$O_2$ consumption and cardiac output were measured by Fick's method. Endotracheal pressure was measured by giving 300 ml of tidal volume. Urine was collected from the beginning of the procedure to 3 hours postoperatively.

Control samples were taken usually before bypass. In group 1 other samples were taken 60 min and 150 min after perfusion started. In group 2 and 3 these were taken 60 min, 120 min and 210 min after perfusion started. The others were at the end of bypass and one hour or some times two hours postoperatively in all groups.

## RESULTS

*1. Mortality and Morbidity* (Tables 1, 2 and 3)

The cause of death were included in four categories; pulmonary insufficiency, cardiac failure, anemia and pneumonia. In group 1; Hypothermic perfusion with 2 hours' cardiac arrest, three dogs were alive and four dogs were dead. One dog died of pulmonary insufficiency, a second of pneumonia three days after the procedure, a third of pulmonary insufficiency and cardiac failure with endocardial bleeding, and last one of cardiac failure with signs of low blood pressure and myocardial bleeding. In group 2, hypothermic perfusion with three hours' cardiac arrest, two dogs lived and four dogs died. Two dogs died of pulmonary insufficiency and the other two of cardiac failure with myocardial and endocardial bleeding. In group 3, normothermic perfusion for four hours as a control of group 2, only one dog died of anemia with low hematocrit and edematous organs. This dog was considered to have been sick because of poor control data. The details of the causes of death are shown in Tables 1 and 2.

The survived dogs were followed until they recovered completely.

The special finding during their recovery was hind leg paralysis (Table 3). In group 1, one of three survivors had hind leg paralysis for 24 hours, in group 2 one of two for 6 days, and in group 3 one of five for 2 days.

TABLE 1. Mortality and Cause of Death

| Group | No. of Cases | Non-Survivor | Cause of Death | | | |
|---|---|---|---|---|---|---|
| | | | Pulmonary Insufficiency | Cardiac Failure | Anemia | Pneumonia |
| Group 1 | 6 | 3 (50%) | 2 | 1 | 0 | 1 |
| Group 2 | 6 | 4 (67%) | 2 | 2 | 0 | 0 |
| Group 3 | 6 | 1 (17%) | 0 | 0 | 1 | 0 |

Group 1..Hypothermic perfusion with 2 hrs' cardiac arrest.
Group 2..Hypothermic perfusion with 3 hrs' cardiac arrest.
Group 3..Normothermic perfusion, control of Group 2.

*2. Blood pressure* (Figs. 1a, 1b and 1c)

In hypothermic perfusion, group 1 and 2, blood pressure dropped rapidly

TABLE 2. Autopsy Findings of Non-Survivors

| Group | Dog Number | Period Until Died | Autopsy Findings |
|---|---|---|---|
| Group 1 | 704 | 15 hours | Both lower lobes are severely atelectatic. |
| | 723 | 3 days | Small indurations are disseminated in both lungs, but no atelectasis. |
| | 771 | 15 hours | Severe atelectasis in left upper lobe, but right lung is normal. Endocardial bleeding in both right and left ventricles. Much abdominal fluid. Mucous membrane of intestine is hemorrhagic. |
| Group 2 | 746 | 12 hours | Small amount of fluid in chest cavity. Both lungs are atelectatic, but left lower lobe is more severe than right lobe. Petechien in kidnies. |
| | 760 | 2 days | Both lungs are atelectatic, but most severe in right lung. |
| | 764 | 5 hours | No atelectasis in lungs. Severe myocardial and endocardial bleeding. |
| | 768 | 4 hours | No atelectasis in lungs, but they are very anemic. Both ventricles have endocrdial bleeding. |
| | 770 | 3 hours | No atelectasis in lungs. Organs are very pale. Much fluid in abdominal cavity, in stomac, and in intestine. Alimentary tract is edematous. |

Group 1..Hypothermic perfusion with 2 hours' cardiac arrest.
Group 2..Hypothermic perfusion with 3 hours' cardiac arrest.

TABLE 3. Postoperative Hind Leg Paralysis in Survivors

| Group | Survival Rate | Dog Number | Hind Leg Paralysis |
|---|---|---|---|
| Group 1 | 50% | 701 | No Paralysis |
| | | 719 | 24 Hours |
| | | 730 | No Paralysis |
| Group 2 | 33% | 739 | 6 Days |
| | | 751 | No Paralysis |
| Group 3 | 83% | 742 | No Paralysis |
| | | 750 | No Paralysis |
| | | 758 | No Paralysis |
| | | 762 | 2 Days |
| | | 766 | No Paralysis |

Group 1..Hypothermic perfusion with 2 hrs' cardiac arrest.
Group 2..Hypothermic perfusion with 3 hrs' cardiac arrest.
Group 3..Normothermic perfusion, control of Group 2.

with cooling. After reduction of the flow rate and cardiac standstill by hypothermia, it came down to 30 mmHg and this pressure was kept until rewarming began. With rewarming, the heart restores its own beat and the pressure

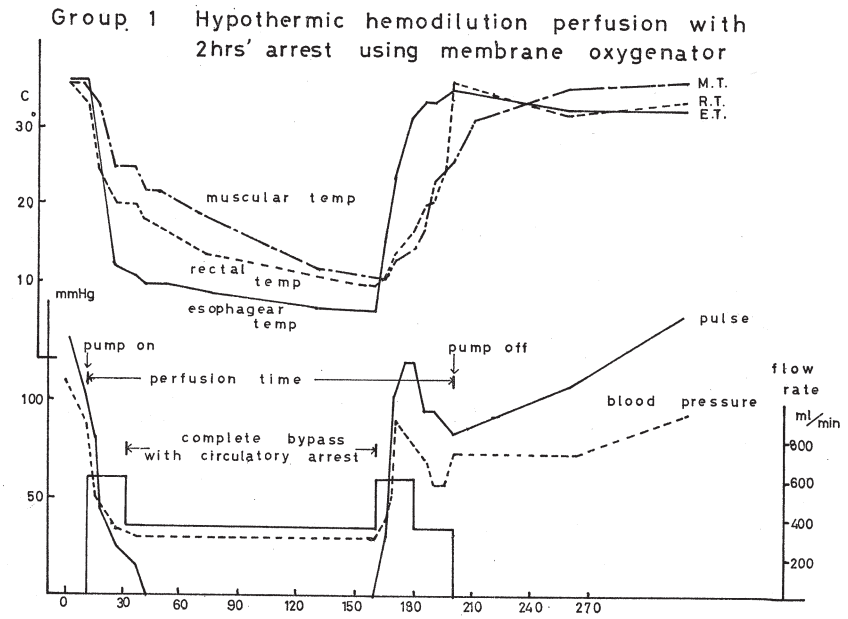


FIG. 1 a. Changes in temperature, blood pressure, pulse rate and flow rate in group 1 (E.T.; Esophageal temperature, R.T.; Rectal temperature, and M.T.; Muscular temperature).

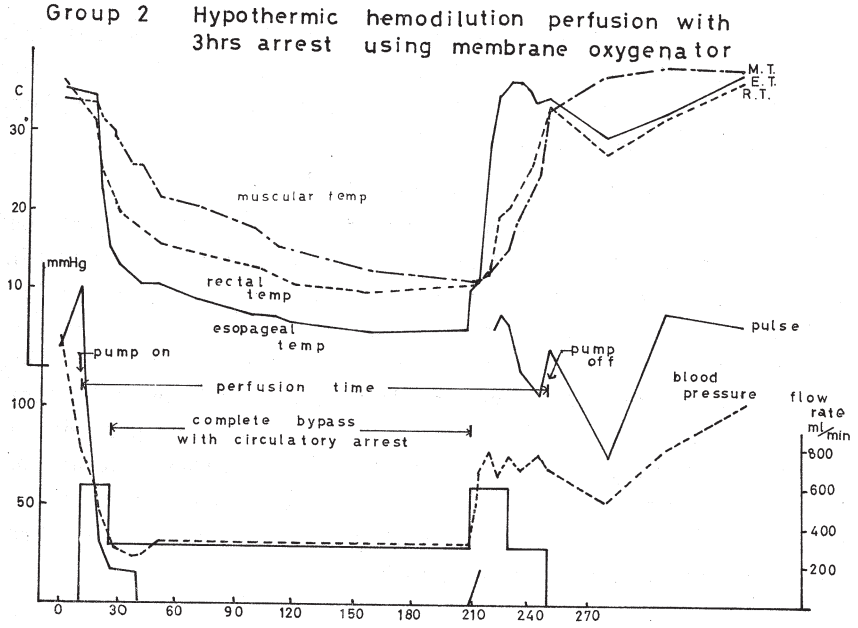


FIG. 1 b. Changes in temperature, blood pressure, pulse rate and flow rate in group 2 (E.T.; Esophageal temperature, R.T.; Rectal temperature, M.T.; Muscular temperature).

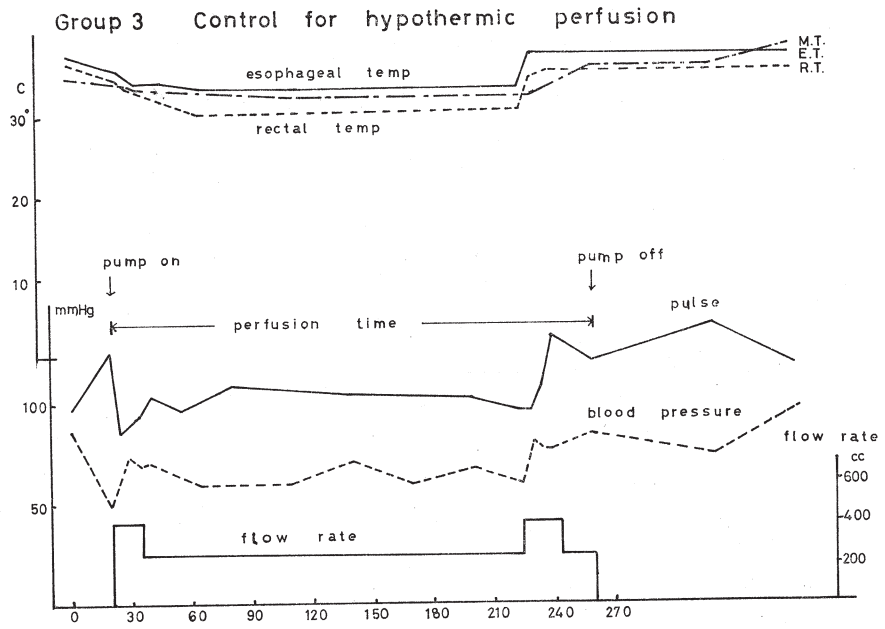


FIG. 1 c. Changes in temperature, blood pressure, pulse rate and flow rate in group 3 (E.T.; Esophageal temperature, R.T.; Rectal temperature, and M.T.; Muscular temperature).

became gradually high. Most of the non-survivors had lower values than the survivors during rewarming or postoperatively. In normothermic perfusion, group 3, survivors had more than 60 mmHg in mean pressure throughout the perfusion except for short time at the beginning of the perfusion.

*3. Cardiac rate* (Figs. 1 a, 1 b and 1 c)

In hypothermic perfusion, groups 1 and 2, by cooling cardiac rate became extremely slow within 30 min. The heart came to a complete standstill. In group 1, all of the dogs had no ventricular fibrillation during cooling and restored their own heart beat spontaneously during rewarming. In group 2, one dog had ventricular fibrillation 25 min after pump on and two dogs at the beginning of rewarming. One was defibrillated easily but the other was very difficult to be defibrillated for 20 min. In normothermic perfusion, group 3, most of the dogs maintained more than 100/min in cardiac rate and had no vetricular fibrillation. Bradycardia at the end of perfusion and in the first postoperative hour had a close relation with pulmonary insufficiency or cardiac failure. This also indicates poor prognosis.

*4. Temperature*

Temperature was regulated by the heatexchanger. In hypothermic perfusion groups, from cooling to rewarming, temperature difference between

esophagus and rectum was kept very small, 1-2°C, but that between thigh and esophagus was usually about 10°C. With rewarming esophageal temperature rose up quickly. Within 15 min. it reached up to 35°C while others remained still low. When rectal temperature came back to 33°C, pump was stopped. After the pump off dogs were rewarmed by means of blanket and infrared lamp. In normothermic group body temperature was also controlled by heatexchanger not to be below 34°C in esophageal temperature. Temperature gradient between esophagus and rectum was kept within 4°C (Figs. 1a, 1b and 1c).

*5. Blood pooling*

In this series of experiment, much saline had to be given to dogs in order to maintain adequate perfusion, and after the perfusion all blood left in the extracorporeal circulation system was returned to the dogs. These fluid and blood were considered to be blood pooling. The average volume taken per dog was 87.0 ml/kg in group 1, 93.7 ml/kg in group 2 and 100.0 ml/kg in group 3 as the control of group 2. In group 3, non-survivors took extremely much fluid. In hypothermic group, no relation with blood pooling between survivors and non-survivors was seen (Fig. 2).

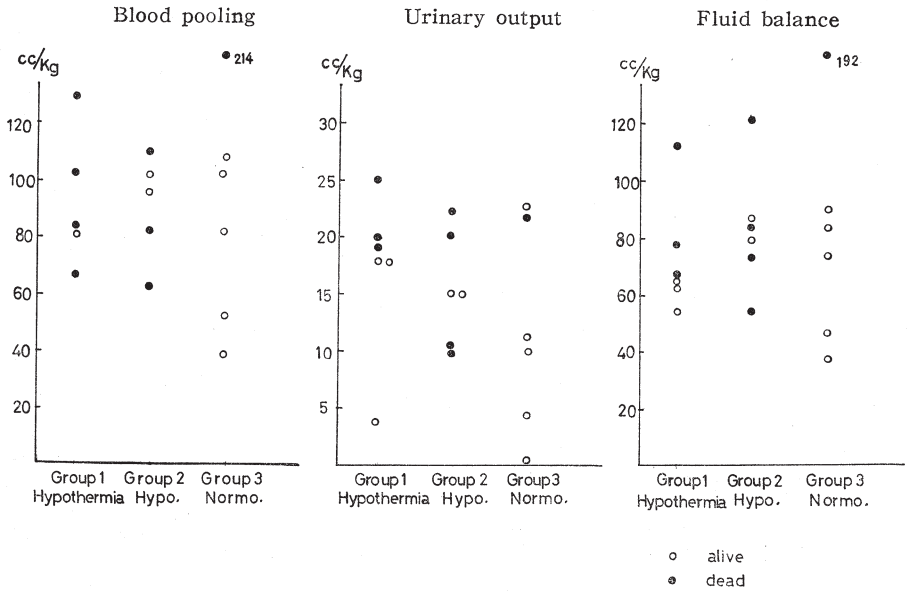


FIG. 2. Blood pooling, Urine output, and Fluid balance in each group were shown.

*6. Urinary output*

Urine was collected by catheter throughout the perfusion and until 3 hours postoperatively. The more fluid the dogs took during the perfusion the more

urinary output they had. Average volume is 15.6 ml/kg in group 1, 13.8 ml/kg in group 2 and 11.8 ml/kg in group 3. Even survived dogs in group 3 had very small amount of urinary output.

*7. Fluid balance*

The fluid which was given during perfusion and within 3 hours postoperatively was called "pooling of fluid" and the urine which was collected during the same period was named "urinary output". Therefore, pooling of fluid minus urinary output, the real amount of fluid pooled in the body, was named here fluid balance. Its average volume is 70 ml/kg in group 1, 79.8 ml/kg in group 2 and 83.0 ml/kg in group 3. Individual data are shows in Fig. 2.

*8. Hematocrit*

Hematocrit before the perfusion ranged from 54% to 36% in three groups. Immediately after perfusion started the hematocrit became very low. During the perfusion it remained in almost the same value. After the perfusion it increased in value by means of giving back the blood left in the circuit. All survivors had hematocrit above 20% during the perfusion. In group 1, some of the non-survivors had high hematocrit postoperatively. In group 3 all survivors ranged from 38% to 28% in hematocrit while one non-survivor had low hematocrit below 20% during the perfusion (Fig. 3).

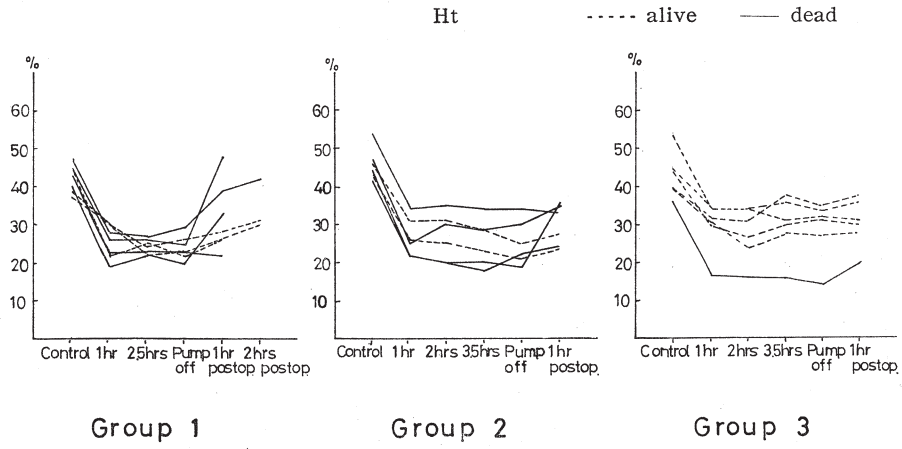


FIG. 3. Hematocrit during perfusion became very low. Hematocrit below 20% may be considered to be one of the causes of death.

*9. Endotracheal pressure*

Percent changes of endotracheal pressure are presented in Fig. 4. The non-survivors never showed high endotracheal pressure during and after the perfusion. High endotracheal pressure was noted in the survivors rather than in the non-survivors.

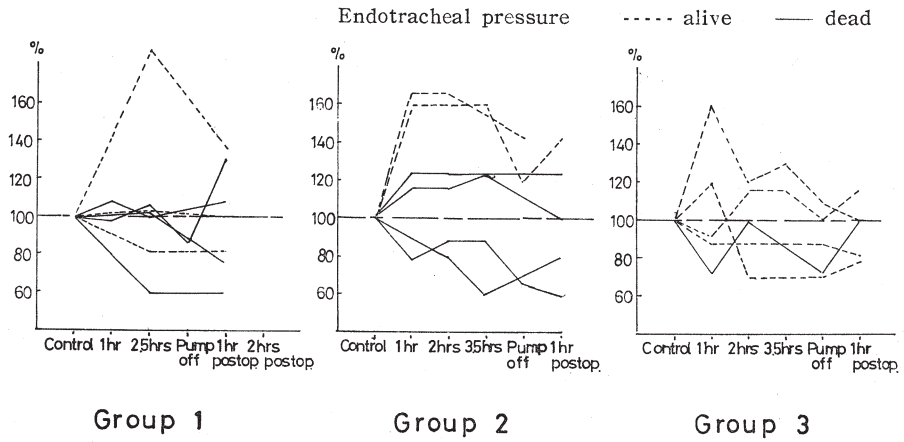


FIG. 4. % Change in endotracheal pressure; high endotracheal pressure was noted in survivoirs rather than in non-survivors.

*10. Metabolism*

$O_2$ A-V difference, as shown in Fig. 5, was small in hypothermia. In group 2, some of the non-survivors had comparatively larger difference than the survivors. The average value was 5.0 ml/dl during normothermic perfusion, but 1.5 ml/dl during hypothermic perfusion. By this fact the efficiency of the oxygenator used was evaluated to be about 15 ml/square meter.

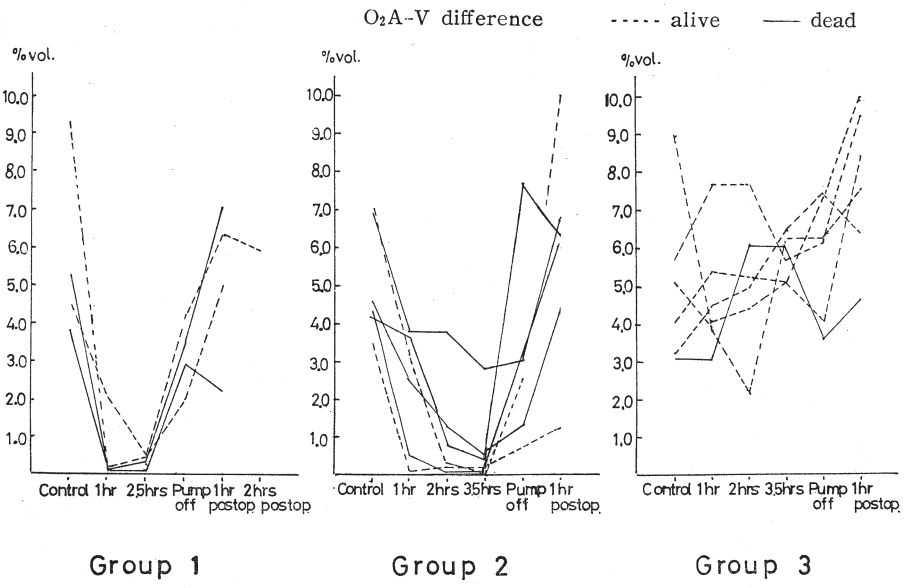


FIG. 5. A-V $O_2$ difference during cardiac arrest below 10°C was almost zero in hypothermic groups.

TABLE 4. Metabolic Changes in Arterial Blood: Average Values

| | $pO_2$ (mmHg) | | | $O_2$ Saturation (%) | | | $O_2$ Consumption (ml/kg/min) | | | Cardiac Output (ml/kg/min) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 |
| Control | 99.8 | 99.0 | 240 | 97.21 | 98.05 | 98.62 | 8.7 | 6.8 | 8.2 | 187 | 155 | 185 |
| 1 hour | 466 | 435 | 76 | 99.69 | 98.87 | 80.8 | — | — | — | — | — | — |
| 2 honrs | — | 608 | 70.6 | — | 100.0 | 79.38 | — | — | — | — | — | — |
| 2.5 hours | 618 | — | — | 100.0 | — | — | — | — | — | — | — | — |
| 3.5 hours | — | 646 | 65 | — | 100.0 | 74.45 | — | — | — | — | — | — |
| End of perfusion | 154 | 216 | 65.1 | 91.55 | 90.8 | 74.1 | — | — | — | — | — | — |
| 1 hour postop. | 96 | 278 | 237 | 94.27 | 96.45 | 98.76 | 9.3 | 8.3 | 7.2 | 166 | 138 | 91 |
| 2 hours postop. | 82 | — | — | 91.1 | — | — | — | — | — | — | — | — |

Group 1..Hypothermic perfusion with 2 hours' cardiac arrest.
Group 2..Hypothermic perfusion with 3 hours' cardiac arrest.
Group 3..Normothermic perfusion, contol of Group 2.

Arterial blood $pO_2$, oxygen saturation, oxygen consumption and cardiac output are shown in Table 4. In the hypothermic perfusion—group 1 and group 2—$pO_2$ and oxygen saturation during the perfusion became extremely high while they became gradually low in the normothermic perfusion—group 3. As to $pO_2$, average value of non-survivors both in the hypothermic and normothermic perfusion was higher than that of survivors. Individual data

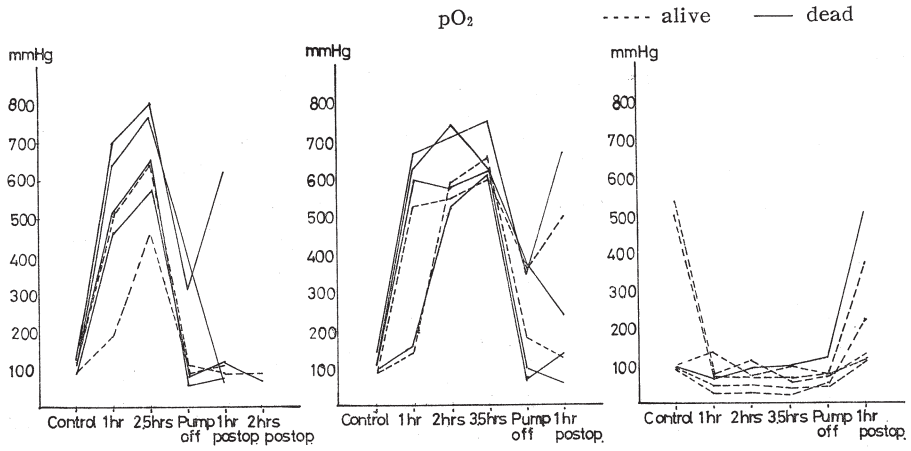


FIG. 6. $pO_2$ in arterial blood during perfusion was extremely high in hypothermic groups instead of becoming gradually low in normothermic group.

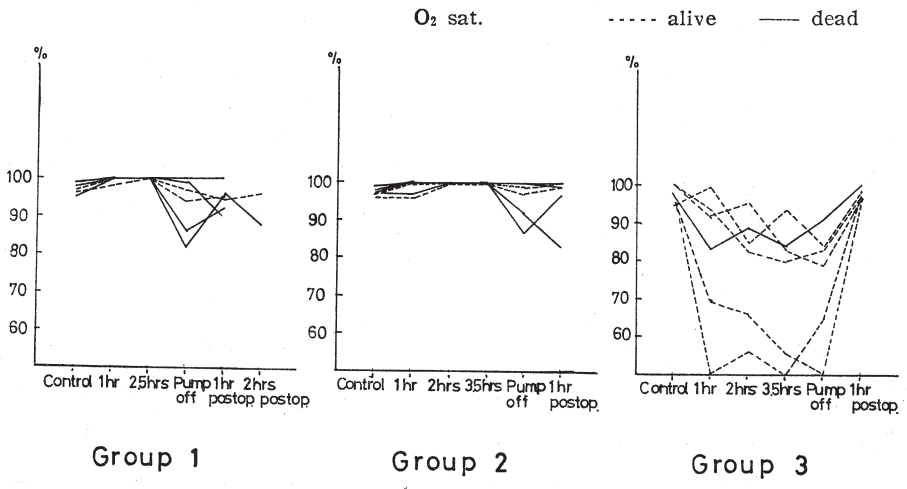


FIG. 7. $O_2$ saturation in arterial blood during perfusion was near 100%, but low $O_2$ saturation after pump off indictes poor prognosis in hypothermic groups.

are presented in Figs. 6 and 7. Low $O_2$ saturation after pump off indicated poor prognosis in hypothermic groups.

$O_2$ consumption was apt to increase after the perfusion in hypothermic groups but it decreased postoperatively in normothermic group.

Cardiac output decreased after the perfusion remarkablly in three groups (Fig. 8).

Average values of pH, $pCO_2$, buffer base, and alkali reserve ($HCO_3^-$) are

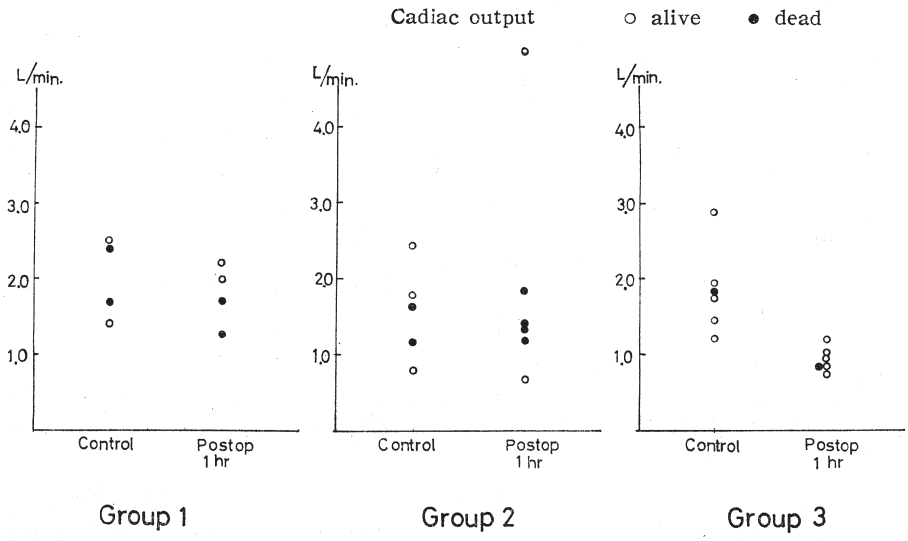


FIG. 8. Cardiac output decreased after perfusion in each group.

TABLE 5. Metabolic Changes in Arterial Blood: Average Values

| | pH | | | $pCO_2$ (mmHg) | | | Buffer Base (mEq/L) | | | $HCO_4^-$ (mEq/L) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 |
| Control | 7.475 | 7.569 | 7.555 | 23.2 | 17.96 | 18.38 | 41.8 | 43.7 | 43 | 17.1 | 15.9 | 15.9 |
| 1 hour | 7.021 | 6.996 | 7.086 | 48.7 | 56.25 | 51.5 | 28.2 | 28.5 | 31.3 | 12.86 | 13.2 | 14.7 |
| 2 hours | — | 6.930 | 7.013 | — | 61.58 | 46.8 | — | 26.5 | 31.8 | — | 12.9 | 14.6 |
| 2.5 hours | 6.941 | — | — | 58.3 | — | — | 25.4 | — | — | 12.35 | — | — |
| 3.5 hours | — | 6.891 | 7.04 | — | 60.3 | 49.9 | — | 24.7 | 29.8 | — | 11.4 | 13.8 |
| End of perfusion | 7.142 | 7.091 | 7.002 | 32.4 | 34.5 | 49.55 | 28.6 | 26.2 | 27.4 | 10.68 | 10.10 | 12.0 |
| 1 hour postop. | 7.253 | 7.201 | 7.362 | 27.3 | 21.7 | 23.1 | 31.2 | 30.1 | 32.5 | 11.36 | 9.7 | 11.2 |
| 3 hours postop. | 7.299 | — | — | 34.6 | — | — | 35.0 | — | — | 15.23 | — | — |

Group 1..Hypothermic perfusion with 2 hours' cardiac arrest.
Group 2..Hypothermic perfusion with 3 hours' cardiac arrest.
Group 3..Normothermic perfusion, control of Group 2.

shown in Table 5. The average value of arterial pH, buffer base and alkali reserve dropped during the perfusion. However, after the perfusion they tended to return except for alkali reserve. Individual data are shown in Figs. 9, 10, 11 and 12. pH values were higher in the survivors than in the non-survivors postoperatively in three groups. Buffer base and alkali reserve showed no particular difference between survivors and non-survivors in hypo-

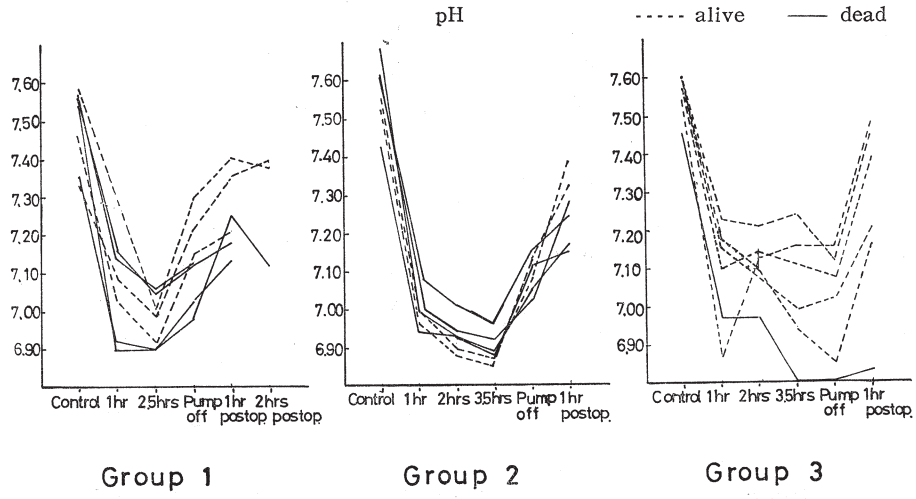


FIG. 9. pH dropped during perfusion, but after perfusion returned to near pre-perfusion value in survivoirs. In non-survivoirs it was still low after perfusion.

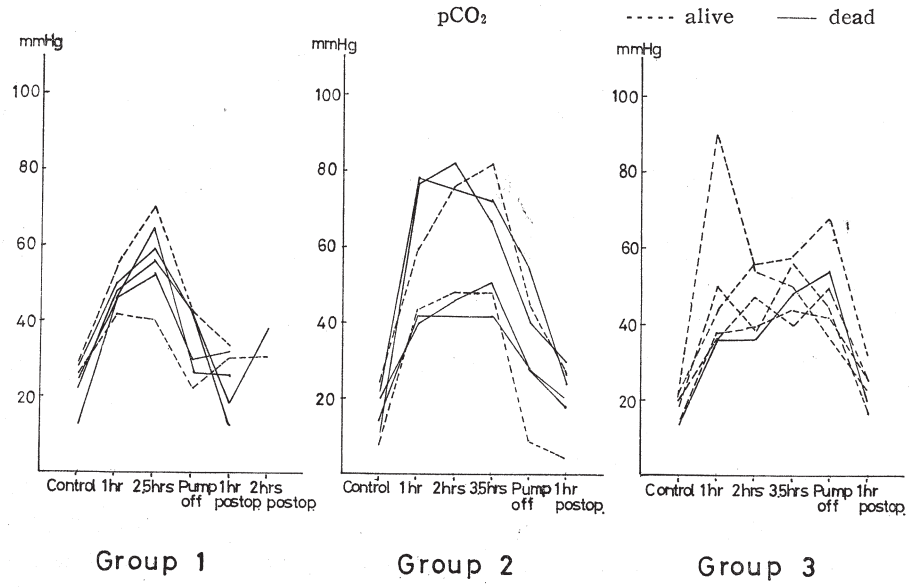


FIG. 10. $pCO_2$ became very high during perfusion more than 50 mmHg, but it's correlation between survivoirs and non-survivoirs was not known.

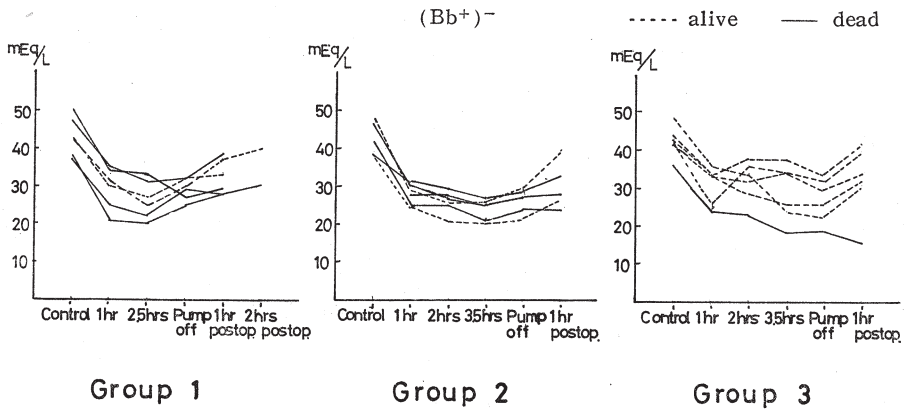


FIG. 11. Buffer base dropped during perfusion. It tends to come back to preperfusion level after perfusion.

thermic groups, but in group 3—normothermic perfusion, non-survivors had far lower value than survivors. The value of $pCO_2$ became very high during the perfusion in three groups. In group 1, the average value was 58.3 mmHg, in group 2, 61 mmHg and in group 3, 49.9 mmHg. No difference between survivors and non-survivors was recognized (Fig. 10).

*11. Electrolytes*

Serum sodium and potassium were measured before and after the perfusion

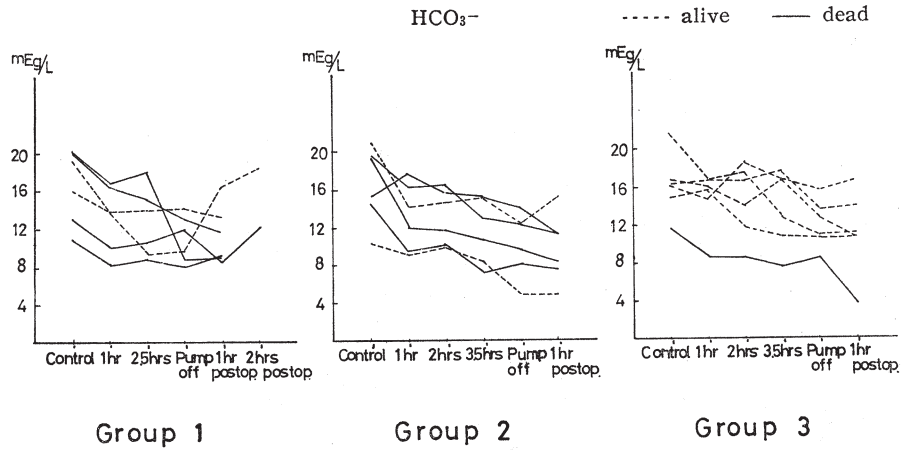


FIG. 12. Changes in serum $HCO_3^-$ in each group.

in group 2 and group 3. The average value of serum sodium was 143 mEq/L before the perfusion and 146 mEq/L postoperatively in grup 2, and it was 149 mEq/L and 151 mEq/L respectively in group 3. Generally, the value increased slightly after the perfusion.

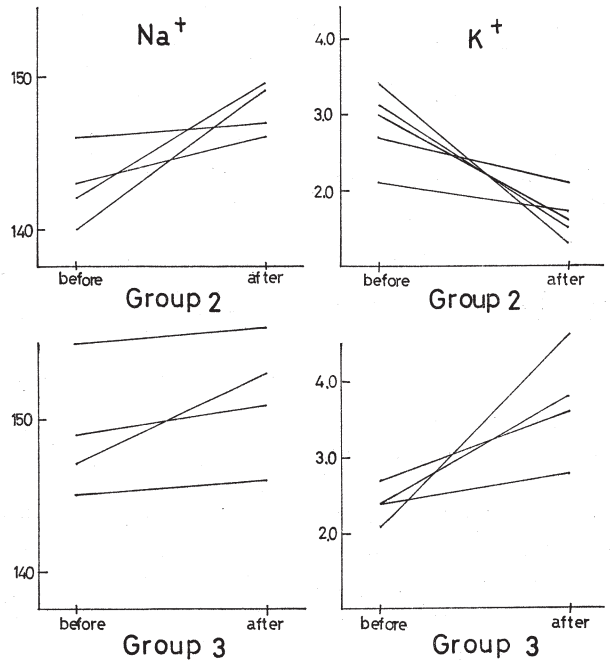


FIG. 13. After perfusion serum $Na^+$ increased. As to serum $K^+$ it decreased remarkablly in hypothermic groups, but increased markedly in normothermic group.

The average value of serum potassium decreased after perfusionin group 2—hypothermic perfusion, but increased in group 3—normotheric perfusion.

## DISCUSSION

The manifestation of complication during long term extracorporeal circulation seems te be as follows; (a) Cardiopulmonary collapse during and after the perfusion without response to blood transfusion. This is very similar in this respect to irreversible shock and is usually associated with blood pooling in chest, abdominal cavities and viscera—mainly lung, liver and bowels. (b) Respiratory insufficiency with or without pulmonary edema. This is also similar to physiologic and pathological changes occuring in the lung during shock. This is rarely associated with low blood pressure in the case of extracorporeal circulation. This is, however, often followed by death. (c) neurological complication—coma, or convulsion, although rarely seen, can not be ruled out in early death. The problem of hind legs weekness or paralysis, usually transitory, remains unsolved. These complications following prolonged perfusion may also occur in profound hypothermia.

Hypothermia combined with extracorporeal circulation has been widely used in open heart surgery since 1957[3] with many physiological advantages such as prevention of red cell destruction[4] and reduced oxygen consumption[5] in hypothermia. Profound hypothermia with circulatory arrest obtained by cardiopulmonary bypass was introduced by Drew and Anderson[6], Shield and Lewis[7], and developed by Lessage and Sealy[8], and Johnston and Gerbode[9]. One of the limiting factors in using this technique in open heart surgery is that only 60 minutes of circulatory arrest at 10°C is tolerated. Lessage and his co-worker reported in 1963[10] high survival rate in dogs which were subjected to deep hypothermia (below 10°C) with 2 hours' cardiac arrest, during the time of which circulation was maintained with very low flow rate.

From their study it may be inffered that mortality and morbidity are directly related to the flow rate and blood trauma among many factors. Anaphylactoid reaction was a definite factor in mortality and was reflected in the data from their experimental extracorporeal circulation. For this reason the author avoided using blood to prime the system. However, blood is far from being the only source of anaphylactoid reaction. Foreign proteins, peptone, endotoxin, toxin of traumatized cell crushes or anoxia are also responsible for shock.

The author, this time, primed the whole circuit of bypass machine with normal saline and added only normal saline during the perfusion to maintain adequate perfusion for elimination of homologous blood reaction[11]. The membrane oxygenator—least traumatic oxygenator was used. This oxygenator has a lesser potential factor for denaturation of protein than the disc or babble

oxygenator[12]. Disadvantage of this oxygenator, however, is that oxygen uptake is poorer than the other type of oxygenator. Teflon membrane, 3/4 mil of thickness, has only 25 ml/min/sq.m of oxygen uptake. Hypotherimia covers this disadvantage with saving surface area and priming volume. Priming volume in the membrane oxygenator which has one square meter of surface area is within 100 ml. Extracorporeal circulation with the membrane oxygenator requires much less priming volume than that with the dis coxygenator. In this series of experiment only 450 ml of normal saline is primed in the bypass circuit.

Throughout the perfusion, partial perfusion was used. By means of blood cooling combined with surface cooling, temperature is lowered below 10°C, and cardiac arrest is tolerable for two or three hours. During such low temperature oxygen supply with membrane oxygenator was sufficient enough and rapid rewarming was done. After the bypass was stopped all blood within the system was returned to the subject.

It is very difficult to measure anaphylactoid reaction quantitatively. Blood pressure and venous pressure in relation to shock-like manifestation were recorded. Amount of blood pooling and quantity of fluid necessary to maintain blood pressure may be the best parameters to measure the degree of shock. For the measurement of cellular anoxia and metabolic acidosis, blood analysis was done. These parameter before, during and after bypass were essentially the same as those obtained by Dr. Lessage and his coworkers[10] (deep hypothermia with disc oxygenator primed with homologous blood and normal sailine 1 : 1 ratio). Any better results were not obtained in hypothermic groups, even though membrane oxygenator and no homologous blood were used. Satisfactory results, however, were obtained in normothermic perfusion with membrane oxygenator and no homologous blood. Its real value remains unknown during profound hypothermia. If oxygen uptake of membrane oxygenator is satisfactory, perfusion carried out by membrane oxygenator primed with no homologous blood seems to be the best. Oxygen uptake of this oxygenator, however, is still not enough to fill oxygen demand of the body during normothermic perfusion with complete bypass. As long as this oxygenator is used hypothermia must be used together at the present stage.

Recently, R. H. R. Belsey[13] reported 265 cases of profound hypothermia obtained by blood stream cooling in cardiac surgery with total postoperative mortality 18% including 120 min of circulatory arrest under 10°C. In his report, it is described that with controlling $pCO_2$ at 40 mmHg by giving carbon dioxide during the perfusion, better results were obtained than without. In another paper to be published by the author, mortality was not improved by using $CO_2$ during pertusion in profound hypothemia.

In case of the membrane oxygenator, $pCO_2$ during the perfusion was higher than 40 mmHg both in normothermia and in hypothermia. The values

of $pCO_2$ do not appear to be related to mortality and morbidity.

In profound hypothermia, 60 minutes of circulatory arrest may be tolerated at 10°C, but by maintaining the circulation at low flow rate (30 ml/min), 120 minutes of cardiac arrest may be tolreated at 10°C whether membrane oxygenator and no homologous blood are used or not.

SUMMARY

With the membrane oxygenator primed with small amounts of normal saline, low flow perfusion was carried out under profound hypothermia and normothermia.

In groups 1 and 2 (hypothermic group) survivors were less than in group 3 (normothermic group). Profound hypothermia below 10°C has less advantage than normothermia.

In order to clarify the nature of mortality and morbidity in this study, blood pooling, urinary output, fluid balance, hematocrit, endotracheal pressure, A-V $O_2$ difference, $paO_2$, arterial oxygen saturation, cardiac output, pH, $paCO_2$, buffer base, and serum electrolytes were investigated before, during and after the perfusion.

Changes of these parameters were very similar to those measured during shock. They are most outstanding characteristics of postperfusion death.

Extracorporeal system used in this study is good enough to perfuse dogs for more than four hours in normothermia and for a little shorter time in profound hypothermia.

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