Systemic hypothermia is useful in protecting various organs from the ischemia induced by the circulatory arrest which is required in cardiac surgery and transplantation. This conclusion is supported by multiple experimental data which demonstrate that the tissue metabolic ratio and oxygen consumption decrease in accordance with a fall in body temperature [21]. In recent veterinary surgery, the supportive method of cardiopulmonary bypass (CPB) has been established. However, since CPB is expensive and labor-intensive, it is not widely used. Less expensive and simpler supportive protocols for cardiac surgery, including hypothermia or cross-circulation, have been tested experimentally [3, 6, 7, 9, 11, 17]. Successful open-heart surgery under hypothermic anesthesia alone has been reported [8, 12, 13, 18]. While surface-induced hypothermic anesthesia is the simplest technique, it is generally combined with ether inhalation. Abdominal cavity cooling, which is another method for inducing hypothermic anesthesia, can give more efficient induction of hypothermic anesthesia than surface-induced hypothermia because of a more abundant blood supply to the peritoneum [14, 15, 22].

This study was designed to investigate the potential of circulatory arrest under systemic hypothermic anesthesia, using the abdominal cavity cooling method.

MATERIALS AND METHODS

Preoperative treatment: Eighteen beagles (1–5 years old), each weighing 10.5 ± 2.3 kg, were used in these experiments. All dogs were judged as being very sound in physical and laboratory examinations. They were fasted for 24 hr, and were given no water for 12 hr before surgery. One hr and 30 min before anesthetic induction, both atropine sulfate (0.025 mg/kg b.w. i.m.) and chlorpromazine (0.5 mg/kg i.m.) were administered. Chlorpromazine was also injected 10 min prior to surgery (Fig. 1).

Anesthesia and preparation: Induction of anesthesia was achieved with sodium thiopental (25 mg/kg b.w. i.v.). After intubation, isoflurane (0.5–2%) was inhaled with pure oxygen and maintained. 3Fr and 5Fr polyethylene catheters were placed in the aortic arch via the left carotid artery and the right atrium via the left jugular vein, respectively. These catheters were also used as the blood sampling route in order to check hematological parameters, including hematocrit (Ht), total protein (TP), and arterial blood pH and gases every 30 min. Intra-cardiovascular pressures were recorded with a lead II electrocardiogram. Urine was collected from a catheter placed into the bladder and the output was calculated. Esophageal temperature was measured using a temperature-monitoring system (CTM-303, TERUMO, Tokyo).

Cooling and surgery: Pancuronium bromide (0.05 mg/kg i.v.) was administered before cooling started. The cooling method, which was referred to in previous reports [4, 5, 14, 15, 22], consisted of placing aseptic, crushed ice made from injectable lactated Ringer’s solution into the abdominal cavity. This manipulation was repeated as required. An ice bag was also applied to the head. Low molecular weight dextran (LMWD: 15 ml/kg i.v.) was infused to blood dilution continuously between 25–35°C of the esophageal temperature. Mechanically controlled ventilation, using a volume-limited-respirator (ACE-3000 ACOMA), maintained respiratory alkalosis with monitoring of blood gases, including arterial blood pH and PaCO₂, throughout the cooling period. Respiration rate, tidal volume, and inspiratory oxygen fraction (FiO₂) were established at 15–
25 breaths/min, 20–25 ml/kg, and 1.0, respectively.

When the esophageal temperature reached 30°C, a thoracotomy was performed through the left fifth intercostal space, and then an incision was made through the pericardium to expose the heart. A 4Fr catheter was inserted into the aortic root, and attached to the aortic wall with purse-string sutures (4–0 polypropylene sutures). A 15Fr catheter was placed into the left atrium from the auricle, and attached with purse-string sutures (4–0 polypropylene sutures). A 15Fr tube attached between these two catheters, bypassing the circulation in the direction of the aorta from the left atrium (left heart bypass) was created to supply oxygen to the coronary blood flow (Fig. 2). Cooling or warming the blood in this bypass supportively increased thermal efficiency in the heart. At the end of this procedure, heparin sodium anticoagulant (50 IU/kg) was administered intravenously.

**Cardiac arrest:** At the esophageal temperature of 20–23°C, the caudal vein, pulmonary artery and aorta were clamped. After confirming the reduction of cardiac volume resulting from decreasing venous return, the heart was arrested by infusing Young’s solution at 4°C (1 ml/kg b.w.) [6–8, 11] into the aortic root. Every 20 min, 2 ml/kg b.w. of cold crystalloid solution containing 20% mannitol, 7% NaHCO₃, KCl, and insulin was perfused into the coronary artery via the aortic root, causing cardioplegia. Controlled mechanical ventilation was continued to prevent alveolar collapse during cardiac arrest. When the systemic circulation had stopped, the left atrium was incised and continuously sutured in one layer with a 6–0 polypropylene suture. The arresting time was found to be about 20–30 min (Table 1).

**Resuscitation**

Cardiac arrest: At the esophageal temperature of 20–23°C, the caudal vein, pulmonary artery and aorta were clamped. After confirming the reduction of cardiac volume resulting from decreasing venous return, the heart was arrested by infusing Young’s solution at 4°C (1 ml/kg b.w.) [6–8, 11] into the aortic root. Every 20 min, 2 ml/kg b.w. of cold crystalloid solution containing 20% mannitol, 7% NaHCO₃, KCl, and insulin was perfused into the coronary artery via the aortic root, causing cardioplegia. Controlled mechanical ventilation was continued to prevent alveolar collapse during cardiac arrest. When the systemic circulation had stopped, the left atrium was incised and continuously sutured in one layer with a 6–0 polypropylene suture. The arresting time was found to be about 20–30 min (Table 1).

Resuscitation and rewarming: After de-aeration and washout of the crystalloid solution from the coronary circulation, all the vascular clamps were released, and warm blood was circulated in the left heart bypass. To reperfuse the coronary blood flow, cardiac massage, injection of noradrenaline, and defibrillation were performed as required. When the heart beat was stable, the abdominal cavity was actively warmed by circulation of 40°C aseptic saline. At the esophageal temperature of 30°C, the left heart bypass was removed, and then the surgical incisions in the thorax...
and abdomen were sutured in the standard manner. Before closing the thorax, a 16Fr silicon tube was inserted for intrathoracic drainage. Using a heat mat, rewarming continued until the esophageal temperature reached 38°C.

Post-operative care included blood transfusion, antibiotics, and cardiotonic drugs as required. A transfusion of 200–400 ml of blood, depending on the volume of pre-operative blood and the bleeding volume, was given based on a cross-matching test performed before the operation.

Statistics: Measurements are expressed as the mean ± SD. Significance of differences among parameters were determined by analysis of variance, and Scheffe’s method was used for simultaneous multiple comparisons. Differences in P value less than 0.05 were considered to be significant.

RESULTS

The recoveries of the dogs fell into three categories, as follows, 1) recovery without any complications-11 dogs (group 1), 2) not extubated with spontaneous breathing-4 dogs (group 2), 3) no reappearance of heart beat-3 dogs (group 3).

Cooling proceeded successfully without any fatal arrhythmia in all groups. The time required to arrest the hearts (cooling time), the fall in esophageal temperature per min (cooling rate), and circulatory arresting time (arresting time), were not significantly different among the three groups (Table 1). The time required to resuscitate the hearts (resuscitation time) and the rise in esophageal temperature per min (warming rate) were not significantly different between groups 1 and 2 (Table 1). In all groups, blood dilution by LMWD infusion resulted in decreases of Ht and TP during the cooling process. Further decrease of these values due to surgical bleeding was resolved by blood transfusion.

Pathologically, pulmonary damage from hemorrhage and/or edema occurred in group 2. In group 3, severe pulmonary and myocardial damage was observed.

Hemodynamics: During the cooling period, heart rhythms remained stable without any serious arrhythmia in all the dogs. Heart rates (HR) and mean arterial blood pressures (mABP) decreased with decreasing esophageal temperature. Decreases of HR and mABP were not significantly different among the three groups. During the rewarming phase, HR and mABP increased with rising esophageal temperature in groups 1 and 2. These increases due to rewarming were symmetrical with the decreases caused by cooling (Fig. 3).

Arterial blood pH and gases: During the cooling phase, the arterial blood pH rose gradually as PaCO₂ decreased due to hyperventilation. Just before arrest and immediately after resuscitating the hearts, measurements of arterial blood pH and PaCO₂ showed no significant differences among the three groups. During the rewarming phase, blood pH and PaCO₂ levels were consistent with the changes of cooling phase in groups 1 and 2.

Hyperoxemia persisted until immediately prior to cardiac arrest in all groups. Circulatory arrest resulted in a remarkable decrease of PaO₂. Immediately after resuscitating the hearts, group 1 still showed hyperoxemia while groups 2 and 3 showed normoxemia and mild hypoxemia, respectively. PaO₂ in group 1 was significantly higher than that in group 3 (Table 2).

DISCUSSION

Open-heart surgical procedures are accomplished under cardioplegia, using cardiopulmonary bypass (CPB), cross-circulation, or hypothermic anesthesia [3, 6, 7, 9, 11, 17]. The present study investigated whether abdominal cavity cooling, which is one of the methods for inducing

Table 1. The time of each stage and change in temperature per minute

<table>
<thead>
<tr>
<th></th>
<th>Cooling Time</th>
<th>Cooling Rate</th>
<th>Arrest Time</th>
<th>Resuscitation Time</th>
<th>Rewarming Time</th>
<th>Rewarming Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time: min.</td>
<td>Rate: °C/min</td>
<td>Time: min.</td>
<td>Time: min.</td>
<td>Time: min.</td>
<td>Time: °C/min.</td>
</tr>
<tr>
<td>1</td>
<td>101.6 ± 11.8</td>
<td>0.11 ± 0.02</td>
<td>20.0 ± 4.5</td>
<td>10.0 ± 5.1</td>
<td>97.5 ± 59.6</td>
<td>0.07 ± 0.05</td>
</tr>
<tr>
<td>2</td>
<td>108.3 ± 7.8</td>
<td>0.11 ± 0.02</td>
<td>24.6 ± 10.9</td>
<td>17.8 ± 19.4</td>
<td>110.0 ± 18.2</td>
<td>0.06 ± 0.02</td>
</tr>
<tr>
<td>3</td>
<td>130.5 ± 17.3</td>
<td>0.08 ± 0.02</td>
<td>24.0 ± 10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Schema of left heart bypass (the aorta from the left atrium).
Fig. 3. Changes of body temperature (B.T.), heart rate (H.R.), arterial blood pressure (ABP), systolic arterial blood pressure (sABP), diastolic arterial blood pressure (dABP), hematocrit (Ht), and total protein (TP) in group 1 (recovery without any complications).

Table 2. Changes of arterial blood pH and gases during circulatory arrest

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>PaCO₂ (mmHg)</th>
<th>PaO₂ (mmHg)</th>
<th>BE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>1</td>
<td>7.57 ± 0.09</td>
<td>7.54 ± 0.18</td>
<td>20.3 ± 5.5</td>
<td>25.4 ± 14.6</td>
</tr>
<tr>
<td>2</td>
<td>7.58 ± 0.08</td>
<td>7.42 ± 0.13</td>
<td>16.6 ± 4.3</td>
<td>22.9 ± 10.3</td>
</tr>
<tr>
<td>3</td>
<td>7.63 ± 0.11</td>
<td>7.45 ± 0.13</td>
<td>18.0 ± 7.5</td>
<td>34.3 ± 27.8</td>
</tr>
</tbody>
</table>

*: p<0.05 comparing before and after. **: p<0.05 comparing group 1 with group 3.

hypothermic anesthesia, can create cardioplegia for application in open-heart surgery without using CPB. The results could be divided into three categories. Eleven dogs recovered without any serious complications after 21 ± 7 min of circulatory arrest without CPB for cardiac surgery (survival rate, 61.1%) (group 1). This group also showed no postoperative neurological abnormalities. Four dogs developed fatal hypoxemia after extubation, although they spontaneously regained breathing and consciousness (group 2). In another three dogs, the hearts could not be resuscitated (group 3). This survival rate was lower than that previously reported using surface-induced hypothermia [13].

Hemodynamic changes induced by circulatory arrest and reperfusion can cause damage to the essential organs. Previous studies have shown that sufficient brain and myocardial protection during circulatory arrest can lead to good prognosis with or without CPB [2, 16, 20, 21, 24]. It was reported that protection of the myocardium and the brain is the most important factor governing the success of cardiac surgery [10, 19, 20]. In the present study, the seven dogs in the non-awakening groups appear to have received inadequate pulmonary and myocardial protection. Pathologically, pulmonary damage from hemorrhage and/or edema was seen in groups 2 and 3. Severe myocardial damage resulted in group 3, which is suggested to have contributed to failure of sinus rhythm. These pathological observations corresponded to the changes in PaO₂. The PaO₂ levels immediately after resuscitation procedures in groups 2 and 3 were lower than in group 1, with a significant difference between groups 1 and 3. These results suggested that maintaining a hyperoxemic state during cardiac resuscitation can be important in achieving success.

In human transplantation, the abdominal cavity cooling method can be applied to patients in order to preserve multiple organs [4, 14, 15, 22]. This method has several advantages, as follows: 1) no warm ischemia in abdominal organs, 2) a very safe and simple induction without causing fatal arrhythmia, 3) a short induction time to the hypothermic stage [22]. These advantages result from the
facts that the peritoneal area is almost equal to the body surface area, and that the peritoneal blood supply is more abundant than the supply to the body surface [15, 22]. In this study, since only the esophageal temperature was evaluated, the core temperature in various essential organs could not be estimated. Cooling progressed successfully without any fatal arrhythmia, consistent with previous reports. Cooling time until arrest of the hearts was 108 ± 15 min in all dogs and there was no significant difference among the three groups. Although the cooling time by this procedure was not shorter than that of the alternative cooling method (i.e., surface-induced cooling) [3, 6–8, 11–13], it appeared that the abdominal cavity cooling method can satisfactorily control the cooling rate.

The blood acid-base balance is not known in detail and the optimum conditions during hypothermia have not yet been defined. In this study, the blood pH indicated respiratory alkalosis (blood pH 7.4–7.7 and PaCO2 10–25 mmHg) during the cooling period. The alkalemia before cardiac arrest may suppress the development of acidemia during circulatory arrest. It was concluded that: 1) open-heart surgery can be accomplished without CPB under hypothermia created by the abdominal cavity cooling method, and 2) protection of the lungs as well as the myocardium can be important to the success of the operation.

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Fig. 4. Changes of arterial blood pH and gases in group 1 (recovery without any complications).
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