Effects of dobutamine and norepinephrine on oxygen availability in tamponade-induced stagnant hypoxia: A prospective, randomized, controlled study

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Objectives: To explore the effects of dobutamine and norepinephrine on the global cardiovascular response and on the relationship between oxygen uptake ($\dot{V}_O_2$) and oxygen delivery ($\dot{D}_O_2$) during an acute reduction in blood flow associated with tamponade.

Design: Prospective, randomized, controlled acute intervention study.

Setting: University intensive care unit (ICU) laboratory.

Subjects: Twenty healthy, anesthetized mongrel dogs, weighing 19 to 28 kg.

Interventions: Six dogs served as control, seven dogs were given 10 $\mu$g/kg/min of dobutamine and another seven dogs were given 1 $\mu$g/kg/min of norepinephrine. Data were collected at graded incremental levels of intrapericardial pressure.

Measurements and Main Results: $\dot{V}_O_2$ was derived from expired gas analysis and $\dot{D}_O_2$ was calculated from the product of thermodilution cardiac index and arterial oxygen content. In each animal, two catheters were inserted into the pericardium to induce tamponade by saline infusion and to measure the intrapericardial pressure. The critical $\dot{D}_O_2$ value, below which $\dot{V}_O_2$ decreased, was found at 9.4 ± 1.3 mL/kg/min in the control animals. When $\dot{D}_O_2$ decreased to below this critical value, lactic acidosis developed. Dobutamine and norepinephrine, at the dose that was administered, significantly increased cardiac index and $\dot{D}_O_2$. Critical $\dot{D}_O_2$ was slightly higher in the treated than in the control animals (12.1 ± 1.6 mL/kg/min in dobutamine and 13.2 ± 0.5 mL/kg/min in norepinephrine, NS). $\dot{V}_O_2$ at critical $\dot{D}_O_2$ was significantly higher in the treated groups than in the control group (7.7 ± 1.1 mL/kg/min in the dobutamine group and 7.9 ± 0.9 mL/kg/min in the norepinephrine group vs. 5.4 ± 0.4 mL/kg/min in control, both $p < .01$). There was no significant difference in the critical oxygen extraction ratio and the slope of the supply-dependent line between the three groups.

In dobutamine-treated animals, cardiac index, $\dot{D}_O_2$, and $\dot{V}_O_2$ were better maintained for any intrapericardial pressure than in the other groups. Critical intrapericardial pressure, at which $\dot{V}_O_2$ started to decrease, was significantly higher in the dobutamine-treated group than in the control group (13.8 ± 2.3 vs. 9.3 ± 1.2 mm Hg, $p < .05$). At critical $\dot{D}_O_2$, the mean blood lactate concentration was also lower in the dobutamine-treated animals than in the other animals (2.1 ± 0.3 vs. 4.1 ± 0.7 mmol/L in control and 3.8 ± 0.4 mmol/L in the norepinephrine group, both $p < .05$).

Conclusions: During low-flow states associated with tamponade, both dobutamine and norepinephrine at the dose used increased cardiac index, $\dot{D}_O_2$, and $\dot{V}_O_2$, but dobutamine delayed the onset of tissue hypoxia by further increasing blood flow and oxygen availability. In the conditions of the present study, neither agent significantly influenced the oxygen extraction capabilities of the body. (Crit Care Med 1994; 22:299-305)

Key Words: dobutamine; norepinephrine; cardiac tamponade; hemodynamics; oxygen delivery; hypoxia; tissue oxygenation; lactate; low flow

Cardiac tamponade is a life-threatening condition that can acutely reduce blood flow and compromise tissue perfusion. Although the definitive treatment of tamponade is the removal of the excessive pericardial fluid, it is essential to transiently support the cardiovascular system before the pericardial tap can be performed. Various catecholamines have been tried for this purpose. Strong $\alpha$-adrenergic receptor stimulation with an agent like norepinephrine may restore arterial
pressure by increasing peripheral tone, but may also reduce cardiac output and oxygen delivery (DO₂) (1). On the other hand, β-adrenergic receptor stimulation with isoproterenol may better maintain cardiac output but may also decrease tissue perfusion pressure (2). Comparing the effects of isoproterenol, dopamine, and norepinephrine in patients with tamponade, Martins and colleagues (3) observed that cardiac output increased with isoproterenol and dopamine and not with norepinephrine, but only norepinephrine increased arterial pressure. It thus appears that an ideal pharmacologic agent for the treatment of tamponade should sustain myocardial contraction while maintaining tissue perfusion pressure. Such a pharmacologic profile may be met by dobutamine, a synthetic catecholamine with predominant β-adrenergic but also with moderate α-adrenergic receptor-mediated actions (4, 5), which has almost entirely replaced isoproterenol as an inotropic agent in critically ill patients (5, 6). However, the effects of dobutamine in tamponade have not been well investigated.

The effects of adrenergic agents on peripheral oxygen extraction capabilities have not been well defined. In the isolated dog hindlimb muscle, norepinephrine increased oxygen uptake (VO₂) but not oxygen extraction when blood flow was either preserved or acutely reduced (7, 8). The effects of dobutamine on oxygen extraction capabilities have not been well studied. Dopamine, a β₂-adrenergic receptor agonist, increases cardiac output and DO₂, but does not improve oxygen extraction (9).

We hypothesized that dobutamine and norepinephrine could exert beneficial effects on the maintenance of oxygen availability during tamponade, but by different mechanisms. With its strong vasoconstrictive effects, norepinephrine may help to maintain tissue perfusion pressure and, thereby, perhaps the oxygen extraction capabilities. On the other hand, dobutamine may better maintain blood flow to the tissues but might reduce the oxygen extraction by altering the distribution of blood flow. Therefore, the present study explored the effects of dobutamine and norepinephrine on the global cardiovascular response, as well as on the oxygen extraction capabilities during an acute reduction in blood flow associated with tamponade.

MATERIALS AND METHODS

Surgical Preparation. The experimental protocol was approved by the Institutional Review Board of animal research; care and handling of the animals were in accord with National Institutes of Health guidelines. Twenty mongrel dogs ranging in weight from 19 to 28 kg were anesthetized with sodium pentobarbital, administered as an initial slow bolus of 30 mg/kg iv followed by a constant infusion of 4 mg/kg/hr, using an infusion pump (Infusomat II, B. Braun, Melsungen, FRG). After endotracheal intubation, the dogs were ventilated with room air using a ventilator (Servo 900B, Siemens-Elema, Solna, Sweden). Controlled ventilation was facilitated with pancuronium bromide at 0.15 mg/kg initially, followed by an infusion at 0.075 mg/kg/hr. Respiratory rate was set at 12 breaths/min and tidal volume was adapted to keep end-tidal CO₂ tension between 28 and 38 torr (3.7 and 5.1 kPa). Exhaled gases were directed through a mixing chamber for sampling of expired oxygen fractions (FeO₂). The gas analyzers for expired oxygen (P.K. Morgan, Chatham, UK) and CO₂ (47210A Capnometer, Hewlett Packard, Waltham, MA) were calibrated before the experiment. Expired minute volume was measured with a spirometer (Haloscale Wright Respironometer, Edronton, London, UK) over a 2-min period. Electrocardiogram (EKG) was continuously monitored throughout the study.

Polyethylene cannulas were inserted into: a) the left femoral artery for monitoring of arterial blood pressure and withdrawal of arterial blood samples; b) the right femoral vein for intravenous saline infusion; c) the left forepaw vein for continuous administration of pentobarbital; and d) the right forepaw vein for the administration of dobutamine or norepinephrine. A balloon-tip pulmonary artery catheter (93A-131-7F, Baxter Edwards Critical-Care, Irvine, CA) was inserted through the right external jugular vein under guidance of pressure waves, as determined from a four-channel monitor (Sirecust 302A, Siemens, Erlangen, FRG). A left thoracotomy between the fourth and fifth intercostal space was performed with bleeding controlled by electrocautery. Via two separate 2- to 3-mm incisions in the anterior pericardium, two 16-gauge polyethylene catheters (Intracath, Deseret Medical, Sandy, UT) with multiple side holes were positioned in the pericardial space with their tips adjacent to the diaphragmatic surface of the left ventricle. The catheters were secured with purse-string sutures and medical glue. The thoracic cavity was then carefully closed in three layers. A chest tube (Trocar catheter A75, 28Ch-40cm, Argyle, Tullamore, Ireland) was inserted through the seventh intercostal space to allow gentle chest suction. One pericardial catheter was used to infuse saline into the pericardial cavity, and the other catheter was used to measure intrapericardial pressure. All pressure transducers were connected to an amplifier (2600S recorder, Gould, Cleveland, OH), zeroed against atmospheric pressure at the midchest level, and calibrated before each pressure measurement. The temperature of the animals was maintained.
constant using a warming blanket or iced pads throughout the study.

**Experimental Protocol.** After the surgical preparation, the dog was placed in the supine position and permitted to stabilize for 30 mins. The pericardial cavity was emptied using a 5-mL syringe to ensure a slightly negative intrapericardial pressure before the measurements started. The dogs were randomly divided into three groups: control (n = 6), dobutamine (n = 7), and norepinephrine (n = 7).

The adrenergic solutions were prepared in concentrations of 1 mg/mL of dobutamine and 0.16 mg/mL of norepinephrine in a 50-mL syringe (Perfusor Akuport, ED-EDL, Melsungen, FRG). The doses administered were 10 µg/kg/min for dobutamine and 1 µg/kg/min for norepinephrine. The infusion of adrenergic agents was started after the baseline measurements and continued throughout the study. Thirty minutes after the initial therapy, measurements were repeated in the adrenergic agent groups. A continuous intrapericardial infusion of normal saline that was heated to 37°C was started (infusion pump Infusomat II, B. Braun) at 40 mL/hr for the first hour and 30 mL/hr thereafter. When the mean arterial pressure had declined to 30% of the baseline level, the dog was considered to be in a decompensatory state and the data collection was ended.

Measurements of heart rate, arterial pressure, pulmonary arterial pressure, right atrial pressure, pulmonary artery occlusion pressure, intrapericardial pressure, cardiac index, \( \text{FEO}_{2} \), end-tidal \( \text{CO}_2 \) tension, respiratory rate, expired minute volume, and core temperature were repeated every 15 mins during the study. Pressures were determined from a strip-chart recorder (2600S recorder, Gould) at end-expiration. Cardiac output was measured by the thermodilution technique (computer COM-2, Baxter Edwards Critical-Care) using three to five injections of 5-mL cold 5% dextrose in ice water. Each injection was started at end-inspiration. After each cardiac output determination, arterial and mixed venous blood samples were simultaneously withdrawn for immediate measurements of arterial and mixed venous blood gases (ABL2 Radiometer, Copenhagen, Denmark). Total hemoglobin concentration, arterial and mixed venous oxygen saturation were measured by a cooximeter calibrated for dog blood (282, Instrumentation Laboratories, Lexington, MA). Arterial blood lactate concentration was determined by an automated analyzer (lactate analyzer 640, Kontron Instruments, Basel, Switzerland). \( \text{DO}_2 \) was calculated as the product of cardiac index and arterial oxygen content. Oxygen consumption \( (\text{VO}_2) \) was determined by the following formula: \( \text{VO}_2 \) (mL/kg/min) = \( \frac{[\text{O}_2 \text{ consumption} - \text{HR} \times \text{O}_{2} \text{ delivery}]}{\text{HR} \times \text{weight} (\text{kg})} \), where \( \text{O}_2 \text{ consumption} \) and \( \text{O}_{2} \text{ delivery} \) represent expired \( \text{CO}_2 \) fraction and inspired oxygen fraction, respectively. The oxygen extraction ratio was calculated as the ratio of \( \text{VO}_2/\text{DO}_2 \).

**Statistical Methods.** A dual-line regression method (10) was used to determine the critical \( \text{DO}_2 \) in each individual animal from a plot of \( \text{VO}_2 \) vs. \( \text{DO}_2 \). Linear regression by best fit was used to calculate straight lines for the supply-dependent and supply-independent \( \text{VO}_2/\text{DO}_2 \) relationship. The point of intersection of the two regression lines defined the critical \( \text{DO}_2 \) and the corresponding critical \( \text{VO}_2 \). The critical oxygen extraction ratio was calculated as the ratio of \( \text{VO}_2 \) over \( \text{DO}_2 \) at critical \( \text{DO}_2 \). Critical intrapericardial pressure and blood lactate represent intrapericardial pressure and blood lactate values at critical \( \text{DO}_2 \) respectively. An analysis of variance (ANOVA) for repeated measurements followed by Dunnett multivariate analysis test were used for statistical evaluation. A \( p < 0.05 \) was considered statistically significant. All values are expressed as mean ± sd.

**RESULTS**

**Control Conditions.** The progressive increase in intrapericardial pressure resulted in gradual reductions in arterial pressure and cardiac index. Heart rate did not change significantly until intrapericardial pressure reached 10 mm Hg (Table 1 and Fig. 1). During the initial stages of tamponade, the decreases in cardiac index and \( \text{DO}_2 \) were compensated by an increase in oxygen extraction ratio so that \( \text{VO}_2 \) remained constant. When intrapericardial pressure reached higher levels, \( \text{VO}_2 \) decreased and blood lactate concentrations increased simultaneously (Fig. 2). No dog survived when intrapericardial pressure exceeded 13 mm Hg (Fig. 3). The critical \( \text{DO}_2 \) was found at 9.4 ± 1.3 mL/kg/min. The corresponding critical intrapericardial pressure was 9.3 ± 1.2 mm Hg (Table 2).

**Effects of Adrenergic Agents.** Before cardiac tamponade, norepinephrine and especially dobutamine at the dose used increased heart rate, stroke volume, cardiac index, and \( \text{DO}_2 \) without significant influence on pressures. Dobutamine infusion was also associated with an increase in \( \text{VO}_2 \) despite a reduction in oxygen extraction ratio (Figs. 1 and 2). There were no significant changes in \( \text{Pao}_2 \) (data not shown) or in blood lactate (Fig. 2).

During cardiac tamponade, cardiac index, \( \text{DO}_2 \), and \( \text{VO}_2 \) were higher, and oxygen extraction ratio was lower at any intrapericardial pressure in the two treated groups, especially in the dobutamine group. However, mean arterial pressure had a similar course in the treated and the control groups (Fig. 1). The systemic
Table 1. Effects of dobutamine and norepinephrine on heart rate, stroke volume, pulmonary arterial, and cardiac filling pressures (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
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</thead>
<tbody>
<tr>
<td>Heart Rate (beats/min)</td>
<td></td>
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</tr>
<tr>
<td>Ctrl (n = 6)</td>
<td>149 ± 25</td>
<td>147 ± 23</td>
<td>146 ± 23</td>
<td>152 ± 23</td>
<td>141 ± 25</td>
<td>131 ± 24</td>
<td>89 ± 25* (n = 5)*</td>
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<tr>
<td>DOB (n = 7)</td>
<td>152 ± 26</td>
<td>192 ± 30*</td>
<td>181 ± 20*</td>
<td>182 ± 19*</td>
<td>183 ± 20*</td>
<td>176 ± 28*</td>
<td>153 ± 58*</td>
</tr>
<tr>
<td>NOR (n = 7)</td>
<td>159 ± 33</td>
<td>174 ± 29</td>
<td>172 ± 29</td>
<td>170 ± 25</td>
<td>164 ± 29</td>
<td>174 ± 35</td>
<td>143 ± 76</td>
</tr>
<tr>
<td>Stroke Volume (mL/beat)</td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>26.0 ± 9.6</td>
<td>25.7 ± 8.2</td>
<td>23.7 ± 10.9</td>
<td>18.0 ± 8.4</td>
<td>15.0 ± 6.9</td>
<td>13.7 ± 7.6</td>
<td>10.5 ± 4.6* (n = 5)</td>
</tr>
<tr>
<td>DOB (n = 7)</td>
<td>24.8 ± 9.9</td>
<td>34.6 ± 17.4*</td>
<td>30.3 ± 9.3*</td>
<td>28.6 ± 9.8</td>
<td>26.8 ± 13.3</td>
<td>27.5 ± 14.3*</td>
<td>15.8 ± 9.8*</td>
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<tr>
<td>NOR (n = 7)</td>
<td>22.2 ± 7.3</td>
<td>24.9 ± 6.6</td>
<td>26.6 ± 4.5</td>
<td>23.3 ± 7.0</td>
<td>17.9 ± 4.8</td>
<td>11.6 ± 5.2</td>
<td>8.3 ± 2.5* (n = 6)</td>
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<td>MPAP (mm Hg)</td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>15.1 ± 4.3</td>
<td>14.3 ± 5.8</td>
<td>15.1 ± 4.7</td>
<td>19.9 ± 5.8</td>
<td>22.8 ± 9.0</td>
<td>17.8 ± 6.7</td>
<td>16.4 ± 4.0 (n = 5)</td>
</tr>
<tr>
<td>DOB (n = 7)</td>
<td>16.1 ± 3.6</td>
<td>14.1 ± 6.7</td>
<td>14.7 ± 6.8</td>
<td>16.1 ± 6.2</td>
<td>16.0 ± 5.4</td>
<td>14.4 ± 4.1</td>
<td>11.5 ± 3.6*</td>
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<tr>
<td>NOR (n = 7)</td>
<td>12.5 ± 3.1</td>
<td>13.9 ± 3.7</td>
<td>15.2 ± 3.6</td>
<td>15.9 ± 3.1</td>
<td>16.8 ± 3.4</td>
<td>14.7 ± 2.6</td>
<td>13.7 ± 4.4 (n = 6)</td>
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<tr>
<td>PAOP (mm Hg)</td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>2.8 ± 1.7</td>
<td>2.7 ± 1.5</td>
<td>4.6 ± 1.9*</td>
<td>5.6 ± 1.2</td>
<td>6.9 ± 1.5*</td>
<td>8.1 ± 1.4*</td>
<td>10.0 ± 1.0* (n = 6)</td>
</tr>
<tr>
<td>DOB (n = 7)</td>
<td>2.5 ± 1.8</td>
<td>2.0 ± 1.4</td>
<td>3.3 ± 0.5*</td>
<td>4.5 ± 1.2</td>
<td>6.3 ± 1.3</td>
<td>7.3 ± 0.8</td>
<td>8.3 ± 1.3*</td>
</tr>
<tr>
<td>NOR (n = 7)</td>
<td>2.9 ± 1.7</td>
<td>2.9 ± 1.2</td>
<td>3.7 ± 1.5</td>
<td>5.2 ± 1.9*</td>
<td>6.1 ± 1.2*</td>
<td>7.6 ± 1.1*</td>
<td>9.0 ± 1.0* (n = 6)</td>
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<td>RAP (mm Hg)</td>
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</tr>
<tr>
<td>Ctrl (n = 6)</td>
<td>1.7 ± 1.3</td>
<td>1.8 ± 1.8</td>
<td>3.3 ± 2.2</td>
<td>5.4 ± 2.1*</td>
<td>8.6 ± 3.7</td>
<td>9.6 ± 2.3*</td>
<td>12.1 ± 2.9* (n = 5)</td>
</tr>
<tr>
<td>DOB (n = 7)</td>
<td>2.1 ± 1.8</td>
<td>2.0 ± 1.3</td>
<td>2.7 ± 1.0</td>
<td>4.6 ± 1.1*</td>
<td>5.6 ± 0.9</td>
<td>7.6 ± 0.5*</td>
<td>10.1 ± 1.1*</td>
</tr>
<tr>
<td>NOR (n = 7)</td>
<td>1.7 ± 1.0</td>
<td>1.3 ± 1.1</td>
<td>2.5 ± 0.9</td>
<td>4.5 ± 1.2</td>
<td>6.7 ± 2.0</td>
<td>5.5 ± 1.9*</td>
<td>9.9 ± 0.9* (n = 6)</td>
</tr>
</tbody>
</table>

Ctrl, control; DOB, dobutamine; NOR, norepinephrine; MPAP, mean pulmonary arterial pressure; PAOP, pulmonary artery occlusion pressure; RAP, right atrial pressure.
*p < .05 vs. baseline; **p < .05 vs. Ctrl; *the number of surviving animals at 10 mm Hg intrapacardial pressure is indicated between parentheses.

The pressure-flow relationship showed that for any mean arterial pressure, cardiac index was higher in the dobutamine-treated group than in the other groups (Fig. 4).

In the dobutamine group, blood lactate measurements remained lower than in the control group and significantly increased only when intrapacardial pressure reached higher concentrations (Fig. 2). The dobutamine-treated animals tolerated higher intrapacardial pressure values. Survival was greater in the dobutamine-treated than in the control group when intrapacardial pressure reached 13 mm Hg (p < .05, Fig. 3). The critical intrapacardial pressure was also significantly higher in the dobutamine-treated than in the control group (Table 2).

Although both critical Do2 and critical Vo2 values were higher in the groups that were treated with adrenergic agents than in the control dogs, only the difference in critical Vo2 reached statistical significance. There was no significant difference in critical oxygen extraction ratio between any paired groups (Table 2). The slope of the Vo2/Do2 dependency lines was also similar in the three groups (Fig. 5). In the dobutamine-treated group, blood lactate concentrations at critical Do2 were significantly lower than in the other two groups (Table 2). There was a strong correlation between oxygen extraction values derived from Vo2/Do2 and those values calculated from the Fick equation (r2 = .86, p < .01).

**DISCUSSION**

In physiologic conditions, as systemic Do2 diminishes, Vo2 is maintained relatively constant over a wide range of Do2 by an increase in tissue oxygen extraction. When Do2 decreases below a critical value, oxygen extraction cannot sufficiently compensate for the decrease in Do2, so that Vo2 becomes Do2-dependent. This so-called supply dependency is associated with the development of tissue anaerobic metabolism reflected by lactic acidosis (11, 12).

The present study focused on the effects of adrenergic agents on the Vo2/Do2 relationship and peripheral oxygen extraction during an acute reduction in blood flow induced by tamponade. Principal findings of the present study are that dobutamine and norepinephrine increased Do2 and Vo2, but neither agent at the doses used influenced the oxygen extraction capabilities of the body. As in previous studies assessing the hemodynamic effects of adrenergic agents on experimental cardiac tamponade (2, 3), the animals were anesthetized with pentobarbital, mechanically ventilated, and paralyzed, with constant body temperature to keep...
oxygen demand stable. Our protocol allowed us to administer only one dose of each adrenergic agent so that a dose-response relation for each agent was not obtained. We chose 1 μg/kg/min of norepinephrine and 10 μg/kg/min of dobutamine because these are moderate doses of each catecholamine. In normal control dogs, Melchior et al. (13) reported that cardiac output and stroke volume increased significantly at a dose of 0.5 μg/kg/min and not more than 1.5 μg/kg/min of norepinephrine. Dobutamine at 10 μg/kg/min has been reported to significantly increase cardiac output and Do₂ in animals and in human patients (5).

A progressive increase in intrapericardial pressure resulted in gradual reductions in cardiac index and arterial pressure. At the doses used, both dobutamine and norepinephrine significantly increased cardiac index and Do₂ throughout the study, but dobutamine maintained a higher cardiac index than the other groups for any given measurement of intrapericardial pressure. This higher blood flow was related to increases in both stroke volume and heart rate. Neither dobutamine nor norepinephrine significantly altered arterial pressure, even though norepinephrine had stronger vasoconstrictor effects than dobutamine. In contrast, dobutamine-treated animals maintained a higher cardiac index for any arterial pressure than in the other groups.

For any given intrapericardial pressure, higher Vo₂ was maintained in the treated groups, and particularly
Table 2. Selected values at critical oxygen delivery (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Critical $\dot{D}O_2$ (mL/kg/min)</th>
<th>$\dot{V}O_2$ (mL/kg/min)</th>
<th>Oxygen Extraction Ratio (%)</th>
<th>Intrapericardial Pressure (mm Hg)</th>
<th>Arterial Blood Lactate (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9.4 ± 1.3</td>
<td>5.4 ± 0.4</td>
<td>60 ± 17</td>
<td>9.3 ± 1.2</td>
<td>4.1 ± 0.7</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>12.1 ± 1.6</td>
<td>7.7 ± 1.1*</td>
<td>67 ± 15</td>
<td>13.8 ± 2.3*b</td>
<td>2.1 ± 0.3*c</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>13.2 ± 0.9</td>
<td>7.9 ± 0.9*</td>
<td>64 ± 13</td>
<td>19.4 ± 1.9</td>
<td>3.8 ± 0.4</td>
</tr>
</tbody>
</table>

$\dot{D}O_2$, oxygen delivery; $\dot{V}O_2$, oxygen consumption.

*p < .01 vs. control; **p < .05; **p < .05 vs. norepinephrine.

Figure 3. Survival rates according to the increment of intrapericardial pressure in the adrenergic-treated and in the control groups.

The dobutamine-treated group, than in the control group. This observation was not unexpected. By activation of adenylyl cyclase, the adrenergic agents induce an increase in cyclic adenosine monophosphate (cAMP), which can stimulate various cell reactions and thereby increase the cellular oxygen requirements (14). An increase in $\dot{V}O_2$ has been sometimes reported in response to the administration of dobutamine (5, 6) and norepinephrine (7, 8, 13–15). Some increase in $\dot{V}O_2$ during adrenergic therapy could be also related to an increase in global oxygen demand associated with the increase in blood flow to some organs, including the heart (7, 8, 14, 16).

Oxygen extraction capabilities are closely related to the vascular tone and the effective capillary density, i.e., the surface area available for exchange and capillary-to-cell diffusion distances (17). By increasing vascular tone, norepinephrine may limit the maldistribution of blood flow through non-nutritive channels, but may also decrease capillary density and thus increase the distance for oxygen diffusion from the capillaries to the cells. On the other hand, the predominant $\beta$-adrenergic receptor mediated actions of dobutamine may increase capillary density but may also alter the peripheral distribution of blood flow. In hypoxic dogs, King and Cain (18) observed that the $\beta_1$- and $\beta_2$-adrenergic receptor stimulation with isoproterenol increased blood flow in muscle but did not improve oxygen extraction, probably because the increased blood flow was directed throughfare, non-nutritive channels. In the present study, a higher critical $\dot{V}O_2$ was associated with a slightly higher critical $\dot{D}O_2$ both in the dobutamine- and norepinephrine-treated dogs so that no difference in critical oxygen extraction ratio was found between any paired group. The slope of the supply-dependent regression line and the intercept were identical in the adrenergic-treated and in the control group. Thus, neither dobutamine nor
norepinephrine at the dose used significantly increased body oxygen extraction capabilities in the present study.

The present observations appeared consistent with some prior studies by Chapler et al. (7) and Cain and Chapler (8), indicating that the administration of norepinephrine could increase $\Delta V_{\text{oxygen}}$, but not oxygen extraction in dog hindlimb when blood flow was either acutely reduced (7) or kept constant (8). Another recent study showed no significant effect of dobutamine on the oxygen extraction capabilities during hemorrhage in dogs (19). Our present study investigated only the global effects of dobutamine and norepinephrine, but some differences may exist in oxygen extraction capabilities among the organs (9).

However, globally, dobutamine-treated dogs better tolerated the increase in intrapericardial pressure. A higher $\Delta V_{\text{oxygen}}$ was maintained throughout the experiment and their critical $\Delta V_{\text{oxygen}}$ appeared at a greater intrapericardial pressure than in the other groups. Dobutamine infusion was associated with lower blood lactate at and below critical $\Delta V_{\text{oxygen}}$. Survival was also prolonged in dobutamine-treated animals. This study suggests that dobutamine may be superior to norepinephrine in maintaining oxygen availability to the tissues when blood flow is acutely reduced by pericardial tamponade. These observations may have clinical implications in the cardiovascular support of the patient with tamponade before drainage of the obstructing fluid can be obtained.

REFERENCES

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