Whole Body Oxygen Consumption after Hypothermic Cardiopulmonary Bypass

Kazuo MARUYAMA, Hiroshi HASHIMOTO, Kazutoshi NAKAMURA, Yasushi NAKAI, Hirofumi UTSUNOMIYA, Junko MARUYAMA, Kunihiko KONISHI and Mannosuke MUNEYUKI

Whole body oxygen consumption and the substrate for energy production during the post-bypass period have not been clarified. We hypothesized that the substrate composition for energy production during post-bypass period might be different from that during pre-bypass period because of surgical diabetic state induced by hypothermic cardiopulmonary bypass (CPB). We measured whole body oxygen consumption, carbon dioxide production and respiratory quotient by the gas exchange method using the Datex Deltatrac before and after hypothermic cardiopulmonary bypass. We also measured oxygen consumption by Fick's principle. Whole body oxygen consumption ($P < 0.001$) and carbon dioxide production ($P < 0.05$) increased significantly above pre-CPB values after the termination of CPB. Respiratory quotient ($P < 0.01$) decreased significantly below pre-CPB values after the termination of CPB. We conclude that oxygen consumption increased significantly above pre-bypass values after the termination of hypothermic cardiopulmonary bypass at least under the fentanyl, diazepam, chlorpromazine anesthesia with continuous infusion of nitroglycerin and nicardipine. The changes in respiratory quotient suggest a relatively higher ratio of lipid metabolism for energy production during post-bypass period. (Key words: oxygen consumption, cardiopulmonary bypass, gas change method)

(Maruyama K, Hashimoto H, Nakamura K, et al.: Whole body oxygen consumption after hypothermic cardiopulmonary bypass. J Anesth 7:1–7, 1993)

Whole body oxygen consumption ($\dot{V}O_2$) decreases during hypothermic (25°C) cardiopulmonary bypass (CPB) by nearly 50%[1]. Reduction in $\dot{V}O_2$ during hypothermic CPB was reversed during normothermic CPB after rewarming, and $\dot{V}O_2$ in the post-bypass period was not different from the pre-bypass values in which anesthesia included 100 $\mu g \cdot kg^{-1}$ fentanyl and diazepam[2]. Another study suggested that metabolic demands increased during post-bypass period and ventilation should be adjusted[3]. The difference of the results might be due to anesthesia protocol, the use of vasodilators and cathecolamines during bypass and post-bypass periods and the presence or abscence of temperature drop after CPB. Hyperglycemia due to dimin-

Departments of Anesthesiology and the Intensive Care Unit, Mie University Hospital, Tsu, Japan

Address reprint requests to Dr. Maruyama: Department of Anesthesiology, Mie University Hospital, 2-174, Edobashi, Tsu, Mie, 514 Japan

ished utilization and increased mobilization of glucose during CPB has been observed[4] and lipid metabolism is dominant during CPB[5], suggesting the use of free fatty acid as a substrate for energy production during the bypass period. We hypothesized that the substrate composition for energy production during post-bypass period might be different from that during pre-bypass period because of surgical diabetic state induced by CPB. The respiratory quotient, ratio of carbon dioxide output to oxygen usage, is useful to estimate ratio of carbohydrate and fat metabolism[6]. In this study oxygen consumption and carbon dioxide production were measured by the gas exchange method using the Datex Deltatrac[7,8], which allows for continuous measurements and gives a calculation of average oxygen consumption, carbon dioxide production ($\dot{V}CO_2$) and the respiratory quotient during the specified period. We also measured $\dot{V}O_2$ by the Fick's principle.

Patients and Methods

Nine adult patients undergoing cardiac surgery were studied (five men and four women, aged 26–73 yr [mean ± SD, 57.7 ± 13.6]). Six were undergoing coronary artery bypass grafting, two were undergoing mitral valve replacement and one undergoing aortic valve replacement. The average body weight and height were 59.1 ± 8.7 kg and 162.6 ± 7.2 cm respectively. None of them had diabetes mellitus preoperatively. All patients were chronic user of nitrates and calcium channel blockers.

Patients were premedicated with morphine hydrochloride (7–10 mg intramuscularly) and scopolamine sulfate (0.3–0.5 mg subcutaneously) 45 min before surgery. Anesthesia was induced with 60–75 $\mu g \cdot kg^{-1}$ fentanyl, followed by 12–16 mg vecuronium or 4–8 mg pancuronium with 100% oxygen, with 2–10 mg diazepam on occasion. The trachea was intubated orally after intratracheal injection of 150 mg lidocaine for topical anesthesia. The radial artery was catheterized percutaneously with a 5.0 cm, 19-gauge Teflon catheter. A Swan-Ganz catheter was inserted via the right internal jugular vein into the pulmonary artery and cardiac output was measured by thermodilution method. Arterial blood and mixed venous blood gas analysis was performed by IL1400 (Instrumentation Laboratories, MA) and the hemoglobin concentration and oxygen saturation of hemoglobin were measured by a cooximeter, IL482 (Instrumentation Laboratories, MA). The arteriovenous oxygen content difference [$C(a\text{-}v)O_2$] was obtained and $\dot{V}O_2$ was calculated by Fick's principle ($\dot{V}O_2$ = cardiac output × [$C(a\text{-}v)O_2$]).

The patients were mechanically ventilated by Servo ventilator 900B or 900C (Siemens-Elema, Sweden) with a tidal volume of 6.5–11.5 $ml \cdot kg^{-1}$ at a ventilator rate of 10–15 $breath \cdot min^{-1}$. Deltatrac (Datex/Instrumentarium, Finland) was connected to the outlet port of a Servo ventilator to measure $\dot{V}O_2$, $\dot{V}CO_2$ and respiratory quotient. The Deltatrac, a new gas exchange monitor, generates a constant flow containing the expired gas and measures the gas concentration both upstream and downstream of the constant flow, allowing the calculation of $\dot{V}O_2$ and $\dot{V}CO_2$ by gas dilution principle[7,8]. The accuracy of the $\dot{V}O_2$ and $\dot{V}CO_2$ measured by the Deltatrac has been shown[7,8] *in vivo* and *in vitro* situations, in which the Deltatrac's measurements of $\dot{V}O_2$ and $\dot{V}CO_2$ were within ± 7% of values predicted from CO_2 and N_2 simulations. Although values obtained by Fick's principle were snapshot values of oxygen consumption, there was significant positive correlation between $\dot{V}O_2$ values obtained by the Deltatrac and Fick's princi-

ple (r=0.66, $P < 0.01$). The oxygen and carbon dioxide gas sensors of the Deltatrac were calibrated with 5.12% CO_2 and 100% O_2 respectively before measurement. $\dot{V}O_2$ and $\dot{V}CO_2$ measurements by the Deltatrac were performed for twenty minutes and average values per one minute were obtained at two time points: after induction of anesthesia but before CPB, and 60 minutes after the completion of CPB. At the same time $\dot{V}O_2$ measurements using the Fick's principle were also made with both before and after CPB.

Anesthesia was maintained with 10–20 $\mu g \cdot kg^{-1}$ fentanyl or 10 mg intravenous diazepam and 50% oxygen in the mixture of air and oxygen until the start of CPB. Total dosage of fentanyl before start of CPB was 97 ± 10 $\mu g \cdot kg^{-1}$. Supplemental dose of pancuronium (4 mg) were administered before measurements of $\dot{V}O_2$. Within 5–10 min after the initiation of CPB, 1 mg of fentanyl, 0.38–1.70 $mg \cdot kg^{-1}$ chlorpromazine and 30 $mg \cdot kg^{-1}$ methylprednisolone were administered to all patients. CPB was maintained at a flow rate of 2.2 $litre \cdot min^{-1} \cdot m^{-2}$ of body surface area with perfusion pressure between 30–70 mmHg (48 ± 12 mmHg) by roller pumps and membrane oxygenator with a heat exchanger. The pump-oxygenator system was primed with 250–300 ml of 10 per cent low-molecular-weight dextran in half saline, 250–300 ml of 20 per cent mannitol in water, 1000 ml of lactated Ringer's solution, and 60 ml of 7 per cent sodium bicarbonate. The duration of CPB was 133 ± 21 min and aorta cross clamp time was 77 ± 28 min. The combined continuous infusion of nitroglycerin (Nippon Kayaku, Japan), at a dose of 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and nicardipine (Yamanouchi, Japan), at a dose of 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$, was started immediately before induction of anesthesia and was continued throughout surgery. Seven patients required inotropic support (5–15 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine) after CPB.

The nasopharyngeal temperature was 36.2 ± 0.2°C and rectal temperature was 36.3 ± 0.2°C during measurements of $\dot{V}O_2$ before CPB. The body was cooled to 25.3 ± 1.0°C at nasopharyngeal temperature and 26.6 ± 0.6°C at rectal temperature. After CPB nasopharyngeal temperature was 36.1 ± 0.3°C and rectal temperature was 36.5 ± 0.2°C during measurements of $\dot{V}O_2$ with no significant difference compared to the pre-CPB values.

Statistical Analysis

Values were described by mean ± standard deviation (SD). Student's t-test (paired) was used for analysis of changes between pre-and post-bypass period. Liner regression analysis was employed to make the correlation between values obtained by the Deltatrac and Fick's principle. A P value of < 0.05 was considered to indicate a statistically significant difference.

Results

There was no significant difference between pre-CPB and post-CPB values in nasopharyngeal and rectal temperature as described in methods. $\dot{V}O_2$, measured by the Deltatrac, increased significantly to 138.3 ± 18.4 $ml \cdot min^{-1} \cdot m^{-2}$ above its pre-CPB values of 103.0 ± 20.0 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.001$) (fig. 1). $\dot{V}O_2$, measured by the Fick's principle at the same time, also increased significantly to 140.0 ± 19.9 $ml \cdot min^{-1} \cdot m^{-2}$ above its pre-CPB values of 99.3 ± 14.0 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.01$) (fig. 1). There was significant positive correlation between the values obtained by the Deltatrac and Fick's principle (r=0.66, $P < 0.01$) (fig. 2). $\dot{V}CO_2$ increased significantly to 96.2 ± 8.6 $ml \cdot min^{-1} \cdot m^{-2}$ above pre-CPB values of 85.4 ± 7.8 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.05$)

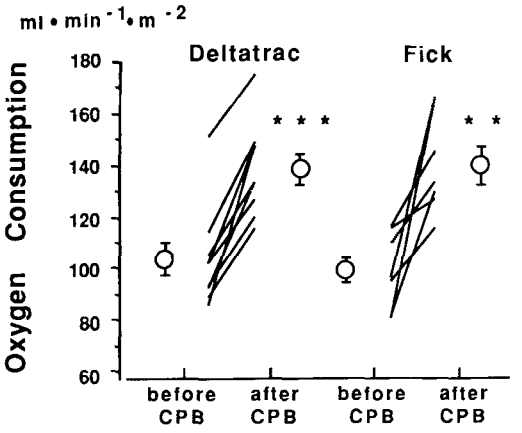

Fig. 1. Whole body oxygen consumption before and after hypothermic cardiopulmonary bypass.

Whole body oxygen consumption ($\dot{V}O_2$) measured by the Deltatrac (n=9) increased significantly to 138.3 ± 18.4 $ml \cdot min^{-1} \cdot m^{-2}$ above its pre-CPB values of 103.0 ± 20.0 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.001$). $\dot{V}O_2$ measured by the Fick's principle (n=7) at the same time also increased significantly to 104.0 ± 19.9 $ml \cdot min^{-1} \cdot m^{-2}$ above its pre-CPB values of 99.3 ± 14.0 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.01$).

Abbreviations: CPB, cardiopulmonary bypass. Values are mean ± SD. $^{**}P < 0.01$, significantly different from values before CPB. $^{***}P < 0.001$, significantly different from values before CPB.

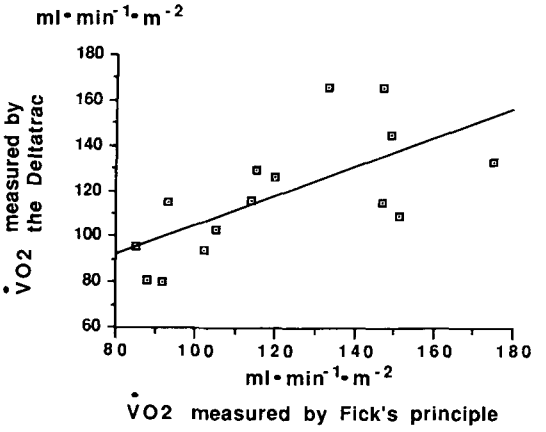

Fig. 2. Correlation between the values of whole body oxygen consumption obtained by the Deltatrac and Fick's principle.

There was significant positive correlation between the values obtained by the Deltatrac and Fick's principle (n=15, r=0.67, slope=0.64, $P < 0.01$).

(fig. 3). The respiratory quotient decreased significantly from pre-CPB values of 0.82 ± 0.15 to post-CPB values of 0.70 ± 0.08 ($P < 0.01$) (fig. 4).

The changes in hemodynamics and arterial blood gas values are shown in table 1. Cardiac index ($P < 0.001$) and heart rate ($P < 0.001$) increased significantly above pre-CPB values after the termination of CPB. Systolic arterial pressure ($P < 0.005$) and total peripheral vascular resistance ($P < 0.001$) decreased significantly after the termination of CPB. Arteriovenous oxygen difference decreased after CPB ($P < 0.05$). There was no change in pulmonary capillary wedge pressure between pre- and post-CPB. The arterial pH ($P < 0.001$), oxygen tension ($P < 0.05$) and base excess ($P < 0.001$) decreased significantly below pre-CPB values after the termination of CPB. Arterial carbon dioxide tension increased significantly above pre-CPB values ($P < 0.005$).

Discussion

Whole body oxygen consumption and carbon dioxide production increased significantly above pre-CPB values after the termination of CPB. Respiratory quotient decreased significantly below pre-CPB values after the termination of CPB.

The depth of anesthesia during post-bypass period might be different from pre-bypass period and may cause the increase in $\dot{V}O_2$ during post-bypass period. Whole body oxygen consumption is determined by various factors such as muscle activity, body temperature and secretion of catecholamine. General anesthesia does not always cause a decrease in whole body oxygen consumption[9]. Morphine decreased

Table 1. Hemodynamics and Blood gas values

	Before CPB (n=9)	After CPB (n=9)
Cardiac index ($l \cdot min^{-1} \cdot m^{-2}$)	2.67 ± 1.2	4.96 ± 1.4***
Systolic arterial pressure (mmHg)	132 ± 12	101 ± 17**
SVRI (dyne·sec·cm^{-5})	3009 ± 1214	1108 ± 432***
Heart rate (min^{-1})	74 ± 16	116 ± 11***
PCWP (mmHg)	7.1 ± 5.1	9.0 ± 3.9
Pa_{O_2} (mmHg)	173.0 ± 53.8	140.0 ± 58.6*
Pa_{CO_2} (mmHg)	33.5 ± 4.7	38.5 ± 3.9**
pH	7.46 ± 0.03	7.26 ± 0.05***
Base excess ($mEq \cdot l^{-1}$)	1.0 ± 1.3	−8.5 ± 1.6***
Hemoglobin ($g \cdot dl^{-1}$)	12.9 ± 2.5	12.2 ± 0.9
C(a-v)O_2 (Vol%O_2)	4.17 ± 0.58	3.14 ± 0.66**

Abbreviations; PCWP, pulmonary capillary wedge pressure; SVRI, systemic vascular resistance index; C(a-v)O_2, arteriovenous oxygen difference.

*$P < 0.05$, **$P < 0.005$, ***$P < 0.001$ significantly different from the values before CPB.

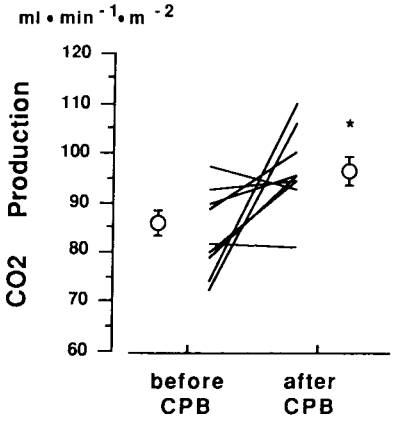

Fig. 3. Carbon dioxide production before and after hypothermic cardiopulmonary bypass.

Carbon dioxide production (n=9) increased significantly to 96.2 ± 8.6 $ml \cdot min^{-1} \cdot m^{-2}$ above pre-CPB values of 85.4 ± 7.8 $ml \cdot min^{-1} \cdot m^{-2}$ ($P < 0.05$).

Abbreviations as in figure 1. CO_2, Carbon dioxide. Values are mean ± SD. *$P < 0.05$, significantly different from values before CPB.

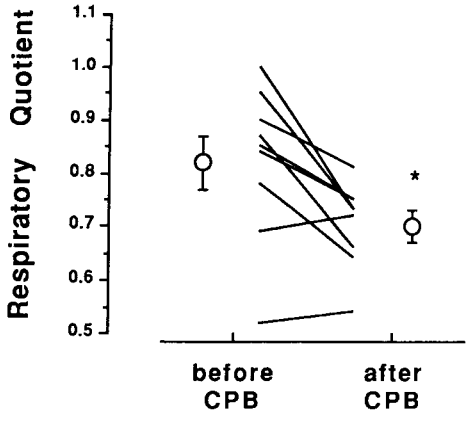

Fig. 4. Changes in respiratory quotient before and after hypothermic cardiopulmonary bypass.

Respiratory quotient (n=9) decreased significantly from pre-CPB values of 0.82 ± 0.15 to post-CPB values of 0.70 ± 0.08 ($P < 0.01$).

Abbreviations as in figure 1. Values are mean ± SD. *$P < 0.01$, significantly different from values before CPB.

$\dot{V}O_2$ by 9–21%[10] and a combination of meperidine, promethazine and chlorpromazine reduced $\dot{V}O_2$ by 34%[11]. Sedation, with a sedative-hypnotic such as diazepam, also reduces oxygen consumption in certain cases. Metabolism may have reduced drug levels so that patients were lighter. A study measur-

ing the changes of $\dot{V}O_2$ during post-bypass period revealed that $\dot{V}O_2$ increased maximally by 180 min post-bypass compared to the 90 min post-bypass value (baseline measurement), in which anesthesia was carried out by 40 $\mu g \cdot kg^{-1}$ fentanyl and isoflurane[12]. Another study, in which $\dot{V}O_2$ was measured during post-bypass period under 100 $\mu g \cdot kg^{-1}$ fentanyl and diazepam anesthesia, showed no changes[2] compared to the values during pre-bypass period. Dopamine administration during post-bypass period might partly contribute the post-bypass increase in $\dot{V}O_2$ because an increase in oxygen consumption with dopamine has been reported[13]. Carbon dioxide production increased and consequently arterial carbon dioxide tension increased after the termination of CPB under the same ventilator setting, which is consistent with an earlier study suggesting that metabolic demands increase during the post-bypass period and ventilation should be adjusted[3].

Hyperdynamic state and metabolic acidosis were present after CPB. This metabolic acidosis is presumably from lactic acid accumulation as other causes of new metabolic acidosis during post-CPB are very unlikely. High cardiac index might be caused by low total peripheral vascular resistance after CPB. The narrowed arteriovenous oxygen difference and metabolic acidosis after CPB might suggest that the cardiac output was adequate but maldistributed peripherally. It is likely that the use of chlorpromazine may have produced some of these effects. Effect of combined infusuion of nitroglycerin and nicardipine is intensified after CPB, inducing more peripheral vasodilation than pre-bypass period[14], which might induce peripheral arteriovenous shunt. Another possibility is the increase in cardiac output is still inadequate in view of the increased metabolic demand. If so, the widened arteriovenous oxygen difference should be observed. There was no difference in body temperature and hemoglobin concentration during both measurements of $\dot{V}O_2$. Although a nerve stimulator was not used to assess the neuromuscular blockade, we gave supplemental doses of relaxant before each measurement of $\dot{V}O_2$. No shivering was observed throughout the course.

Lipid metabolism for energy production might be dominant during post-bypass period because respiratory quotients during the post-bypass period (0.70 ± 0.03) approached the value for fat metabolism, 0.71. The respiratory quotient (ratio of carbon dioxide output to oxygen usage) is useful to estimate relative ratio of carbohydrate and fat metabolism. Our results indicate approximate ratio of carbohydrate and fat metabolism. We were unable to measure protein metabolism to assess its impact on substrate utilization for energy production[6]. Usually a respiratory quotient of 0.85 indicates approximately equal utilization of carbohydrate and fat[6]. Respiratory quotient before CPB was 0.82 ± 0.05, greater than post-CPB values, suggesting that ratio of carbohydrate metabolism during pre-bypass period is higher than post-CPB period. Diminished utilization and increased mobilization of glucose during CPB has been observed[4] and lipid metabolism is dominant during CPB[5], causing hyperglycemia and the high non-esterified fatty acid levels in the blood. Failure of insulin secretion during surgery[15] and especially during hypothermic CPB[4] have been pointed out and referred to as "surgical diabetes". Failure to metabolize carbohydrates in sufficient quantity and diminished carbohydrates in the cell cause rapid metabolism of fat. In diabetes mellitus little carbohydrate is utilized by the body, and consequently, most of the energy is

derived from fat. Although carbohydrate could be used before CPB, the patients might be under the surgical diabetic state during post-bypass period and use less carbohydrate than in the pre-bypass period.

We conclude that oxygen consumption and carbon dioxide production increased significantly above pre-CPB values after the termination of hypothermic CPB at least under the fentanyl, diazepam, clorpromazine anesthesia with continuous infusion of nitroglycerin and nicardipine. Respiratory quotient decreased to 0.70 significantly below pre-CPB values after the termination of CPB, suggesting a relatively higher ratio of lipid metabolism for energy production during the post-bypass period.

Acknowledgments: The authors thank Prof. Evans CW in Mie University for preparing manuscript.

(Received Mar. 19, 1992, accepted for publication Apr. 17, 1992)

References

1. Tinker JH, Roberts SL: Management of cardiopulmonary bypass, in Kaplan JA. (ed): Cardiac Anesthesia second ed. Philadelphia, WB Saunders, 1987, pp. 896–926
2. Murkin JM, Farrar JK, Tweed WA, et al: Cerebral versus systemic oxygen consumption during high-dose narcotic anaesthesia for cardiac surgery. Can Anaesth Soc J 32:S63–64, 1985
3. Sladen RN: Temperature and ventilation after hypothermic cardiopulmonary bypass. Anesth Analg 64:816–820, 1985
4. Yokota H, Kawashima Y, Takao T, et al: Carbohydrate and lipid metabolism in open-heart surgery. J Thorac Cardiovasc Surg 73:543–549, 1977
5. Moffitt EA, Rosevear JW, Molnar GD, et al: The effects of glucose-insulin-potassium solution on ketosis following cardiac surgery. Anesth Analg 50:291, 1971
6. Guyton AC: Dietary balances, regulation of feeding; obesity and starvation, Textbook of Medical Physiology. Philadelphia, WB Saunders, 1976, pp. 970–978
7. Takala J, Keinanen O, Vaisanen P, et al: Measurement of gas exchange in intensive care: Laboratory and clinical validation of a new device. Crit Care Med 17:1041–1047, 1989
8. Weissman C, Sardar A, Kemper M: In vitro evaluation of compact metabolic measurement instrument. J Parenteral Enteral Nutrition 14:216–221, 1990
9. Mikat M, Peters J, Zindler M, et al: Whole body oxygen consumption in awake, sleeping, and anesthetized dogs. Anesthesiology 60:220–227, 1984
10. Rouby JJ, Eurin B, Glaser P, et al: Hemodynamic and metabolic effects of morphine in the critically ill. Circulation 64:53–59, 1981
11. Baum D, Brown AC, Church SC: Effect of sedation on oxygen consumption of children undergoing cardiac catheterization. Pediatrics 39:891–895, 1967
12. Ralley FE, Carli F, Ramsay JG, et al: Oxygen consumption and carbon dioxide production in patients following open heart surgery. Can Anaesth Soc J 33:S70–71, 1986
13. Westenskow DR, Huffaker JK, Stanley TH: The effect of dopamine, atropine, phenylephrine and cardiac pacing on oxygen consumption during fentanyl-nitrous oxide anaesthesia in the dog. Can Anaesth Soc J 28:121–124, 1981
14. Maruyama K, Horiguchi R, Hashimoto H, et al: Effect of combined infusion of nitroglycerin and nicardipine on femoral-to-radial arterial pressure gradient after cardiopulmonary bypass. Anesth Analg 70:428–432, 1990
15. Hall GM, Walsh ES, Paterson JL, et al: Low-dose insulin infusion and substrate mobilization during surgery. Br J Anaesth 55:939–945, 1983