Cardiothoracic Anesthesia, Respiration and Airway

Hepatosplanchnic oxygenation is better preserved during mild hypothermic than during normothermic cardiopulmonary bypass

[L'oxygénation hépatosplanchnique est mieux préservée pendant la circulation extracorporelle sous légère hypothermie que sous normothermie]

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Purpose: To assess and compare the effects of normothermic and mild hypothermic cardiopulmonary bypass (CPB) on hepatosplanchnic oxygenation.

Methods: We studied 14 patients scheduled for elective coronary artery bypass graft surgery who underwent normothermic (>35°C; group I, *n*=7) or mild hypothermic (32°C; group II, *n*=7) CPB. After induction of anesthesia, a hepatic venous catheter was inserted into the right hepatic vein to monitor hepatic venous oxygen saturation ($ShvO_2$) and hepatosplanchnic blood flow by a constant infusion technique that uses indocyanine green.

Results: The $ShvO_2$ decreased from a baseline value in both groups during CPB and was significantly lower at ten minutes and 60 min after the onset of CPB in group I (39.5 ± 16.2% and 40.1 ± 9.8%, respectively) than in group II (61.1 ± 16.2% and 61.0 ± 17.9%, respectively; $P < 0.05$). During CPB, the hepatosplanchnic oxygen extraction ratio was significantly higher in group I than in group II (44.0 ± 7.2% *vs* 28.7 ± 13.1%; $P < 0.05$).

Conclusion: Hepatosplanchnic oxygenation was better preserved during mild hypothermic CPB than during normothermic CPB.

Objectif : *Évaluer et comparer les effets de la circulation extracorporelle (CEC), sous normothermie ou hypothermie légère, sur l'oxygénation hépatosplanchnique.*

Méthode : *Nous avons étudié 14 patients devant subir un pontage aortocoronarien avec CEC sous normothermie (> 35 °C; groupe I, n = 7) ou hypothermie légère (32 °C; groupe II, n = 7). Après l'induction de l'anesthésie, un cathéter a été inséré dans la veine hépatique droite pour permettre de vérifier la saturation en oxygène du sang veineux hépatique (SO_2vh) et le débit sanguin hépatosplanchnique par une perfusion constante utilisant le vert d'indocyanine.*

Résultats : *La SO_2vh a diminué de sa valeur de base dans les deux groupes et a été significativement plus basse à 10 minutes et à 60 min après le début de la CEC dans le groupe I (39,5 ± 16,2 % et 40,1 ± 9,8 %, respectivement) que dans le groupe II (61,1 ± 16,2 % et 61,0 ± 17,9 %, respectivement; $P < 0,05$). Le taux d'extraction d'oxygène hépatosplanchnique pendant la CEC a été significativement plus élevé dans le groupe I que dans le groupe II (44,0 ± 7,2 % vs 28,7 ± 13,1 %; $P < 0,05$).*

Conclusion : *L'oxygénation hépatosplanchnique a été mieux préservée pendant la CEC sous hypothermie légère que sous normothermie.*

NORMOTHERMIC cardiopulmonary bypass (CPB) is now commonly used in cardiac surgery, mainly because of the lack of the adverse effects of hypothermia and rewarming.[1] However, the increased oxygen demand associated with normothermia may compromise tissue oxygenation as a result of the reduced oxygen delivery caused by hemodilution. Although reports on CPB are conflicting, some studies indicated greater increases in splanchnic *vs* systemic oxygen extraction.[2–4] We hypothesized that this imbalance

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Accepted for publication May 31, 2001.

Revision accepted July 27, 2001.

between oxygen demand and supply would be greater during normothermic than mild hypothermic CPB. To test this hypothesis, we investigated changes in hepatic venous oxygen saturation ($ShvO_2$), hepatosplanchnic blood flow, and oxygen delivery during mild hypothermic and normothermic CPB.

Patients and methods

After obtaining approval from the Ethics Committee and informed consent from the patients, we randomly allocated 14 otherwise healthy patients undergoing elective coronary artery bypass graft surgery into the normothermic (group I, *n*=7) and the mild hypothermic (group II, *n*=7) groups.

After premedication with 10 mg diazepam *po*, anesthesia was induced with 0.2 $mg \cdot kg^{-1}$ midazolam and 5 $\mu g \cdot kg^{-1}$ fentanyl; tracheal intubation was facilitated with 0.1 $mg \cdot kg^{-1}$ vecuronium. Anesthesia was maintained with 15 $\mu g \cdot kg^{-1}$ fentanyl, vecuronium, 4 $mg \cdot kg^{-1} \cdot hr^{-1}$ propofol and 50% oxygen in air. In addition to radial and pulmonary artery catheters for routine monitoring, a hepatic venous catheter (Harmac Medical Products, USA.) was inserted into the right hepatic vein via the right femoral vein under fluoroscopic guidance.

Non-pulsatile CPB used a membrane oxygenator, priming with crystalloid solution and a pump flow of 2.3–2.5 $L \cdot min^{-1} \cdot m^{-2}$. A mean arterial pressure (MAP) of 50–90 mmHg was maintained by phenylephrine infusion and a hematocrit greater than 20% by transfusion of packed red cells if needed. The target nasopharyngeal temperature was above 35°C for the normothermic group and at 32°C for the mild hypothermic group. After CPB, the cardiac index (CI) was maintained above 3.0 $L \cdot min^{-1} \cdot m^{-2}$ by administering dopamine or dobutamine or both.

Administration of 1–2 $mg \cdot kg^{-1} \cdot hr^{-1}$ propofol for sedation in the intensive care unit was discontinued and patients extubated when awake and their blood gas analysis comparable to that before surgery. Lactated Ringer's solution (2–3 $mL \cdot kg^{-1} \cdot hr^{-1}$), colloids and packed red blood cells were administered to maintain a CVP of 8–14 mmHg, a pulmonary artery occlusion pressure of 5–12 mmHg, and a hematocrit above 30%.

Hemodynamic variables, arterial, mixed venous, and hepatic venous blood gases, and hepatic venous lactate concentrations were measured: 1) after the induction of anesthesia; 2) ten minutes and; 3) 60 min after the onset of CPB; 4) at the unclamping of the aorta; 5) at the cessation of CPB; 6) at the end of the operation; 7) six hours and; 8) 24 hr after the end of the operation.

Hepatic blood flow was determined by a primed (6 mg), continuous infusion (1 $mg \cdot min^{-1}$) of indocyanine green (ICG)[5] into a central venous catheter: 1) after the induction of anesthesia; 2) during the steady state of CPB; and 3) after cessation of the CPB. Arterial and hepatic venous ICG concentrations were in steady-state plateaus at each measurement.

Various oxygen-utilization variables calculated by standard formulae were systemic oxygen delivery index (DO_2I), consumption index (VO_2I) and extraction ratio (OER), and hepatosplanchnic oxygen delivery index (DO_2splI), consumption index (VO_2splI), and extraction ratio (OERspl).

All data are expressed as means ± SD. One-way analysis of variance was followed by Bonferroni test for intragroup comparisons and by Student t test for intergroup comparisons. A *P* value of less than 0.05 was considered significant.

Results

No significant differences were found between groups in patient height and weight, dosage of phenylephrine and catecholamines, duration of CPB (mean, 146 min), aortic clamping (123 min), and operation (352 min). Furthermore, neither CI, MAP, nor hemoglobin concentrations differed between groups during the study period (Table I). In group I, mixed venous oxygen saturation (SvO_2) decreased early in the course of CPB, while in group II, it decreased at the time of rewarming. The changes in both VO_2I and OER during CPB also differed largely between groups: they increased in group I and decreased in group II. Postoperatively, these levels significantly increased in both groups with no differences between groups. Hepatic venous lactate concentrations were higher in group II than in group I throughout the observation period.

As shown in the Figure, $ShvO_2$ decreased from a baseline value in both groups during CPB; at ten minutes and 60 min after the onset of CPB, it was lower in group I than in group II. Changes in hepatic blood flow (SBFI) and oxygen-utilization variables are summarized in Table II. Changes in SBFI were not found during CPB in either group. DO_2splI was significantly decreased to a similar degree during CPB in both groups. In group I, VO_2splI was markedly increased from baseline value during CPB, while in group II, no increase was found at any time point studied. OERspl was increased in both groups during CPB, more in group I than in group II. The alanine aminotransferase and total bilirubin measured on postoperative days one, three, and seven did not show any major change in either group.

TABLE I Systemic hemodynamic and oxygen-utilization variables, lactate concentrations, and nasopharyngeal temperatures

		during CPB			*after CPB*		*ICU*	
Variable	*Baseline*	*10 min*	*60 min*	*Aorta unclamp*	*10 min*	*60 min*	*6 hr*	*24 hr*
CI (L·min^{-1}·m^{-2})								
normothermic	2.1 ± 0.6	2.3 ± 0.2	2.3 ± 0.2	2.3 ± 0.2	3.7 ± 1.5*	4.0 ± 1.4*	3.2 ± 0.5*	3.2 ± 0.5*
hypothermic	2.6 ± 0.9	2.3 ± 0.2	2.3 ± 0.2	2.3 ± 0.2	3.4 ± 0.6*	3.1 ± 0.5	2.9 ± 0.5	3.1 ± 0.3
MAP (mmHg)								
normothermic	79 ± 8	58 ± 11*	69 ± 5*	61 ± 6*	63 ± 9*	67 ± 10*	69 ± 8*	81 ± 8
hypothermic	75 ± 9	61 ± 16*	71 ± 11	66 ± 9	67 ± 6	69 ± 7	73 ± 12	76 ± 10
Hb (g·dL^{-1})								
normothermic	12.8 ± 1.4	7.9 ± 0.5*#	8.5 ± 1.6*	8.1 ± 0.7*	8.2 ± 0.7*	10.1 ± 1.2*	11.2 ± 1.7*	10.9 ± 1.4*
hypothermic	12.1 ± 1.5	6.5 ± 1.3*	7.6 ± 0.9*	7.9 ± 0.9*	8.3 ± 0.7*	9.6 ± 0.6*	11.8 ± 0.4	11.7 ± 0.8
SvO_2 (%)								
normothermic	85.2 ± 5.5	81.5 ± 5.1	75.5 ± 2.2*#	75.6 ± 3.7*	81.8 ± 4.6	83.9 ± 6.6	66.5 ± 7.4*	68.6 ± 6.6*
hypothermic	82.3 ± 5.9	84.6 ± 5.8	87.4 ± 2.9	75.8 ± 2.8	80.0 ± 3.9	79.5 ± 4.3	69.0 ± 8.4*	70.2 ± 8.2*
DO_2I (mL·min^{-1}·m^{-2})								
normothermic	361 ± 94	249 ± 21*#	267 ± 44*	255 ± 19*	418 ± 187	513 ± 112*	472 ± 67*	468 ± 77*
hypothermic	428 ± 159	206 ± 35*	240 ± 29*	251 ± 26*	388 ± 78	472 ± 154	454 ± 79	485 ± 50
VO_2I (mL·min^{-1}·m^{-2})								
normothermic	53 ± 20	46 ± 13#	65 ± 9#	62 ± 7	70 ± 14	85 ± 47*	155 ± 45*	142 ± 29*
hypothermic	73 ± 31	30 ± 8*	30 ± 7*	60 ± 9	78 ± 25	82 ± 21	134 ± 36*	132 ± 36*
OER (%)								
normothermic	14.8 ± 5.5	18.5 ± 5.2	24.5 ± 2.2*#	24.4 ± 3.7*	18.2 ± 4.5	16.1 ± 6.6	32.8 ± 7.1*	30.7 ± 6.6*
hypothermic	17.5 ± 5.9	15.4 ± 5.7	12.6 ± 2.9	24.1 ± 2.8*	20.0 ± 3.8	20.5 ± 4.3	30.2 ± 8.6*	27.9 ± 8.6*
Lactate-hv (mM·L^{-1})								
normothermic	0.7 ± 0.6	1.5 ± 0.7#	1.4 ± 0.7#	1.8 ± 1.0#	2.4 ± 1.2*#	2.5 ± 1.4*#	4.6 ± 3.3*	1.9 ± 0.7
hypothermic	1.0 ± 0.6	2.2 ± 0.4*	2.8 ± 0.6*	2.9 ± 0.8*	4.2 ± 0.8*	4.4 ± 1.0*	5.4 ± 1.0*	2.2 ± 0.5*
NT (°C)								
normothermic	36.2 ± 0.4	35.3 ± 0.5*#	36.4 ± 0.1#	36.2 ± 0.2#	35.9 ± 0.4	36.0 ± 0.3	37.2 ± 0.7*	37.4 ± 0.4*
hypothermic	36.2 ± 0.4	32.8 ± 1.5*	32.3 ± 0.8*	33.4 ± 0.9*	36.1 ± 0.4	36.0 ± 0.1	37.4 ± 0.4*	37.4 ± 0.3*

Values are expressed as means ± SD. CPB=cardiopulmonary bypass; ICU=intensive care unit; CI=cardiac index,;MAP=mean arterial pressure; Hb=hemoglobin; DO_2I=oxygen delivery index; VO_2I=oxygen consumption index; OER=oxygen extraction ratio; Lactate-hv=hepatic venous lactate concentration; NT=nasopharyngeal temperature. *P <0.05 compared with baseline; #P <0.05 compared with mild hypothermic group.

TABLE II Hepatosplanchnic blood flow and oxygen-utilization variables

Variables	*Baseline*	*During CPB*	*After CPB*
SBFI (mL·min^{-1}·m^{-2})			
normothermic	693 ± 188	601 ± 154	859 ± 347
hypothermic	670 ± 327	678 ± 300	917 ± 222
DO_2splI (mL·min^{-1}·m^{-2})			
normothermic	103 ± 22	67 ± 14*	111 ± 36
hypothermic	97 ± 39	65 ± 25*	111 ± 25
VO_2splI (mL·min^{-1}·m^{-2})			
normothermic	13.5 ± 4.9	29.0 ± 4.5*#	17.9 ± 8.1
hypothermic	14.1 ± 8.1	15.4 ± 6.2	21.7 ± 7.9
OERspl (%)			
normothermic	13.4 ± 5.9	44.0 ± 7.2*#	17.9 ± 10.2
hypothermic	16.3 ± 10.0	28.7 ± 13.1*	20.5 ± 8.2

Values are expressed as means ± SD. CPB=cardiopulmonary bypass; SBFI=hepatosplanchnic blood flow index; DO_2splI=hepatosplanchnic oxygen delivery index; VO_2splI=hepatosplanchnic oxygen consumption index; OERspl=hepatosplanchnic oxygen extraction ratio. *P <0.05 compared with baseline; #P <0.05 compared with mild hypothermic group.

Discussion

We observed that oxygen consumption exceeded oxygen delivery specifically in the hepatosplanchnic region (Table II), resulting in a marked reduction in $ShvO_2$ (Figure). In addition, we could demonstrate that a small difference in systemic temperature had an important effect on the hepatosplanchnic oxygen balance; normothermic CPB further exacerbated the imbalance of oxygen demand and supply.

The lactate concentrations in the hepatic vein were higher during mild hypothermia. Anaerobic metabolism in the hepatosplanchnic region may have been more pronounced during mild hypothermic than during normothermic CPB. However, other contributors to these high concentrations of lactate may include a decrease in lactate metabolism secondary to systemic hypothermia and an increase in lactate production outside the splanchnic region.[6,7] Thus, the increased lactate concentrations may not always indicate the presence of hepatosplanchnic hypoperfusion.

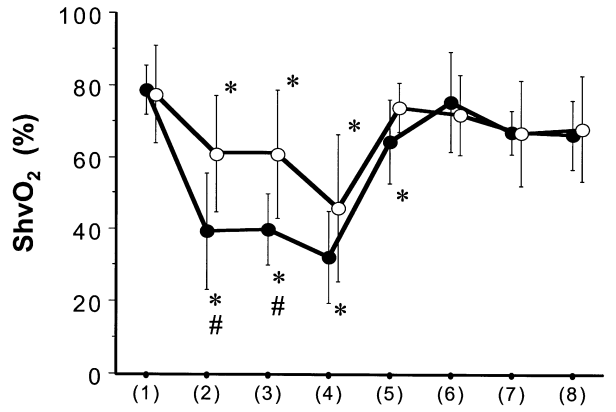

FIGURE Hepatic venous oxygen saturation($ShvO_2$) in normothermic group (•) and in mild hypothermic group (○).
*P <0.05 compared with baseline, #P <0.05 compared with mild hypothermic group. 1) after the induction of anesthesia; 2) ten minutes after the onset of CPB; 3) 60 min after the onset of CPB; 4) at unclamping of the aorta; 5) at the cessation of CPB; 6) at the end of operation; 7) six hours after the operation; 8) 24 hr after the operation.

Liver dysfunction does not constitute a major cause of morbidity after CPB. Despite the presence of severe hepatic venous oxygen desaturation, postoperative liver function tests did not show any major abnormalities in either group. Possible explanations include a very transient decrease in $ShvO_2$, the limited number of patients studied and their relatively low-risk, preservation of hepatosplanchnic blood flow during CPB, and fully developed compensation mechanisms in the liver.[8,9] However, a perioperative decrease in $ShvO_2$ to below 30% during liver resection is associated with postoperative liver dysfunction.[10] In the present study, hepatosplanchnic oxygenation was better preserved during mild hypothermic than normothermic CPB. However, the limits of compensation and the duration of tolerance for hepatic venous hypoxia are not yet known.

Acknowledgements

We thank Mr. Kamiyashiki and Mr. Someya for their technical assistance (Division of Medical Engineering in our institute). This work was supported by the institutional research fund of Saitama Cardiovascular and Pulmonary Center.

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