Changes in gastric intra-mucosal pH and circulating blood volume following coronary artery bypass grafting

Satoshi Ohki MD,* Fumio Kunimoto MD,†
Yukitaka Isa MD,† Hiroshi Tsukagoshi MD,†
Susumu Ishikawa MD,* Akio Ohtaki MD,*
Toru Takahashi MD,* Tetsuya Koyano MD,*
Noboru Oriuchi MD,‡ Yasuo Morishita MD*

Purpose: To determine the changes in gastric intramucosal pH (pHi) following coronary artery bypass grafting (CABG) in comparison with systemic hemodynamic variables and circulating blood volume (BVC).

Methods: Twenty patients who underwent CABG under mild hypothermic cardiopulmonary bypass (CPB) were included. Hemodynamic variables and the values of pHi were obtained at 3, 6, 12 and 24 hr after admission to the intensive care unit (ICU). The pHi was measured by gastric tonometric catheter. The BVC was measured by carbon monoxide (CO)-labeled hemoglobin (CO-Hb) dilution method (CO method) at 6 and 24 hr after ICU admission.

Results: Systemic vascular resistance index (SVRI) and pulmonary vascular resistance index (PVRI) decreased with time. Systemic oxygen delivery index (DO_2I) and systemic oxygen consumption index (VO_2I) showed a gradual increase during the study period. By contrast, pHi decreased to the lowest value (7.26 ± 0.05) at six hours and returned to normal levels (7.34 ± 0.04) at 24 hr after ICU admission. Changes in BVC between six and 24 hr ranged from -242 ml to 978 ml (mean, 334 ± 338 ml). The pHi increased in patients whose BVC increased by > 300 ml. Mean fluid balance was negative in this period (-386 ± 667 ml; range, $-1786 - + 423$ ml).

Conclusion: The pHi showed the lowest value at six hours and returned to normal at 24 hr after ICU admission. The pHi increased with the decrease in vascular resistance and with the increases in BVC in this period. The improvement of pHi, an indicator of splanchnic perfusion, appears to be related to systemic vasodilatation and an increase in BVC.

Objectif : Déterminer les changements de pH gastrique intramuqueux (pHi) qui suivent un pontage aortocoronarien, comparés aux variables hémodynamiques générales et au volume sanguin circulant (VSc).

Méthode : Vingt patients qui ont subi un pontage aortocoronarien sous circulation extracorporelle (CEC) légèrement hypothermique ont participé à l'étude. Les variables hémodynamiques et le pHi ont été mesurés à 3, 6, 12 et 24 h après l'admission à l'unité des soins intensifs (USI). La mesure du pHi a été faite avec un cathéter gastrique tonométrique. Le VSc a été mesuré par la méthode de dilution de l'hémoglobine marquée à l'oxyde de carbone (CO-Hb), à 6 et à 24 h après l'admission à l'USI.

Résultats : L'indice de résistance vasculaire générale (IRVG) et l'indice de résistance vasculaire pulmonaire (IRVP) ont baissé en fonction du temps. L'indice de distribution d'oxygène générale (DO_2I) et l'indice de consommation d'oxygène générale (VO_2I) ont affiché une augmentation graduelle pendant l'étude. Par ailleurs, le pHi a présenté sa plus basse valeur ($7,26 \pm 0,05$) à six heures et est revenu à la normale ($7,34 \pm 0,04$) à 24 h après l'admission à l'USI. Le VSc s'est modifié entre 6 et 24 h, de -242 ml à 978 ml (moyenne, 334 ± 338 ml). Le pHi s'est élevé chez les patients dont le VSc a augmenté de > 300 ml. Le bilan hydrique moyen a été négatif pendant cette période (-386 ± 667 ml; limites, $-1786 - + 423$ ml).

Conclusion : Le pHi le plus bas a été noté à 6 h et est revenu à la normale à 24 h après l'admission à l'USI. Le pHi a augmenté selon la baisse de résistance vasculaire et l'augmentation du VSc pendant ce temps. L'amélioration du pHi, un indicateur de perfusion splanchnique, semble relié à une vasodilatation générale et à une augmentation du VSc.

From the Second Department of Surgery,* Intensive Care Unit† and Department of Nuclear Medicine,‡ Gunma University School of Medicine, Maebashi, Gunma, Japan.

Address correspondence to: Satoshi Ohki MD, Second Department of Surgery, Gunma University School of Medicine, 3-39-15, Showa-Machi, Maebashi, Gunma, 371-8511, Japan. Phone, Fax: 81-27-220-8245; E-mail: ohkisato@akagi.sb.gunma-u.ac.jp

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HEMODYNAMIC formation after cardiac surgery is characterized by an increase in systemic vascular resistance due to hypothermia, circulating vasoconstrictive mediators, sympathetic nerve activation or uncorrected blood volume.¹⁻³

In the early postoperative stage, patients are treated with inotropics, vasodilators and infusion of blood products or plasma expanders to improve tissue perfusion according to systemic arterial pressure (SAP), cardiac output, pulmonary capillary wedge pressure (PCWP) or central venous pressure (CVP). However, these values represent only an average of systemic hemodynamic status and do not give information about tissue perfusion.⁴ Fiddian-Green *et al.* developed a new method to estimate gastric intramucosal pH (pHi) using a tonometric catheter.⁵ The pHi is an indicator of tissue perfusion and its usefulness has been reported in a variety of patients.⁶⁻¹⁰ In patients undergoing open-heart surgery, Fiddian-Green reported that the postoperative complication and mortality rate was high in patients with low pHi (pHi <7.32).¹¹ Landow *et al.*¹² and Niinikoski *et al.*¹³ showed a decrease in pHi in patients undergoing cardiac surgery. We hypothesized that reduced blood volume is a major contributor to the postoperative decrease in pHi.¹⁴ In this study, we determined the changes in pHi following coronary artery bypass grafting (CABG) in comparison with circulating blood volume (BVC) and systemic hemodynamic variables. BVC was measured by the carbon monoxide (CO)-labeled hemoglobin (CO-Hb) dilution method (CO method). The clinical usefulness of the CO method for blood volume measurement was previously reported¹⁵ as a simple and safe method without the risk of exposure to radioactivity. Obata *et al.* reported high predictive value of circulating blood volume measurement using CO method in animal hemorrhage model¹⁶ and we recently reported the accuracy and precision of the CO method in humans.¹⁷

Patients and methods

Patients

The protocol was approved by the Gunma University Ethical Committee for Human Research. A total of 20 patients (12 male and eight female) who underwent CABG and were admitted to the intensive care unit (ICU) of the Gunma University Hospital from April 1997 to March 1998 were included in this study. The day before surgery, patients were informed of the purposes of the study and the procedures involved, and written consent was obtained. Patients with 1) renal, hepatic or gastrointestinal disease, 2) low left ventricular ejection fraction (LVEF) < 40%, as determined by

preoperative echocardiography, 3) low cardiac output syndrome (LOS) with cardiac index < 2.5 L·min⁻¹·m⁻², 4) or postoperative bleeding > 500 ml for six hours after admission to the ICU were excluded from the study. Anesthesia was induced with 12-20 µg·kg⁻¹ fentanyl, 0.4-1.0 mg·kg⁻¹ midazolam and 0.1 mg·kg⁻¹ vecuronium and maintained by additional doses of fentanyl. Following median sternotomy and pericardotomy, 3 mg·kg⁻¹ heparin were administered and CPB was instituted with an arterial line into the ascending aorta and venous lines. A single two-stage venous cannula was used for CABG. Non-pulsatile, hypothermic cardiopulmonary bypass was conducted in standard fashion using a membrane oxygenator including a heat exchanger (AFFINITY, AVECOR Cardiovascular Inc. Plymouth, MN) and roller pump (TOW NOK, Tonokura Ika Kogyo Co., Ltd., Tokyo, Japan). When the esophageal temperature reached 28-30°C, the ascending aorta was cross-clamped. Cold blood cardioplegia and topical hypothermia with ice slush were used for myocardial protection. Rectal temperature was maintained at 28 to 30°C in all patients.

All patients were given a low dose of catecholamines (≤ 3 µg·kg⁻¹·min⁻¹ dopamine and ≤ 3 µg·kg⁻¹·min⁻¹ dobutamine), 1 µg·kg⁻¹·min⁻¹ diltiazem and 0.5-1 µg·kg⁻¹·min⁻¹ nitroglycerin after surgery. No patients received blood transfusion but each received 476 ± 96 ml albumin 4% solution, 1508 ± 160 ml lactated Ringer's solution and 1238 ± 121 ml of glucose 5% solution during the study. For the first six hours after ICU admission, the lungs of all patients were mechanically ventilated and the endotracheal tubes were removed 24 hr after ICU admission in 18 of 20 patients. Two elderly patients (71, 72 yr) needed 5 cmH₂O pressure support ventilation (PSV) over 24 hr in ICU, but they were successfully weaned from the ventilators after this study. The postoperative courses were uneventful in all patients with no episodes of low cardiac output syndrome or major complications.

Study protocol

Hemodynamic variables and values of pHi were obtained at 3, 6, 12 and 24 hr after ICU admission. The BVC was measured by the CO method at 6 and 24 hr after ICU admission.

A pulmonary artery catheter (93A-750H-7.5F, Baxter, Irvine, CA) was inserted via the right internal jugular vein and a small polyethylene catheter was introduced into the radial artery after induction of anesthesia. A gastric intramucosal pH catheter (TRIP NGS CATHETER, Tonometrics, Inc., Hopkinton, MA) was placed in the stomach immediately after admission to the ICU. The catheters were fixed at 50

– 60 cm from incisors and correct positioning was confirmed by auscultation of gurgling sound of injected air and by X-ray. Using these catheters, both the hemodynamic variables and pHi were measured at 3, 6, 12 and 24 hr after ICU admission. The catheters were removed after the end of the study. The tonometric method for calculating pHi has been previously described.⁵ Briefly, the gas-permeable balloon of the tonometer filled with 2.5 ml saline solution was placed in the stomach. After 30 min, 1 ml saline was aspirated and discarded (dead space). The remaining 1.5 ml were aspirated and analyzed for P_{CO_2} in a blood gas analyzer. The P_{CO_2} was corrected to steady state P_{CO_2} (P_{ssCO_2}). Henderson-Hasselbalch's equation was used for the calculation of pHi: $pHi = 6.1 + \log (B/0.03 \times P_{ssCO_2})$, where B is the arterial bicarbonate concentration, P_{ssCO_2} was obtained using the slide calculator provided by the manufacturer which transforms P_{CO_2} to P_{ssCO_2} using a correction factor (CF). Blood lactate concentrations were measured with a glucose-lactate-electrolyte analyzer (EML-105, Radiometer, Copenhagen, Denmark).

Measurement of BVc

THE CO METHOD

The accuracy and precision of the CO method in

humans was reported recently.¹⁷ In that paper, we simultaneously measured BVc using the ^{51}Cr method as well as the CO method and verified the accuracy and precision of the CO method by comparing the values obtained from the CO method with those from the ^{51}Cr method which is widely accepted as a standard method for BVc measurement. Small mean differences and standard deviations between the CO method and the ^{51}Cr method (-70.2 ± 184.8 ml) and small percentage errors ($-0.49 \pm 1.29\%$) indicated the accuracy and precision of the CO method, and a close correlation was observed ($r=0.97$). The BVc was calculated from the following equation:

$$BVc \text{ (ml)} = V_i \text{ (ml)} \times Hb_i / Hb_b \text{ (g·dl}^{-1}) \times CO-Hb_i / (CO-Hb_z - CO-Hb_b) \text{ (\%)}$$

where V_i = injected volume of CO-labeled blood; Hb_i , $CO-Hb_i$ = hemoglobin and CO-Hb concentration in CO-labeled blood; Hb_b , $CO-Hb_b$ = hemoglobin and CO-Hb concentration in circulating blood before injection of CO-labeled blood; $CO-Hb_z$ = the extrapolated zero-time intercept of CO-Hb concentration in circulating blood. Blood hemoglobin and CO-Hb concentration were measured with a blood gas analyzer with oximetry (ABL520, Radiometer, Copenhagen, Denmark).

Statistical analysis

All data are presented as mean $\pm$ SD. Consecutive data were analyzed by one way analysis of variance (ANOVA) for repeated measures and a post hoc test was performed using the Scheffe's test. Linear regression analysis was used to test the relationship between the increase in BVc and the increase in pHi. Differences were considered significant at $P < 0.05$ (Macintosh program, Statview 4.01; Abacus Concepts, Berkeley, CA).

TABLE I Patient characteristics and surgical data (mean $\pm$ SD (range))

n	20
Male/Female	12/8
Age (yr)	62.0 $\pm$ 6.4 (52 - 75)
Weight (kg)	50.0 $\pm$ 9.5 (37.3 - 70.3)
Body surface area (m ²)	1.47 $\pm$ 0.16 (1.24 - 1.84)
Cross-clamp time (min)	80.4 $\pm$ 16.9 (56 - 124)
CPB time (min)	111.3 $\pm$ 21.7 (78 - 158)

CPB = cardiopulmonary bypass.

TABLE II Postoperative hemodynamic data (mean $\pm$ SD)

		3 hr	6 hr	12 hr	24 hr
HR	(beats·min ⁻¹)	98.5 $\pm$ 17.2	96.1 $\pm$ 10.2	92.1 $\pm$ 9.0	95.8 $\pm$ 12.5
CI	(L·min ⁻¹ ·m ⁻²)	3.7 $\pm$ 0.9	3.9 $\pm$ 0.9	3.9 $\pm$ 0.9	3.9 $\pm$ 0.8
MAP	(mmHg)	79.9 $\pm$ 12.7	82.6 $\pm$ 11.4	80.1 $\pm$ 11.3	75.9 $\pm$ 12.1
MPAP	(mmHg)	21.9 $\pm$ 13.8	19.8 $\pm$ 6.7	19.1 $\pm$ 6.6	16.9 $\pm$ 6.4
CVP	(mmHg)	3.7 $\pm$ 2.1	4.1 $\pm$ 2.1	4.6 $\pm$ 2.3	5.3 $\pm$ 3.2
PCWP	(mmHg)	6.7 $\pm$ 3.7	7.3 $\pm$ 3.0	7.3 $\pm$ 3.0	7.9 $\pm$ 3.4
SVRI	(dyne·sec·cm ⁻⁵ ·m ²)	1736 $\pm$ 466	1644 $\pm$ 415	1538 $\pm$ 319	1447 $\pm$ 420*
PVRI	(dyne·sec·cm ⁻⁵ ·m ²)	288 $\pm$ 99	249 $\pm$ 91	209 $\pm$ 64†	178 $\pm$ 69†

HR=heart rate; CI=cardiac index; MAP=mean arterial pressure; MPAP=mean pulmonary artery pressure; CVP=central venous pressure; PCWP=pulmonary capillary wedge pressure; SVRI=systemic vascular resistance index; PVRI=pulmonary vascular resistance index.

* $P < 0.05$, † $P < 0.01$ compared with value at three hours after ICU admission

FIGURE 1 Changes in systemic oxygen delivery index (DO_2I) (closed circles) and systemic oxygen consumption index (VO_2I) (open circles) (top), arterial pH (pHa) (closed squares) and gastric intramucosal pH (pHi) (open squares) (bottom) from three to 24 hr after ICU admission. Values are mean $\pm$ SD * $P < 0.05$ compared with value at six hours after ICU admission.

Results

The patient characteristics, aortic cross-clamp and CPB times are shown in Table I. Body weight increased by 2.0 ± 0.9 (range, 1.0-3.4) kg after surgery. There were no differences in heart rate (HR), cardiac index (CI), CVP or PCWP throughout the study period. The pulmonary vascular resistance index (PVRI) and systemic vascular resistance index (SVRI) were lower at 24 hr after ICU admission than at three hours after ICU admission (Table II). Lactate levels decreased at 12 hr (4.0 ± 1.3 mmol·l⁻¹) and 24 hr (2.5 ± 0.6 mmol·l⁻¹) after ICU admission compared with those at three hours (7.1 ± 2.1 mmol·l⁻¹) after ICU admission ($P < 0.01$). Systemic oxygen delivery index (DO_2I) and systemic oxygen consumption index (VO_2I) gradually increased toward the end of the study. The pHi was at its lowest

FIGURE 2 Changes in pHi and circulating blood volume from six to 24 hr after ICU admission. Closed circles indicate the value at six hours after ICU admission. Open circles indicate the value at 24 hr after ICU admission.

FIGURE 3 Relationship between changes in pHi and circulating blood volume from six to 24 hr after ICU admission.

value six hours after ICU admission (7.26 ± 0.05) and recovered to normal levels at 24 hr (7.34 ± 0.04) (Figure 1). The serum bicarbonate concentrations obtained at 3, 6, 12 and 24 hr after ICU admission were 21.4 ± 2.3 , 23.1 ± 2.4 , 24.8 ± 2.1 and 26.8 ± 1.8 , respectively. Figure 2 shows changes in pHi and BVC between six and 24 hr. Changes in BVC between six and 24 hr ranged from -242 ml to 978 ml (mean, 334 ± 338 ml). The pHi increased in patients whose BVC increased by > 300 ml. Mean fluid balance was negative in this period (-386 ± 667 ml; range, -1786 - +423 ml). A correlation was observed between increases in BVC and pHi ($r^2=0.42$) (Figure 3).

Discussion

Mythen reported that perioperative plasma volume expansion reduced the incidence of gut mucosal hypoperfusion during cardiac surgery.¹⁴ We attempted to determine changes in pHi and BVc in patients after CABG in this study. There were two major findings in this study. First, pHi decreased at six hours after ICU admission when both the systemic hemodynamics and oxygen balance were within normal ranges and then recovered to normal at 24 hr. The decrease in pHi observed at six hours after ICU admission may be due to; 1) limited blood flow to splanchnic organs by residual vasoconstrictors which might have been released during CPB and selectively acted on splanchnic vasculature,³ or 2) reduced blood flow due to the blood flow shift from splanchnic organs to the muscle or skin where vasodilatation occurred in the late rewarming stage.¹⁸ Second, the lowered pHi increased with the increase in BVc, indicating correlation between increases in pHi and BVc. This finding suggests that the recovery of pHi between six and 24 hr after ICU admission may be a result of improved splanchnic perfusion through the increase in BVc from systemic vasodilation. Vascular resistance also decreased toward the end of the study period. Our results suggest that both vasodilatation and normalization of BVc are important to maintain systemic circulation and splanchnic perfusion after open-heart surgery with CPB. In this study, a low dose of vasoconstrictor such as dopamine and vasodilators such as diltiazem and nitroglycerin were administered postoperatively. Results might be modified by these vasoactive drugs. Further studies are required to clarify the effects of vasoactive drugs on pHi and BVc.

Care is necessary in the interpretation of the pHi data. Henderson-Hasselbalch's equation was used for the calculation of pHi. However, neither intramural P_{CO_2} nor gastric intramural HCO_3^- can be measured directly. Heard *et al.* reported intraluminal CO_2 formation can be prevented by the use of H_2 -blockers because CO_2 was produced by the titration of secreted HCO_3^- in the acid environment of the stomach.⁷ On the other hand, Fiddian-Green *et al.* reported that back-diffusion CO_2 did not influence pHi measurement.¹⁹ In our study, no patients received H_2 -blockers and gastric juice was drained through the gastric catheter. Therefore, CO_2 production due to the titration might be minimal in this study. The pHi was also defined by the arterial bicarbonate concentration. The considerable increase in pHi at 24 hr was partly a result of the increase in arterial bicarbonate concentration. However, perhaps the major factor in the increase in pHi was the decrease in P_{CO_2} in gastric

mucosa during the study because the increase in arterial pH was small and insignificant.

A potential source of error is measurement of saline P_{CO_2} by different clinical blood gas analyzers, however, ABL520 which was used in this study had reasonable bias and good reproducibility.²⁰

In spite of the negative fluid balance (-386 ± 667 ml) between six and 24 hr, BVc increased in 18 of 20 patients in this period. It is recognised that extracellular fluid (ECF) volume increases during open-heart surgery with CPB. The increased ECF, thereafter, is reabsorbed into the intravascular space and excreted, resulting in diuresis.²¹ Negative fluid balance was a result of high urine output in the diuretic phase. Therefore, the increase in BVc observed in our study might be a result not only of postoperative transfusion but also of reabsorption of ECF into the vascular space.

In conclusion, pHi was lowest at six hours after ICU admission and returned to normal at 24 hr. Vascular resistance decreased and pHi increased with an increase in BVc in this period. The improvement of pHi, an indicator of splanchnic perfusion, appears to be related to systemic vasodilatation and an increase in BVc.

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