A marked increase in gastric fluid volume during cardiopulmonary bypass

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Major physiological stress occurs during cardiac surgery with cardiopulmonary bypass. This is related to hypothermia and artificial organ perfusion. Thus, serious gastrointestinal complications, particularly upper gastrointestinal bleeding, sometimes follow cardiac surgery. We have compared the antisecretory effects of a preanesthetic H2 antagonist (roxatidine, cardiopulmonary bypass-H2 group, n = 15) and a proton pump inhibitor (rabeprazole, cardiopulmonary bypass-PPI group, n = 15) in patients undergoing cardiac surgery with cardiopulmonary bypass, and also compared in patients undergoing an off-pump coronary artery bypass graft surgery (off-pump cardiopulmonary bypass-H2 group, n = 15). Gastric pH (5.14 ± 0.61) and gastric fluid volume (13.2 ± 2.4 mL) at the end of surgery in off-pump cardiopulmonary bypass-H2 group was significantly lower and higher than those in both cardiopulmonary bypass-H2 (6.25 ± 0.54, 51.3 ± 8.0 mL) and cardiopulmonary bypass-PPI (7.29 ± 0.13, 63.5 ± 14.8 mL) groups, respectively although those variables did not differ between groups after the induction of anesthesia. Plasma gastrin (142 ± 7 pg/mL) at the end of surgery and maximal blood lactate levels (1.50 ± 0.61 mM) in off-pump cardiopulmonary bypass-H2 group were also significantly lower than those in both cardiopulmonary bypass-H2 (455 ± 56 pg/mL, 3.97 ± 0.80 mM) and cardiopulmonary bypass-PPI (525 ± 27 pg/mL, 3.15 ± 0.44 mM) groups, respectively. In addition, there was a significant correlation between gastric fluid volume and maximal blood lactate (r = 0.596). In conclusion, cardiopulmonary bypass may cause an increase in gastric fluid volume which neither H2 antagonist nor PPI suppresses. A significant correlation between gastric fluid volume and maximal blood lactate suggests that gastric fluid volume may predict degree of gastrointestinal tract hypoperfusion.

Key Words: cardiopulmonary bypass, gastrointestinal ischemia, gastric acidity, H2 antagonists, proton pump inhibitors

Materials and Methods

With University Ethics Committee approval and informed consent, 45 adult patients undergoing cardiac surgery were recruited in the study. Number of patients in each group was determined by power analysis using our previous study data. Thirty patients undergoing cardiac surgery under CPB were randomly assigned to two groups: CPB-H2 and CPB-PPI group (n = 15 each). Another 15 patients were scheduled to undergoing off-pump coronary artery bypass grafting (OPCAB) surgery. In the CPB-H2 and OPCAB-H2 groups, patients were given ranitidine 75 mg orally at 9:00 pm on the day before the surgery and 2 h before the induction of anesthesia. In the CPB-PPI group, patients were premedicated with rabeprazole 20 mg orally at 9:00 pm on the day before the surgery and 2 h before the induction of anesthesia. Because only ranitidine has been approved as an oral preanesthetic H2 antagonist by our Ministry of Health, Labor and Welfare in Japan, famotidine or omeprazole was not used. All patients were hospitalized for at least the night before surgery and were fasted from the first anesthetic premedication (i.e., 9:00 pm). The researchers and patients were blinded to preanesthetic medication.

Anesthesia was induced with propofol 0.5–1.5 mg/kg, ketamine 0.5–1.0 mg/kg, and fentanyl 5 µg/kg and maintained with propofol 3–7 mg·kg−1·h−1, ketamine 0.5–1.0 mg·kg−1·h−1, and fentanyl 4–8 µg/kg. The trachea was intubated after muscle relaxation facilitated with vecuronium 0.1 mg/kg IV. Muscle relaxation was maintained with an IV bolus of vecuronium that was given 1 mg every 30 min. A gastric tube (Argyle® Salem Sump Tube, Japan

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were also significantly lower in OPCAB-H (Fig. 1A and B). Plasma gastrin and maximal blood lactate levels did not differ between groups after the induction of anesthesia.

Gastric pH and volume at the end of surgery in OPCAB-H group was significantly lower and higher than those in both CPB-H group and CPB-PPI groups, respectively although those variables did not differ between groups after the induction of anesthesia (Fig. 1A and B). Plasma gastrin and maximal blood lactate levels were also significantly lower in OPCAB-H group than those in both CPB-H and CPB-PPI groups (Fig. 1C and D). In addition, there was a significant correlation between gastric fluid volume and maximal blood lactate level (Fig. 2; r = 0.596; p<0.01).

There were fewer patients showing critical factors for acid aspiration pneumonia (pH<2.5 or gastric fluid volume>25 mL) in the OPCAB-H group (Table 3).

### Discussion

CPB patients (CPB-H: and CPB-PPI groups) had higher gastric pH and volume compared to those in the OPCAB-H group. H2 antagonist and PPI were effective, gastric fluid volume should have been reduced with higher pH. Thus, higher gastric pH may not imply that these anti-acid agents suppressed gastric acid secretion. Where did gastric fluid volume come from? Several reports indicate that the CPB causes intestinal hypoperfusion which impairs small intestinal transport and increases intestinal permeability. Tsunooka and colleagues reported that serum diamine oxidase activity, an index of small intestinal ischemia, rose significantly during the CPB in patients undergoing coronary artery bypass grafting. The activity was unchanged in patients undergoing OPCAB. In addition, serum lactate mirrored the changes in diamine oxidase activity. Similarly, blood lactate was significantly higher in the CPB groups than that in the OPCAB group in the present study. As lactate production increases as a consequence of tissue hypoxia, high blood lactate levels may also indicate intestinal hypoperfusion during CPB. As there was a significant correlation between gastric fluid volume and maximal blood lactate levels in the present study, intestinal hypoperfusion due to CPB could increase GI microvascular permeability to increase gastric fluid volume. Therefore, either gastric fluid volume or blood lactate may be an index of GI tract hypoperfusion.

Critical factors for acid aspiration pneumonia in adults have been considered to comprise gastric pH below 2.5 and a fluid volume above 25 mL. In the present study, 12 and 10 of 15 patients with more than 25 mL of gastric contents in the CPB-H and CPB-PPI groups have a higher postoperative risk of acid aspiration pneumonia. Into the OPCAB-H group only 2 of 15 patients had gastric contents in excess of 25 mL. Thus, gastric tube should be inserted after removal of transesophageal echocardiographic probe.

To determine the precise mechanism regarding the increase of gastric fluid volume by CPB, we should have placed the gastric tube just after termination of CPB rather than just before the end of surgery.

### Table 1. Patient characteristics

| Group    | n   | Sex (M/F) | Age (yr) | Ht (cm) | Wt (kg) | Duration (min) |
|----------|-----|-----------|----------|---------|---------|----------------|
| CPB-H2   | 15  | 4/11      | 60 ± 12  | 157 ± 10| 56 ± 14 | 439 ± 88*       |
| CPB-PPI  | 15  | 7/8       | 64 ± 11  | 158 ± 9 | 64 ± 11 | 441 ± 146*      |
| OPCAB-H2 | 15  | 5/10      | 67 ± 10  | 157 ± 9 | 60 ± 10 | 342 ± 57        |

Data are either number of patients or Mean ± SD as appropriate. Ht: height, Wt: weight, Ane: anesthesia, Surg: surgery, CPB: cardiopulmonary bypass, (—): no application, *p<0.01 vs OPCAB-H.

### Table 2. Details of cardiac procedures

| Type of cardiac surgery       | Group          |
|-------------------------------|----------------|
|                               | CPB-H2 | CPB-PPI | OPCAB-H2 |
| CABG                          | 1      | 1      | 15      |
| CABG + Dor’s ope              | 2      | 0      | (—)     |
| CABG + Dor’s ope + MVP        | 1      | 0      | (—)     |
| CABG + AVR                    | 2      | 4      | (—)     |
| CABG + MVP                    | 1      | 1      | (—)     |
| AVR                           | 1      | 1      | (—)     |
| TVR                           | 1      | 1      | (—)     |
| MVR or MVP                    | 4      | 1      | (—)     |
| MVR + TAP                     | 2      | 0      | (—)     |
| MVR + AVR                     | 0      | 1      | (—)     |
| ASD                           | 0      | 1      | (—)     |
| ASD + VSD                     | 0      | 1      | (—)     |
| ASD + MVP                     | 0      | 1      | (—)     |
| As-Ao Replacement + AVR       | 0      | 1      | (—)     |
| As-Ao Replacement             | 0      | 1      | (—)     |
| Total Arch Replacement        | 0      | 1      | (—)     |

CABG: coronary artery bypass grafting, ope: operation, MVR: mitral valve replacement, MVP: mitral valve plasty, AVR: aortic valve replacement, TAP: tricuspid annuloplasty, TVR: tricuspid valve replacement, ASD: atrial septal defect, VSD: ventricular septal defect, As-Ao: ascending aorta, Ds-Ao: descending aorta, (—): no application.
of surgery in the present study. However, as OPCAB-H₂ group data clearly suggest that an increase in gastric fluid volume may be due to CPB as cardiac surgery per se would not increase gastric fluid volume.

The present data indicate that both H₂ antagonist and PPI cannot inhibit an increase in gastric fluid volume. Should these agents be given as anesthetic premedication? If neither are given, most of patients would have a high risk of acid aspiration pneumonia during the induction of anesthesia as we previously found that patients without prophylaxis showed low gastric pH (2.2 ± 1.2) and high volume (20 ± 18 mL).¹⁶ In addition, the chief GI complication following CPB is GI bleeding secondary to gastric or duodenal ulceration.¹⁷ Therefore, perioperative gastric acid suppression is necessary. Which anti-acid agent is suitable to suppress gastric acidity in patients undergoing cardiac surgery H₂ antagonist or PPI? Wagner and colleagues¹⁵ reported that perioperative administration of famotidine (H₂ antagonist) suppresses gastric secretion in cardiac patients. Hata and colleagues¹⁸ compared three agents (n = 70 each): teprenone 150 mg/day (mucosal protection), ranitidine 300 mg/day (H₂ antagonist) and rabeprazole 10 mg/day (PPI) to prevent postoperative the upper GI complications in patients undergoing cardiac surgery with CPB. They found that the incidences of hemorrhagic gastritis and active ulceration were significantly lower in patients with rabeprazole.

Fig. 1. Changes in gastric pH (A), gastric fluid volume (B), plasma gastrin (C) and maximal blood lactate level (D) at the beginning and end of surgery. Pre: before cardiopulmonary bypass (CPB), Post: after cessation of CPB, Mean ± SEM, *p<0.01 vs Pre, *p<0.01 vs OPCAB-H₂ group.

Fig. 2. Correlation between gastric fluid volume and maximal blood lactate (r = 0.596, p<0.01).
Therefore, preanesthetic PPI may be the most appropriate anti-
acid for patients undergoing cardiac surgery with CPB.

In conclusion, the present study suggests that both gastric fluid
volume and blood lactate level may predict the degree of GI tract
hypoperfusion. As CPB often increases gastric fluid volume more
than 25 mL, gastric tube should be placed before the end of
surgery.

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Abbreviations

CABG coronary artery bypass graft
CPB cardiopulmonary bypass
GI gastrointestinal
GV gastric fluid volume
NSAIDs nonsteroidal antiinflammatory drugs
OPCAB off-pump coronary artery bypass grafting
PPI proton pump inhibitor

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