Artificial Organs
30(7):548–553, Blackwell Publishing, Inc.

Gastrointestinal Motility During Cardiopulmonary Bypass: A Sonomicrometric Study

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Abstract: Cardiopulmonary bypass (CPB) is known to impair the integrity of the gastrointestinal tract. However, little is known about the movement behavior of the gastrointestinal tract during CPB. This study was aimed to assess the gastrointestinal motility with sonomicrometry, a distance measurement using ultrasound, in a porcine model of CPB. Twelve pigs weighing 70–112 kg were having a standard hypothermic CPB for 120 min either with the nonpulsatile flow ($n = 6$) or the pulsatile flow ($n = 6$). Before CPB, piezoelectric echo crystals were placed either along the longitudinal or the circular axis of the pylorus. Patterns of gut movement and the total sonomicrometric activity (TSA) were recorded at several time intervals during experiments as qualitative and quantitative parameters of gut motility. Results showed that the intact regular rhythmic pattern of gut movement was detected before CPB. This pattern changed little when CPB started, but it disappeared at 60 min when the body temperature lowered down to 32°C. During the same period, the TSA reduced significantly along the longitudinal as well as the circular directions of the pylorus. There was no significant difference between the nonpulsatile and pulsatile groups. Gut blood flow reduced significantly in both groups, but it was not associated with the reduced sonomicrometric activity. In conclusion, gastrointestinal motility during CPB can be measured qualitatively and quantitatively by sonomicrometry in a large animal model. Suppression of gut motility during CPB does not seem to be associated with the mode of perfusion but with the reduced body temperature during the hypothermic phase of CPB.
Key Words: Cardiopulmonary bypass—Gastrointestinal motility—Sonomicrometry.

Cardiopulmonary bypass (CPB) has been successfully applied in open-heart surgery for the past five decades (1). However, due to the nonphysiological behaviors of the heart-lung machine, such as the nonpulsatile perfusion flow, induced hypothermia, and dilution of circulating blood with the priming solution, patients are still vulnerable to postoperative complications and organ dysfunction as a result of poor organ perfusion during CPB (2,3). The gastrointestinal tract is one of the organs that is known to be affected by CPB (4–6). In the past, efforts have been made to measure mesenteric blood flow, gastric mucosal perfusion, and gut permeability (7–9). However, little is known about gut motility, namely the movement behavior of the gastrointestinal tract during CPB.

Sonomicrometry is a well-known diagnostic technique for its cardiac applications (10–12). One of its main features is to record the shortening of myocardial segment length during heart movement during which a pair or several pairs of echo crystals are imbedded in the myocardium to access the distance of two relevant points over the elapsed time. With this principle, sonomicrometry has also been suggested to be used for monitoring the gastrointestinal motility in a rat model (13,14). In this study, we sought to explore the feasibility of using the sonomicrometric technique in a large animal model to either qualify or quantify the movement of the gastrointestinal tract during CPB. Furthermore, we hypothesized that the pulsatile perfusion flow would be better than the nonpulsatile flow in maintaining the gastrointestinal motility during CPB surgery.

Received September 2005; revised January 2006.
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METHODS

Animal experiments

Pigs with a body weight of 70–112 kg were prohibited from any food for at least 8 h before operation. All animals received humane care in compliance with

the "Principles of Laboratory Animal Care" by the Dutch animal protection law. The study protocol was approved by the Groningen University Ethical Committee on animal experiments. For all the animals, anesthesia was induced with intramuscular injection of ketamine (10 mg/kg) and diazepam (1 mg/kg) followed by continuous inhalation of 2% isoflurane with 100% oxygen. Muscle relaxation was achieved by continuous infusion of Pavulon (0.05 mg/kg) and analgesia was achieved by intramuscular injection of flunixine meglumine (2 mg/kg). After tracheal intubation and the employment of mechanical ventilation, the animals underwent a midline incision laparotomy to facilitate the measurement of superior mesenteric blood flow and the assessment of gastrointestinal movement. The thorax was opened with a median sternotomy. After systemic heparinization (3 mg/kg), CPB was established with the conventional heart-lung machine consisting of roller pumps and a hollow fiber membrane oxygenator. Venous blood was withdrawn from the right atrium, and arterial blood was returned via the ascending aorta.

CPB and pulsatile perfusion

All the animal experiments were standardized to have a duration of CPB for 120 min, and the aorta was cross clamped for 60 min. The CPB circuit was primed with 1000-mL lactated Ringer's solution and 500-mL 10% hydroxyethyl starch solution. During CPB, the animals were cooled down to 32°C with an average roller pump flow of 60 mL/kg/min by the heart–lung machine. According to the flow pattern during perfusion, the animals were divided into a nonpulsatile group ($n = 6$) perfused with the roller pump and a pulsatile group ($n = 6$) perfused with the roller pump and an additional intra-aortic pulsatile catheter pump. In the pulsatile group, the pulsatile flow was initiated from the beginning of the CPB until the release of the aortic cross clamp by the intra-aortic pulsatile catheter placed via the ascending aorta in the descending aorta. This catheter was connected to a membrane pump and activated by a pneumatical driver with an average pumping flow of 3.1 L/min on a fixed pulse rate of 80/min. Details about the intra-aortic pulsatile catheter pump and the initiation of pulsatile flow have been described previously (15).

Sonomicrometric measurement of gut movement

After laparotomy, each of three piezoelectric echo crystals of 2 mm in diameter (Sonometrics, London, ONT, Canada) was positioned around the pylorus. The first and second crystal were placed along the longitudinal axis of the pylorus to measure the longitudinal movement of the gut, whereas the third crystal was placed vertically to the first crystal to measure the circular movement of the gut. The initial distance between each pair of the two crystals was set to 20 mm. The sonomicrometric data acquisition was made at the baseline after laparotomy; 5 min before the start of CPB; 5, 30, 60, 90 min after the start of CPB; at the end of CPB; and 30 min after the end of CPB. Each data recording lasted for 5 min or 300 s using the digital sonomicrometer connected to a personal computer running SonoLAB software (Sonometrics). To quantitatively assess the movement of the gastrointestinal tract, a simple calculation method was developed to count the total sonomicrometric activities (TSAs) by accumulating all the digital signals recorded within one measurement. The TSA was calculated according to the following formula:

$$TSA\ (\text{units}/\text{min}) = \frac{\textit{Total recorded sonomicrometric activity}\ (\text{unit})}{\textit{Initial distance}\ (\text{mm})/\textit{duration of recording}\ (\text{min})}$$

Gastrointestinal blood flow and hemodynamics

During the experiment, the blood flow to the gastrointestinal tract was measured from the superior mesenteric artery by an ultrasonic flow meter (Transonic Systems Inc., Ithaca, NY, U.S.A.). Hemodynamic data including the mean aortic pressure and the online monitoring of venous oxygen saturation (SvO_2) in the inferior vena cava were monitored, respectively, by an arterial line pressure transducer through the femoral artery, and a Swan-Ganz catheter (Baxter Healthcare Corp., Irvine, CA, U.S.A.) inserted via the femoral vein. These parameters were registered at the similar time points to sonomicrometric measurement. Hemodynamic energy represented by the energy equivalent pressure (EEP) delivered to the gastrointestinal tract either by the pulsatile or nonpulsatile perfusion was calculated with the following formula: EEP (mm Hg) = $(\int fpdt)/(\int fdt)$, where f is the organ blood flow (mL/min), P is the aortic pressure (mm Hg), and dt is the change in time at the end of flow and pressure cycle.

Statistics

Quantitative sonomicrometric data are expressed as mean and the SE of the mean. Data processing and statistical analysis were carried out with the SPSS software (SPSS Inc., Chicago, IL, U.S.A.). A two-way analysis of variance test with repeated measures was performed to examine the significance between the two groups with group-time interaction.

Differences between each time point were examined by the student *t*-test. Association between sonomicrometric activity and gut blood flow was examined by the Pearson's correlation coefficient. A P value of less than 0.05 was considered statistically significant.

RESULTS

Qualitative measurement on the pattern of gut movement

In general, regular movement of the gastrointestinal tract either along the longitudinal or the vertical direction of the pylorus was detected before the start of CPB (Fig. 1). Under the hypothermic conditions during CPB, when the body temperature was cooled down to 32°C, the rhythmic activity of the pylorus disappeared and it was accompanied with a few gut contractions in high amplitude (Fig. 2). At the end of CPB when the body temperature rewarmed to 37°C, the gut rhythmic activity was basically restored. However, there still appeared some irregular large gut movement (Fig. 3).

Quantitative measurement using the TSA

At the baseline, the calculated TSA of gut movement along the longitudinal direction of the pylorus was 63 ± 15 units/min in the nonpulsatile group and 55 ± 6 units/min in the pulsatile group. It changed little in both groups when the animals were perfused 5 min on CPB. A significant drop of TSA was found at 30 min (20 ± 4 units/min, $P < 0.05$) and 60 min (25 ± 4 units/min, $P < 0.05$) after the start of CPB in the nonpulsatile group when the animals were cooled down to 32°C in body temperature. During the similar period of time under hypothermia, there was also a slight nonsignificant drop of TSA in the pulsatile group (41 ± 15 units/min at 30 min and 47 ± 20 at 60 min). TSA rebounded to 76 ± 24 and 86 ± 24 units/min, respectively, in the nonpulsatile and the pulsatile group at 90 min after the start of CPB when animals were rewarmed to 37°C. This high sonomicrometric activity was maintained toward the end of

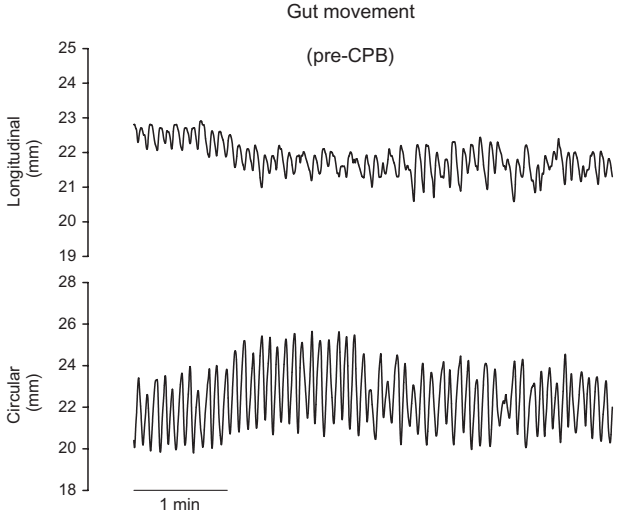

FIG. 1. Regular rhythmic movement of the gastrointestinal tract before the start of CPB (pre-CPB) as detected by sonomicrometric measurement either along the longitudinal or the circular direction of the pylorus. Data were sample traces recorded from one experiment in the nonpulsatile group.

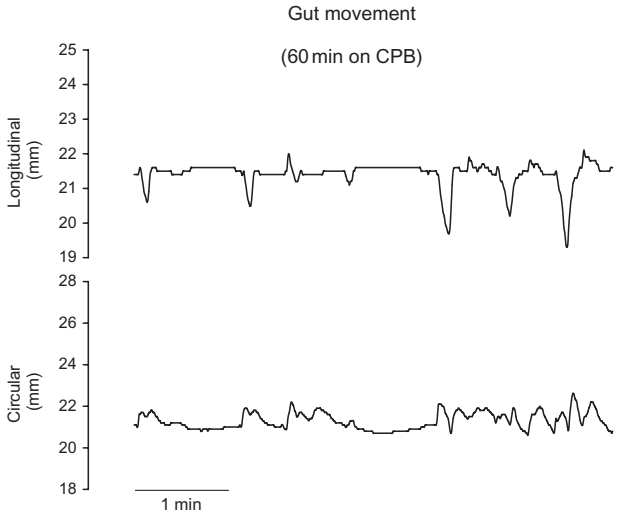

FIG. 2. Regular rhythmic movement of the gastrointestinal tract disappeared at 60 min after the start of CPB (60 min on CPB) when the pig was under systemic hypothermia (32°C), replaced by a few gut contractions with high amplitude detected by sonomicrometry.

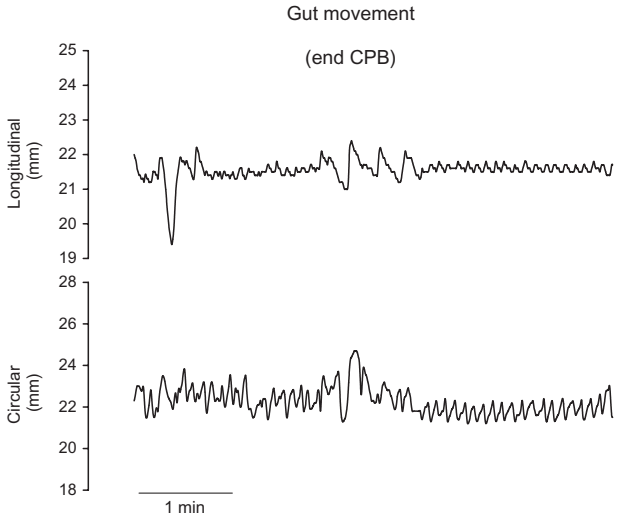

FIG. 3. The sonomicrometric measurements show that the movement rhythm of the gastrointestinal tract resumed, although low in amplitude, at the end of CPB (end-CPB) when the body temperature had been rewarmed to 37°C.

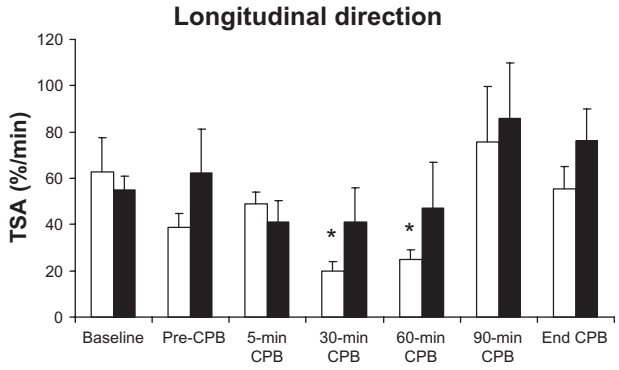

FIG. 4. Gut movement calculated as the TSA from the longitudinal direction of the pylorus during porcine CPB with either the nonpulsatile (open bar box) or the pulsatile flow (closed bar box). TSA reduced significantly in the nonpulsatile group at 30 and 60 min of CPB during the hypothermic phase of CPB when the body temperature dropped to 32°C. Asterisks (*) signify $P < 0.05$ in comparison with the baseline.

CPB. There was no significant difference between the two groups (Fig. 4). TSA along the circular direction was somewhat unstable in a few experiments at the baseline. During CPB, it dropped, respectively, at 30 and 60 min in almost the same pattern as the longitudinal direction in both the nonpulsatile and pulsatile group (Fig. 5).

Gastrointestinal blood flow

The baseline measurement of the blood flow to the superior mesenteric artery was 312 ± 44 mL/min in the nonpulsatile group and 415 ± 71 mL/min in the pulsatile group. This large variation of blood flow did not correlate with the body weight ($r = 0.112$). At 60 min after the start of CPB when the animals were under hypothermia, blood flow to the superior mesenteric artery was 202 ± 60 mL/min in the nonpulsatile group and 343 ± 61 mL/min in the pulsatile group. During the remaining perfusion period until the release of the aortic cross clamp, the blood flow to the superior mesenteric artery was slightly lower in the nonpulsatile group than in the pulsatile group, but the difference was not statistically significant. Gut blood flow did not correlate with the TSA.

Hemodynamics

The mean aortic pressure was 84 ± 8 mm Hg in the nonpulsatile group and 82 ± 4 mm Hg in the pulsatile group at baseline. It dropped to 59 ± 8 and 72 ± 5 mm Hg, respectively, in the nonpulsatile and pulsatile groups 60 min after the start of CPB under hypothermia, and it recovered to 64 ± 4 and 71 ± 8 mm Hg in either groups at the end of CPB. The calculated EEP to the gastrointestinal region was 59 ± 21 mm Hg in the nonpulsatile group and 82 ± 9 mm Hg in the pulsatile group ($P < 0.05$) at 60 min of CPB. Neither blood flow to the superior mesenteric artery nor calculated EEP correlated with gut TSA. Hemodilution as indicated by the hematocrit level was found similar between the two groups, being 25.2 ± 1.2 and $25.0 \pm 1.1\%$, respectively, measured at 60 min after the start of CPB. The online monitoring of SvO_2 was significantly higher in the pulsatile group than in the nonpulsatile group 60 min after the start of CPB (62 ± 10 vs. $49 \pm 7\%$, $P < 0.05$), but there was no significant difference between the two groups after the release of the aortic cross clamp until the end of CPB. There was no correlationship between SvO_2 and the TSA.

DISCUSSION

The gastrointestinal tract is known to be affected by CPB, but little is known about the movement behavior of the gut during CPB (4–9). In this study, we deployed the method of sonomicrometry to qualitatively and quantitatively detect the motility of the gastrointestinal tract. It was found that during the hypothermic phase of CPB, the gut lost its regular rhythmic activity in comparison with its movement pattern before CPB. As a result, there was also a significant drop of the TSA during the hypothermic period of CPB. However, we did not observe a significant difference between the pulsatile and nonpulsatile perfusion flows in gut motility.

Sonomicrometry is the measurement of distance using ultrasound. Transducers commonly called echo crystals can transmit and receive the ultrasound signals from each other within a biological medium at a known velocity. This basic principle of distance mea-

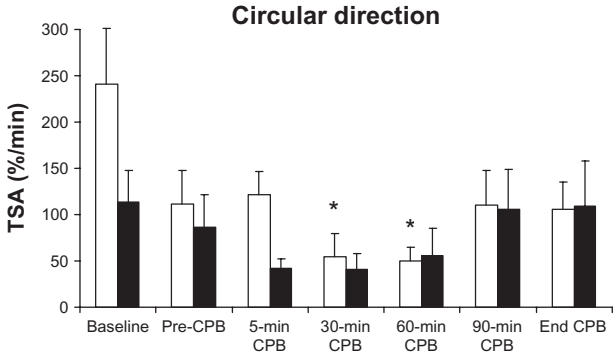

FIG. 5. TSA representing the movement gastrointestinal tract along the circular direction of the pylorus during porcine CPB with either the nonpulsatile (open bar box) or the pulsatile flow (closed bar box). TSA reduced in the nonpulsatile group at 30 and 60 min of CPB during the hypothermic phase of CPB when the body temperature dropped to 32°C. Asterisks (*) signify $P < 0.05$ in comparison with baseline.

surement between crystals makes it possible to accurately record the change of myocardial segment length during heart movement (10–12). For the gastrointestinal system, there are only limited reports in literature using sonomicrometry to study gut motility. In an earlier study, the sonomicrometric technique had been applied to study the motility of canine pylorus (13). However, due to the irregular movement of the gut and the lack of appropriate analytical software to remove the recorded artifacts, there was hardly any progress in using this technique until recently, when Adelson and coworkers reported their experimental work in rats (14). In their study, the sonomicrometric measurement was found to be a reliable method in detecting gastrointestinal response to intravenous injection of cholecystokinin. In the current study, we utilized the similar method described by Adelson and coworkers, but we did so in large animals in a model mimicking the clinical CPB procedure.

Pulsatile perfusion flow is assumed to be beneficial in maintaining gastrointestinal motility because it generates more EEP than the nonpulsatile flow, thus supplying the gut tissue with more hemodynamic energy (16,17). Previous studies have shown that pulsatile flow was associated with an improvement in renal blood flow (18,19). Also, we have reported that implementation of an intra-aortic pulsatile catheter pump to augment abdominal organ perfusion during CPB resulted in significantly higher EEP to the abdominal organs (15). In the current study, however, we did not observe a significant improvement in gastrointestinal motility in animals perfused with the pulsatile flow, although the animals perfused with the nonpulsatile lost more gut mobility during CPB compared to its own baseline activity. This lack of efficiency of pulsatile flow on gastrointestinal mobility is likely due to the adverse effect of hypothermia that had neutralized the beneficial effect of pulsatile flow (20,21). Our results obtained from the current study is thus in agreement with the findings of Ohri and coworkers that although pulsatile flow during CPB was beneficial for gastric mucosal perfusion in patients perfused with the normothermia protocol, the advantage of pulsatility was lost when patients were perfused under hypothermia (22).

Apparently, according to our observation, the gastrointestinal motility during CPB is neither in association with the mesenteric blood flow nor with hemodynamic parameters such as EEP and SvO_2. Although we found a decrease in blood flow to the gastrointestinal flow during hypothermic CPB, this flow drop did not correlate with the TSA. However, a decreased mesenteric blood flow as a result of reduced systemic blood flow did cause an inadequate tissue oxygenation in the gastrointestinal tract (23), a metabolic disturbance that may influence the gastrointestinal motility (24). Furthermore, it is unclear whether Pavulon, a skeletal muscle relaxation drug used during the experiment, would have influenced the gastrointestinal smooth muscles. Overall, the mechanisms of reduced gastrointestinal motility found during the hypothermic CPB need to be further elucidated.

In conclusion, sonomicrometry is a reliable method in detecting the gastrointestinal motility in a large animal model of CPB surgery, by which the measurement can be achieved both qualitatively and quantitatively. Furthermore, this study demonstrates that the pulsatile flow does not seem to be better than the nonpulsatile flow in maintaining the gastrointestinal motility during CPB. Suppression of gut motility during CPB is likely due to the reduced body temperature during the hypothermic phase of CPB, which may in turn contribute to gastrointestinal dysfunction during and after CPB surgery.

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