Small bowel tonometry is more accurate than gastric tonometry in detecting gut ischemia

KEITH R. WALLEY, BYRON P. FRIESEN, MICHAEL F. HUMER, AND P. TERRY PHANG
Program of Critical Care Medicine, Department of Surgery and Pulmonary Research Laboratory, St. Paul’s Hospital, University of British Columbia, Vancouver, British Columbia, Canada V6Z 1Y6

Walley, Keith R., Byron P. Friesen, Michael F. Humer, and P. Terry Phang. Small bowel tonometry is more accurate than gastric tonometry in detecting gut ischemia. J. Appl. Physiol. 85(5): 1770–1777, 1998.—Gastric tonometer PCO2 measurement may help identify gut ischemia in critically ill patients but is frequently associated with large measurement errors. We tested the hypothesis that small bowel tonometer PCO2 measurement yields more accurate information. In 10 anesthetized, mechanically ventilated pigs subject to progressive hemorrhage, we measured gut oxygen delivery and consumption. We also measured tonometer PCO2 minus arterial PCO2 (ΔPCO2) and calculated the corresponding intracellular pH from tonometers placed in the stomach and jejunum. We found that the correlation coefficient (r2) for biphasic gut oxygen delivery-ΔPCO2 relationships was 0.29 ± 0.52 for the gastric tonometer vs. 0.76 ± 0.25 for the small bowel tonometer (P < 0.05). In addition, the critical gastric tonometer ΔPCO2 was excessively high and variable (62.9 ± 39.6) compared with the critical small bowel tonometer ΔPCO2 (17.0 ± 15.0, P < 0.01). Small bowel tonometer PCO2 was closely correlated with superior mesenteric vein PCO2 (r2 = 0.81, P < 0.001), whereas gastric tonometer PCO2 was not (r2 = −0.13, P = not significant). We conclude that measurement of gastric tonometer PCO2 yields excessively noisy and inaccurate data on the onset of gut anaerobic metabolism in hemorrhagic shock. Small bowel tonometer PCO2 is less noisy and, as a result, is superior in detecting gut hypoperfusion and the onset of anaerobic metabolism.

gastric tonometry; small bowel tonometry; intracellular pH; mesenteric ischemia

TONOMETRIC MEASUREMENT of gastric PCO2, and the subsequent calculation of intracellular pH (pHi) (6), is an attractive clinical measurement for several reasons. A greatly elevated tonometer PCO2 measurement, and, by inference, tissue PCO2, suggests the presence of tissue anaerobic metabolism (2, 25), resulting in proton formation (12) and titration of bicarbonate-based buffer systems to produce CO2. A less severely elevated gastric tonometer PCO2 suggests a relative imbalance between local tissue perfusion and metabolic demands (25). Thus, clinically, an increase in tonometer PCO2 is useful in detecting inadequate tissue perfusion even if it has not progressed to frank anaerobic metabolism (28). Gastric tonometer PCO2 measurements have been suggested to be particularly useful in critically ill patients because the gut may become ischemic before other organ systems in hypoperfusion states (7, 20) so that an elevated gastric tonometer PCO2 may be an early and sensitive signal of inadequate perfusion (2, 4). These potentially important measurements have generated a great deal of enthusiasm because they are easily measured clinically by using a device no more invasive than the ubiquitous nasogastric tube in critically ill patients (8). Several important studies have shown potential for significant clinical benefit by using gastric tonometry (4, 8, 9, 15, 16, 18).

Despite the promise of clinical utility, the routine use of gastric tonometers in management of critically ill patients has not been fully embraced in very many critical care units around the world. This is due, in part, to the observation that gastric tonometer PCO2 measurements are noisy, so, although average values in groups of patients may be predictive, they are much less valuable in guiding care in individual patients (23). A number of problems have been identified. Reflux of alkaline duodenal contents into the acidic stomach, or back diffusion of gastric mucosal bicarbonate, produces a significant amount of CO2 unrelated to tissue hypoperfusion (11). Therefore, H2-antagonist treatment has been used when gastric tonometric measurements are to be made (11). Gastric mucosal acid-base balance is complex so that the relationship between pHi and tissue perfusion may not be straightforward (2, 23). In addition, the anatomic blood supply to the stomach is more extensive than that to the small bowel so that the stomach may not be particularly reflective of gut ischemia. Measurement of tonometer-solution PCO2 is another potential source of error (27). Strategies to improve tonometric PCO2 measurement could potentially contribute to the clinical utility of these measurements in critically ill patients.

Because the small bowel is not encumbered with the same problems as the stomach, we postulated that tonometric PCO2 measurements in the small bowel may be superior to those in the stomach. Accordingly, in anesthetized pigs subject to progressive hemorrhage we tested the hypothesis that small bowel tonometer PCO2 measurement is less noisy than gastric tonometer PCO2 measurement and is superior in identifying the onset of gut ischemia.

METHODS

This study was approved by the Animal Care Committee of the University of British Columbia, and the animals were handled in accordance with Canadian and National Institutes of Health guidelines.

Instrumentation. Ten pigs (29 ± 6 kg) were fasted for 12 h and treated with ranitidine (150 mg iv) 2 h before experimentation. The pigs were then sedated with ketamine (500 mg im), followed by thiopental sodium (125–250 mg iv). Anesthesia was maintained during the experiment with halothane (0.5–1.5%) inhalation and ketamine infusion (0.75 μg·kg−1·min−1 iv). The pigs were ventilated via a tracheotomy with a tidal volume of 12 ml/kg at a rate adjusted to maintain arterial PCO2 from 37 to 42 Torr. The inspiratory O2
fraction was set at 0.95 during instrumentation and at 0.21 after instrumentation for the duration of the experiment. A low-compliance catheter was inserted into the left common carotid artery for arterial blood sampling and continuous recording of blood pressure and heart rate. Fluid and drugs were infused through a catheter inserted in the left external jugular vein. A Swan-Ganz catheter was inserted through the right internal jugular vein and advanced into the pulmonary artery for mixed venous blood sampling, temperature measurement, and for measurement of central venous pressure, pulmonary artery pressure, and pulmonary artery occlusion pressure.

A midline laparotomy was performed. The second part of the duodenum and the superior rectal vein at the promontory of the sacrum were tied off to ensure that venous blood from the gut passed through the superior mesenteric vein. Superior mesenteric venous flow was measured by placement of a 1.5-cm ultrasonic flow probe (Transonic Systems, Ithaca, NY) around the superior mesenteric vein just proximal to the junction with the splenic vein. The splenic vein and artery were tied off to prevent autotransfusion, and a catheter to sample superior mesenteric venous blood was inserted via the splenic vein. Tonometers (Tonometrics, Datex Engstrom, Helsinki, Finland) were primed with normal saline. A gastric tonometer was placed in the stomach via the mouth and esophagus. The position was checked manually by palpating the stomach gently. Gastric contents were allowed to drain by gravity after irrigation of the stomach with saline. A small enterotomy was made in the jejunum ~1 m distal to the ligament of Treitz, and a tonometer was advanced 15 cm into the jejunum and fixed in place with suture.

After hemostasis was ensured, the abdominal contents were then carefully returned to the abdomen, the abdomen was closed, and the animals were warmed to ~37.5°C and allowed to stabilize for 30 min. During surgery and stabilization, 500 ml normal saline were intravenously infused. Protocol. After instrumentation and stabilization, oxygen delivery was decreased by hemorrhage of between 2 and 4 ml of blood/min by using a constant-withdrawal pump. Data were measured at the end of the stabilization period (baseline) and then at 30-min intervals during progressive hemorrhage. At each data set, measurements were made of hemodynamic parameters, gut oxygen consumption and delivery, and gastric and small bowel tonometer PCO₂.

In additional control experiments, five pigs were instrumented in exactly the same way. Five repeated measurements at 30-min intervals during aerobic metabolism were performed to determine the baseline variability of gastric and small bowel tonometer PCO₂. All measurements were performed in exactly the same fashion as in the 10 hemorrhagic pigs and at the same time intervals.

Measurements. All expired gas from the sealed ventilator circuit was diverted through a previously validated (22) metabolic monitor (Datex, MRB-1000, Datex) to measure whole body oxygen consumption. Values were determined at each measurement as an average over a 3-min interval. Arterial, mixed venous, and gut venous hemoglobin and oxygen saturations were measured by using an IL 482 CO-oximeter (Instrumentation Laboratories, Lexington, MA). Corresponding blood-gas measurements and tonometer PCO₂ measurements corrected for body temperature were made by using an ABL 30 blood-gas machine (Radiometer, Copenhagen, Denmark). To measure tonometer PCO₂, the first 5 ml of saline were discarded and 2 ml saline from the tonometer catheters were then sampled anaerobically. PCO₂ was measured within 60 s of sampling in all cases. In separate experiments, the flow probe was calibrated in vivo against volumetric flow measurements by utilizing a mesenteric-brachiocephalic shunt for collection of timed volumes over a range of flows from 20 to 800 ml/min and was found to have a mean difference of 0 ± 8% over this range.

Postmortem, retrograde dye injection into the superior mesenteric vein confirmed that venous drainage of the gut being studied was confined to gut between ligatures. The gut from the postpyloric duodenum to the proximal rectum was excised, evacuated, and weighed to express oxygen transport variables per kilogram gut weight.

Analysis. Blood oxygen content was calculated as hemoglobin (g/dl) × 1.39 × blood oxygen saturation (%)+ 0.003 × blood oxygen tension (Torr). Cardiac output was calculated, by using the Fick principle, as whole body oxygen consumption divided by the difference between arterial and mixed venous oxygen contents. Whole body oxygen delivery was calculated as cardiac output multiplied by arterial oxygen content. Gut oxygen delivery (ml O₂·kg⁻¹·min⁻¹) was calculated as superior mesenteric vein blood flow multiplied by arterial oxygen content. Gut oxygen consumption (ml O₂·kg⁻¹·min⁻¹) was calculated as superior mesenteric vein blood flow multiplied by the difference between arterial and gut venous oxygen contents.

Tonometer pH was calculated by using the Henderson-Hasselbalch equation as

\[ \text{pH}_1 = \text{pK}_a + \log_{10}\left(\frac{\left[\text{HCO}_3^\right]}{\left(\text{tonometer PCO}_2 \times k \times 0.03\right)} \right) \]

where acidic dissociation constant (pK_a) = 6.1, [HCO₃⁻] is arterial blood-gas bicarbonate concentration (mmol/l), and tonometer PCO₂ (Torr) is multiplied by a correction factor, k, for an equilibration time of 30 min (k = 1.26, as supplied by Tonometrics).

Gastric ΔPCO₂ equals gastric tonometer PCO₂ minus arterial PCO₂. Small bowel ΔPCO₂ equals small bowel tonometer PCO₂ minus arterial PCO₂.

Biphasic relationships between whole body oxygen delivery and consumption as well as between gut oxygen delivery and consumption were plotted for each animal. In addition, gut oxygen delivery was plotted against gastric ΔPCO₂, gastric pH, small bowel ΔPCO₂, and small bowel pH. We used Samsel and Schumacker's (24) dual-line regression to fit two lines to each of these biphasic relationships. We determined the critical oxygen delivery as the point of intersection of the two lines. The critical oxygen delivery point from the gut oxygen delivery vs. consumption relationship was used to indicate the onset of gut ischemia.

To reflect the scatter of data points around the biphasic linear relationships, the correlation coefficient r² was calculated as 1 minus the sum of squared residuals divided by the sum of squared differences from the mean. We used paired t-tests to test for differences between gastric and small bowel tonometric measurements, choosing P < 0.05 as significant. We used the method of Bland and Altman (1) to compare tonometer PCO₂ measurement with superior mesenteric vein PCO₂ measurement. Data are reported as means ± SD.

RESULTS

Progressive hemorrhage resulted in biphasic relationships between whole body oxygen delivery and consumption (Fig. 1A), with an average r² of 0.92 ± 0.14 and a critical oxygen delivery of 9.5 ± 2.3 ml O₂·kg⁻¹·min⁻¹. Similarly, biphasic gut oxygen delivery-consumption relationships (Fig. 1B) were observed with an average r² of 0.92 ± 0.08, identifying a gut critical oxygen
delivery of 20.3 ± 5.7 ml O$_2$·kg$^{-1}$·min$^{-1}$. In 8 of 10 animals, the onset of gut anaerobic metabolism occurred before whole body anaerobic metabolism, on average for the group, at a whole body oxygen delivery of 12.5 ± 5.2 ml O$_2$·kg$^{-1}$·min$^{-1}$ (P < 0.05 compared with whole body critical oxygen delivery of 9.5 ± 2.2 ml O$_2$·kg$^{-1}$·min$^{-1}$).

In the 10 hemorrhagic animals, the onset of anaerobic metabolism occurred in the sixth to tenth half-hourly measurement set (at the 2.5- to 4.5-h-after-baseline set at time 0). There was no significant difference in ∆PCO$_2$ over time for the first four measurements in each animal. Thus measurable increases in ∆PCO$_2$ due to low flow had not yet occurred. Therefore, we took the first four measurements during aerobic metabolism to define, in each animal, the mean and 95% confidence intervals for ∆PCO$_2$ in that animal. In all 10 animals, small bowel ∆PCO$_2$ increased outside of these 95% confidence intervals at 7.3 ± 2.5 measurement sets (on average at 3.15 h after baseline), whereas the onset of anaerobic metabolism (critical oxygen delivery point) occurred at 7.4 ± 1.6 measurement sets (on average at 3.2 h after baseline). Thus small bowel ∆PCO$_2$ exceeded the 95% confidence interval in each animal at almost the same time as the onset of anaerobic metabolism. Variability in the first four measurements during aerobic metabolism was much greater for gastric ∆PCO$_2$ (width of 95% confidence interval 45 ± 26 Torr) than for small bowel ∆PCO$_2$ (12 ± 12 Torr, P < 0.005). As a result, gastric ∆PCO$_2$ in five animals did not exceed the 95% confidence intervals at any time. In the other five animals gastric ∆PCO$_2$ increased outside the 95% confidence intervals at 8.2 ± 3.0 measurement sets, whereas the onset of anaerobic metabolism occurred at 7.0 ± 1.6 measurement sets.

An alternative approach is to use the 95% confidence intervals from the five control animals to define the ∆PCO$_2$ threshold, recognizing that these data include additional interanimal variability. Repeated measurements in the five control experiments during aerobic metabolism demonstrated a mean gastric ∆PCO$_2$ of 33 ± 39 Torr and a mean small bowel ∆PCO$_2$ of 9 ± 12 Torr. Interanimal variability in gastric ∆PCO$_2$ accounted for >99% of total variability in these data (interanimal mean square divided by total mean square >99%). Thus there were marked differences in ∆PCO$_2$ among different control animals. In contrast, intra-animal variability was small (intra-animal mean square divided by total mean square <1%), which indicates that ∆PCO$_2$ measured repeatedly within one animal was quite stable. ∆PCO$_2$ in individual animals exceeded the group threshold value (upper 95% confidence interval value was 33 Torr) in 8 of 10 animals at 7.1 ± 3.2 sets. In 2 of 10 animals, this threshold value derived from control animals was not exceeded. In contrast, gastric ∆PCO$_2$ exceeded the group threshold value (upper 95% confidence interval value was 110 Torr) in only 5 of 10 animals on average at 4.6 ± 3.5 sets, essentially unrelated to the true onset of anaerobic metabolism. In the other 5 of 10 animals, this threshold value derived from control animals was not exceeded.

Biphasic relationships resulted from plots of gut oxygen delivery vs. gastric pH$_i$, small bowel pH$_i$, gastric ∆PCO$_2$, and small bowel ∆PCO$_2$ (Fig. 2). However, the correlation of small bowel pH$_i$ data points with dual regression lines was significantly greater than the correlation of gastric pH$_i$ data points (P < 0.01) (Fig. 3). Also striking were the differences in gut oxygen delivery-∆PCO$_2$ relationships, where the correlation with dual-line regression for the small bowel ∆PCO$_2$ was greater than the correlation for gastric tonometer ∆PCO$_2$ measurements (Figs. 2 and 4). These data indicate that there was significantly less scatter in small bowel tonometer measurements compared with gastric tonometer measurements around the biphasic relationships.

The critical gastric ∆PCO$_2$ was high and variable (62.9 ± 39.6 Torr), resulting in a low critical gastric pH$_i$ (7.04 ± 0.14). In contrast, the critical small bowel ∆PCO$_2$ was smaller (17.0 ± 15.1, P < 0.01) and less variable (SD 39.6 vs. 15.1, significantly different, P < 0.01) (Fig. 5). As a result, the critical small bowel pH$_i$
(7.29 \pm 0.15) was greater than the critical gastric pH \( i \) (7.04 \pm 0.14, P < 0.01).

Because tonometer and venous PCO2 measurements should reflect tissue PCO2, we compared both gastric tonometer PCO2 and small bowel tonometer PCO2 measurements with superior mesenteric vein PCO2 from all measurement sets in all animals. We used this as an independent assessment of whether gastric or small bowel tonometer measurements were superior in assessing tissue PCO2 in the regional circulation of the gut. Small bowel tonometer PCO2 was closely correlated with superior mesenteric vein PCO2 (\( r^2 = 0.81, P < 0.001 \)), whereas gastric tonometer PCO2 was not (\( r^2 = -0.13, P = \text{not significant} \)) (Fig. 6). By using a Bland-Altman analysis (1), small bowel tonometer PCO2 was significantly more closely related to superior mesenteric vein PCO2 both in mean (P < 0.05) and in the two SD intervals (P < 0.05) (Fig. 7).
To determine whether gastric or small bowel tonometry was best at identifying the onset of gut ischemia, as determined from gut oxygen delivery-consumption relationships, we compared the difference in gut critical oxygen delivery points. There was a small difference in the gut critical oxygen delivery determined from gut oxygen delivery-consumption relationships vs. gut oxygen delivery-small bowel $\Delta$PCO$_2$ relationships (mean difference in estimate of critical gut oxygen delivery $4.4 \pm 3.5$ ml O$_2$·kg$^{-1}$·min$^{-1}$). However, there was significantly greater disparity in estimates of the gut critical oxygen delivery from gut oxygen delivery-consumption relationships and gut oxygen delivery-gastric $\Delta$PCO$_2$ relationships (mean difference 9.3 $\pm$ 5.8 ml O$_2$·kg$^{-1}$·min$^{-1}$, $P < 0.05$).

**DISCUSSION**

Our key findings are that, in this large-animal model, gastric tonometer PCO$_2$ and pH$_i$ measurements were noisy compared with small bowel tonometer PCO$_2$ and pH$_i$ measurements. This resulted in excessively high and variable estimates of gastric $\Delta$PCO$_2$ and pH$_i$ at the onset of gut ischemia. The 95% confidence intervals for gastric $\Delta$PCO$_2$ were wide so that values outside this range did not occur consistently, even though hemorrhagic shock progressed to death. In contrast, small bowel $\Delta$PCO$_2$ exceeded the 95% confidence intervals in all cases at approximately the onset of anaerobic metabolism. Gastric tonometer PCO$_2$ was not closely correlated with superior mesenteric vein PCO$_2$ measurements, and critical oxygen delivery points derived from these measurements were not closely related to the critical oxygen delivery points determined from biphasic gut oxygen delivery-consumption relationships. Small bowel tonometric PCO$_2$ measurement (and the derived pH$_i$ calculation) was superior in all of these respects. This suggests the possibility that small bowel tonometric PCO$_2$ measurement may be clinically useful.

Part of the reason why measures of gut perfusion, such as tonometer PCO$_2$, may be useful is that the gut may be an organ that is particularly sensitive to systemic hypoperfusion (7, 20). For example, Nelson and colleagues (20) found in dogs that the onset of oxygen supply dependency occurred earlier in the gut than in the whole body. Our results confirm these previous observations, supporting the notion that evidence of gut hypoperfusion or ischemia may be an early indicator of inadequate systemic perfusion. In addition, gut ischemia may be important in the pathogenesis of a systemic inflammatory response (5, 7). Intestinal permeability increases after gut ischemia (3), resulting in leakage of bacteria and bacterial products into the portal circulation (10). This results in activation of hepatic Kupffer cells (14) and circulating leukocytes (13, 26). A number of investigators have suggested that
this initiates a subsequent systemic inflammatory response, which may result in distal organ damage and dysfunction (13, 26). Thus there is a strong physiological rationale for monitoring gut perfusion in critically ill patients.

Indeed, a number of studies demonstrate that tonometry may be a useful clinical tool. Gutierrez and colleagues (8) found that, in critically ill patients with an initial gastric tonometer $pH_i > 7.35$, if tonometer-derived $pH_i$ subsequently fell below 7.35, then resuscitation with fluids and dobutamine significantly improved survival. Mohsenifar and colleagues (18) have demonstrated in critically ill patients that a low $pH_i$, calculated from gastric juice $PCO_2$, predicts failure of spontaneous ventilation at the time of extubation. Studies by Marik (15) and by Maynard and colleagues (16) suggest that gastric tonometer-derived $pH_i$ is a more robust predictor of outcome in critically ill patients than hemodynamic measurements and other common predictors. Similarly, Mohsenifar and colleagues (17) found that $pH_i$ was a better predictor of outcome than all other presently used parameters in hemodynamically stable, mechanically ventilated patients. A $pH_i < 7.25$ had a sensitivity of 86% and a specificity of 83% in predicting mortality (17). Thus tonometry has the potential to play an important role in the intensive care unit, adding to other hemodynamic and physiological data in assessing adequacy of perfusion and enhancing prognostic measures, which include severity-of-illness scoring systems such as APACHE II. However, there are problems with gastric tonometer measurements that may have contributed to its limited use in many intensive care units as a clinical tool in individual critically ill patients.

Gastric tonometer $PCO_2$ measurement may be noisy and not accurately reflect gut intramural $PCO_2$ for several reasons. First, the acid-generating gastric mucosa may make the stomach a poor site for tonometry. Accurate gastric tonometry may require pretreatment with $H_2$ antagonists or a proton-pump inhibitor to prevent significant $CO_2$ generation when gastric mucosal bicarbonate diffuses into the lumen or when duodenal contents reflux through the pylorus into the acidic stomach (11). $CO_2$ production from titrating acid and base in this way yields erroneous information because it is unrelated to tissue perfusion. Despite our administration of a high dose of an $H_2$ antagonist in this study, it is conceivable that this effect may have contributed somewhat to our results. Furthermore, gastric intramural $PCO_2$ may not be an accurate reflection of gut intramural $PCO_2$ because the gastric arterial blood supply is more extensive than the blood supply of the gut, which is predominantly via the superior mesenteric artery. Thus gut ischemia does not necessarily indicate gastric ischemia. The lack of correlation between gastric $PCO_2$ and superior mesenteric vein $PCO_2$ and the close correlation between small bowel $PCO_2$ and superior mesenteric vein $PCO_2$ support the idea that it is best to consider the stomach and small bowel to be two different regional circulations. Problems common to all tonometry include that tonometer-measured $PCO_2$ requires a prolonged equilibration time so that a correction factor must be introduced to account for incomplete $CO_2$ equilibration (2). In addition, Takala and colleagues (27) have pointed out that measurement of $PCO_2$ in tonometer saline can introduce marked errors (27). Improved measurements with buffered solutions suggest that tonometry must be carefully done to avoid diffusion of $PCO_2$ from the tonometer solution into the atmosphere.

We found that small bowel tonometer $PCO_2$ measurements appeared to be more accurate and less variable than gastric tonometer $PCO_2$ measurement. Although both gastric and small bowel tonometry detect ischemia (19), compared with gastric tonometry, small bowel tonometry appears to reduce the variability of individual measurement points around biphasic oxygen delivery-consumption relationships and appears to reduce the variability of the critical $\Delta PCO_2$ and $pH_i$. Small bowel tonometry led to a closer estimate of the onset of gut ischemia, as determined from gut oxygen delivery-consumption relationships. The observation that small bowel tonometer $PCO_2$ was closely related to superior mesenteric vein $PCO_2$, whereas gastric tonometer $PCO_2$ was not, suggests that small bowel tonometer $PCO_2$ is the more accurate measurement. By improving the accuracy of tonometer measurements, small bowel tonometry may conceivably improve on the clinical utility of present gastric tonometry. Obviously, surgical placement of a small bowel tonometer, as in this animal experiment, is not clinically realistic. However, the increasing use of duodenal and jejunal feeding tubes in critically ill patients suggests a feasible clinical route.

Our data do not resolve the partly semantic issue of whether $\Delta PCO_2$ measurement or $pH_i$ calculation should be used. $pH_i$ is fundamentally more important than extracellular $pH$ in altering cellular function, including cardiac muscle contraction, synthetic function, and work by cellular membrane ion pumps (29). Fiddian-Green (6) popularized the idea that gastric tonometer measurements of $pH_i$ may reflect intramural $pH$ and, by inference, $pH_i$. Therefore, there was theoretical reason to suspect that tonometer $pH_i$ may be of fundamental importance in assessing tissue acidosis and would be an independent contributory parameter in evaluating hypoperfusion states in critically ill patients (6). However, the calculation of $pH_i$ involves a number of assumptions that are generally not fulfilled (2, 23). For example, the intracellular buffer systems are not predominantly bicarbonate based, and arterial, rather than tissue, bicarbonate measurements are used. Thus these two terms $(pK_a$ and $[HCO_3^-])$ in the three-term Henderson-Hasselbalch equation suffer significant limitations. Schlichtig and Bowles (25) have put tonometer $PCO_2$ measurement on a firm theoretical foundation. They show that decreased flow states will increase tissue, and thus tonometer, $PCO_2$ and that there is a rapid rise in tissue $PCO_2$ at the onset of anaerobic metabolism. There is no need to calculate $pH_i$ because $PCO_2$ measurements can be used directly (2).

On the basis of this, we think that $\Delta PCO_2$ is the appropriate measurement to make. The counterargu-
ment could be made that pH$_i$ is superior because biphasic gut oxygen delivery-pH$_i$ relationships had better correlation coefficients than did gut oxygen delivery-$\Delta$PCO$_2$ relationships. We do not support this line of reasoning because pH$_i$ measurements are less variable due to the logarithmic transformation (Henderson-Hasselbalch equation), which does not improve the value of the measurement in a fundamental way. Furthermore, the inclusion of arterial bicarbonate in pH$_i$ calculation artificially enhances the biphasic relationship because arterial bicarbonate falls as oxygen delivery decreases. This may be considered useful in this controlled setting, starting at a normal acid-base status. However, inclusion of arterial bicarbonate is potentially a detrimental feature in the clinical use of tonometry. For example, patients with primary acid-base disturbances will have erroneously high or low calculated pH$_i$, independent of the presence or absence of true gut ischemia, leading to inappropriate therapy for the critically ill patient (23). Furthermore, during rapid onset of gut ischemia, PCO$_2$ will increase, whereas arterial bicarbonate will not change significantly for a period of time. The difference in pH$_i$ calculation between rapid and slow onset of ischemia once again could lead to clinical confusion and inappropriate management. Therefore, because the primary measurement is PCO$_2$ of the tonometer solution, we agree with a number of other investigators (2, 23, 25) that tonometer PCO$_2$ and, more importantly, the difference in PCO$_2$ between the tonometer solution and arterial blood ($\Delta$PCO$_2$) are the most useful clinical variables.

Surgical instrumentation and measurement techniques may have influenced our results. One possibility is that, in some of the anesthetized, highly instrumented animals in this study, the gastric mucosa was much more susceptible to hemorrhage-induced ischemia than was the gut. Hence the high and variable gastric $\Delta$PCO$_2$. Although this is possible, it is our clinical experience that in patients having septic shock we reasonably frequently observe small bowel ischemia to the point of infarction, whereas we have not yet observed gastric ischemia to the point of infarction. In addition, animal studies suggesting that the gut may become oxygen supply dependent before the whole body have focused on the gut rather than on the stomach (7, 20). The variability of our gastric tonometer PCO$_2$ measurements in control animals was high but similar to other reported values (e.g., 57.2 ± 35.7 Torr in surviving surgical intensive care patients; Ref. 9). Other studies in healthy humans report less variability (48 ± 10 Torr; Ref. 21). It is important to note that >99% of the variability we observed in $\Delta$PCO$_2$ was interanimal variability (individual animal $\Delta$PCO$_2$ differed substantially from other animals), whereas repeated $\Delta$PCO$_2$ measurements within an individual animal were very consistent. Thus the variability in $\Delta$PCO$_2$ among different anesthetized, ventilated, and surgically instrumented pigs was greater than the variability in $\Delta$PCO$_2$ among different healthy humans (21). The tonometer measurements themselves show very little variability when repeated over substantial time intervals in individual animals, suggesting that the tonometer measurements were likely accurate. The concordance of superior mesenteric vein PCO$_2$ and tonometer PCO$_2$ provides independent corroboration of the likely accuracy of the tonometer measurements. The important comparison in our study is between gastric $\Delta$PCO$_2$, which demonstrated high variability, and small bowel $\Delta$PCO$_2$, which demonstrated lower variability. Gastric and small bowel samples were handled in exactly the same manner so that our conclusions likely are not dependent on measurement technique.

In summary, these data suggest that small bowel tonometer PCO$_2$ measurement is superior to gastric tonometer PCO$_2$ measurement in reflecting gut CO$_2$ accumulation, hypoperfusion, and the onset of anaerobic metabolism. This suggests the possibility of enhancing the present clinical utility of gastric tonometer PCO$_2$ and pH$_i$ measurements by small bowel placement of an appropriate tonometer catheter.

Address for reprint requests: K. R. Walley, Pulmonary Research Laboratory, St. Paul’s Hospital, 1081 Burrard St., Vancouver, BC, Canada V6Z 1Y6.

Received 5 November 1997; accepted in final form 25 June 1998.

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