Increased gastric Pco_2 during exercise is indicative of gastric ischaemia: a tonometric study

J J Kolkman, A B J Groeneveld, F G van der Berg, J A Rauwerda, S G M Meuwissen

Abstract

Background—Diagnosis of gastric ischaemia is difficult and angiography is an invasive procedure. Angiographic findings may not correlate with clinical importance.

Aims—To investigate whether tonometric measurement of intragastric Pco_2 during exercise can be used to detect clinically important gastric ischaemia.

Methods—Fourteen patients with unexplained abdominal pain or weight loss were studied. Splanchnic angiography served as the gold standard. Three patients were studied again after a revascularisation procedure. Gastric Pco_2 was measured from a nasogastric tonometer, with 10 minute dwell times, and after acid suppression. Gastric and capillary Pco_2 were measured before, during, and after submaximal exercise of 10 minutes duration.

Results—Seven patients had normal angiograms; seven had more than 50% stenosis in the coeliac (n=7) or superior mesenteric artery (n=4). Normal subjects showed no changes in tonometry. In patients with stenoses, the median intragastric Pco_2 (Pico_2) at rest was 5.2 kPa (range 4.8–11.2) and rose to 6.4 kPa (range 5.7–15.7) at peak exercise; the median intragastric blood Pco_2 gradient increased from 0.0 kPa (range –0.8 to 5.9) to 1.7 kPa (range 0.9 to 10.3; $p<0.01$). Only two subjects had abnormal tonometry at rest; all had supernormal values at peak exercise. The Pco_2 gradient correlated with clinical and gastroscopic severity; in patients reexamined after revascularisation (n=3), exercise tonometry returned to normal.

Conclusion—Gastric tonometry during exercise is a promising non-invasive tool for diagnosing and grading gastrointestinal ischaemia and evaluating the results of revascularisation surgery for symptomatic gastric ischaemia.

(Gut 1999;44:163–167)

Keywords: gastric ischaemia; tonometry; carbon dioxide; exercise test

Symptomatic chronic gastrointestinal ischaemia is rarely diagnosed^{1–4} despite a relatively high prevalence of significant splanchnic atherosclerosis in angiographic^{5–6} and autopsy studies.^{7–8} This discrepancy is explained by the abundant collateral circulation of the gastrointestinal tract, preventing ischaemia if a single

vessel has been occluded.^{1–4} It is therefore widely accepted that surgery is indicated only in patients with multiple vessel occlusions.² In contrast, symptomatic single vessel occlusion, with complete resolution of symptoms after surgery, has been repeatedly reported,^{3–9} and a large retrospective angiographic study found unexplained abdominal complaints to be sevenfold more common in patients with single vessel stenosis than in those with normal angiograms.⁵ The main problem in determining the true incidence of symptomatic splanchnic ischaemia is the lack of a functional test that can identify and grade the severity of gastrointestinal ischaemia.^{3–10} Measurement of intragastric Pco_2 (Pico_2) may be an accurate test for gastrointestinal ischaemia, as ischaemia was invariably associated with an elevated Pico_2 .^{11–14} As most patients with gastrointestinal ischaemia are without symptoms at rest and often have pain postprandially, tonometry during a test meal has been used to provoke ischaemia and to establish the diagnosis.^{15–16} However, a test meal seems unsuitable during tonometry as it may affect the Pico_2 independently of mucosal Pco_2 .¹⁷ We therefore looked for an alternative measure to provoke ischaemia. An exercise test might serve that goal, as it stresses the abdominal vasodilator reserve by diverting blood flow from the splanchnic circulation to the exercising muscles, with a reduction in superior mesenteric artery blood flow of 43%, as shown in healthy subjects.¹⁸

In this study we evaluated the potential value of gastric tonometry during exercise for diagnosing gastrointestinal ischaemia, as compared with angiographic findings, in patients with otherwise unexplained abdominal symptoms.

Methods

The study was conducted according to the guidelines produced by the ethics committee of our institution concerning pilot studies. Fourteen patients (nine women, five men) with a mean age of 56 (range 30–75) years were studied, after informed consent. The medical history was taken and a physical examination performed in all subjects. One patient was enrolled for persisting pain, 18 months after reconstruction for a coeliac artery (CA) compression syndrome; another patient for recurrence of pain 18 months after an abdominal revascularisation procedure for CA and

Abbreviations used in this paper: CA, coeliac artery; IMA, inferior mesenteric artery; Pco_2 , partial pressure of carbon dioxide; Pico_2 , intragastric Pco_2 ; SMA, superior mesenteric artery; cBic, capillary bicarbonate content.

Department of
Gastroenterology,
Medical Spectrum
Twente, Enschede, The
Netherlands
J J Kolkman

Medical Intensive Care
Unit, Free University
Hospital, Amsterdam,
The Netherlands
A B J Groeneveld

Department of
Radiology, Free
University Hospital,
Amsterdam, The
Netherlands
F G van der Berg

Department of
Vascular Surgery, Free
University Hospital,
Amsterdam, The
Netherlands
J A Rauwerda

Department of
Gastroenterology, Free
University Hospital,
Amsterdam, The
Netherlands
S G M Meuwissen

Correspondence to:
Dr J J Kolkman, Medical
Spectrum Twente, PO Box
50,000, 7500 KA Enschede,
The Netherlands.

Accepted for publication
23 September 1998

superior mesenteric artery (SMA) occlusions. The other 12 patients had abdominal pain related to food intake or exercise (n=5), pain combined with weight loss (n=5), or diarrhoea (n=2). The severity of complaints was scored by a symptom score before the tonometry test and angiography on a four point scale: 1, no complaints; 2, minor complaints, no interference with daily activities; 3, moderate complaints, some restrictions of normal daily activities; 4, severe complaints, normal daily activities impossible. In these 12 patients, extensive investigations including gastroscopy, abdominal ultrasonography, barium enema, and abdominal computed tomography had revealed no clues for a diagnosis. In all patients, gastroscopy and angiography were performed within a time frame of two weeks from exercise tonometry. Three patients were reevaluated by angiography and exercise tonometry, one (n=1) or eight weeks (n=2) following reconstructive vascular surgery.

GASTRODUODENOSCOPY

Gastroduodenoscopy was performed within two weeks of tonometry, and the severity of gastroscopic abnormalities was scored on a five point scale: 1, normal findings; 2, oedema; 3, the presence of erosions; 4, localised ulceration; 5, extensive ulceration.

ABDOMINAL ANGIOGRAPHY

Abdominal angiography was performed within two weeks of tonometry, using a Siemens Polytroton (Siemens, Erlangen, Germany) after Ultravist 300 (Schering, Berlin, Germany) as contrast medium. A non-selective bidirectional abdominal aortic angiogram was obtained in all patients, followed by selective angiography of the CA, SMA, and inferior mesenteric artery (IMA), unless the non-selective images showed complete obstruction. The angiograms were judged by two radiologists, blinded to the clinical information, and stenosis was expressed as the percentage change in calibre. When these reports showed conflicting results, a final score was performed to reach consensus. The angiographic findings were scored on a five point scale: 1, normal; 2, more than 50% stenosis of branches; 3, more than 50% stenosis in single main splanchnic vessel; 4, stenosis in two main splanchnic vessels; 5, stenosis in all three splanchnic vessels.

EXERCISE TONOMETRY

For the tonometry study, patients were not allowed to eat or drink from 2200 the night before the day of the study. In the morning, 100 mg of ranitidine was given intravenously to suppress gastric acid secretion.¹⁹ A tonometer (Sigmoid model, Tonometrics, Bethesda, USA), a CO₂ impermeable nasogastric tube with a CO₂ permeable silicone balloon at its tip, was placed intragastrically at 60 cm from the tip of the nose. The Pico₂ was measured as follows. At the start of measurement 2.5 ml saline was infused into the tonometer. After a given dwell time in the tonometer balloon, in this study 10 minutes, the saline was aspirated from the tonometer. The first 1 ml was expelled as it

represents dead space volume, and the Pco₂ was measured from the rest of the saline using a Corning 278 blood gas analyser (Ciba-Corning, Houten, The Netherlands). To calculate steady state Pico₂ during the measurement interval, the measured Pco₂ was multiplied by 1.86, to correct for incomplete equilibration at 10 minutes and the bias of the blood gas analyser.²⁰ An arteriolised capillary blood sample from a warmed finger was drawn, for determination of pH, Pco₂ (Pcco₂), and bicarbonate (cBic) content using the blood gas analyser. The intragastric-blood gradient for Pco₂ was calculated. The Pico₂ was measured twice at rest, during 10 minutes exercise (from 0 to 10 minutes), and three times after exercise: from t=10 to 20, from t=20 to 30, and from t=40 to 50 minutes. The exercise test (from t=0 to 10 minutes) was aimed at a submaximal exercise level of 70–80% of the predicted maximal heart rate²¹ by stepping up and down stairs. The level of exercise was assessed from the percentage of the maximal heart rate at peak exercise²¹ and the decrease in blood bicarbonate content, an indicator of exercise induced anaerobiosis and lactate production.²²

STATISTICAL ANALYSIS

Data are expressed as median and range. The interobserver variability for assessment of angiographic abnormalities was evaluated with the kappa test. Based on the angiographic findings, patients were divided into two groups: those with normal arteries (normal group, n=7), and those with at least one vascular stenosis (stenotic group, n=7). The difference in tonometric parameters between periods was evaluated with the Kruskal-Wallis analysis of variance for repeated measurements followed by a Wilcoxon signed rank test for matched pairs; the differences between groups were evaluated with a Mann-Whitney test. For calculation of sensitivity and specificity of tonometric parameters for the detection of gastric ischaemia, the angiographic findings were used as the gold standard. The normal threshold values were obtained from a human volunteer study²⁰: Pico₂ ≤6.1 kPa, Pco₂ gradient ≤0.8 kPa. The relations between the clinical severity (symptom and gastroscopic score), tonometric parameters, and angiographic severity score, were evaluated using Spearman's rank correlation coefficients. A value of p<0.05 was considered statistically significant.

Results

PATIENT CHARACTERISTICS

Table 1 presents the patients' features. Among patients with stenotic lesions, abdominal pain or discomfort was reported more often compared with those with a normal abdominal angiogram. The triad of abdominal angina (meal related pain, epigastric bruit, and weight loss) was observed in two patients with stenotic lesions.

GASTROSCOPY

In the group with normal angiograms, all subjects had normal gastroscopic findings. In the

Table 1 Clinical characteristics of patients with normal angiograms or stenotic lesions

	Normal group (n=7)	Stenotic group (n=7)
Sex (M/F)	3/4	2/5
Age (years) (range)	56 (32–71)	56 (30–80)
Previous splanchnic artery surgery	0	2
Peripheral vascular disease	2	3
Active smoking (>10 cigarettes/day)	3	5
Pain after a meal	4	5
Pain during exercise	2	6
Weight loss >10%	3	3
Audible epigastric bruit	1	2

Table 2 Sensitivity and specificity for detection of gastric ischaemia

	P_{CO_2}		PCO_2 gradient	
	Sensitivity	Specificity	Sensitivity	Specificity
At rest	29%	100%	14%	100%
Exercise	71%	100%	100%	86%

group with stenotic lesions, two patients had normal findings, one subject showed focal, sharp, delineated white areas with adjacent cyanotic areas, two showed gastritis with erosions, one had gastritis with two ulcers, and one had extensive ulceration in the stomach, with congested mucosa and gastroparesis.

ANGIOGRAPHY

The interobserver agreement between both radiologists was good, with a kappa value of 0.69 for assessment of the roots of the CA, SMA, and IMA and a kappa of 0.88 for the main vessel branches to the stomach. Identification of the left gastric artery and gastroduodenal artery could be achieved in all patients. The right gastric and right and left gastric epiploic arteries could not be identified in four, two, and 12 patients, respectively. In the stenotic group, three patients had occlusion of all three splanchnic vessels, two patients had occlusion of the CA and IMA, one had occlusion of the left gastric artery only, and one had several areas of 50–80% stenosis in branches of the CA and SMA and was later diagnosed as having polyarteritis nodosum.

EXERCISE

The aimed exercise level (70% of maximal predicted heart rate) could not be achieved in two patients with stenotic lesions, because of near exhaustion and abdominal pain, and in one with a normal angiogram, who had low back pain. These two patients in the stenotic group stopped exercise after five minutes; all patients

with normal angiograms could exercise for 10 minutes. In the group with stenoses, four subjects could not climb stairs (all due to abdominal complaints) and the other three climbed 19, 95, and 190 stair steps, respectively. In the group with normal angiograms, two subjects could not climb stairs, due to low back pain. The other five subjects climbed 95 to 190 stair steps. No group differences in percentage of maximal heart rate (median 71% (range 61–87%) in the stenotic versus 77% (range 62–91%) in the normal group; $p>0.05$), or the fall in cBic (median 2.6 mmol/l (range 0.0–4.6) versus median 2.1 mmol/l (range 0.7–5.4), respectively; $p>0.05$) were seen, indicating a similar level of exercise among the groups.

TONOMETRY

Figure 1 shows the time dependent changes in PCO_2 gradient before, during, and after exercise. No difference in both basal P_{CO_2} values was found (median difference -0.1 kPa (range -0.6 to 0.7), coefficient of variation 8%); the mean of these values was taken as resting P_{CO_2} . In patients with normal angiograms the median P_{CO_2} was 4.5 kPa (range 4.4 to 5.5) at rest and 5.1 kPa (range 4.3 to 6.0) during exercise (NS). In this group, the median PCO_2 gradient at rest was -0.5 kPa (range -0.9 to 0.5) and rose slightly to 0.3 kPa (range -0.7 to 0.8) during exercise ($p<0.05$). In the group with splanchnic stenoses, the median P_{CO_2} at rest was 5.2 kPa (range 4.8 to 11.2) and rose to 6.4 kPa (range 5.7 to 15.7) during exercise ($p<0.01$). In this group the median PCO_2 gradient at rest was 0.0 kPa (-0.8 to 5.9) and rose to 1.7 kPa (range 0.9 to 10.3) during exercise ($p<0.05$). The resting P_{CO_2} , but not the PCO_2 gradient, differed between normal and stenotic patients ($p<0.05$ and $p=0.07$, respectively). The P_{CO_2} and PCO_2 gradient during exercise was higher in the stenotic compared with the normal group ($p<0.001$ and $p<0.01$, respectively). No correlation between any tonometer parameter and indicators of exercise level (heart rate, bicarbonate level) was found. Table 2 shows the sensitivity and specificity of tonometry parameters for the detection of gastric ischaemia. In general, tonometry at rest showed poor sensitivity, and the best sensitivity and specificity were obtained with the maximum PCO_2 gradient during or shortly after exercise.

Figure 1 The intra-gastric-blood PCO_2 gradient, before, during, and after exercise in (A) patients with splanchnic stenosis on angiography ($n=7$) and (B) patients with normal angiograms ($n=7$). The dotted line represents the upper level of normal, established in healthy volunteers (Kolkman et al¹⁰). Baseline (resting) values at $t=-10$ minutes; exercise test by stepping stairs from $t=0$ to $t=10$ minutes (grey square); recovery phase at $t=20$, $t=30$, and $t=50$ minutes.

Figure 2 Correlation between tonometry and severity of ischaemia in patients with splanchnic stenosis. (A) Peak PCO₂ gradient versus symptom score ($n=10$; seven patients, three reexamined after surgery). (B) Peak PCO₂ gradient versus gastroscopic score ($n=9$; seven patients, two reexamined after surgery).

POSTOPERATIVE FOLLOW UP

Three patients, who underwent a vascular reconstruction of the splanchnic vessels, were reevaluated postoperatively. Patient A was evaluated one week after surgery. The PCO₂ gradient at rest of 3.9 kPa before the operation decreased to 0.3 kPa after surgery. In patients B and D, the exercise test was repeated eight weeks postoperatively. Both patients were without symptoms, had gained weight, and had a notably increased exercise tolerance. The PCO₂ gradient at peak exercise decreased from 3.7 kPa preoperatively to 0.7 kPa and from 1.7 kPa preoperatively to 0.8 kPa after surgery, for patients B and D, respectively. In the latter patients, initial gastroscopy showed ulceration and gastritis; repeated gastroscopy eight and 10 weeks after surgery showed normal gastric mucosa.

CORRELATIONS

In the patients with stenotic lesions, the maximal PCO₂ gradient during exercise correlated with the severity of ischaemia, as indicated by the symptom score and the gastroscopy score (fig 2; $r_s=0.97$, $p<0.0001$ and $r_s=0.87$, $p<0.01$, respectively). The angiographic score correlated poorly with the symptom score and not with the gastroscopy score ($r_s=0.68$, $p<0.05$ and $r_s=0.44$, $p>0.05$, respectively).

Discussion

This study indicates that measurement of an increased gastric PCO₂ during exercise may identify subjects with symptomatic chronic gastrointestinal ischaemia. The technique could potentially be useful as a screening test in patients with unexplained abdominal complaints and weight loss, for the decision to perform angiography or even reconstructive surgery, or for the assessment of surgical results.

The provocation of gastric ischaemia during peak exercise in patients with stenotic lesions most probably resulted from diversion of blood flow away from the splanchnic area to the exercising muscles.¹⁸ A potential pitfall with exercise as a provocation test is that gastrointestinal ischaemia has been reported after heavy, extended exercise in healthy, well trained individuals.²³ However, with the level of exercise applied in this study, gastrointestinal ischaemia was not observed in subjects with normal angiograms, in contrast to the patients with abnormal angiograms. Although some

patients could not endure the entire 10 minute exercise or walk stairs, no false negative tests were seen. With more precise prediction of the required exercise level, and a more flexible exercise protocol the drawbacks of the current exercise protocol may be overcome in future studies. The undertaking of such studies may be worthwhile as the major advantage of using exercise as provocation is that problems associated with a test meal during tonometry are avoided.¹⁷ The main problem with a test meal is an erroneous increase in Pico₂ from buffering of meal stimulated acid secretion even in the presence of H₂ antagonist treatment, and an initial decrease in Pico₂ due to the dilution effect of the ingested test meal with an atmospheric PCO₂ of 0 kPa.¹⁷ The latter phenomenon probably caused the negative results of tonometry during a test meal to detect ischaemia in a recent prospective study.²⁴ As exercise tonometry is performed in the fasting state, these problems are avoided.

The correlation between peak PCO₂ gradient and the clinical and gastroscopic severity of ischaemia may indicate that exercise tonometry could be used to grade severity of ischaemia. That tonometric variables are related to the degree of ischaemic damage has been shown in several animal studies, where the increase in mucosal and regional venous PCO₂ correlated with the severity of ischaemia.^{12 25-27} It has even been suggested that the stages of hypoperfusion and ischaemia could be derived from tonometry. In experiments with progressive hypoperfusion, the small bowel PCO₂ gradient in dogs was between 1.5 and 2.3 kPa, just below the threshold of anaerobic metabolism, and 5.0 to 10.0 kPa during severe ischaemia with anaerobic metabolism and lactic acidosis.^{26 27} Indeed, in our study, patients with gradients above 2.0 kPa showed more pronounced mucosal damage at gastroscopy, indicating more severe ischaemia. Future studies are needed to confirm the association between severity of ischaemia and tonometry, and whether a critical PCO₂ gradient during exercise tonometry can be identified that separates patients with severe ischaemia, who would likely benefit from surgery, and those with moderate ischaemia who could be managed conservatively.

The poor relation between angiographically proved stenoses and their clinical relevance is in accordance with previous studies.^{3 7} Furthermore, the blood flow parameters obtained with

duplex ultrasonography of the splanchnic vessels may have no relation to the presence or severity of ischaemia, and may have considerable overlap with normal subjects.²⁸ Moreover, with duplex ultrasonography, the visualisation of the CA proved impossible in about 20% of cases.²⁸ Tonometry does not provide data on gastric blood flow or vascular anatomy, but merely on the adequacy of gastrointestinal blood flow.²⁹ In the current study, we measured in the stomach only, and the results might be biased since all patients had CA stenoses. Although the CA is involved in the majority of patients with splanchnic atherosclerosis, gastric tonometry might very well be insensitive in patients with small bowel ischaemia from SMA stenosis with normal CA anatomy, a combination which may occur in 12% of patients.⁵ Theoretically, this may be overcome by placement of a tonometer in the small bowel.¹⁶ Future studies would need to determine whether combined gastric and small bowel PICO₂ measurements might enhance the diagnostic accuracy of exercise tonometry.

In conclusion, gastric tonometry of PICO₂ during exercise may be a promising tool for detection of chronic gastric ischaemia, and possibly of grading of ischaemic severity. Further studies are needed to confirm these preliminary conclusions.

This work was made possible by support of GlaxoWellcome, The Netherlands.

- Crawford ES, Morris GC, Myhre HO, *et al.* Celiac axis, superior mesenteric artery and inferior mesenteric artery occlusion: surgical considerations. *Surgery* 1977;82:856–66.
- MacFarlane SD, Beebe HG. Progress in chronic mesenteric arterial ischemia. *J Cardiovasc Surg* 1989;30:178–84.
- Marston A, Clarke JMF, Garcia Garcia J, *et al.* Intestinal function and intestinal blood supply: a 20 year surgical study. *Gut* 1985;26:656–66.
- Stanton PE, Jr, Hollier PA, Seidel TW, *et al.* Chronic intestinal ischemia: diagnosis and therapy. *J Vasc Surg* 1986;4:338–44.
- Bron KM, Redman HC. Splanchnic artery stenosis and occlusion. Incidence; arteriographic and clinical manifestations. *Radiology* 1969;92:323–8.
- Dick AP. An arteriographic study of mesenteric arterial disease. *Gut* 1967;8:206–20.
- Croft RJ, Menon GP, Marston A. Does “intestinal angina” exist? A critical study of obstructed visceral arteries. *Br J Surg* 1981;68:316–18.
- Järvinen O, Laurikka J, Sisto T, *et al.* Atherosclerosis of the visceral arteries. *Vasa* 1995;24:9–14.
- Loffeld RJLF, Overtoom HAJM, Rauwerda JA. The celiac axis compression syndrome, report of 5 cases. *Digestion* 1995;56:534–7.
- Kolkman JJ, Groeneveld ABJ. Occlusive and non-occlusive gastrointestinal ischemia: a clinical review with special emphasis on the diagnostic value of tonometry. *Scand J Gastroenterol* 1998;33(suppl 225):3–12.
- Antonsson JB, Boyle CC, Kruthoff KL, *et al.* Validation of tonometric measurement of gut intramural pH during endotoxemia and mesenteric occlusion in pigs. *Am J Physiol* 1990;259:G519–23.
- Desai VS, Weil MH, Tang WC, *et al.* Gastric intramural PCO₂ during peritonitis and shock. *Chest* 1993;104:1254–8.
- Poole JW, Sammartano RJ, Boley SJ. Hemodynamic basis of the pain of chronic mesenteric ischemia. *Am J Surg* 1987;153:171–6.
- Tang W, Weil MH, Sun S, *et al.* Gastric intramural PCO₂ as monitor of perfusion failure during hemorrhagic and anaphylactic shock. *J Appl Physiol* 1994;76:572–7.
- Fiddian-Green RG, Stanley JC, Nostrant T, *et al.* Chronic gastric ischemia; a cause of abdominal pain or bleeding identified from the presence of gastric mucosal acidosis. *J Cardiovasc Surg* 1989;30:852–9.
- Boley SJ, Brandt LJ, Veith FJ, *et al.* A new provocative test for chronic mesenteric ischemia. *Am J Gastroenterol* 1991;86:888–91.
- Groeneveld ABJ, Vervloet M, Kolkman JJ. Gastric tonometry in the fed or fasting state? *Crit Care Med* (in press).
- Qamar MI, Read AE. Effects of exercise on mesenteric blood flow in man. *Gut* 1987;28:583–7.
- Kolkman JJ, Groeneveld ABJ, Meuwissen SGM. Effect of ranitidine on basal and bicarbonate enhanced intragastric PCO₂: a tonometric study. *Gut* 1994;35:737–41.
- Kolkman JJ, Groeneveld ABJ, Meuwissen SGM. Characteristics of time-dependent PCO₂ tonometry in the normal human stomach. *Br J Anaesthesiol* 1998;81:669–75.
- Wasserman K, Hansen JE, Sue DY, *et al.* *Principles of exercise testing and interpretation*. Philadelphia: Lea and Febiger, 1987.
- Beaver WL, Wasserman K, Whipp BJ. Bicarbonate buffering of lactic acid during exercise. *J Appl Physiol* 1986;60:472–8.
- Nielsen HB, Svendsen LB, Jensen TH, *et al.* Exercise-induced gastric mucosal acidosis. *Med Sci Sports Exerc* 1995;27:1003–6.
- Geelkerken RH, Schultze Kool LJ, Hermans J, *et al.* Chronic splanchnic syndrome: tonometry as a functional test. *Eur J Surg* 1997;163:115–21.
- Noc M, Weil MH, Sun S, *et al.* Comparison of gastric luminal and gastric wall PCO₂ during hemorrhagic shock. *Circ Shock* 1993;40:194–9.
- Schlichtig R, Bowles SA. Distinguishing between aerobic and anaerobic appearance of dissolved CO₂ in intestine during low flow. *J Appl Physiol* 1994;76:2443–51.
- Zhang H, Rogiers P, De Backer D, *et al.* Regional arteriovenous differences in PCO₂ and pH can reflect critical organ oxygen delivery during endotoxemia. *Shock* 1996;5:349–56.
- Moneta GL, Lee RW, Yeager RA, *et al.* Mesenteric duplex scanning: a blinded prospective study. *J Vasc Surg* 1993;17:79–86.
- Groeneveld ABJ, Kolkman JJ. Splanchnic tonometry: a review of physiology, methodology, and clinical applications. *J Crit Care* 1994;9:198–210.