Clinical Impact of Gastric Exercise Tonometry on Diagnosis and Management of Chronic Gastrointestinal Ischemia

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Background & Aims: **Chronic gastrointestinal ischemia or chronic splanchnic syndrome is a difficult diagnosis. The use of a physiologic test, combined with clinical and anatomic data, should improve diagnostic accuracy. This study evaluates the diagnostic accuracy and clinical impact of gastric tonometry during exercise (GET) in a patient cohort suspected of chronic splanchnic syndrome.** ***Methods:*** **From 1997 to 2000, 102 patients with chronic abdominal pain were analyzed. The workup included GET and selective biplane angiography. The diagnosis of gastrointestinal ischemia was based on consensus in a multidisciplinary working group and sustained on follow-up.** ***Results:*** **Gastrointestinal ischemia was diagnosed in 38 patients. In 33 patients chronic splanchnic syndrome was found, with single vessel involvement in 20 (17 celiac artery, 3 mesenteric superior) and multivessel disease in 13. In 5 patients nonocclusive ischemia was found. By using receiver operator curve analysis, the difference between gastric and arterial partial pressure of carbon dioxide (Pco_2 gradient) proved to be the best GET parameter. The criteria for diagnosing ischemia in GET were Pco_2 gradient >0.8 kPa and increase gastric Pco_2, with base excess decrease <8 mmol/L during exercise. GET had 78% sensitivity and 92% specificity. Twenty-five patients underwent vascular treatment (19 operative, 6 stent/percutaneous transluminal angioplasty). After 4 years of follow-up 83% of patients were alive and free of symptoms.** ***Conclusions:*** **GET is an accurate diagnostic tool to show gastrointestinal ischemia. Including GET into clinical decision making enabled selecting patients with ischemia, who benefited from vascular and medical treatment. These benefits were sustained during 4-year follow-up. GET should be considered in the workup of patients with a suspected diagnosis, of gastrointestinal ischemia.**

The diagnosis of chronic gastrointestinal ischemia is notoriously difficult. Many patients with splanchnic stenoses remain asymptomatic and have no indication for treatment. Other patients develop typical symptoms, including postprandial pain, fear of eating, and weight loss, a condition referred to as chronic splanchnic syndrome (CSS) or chronic mesenteric ischemia. Another patient group consists of those with ischemia and apparently normal splanchnic vessels, a condition referred to as nonocclusive mesenteric ischemia (NOMI), caused by local vasoconstriction related to circulatory (pre)-shock.

It has been shown that the main contributor to the diagnosis is a high degree of clinical suspicion,[1,2] and that detection of a stenosis alone does not prove ischemia.[3–5] It is widely accepted that the gastrointestinal tissue is resistant to ischemia because of the extensive collateral circulation between the 3 main arteries.[6,7] Common clinical knowledge thus dictates that at least 2 of the 3 major splanchnic arteries have to be stenotic to give ischemic symptoms. Studies that reported the rarity of an isolated stenosis of celiac artery (CA) as cause of complaints[8,9] coincide with series showing disappearance of symptoms after treatment of isolated CA stenoses.[10,11]

Therefore, some but not all patients with splanchnic stenoses benefit from treatment. It was acknowledged more than a decade ago that "a functional and physiological test distinguishing symptomatic ischemia, the chronic splanchnic syndrome from non-ischemic stenoses, the chronic splanchnic disease, was urgently warranted."[12] None of the currently available diagnostic modalities, including angiography, duplex ultrasound, and magnetic resonance angiography, could provide that functional information. Measurement of intraluminal partial pressure of carbon dioxide (Pco_2) by tonometry has been shown to provide exactly that information, the presence or absence of is-

Abbreviations used in this paper: BE, base excess; CA, celiac artery; CACS, celiac artery compression syndrome; CSS, chronic splanchnic syndrome; GET, gastric exercise tonometry; NOMI, nonocclusive mesenteric ischemia; $PaCO_2$, arterial partial carbon dioxide pressure; PCO_2 gradient, difference between gastric and arterial PCO_2; $PgCO_2$, gastric intraluminal partial carbon dioxide pressure; PTA, percutaneous transluminal angioplasty; ROC, receiver operator curve; SMA, superior mesenteric artery.

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chemia. In a small pilot study we have shown that gastric exercise tonometry (GET) was able to detect actual ischemia.[13] We have recently validated this exercise test in healthy volunteers and established the optimal exercise intensity level as well as normal threshold values.[14]

The current study was performed to establish the role of GET for detection of gastrointestinal ischemia in a cohort of patients with unexplained chronic abdominal symptoms and to establish its clinical impact for these patients.

Patients and Methods

In our institution a multidisciplinary working group on gastrointestinal ischemia was instituted in 1997. All patients were evaluated for clinical suspicion of chronic gastrointestinal ischemia or because of an incidental finding of splanchnic stenosis on abdominal angiography. A standard protocol was used including a detailed history of complaints by 2 experienced physicians, duplex ultrasound, splanchnic angiography, and GET.

The severity of complaints (upper abdominal pain at "rest," worsening after meal or exercise, and diarrhea) was scored by one of the authors (J.A.O.) by using a symptom score: 0, no complaints; 1, minor complaints not interfering in daily activities; 2, moderate complaints, some restrictions in daily activities; 3, severe complaints, normal activities impossible. The body mass index was calculated (weight/square of length), and the weight loss during the last 6 months was recorded.

Splanchnic Angiography

All patients underwent multiplane intra-arterial digital subtraction angiography of the abdominal aorta and its branches (Philips 3000 Integris system; Philips, Eindhoven, The Netherlands) during injection of 30–40 mL contrast medium (Ioxaglate, Hexabrix; Mallinkrodt, St. Louis, MO). First a nonselective anterior-posterior and lateral aortic angiography was performed, followed by selective cannulation of the splanchnic arteries. The luminal filling of the abdominal aorta, the CA, superior mesenteric artery (SMA), and inferior mesenteric artery was determined. Stenoses were graded by consensus of 2 investigators who were blinded to the patients' symptoms and the results of the other investigations. For comparison we graded these stenoses as absent, insignificant (<50%), mild (50%–70%), major (70%–99%), and occlusion (100%).[15]

Gastric Exercise Tonometry

GET was performed in the afternoon after a light breakfast followed by at least 4 hours of fasting. To prevent intragastric CO_2 production by buffering of gastric acid, 100 mg of ranitidine was administered intravenously 1 hour before the baseline tonometry measurements. A standard balloon-tipped tonometry catheter (Trip sigmoid catheter; Tonometrics, Helsinki, Finland) was inserted nasogastrically and placed at 55 cm from the tip of the nose. Correct placement was checked by aspiration of gastric fluids or fluoroscopy when in doubt. The catheter was attached to an automated air tonometry device (Tonocap; Datex-Ohmeda, Hoevelaken, the Netherlands). The tonometry device measures gastric P_{CO_2} (Pg_{CO_2}) every 10 minutes.

An intravenous catheter was placed in the forearm for intravenous administration of ranitidine. A radial artery catheter was inserted in the nondominant arm to allow arterial blood sampling. The exercise period lasted 10 minutes and followed the last baseline tonometric measurement cycle. Exercise was performed on an electromagnetically braked bicycle ergometer (Lode, Groningen, The Netherlands). During the exercise test a 12-lead electrocardiogram was recorded (Case 12; Marquette Electronics Inc, Milwaukee, WI). The workload was gradually increased and targeted at submaximal work rate level.[14] The maximal workload was estimated by using standard criteria, with age, sex, weight, and forced expiratory volume. The exercise episode was started at 10% of maximal workload, and during the first 4–6 minutes the workload was increased every minute with 10% of maximal workload. The workload was intended to remain constant thereafter at a submaximal exercise level. The exercise intensity was monitored by measuring heart rate, aiming for a heart rate during the last 4–5 minutes of 80% of maximal predicted heart rate, and respiratory quotient, aiming for a recovery quotient of 1.0 in the last 4–5 minutes of the exercise episode. This respiratory quotient was chosen because it indicates the anaerobic threshold.

At these same times, the Pg_{CO_2} was measured by the Tonocap, and the gastric-arterial P_{CO_2} difference or P_{CO_2} gradient was calculated: P_{CO_2} gradient = Pg_{CO_2} − Pa_{CO_2}. The normal upper threshold value for P_{CO_2} gradient during exercise is 0.8 kPa.[14] The means of both baseline measurements were taken as baseline values. The decrease in base excess (BE) (Baseline − Exercise BE value) was used as a measure of exercise intensity because it is closely correlated to arterial lactate levels. All tonometry test results were reviewed by 2 investigators blinded for the other clinical data for determination of interoperator variability.

The Gold Standard for Chronic Gastrointestinal Ischemia

Selective splanchnic arteriography was used as the gold standard for the presence or absence of splanchnic arterial stenosis. Because there is no gold standard for diagnosing chronic splanchnic syndrome (CSS), we decided to rely on a multidisciplinary panel consensus and sustained with careful follow-up, an approach used earlier for diagnoses lacking a gold standard procedure like rheumatoid arthritis.[16]

After completion of all investigations, each case was discussed in the multidisciplinary gastrointestinal working group, and a consensus diagnosis was made. The diagnosis ischemia was made by the panel and was based on (1) a clinical presentation that suggests ischemia (mostly postprandial and post-exercise pain) after consideration of all available investigations, (2) exclusion

of other more prevalent diagnoses, and (3) sustained diagnosis on follow-up. The panel always consisted of at least the gastroenterologist (J.J.K.), vascular surgeon (R.H.G.), and interventional radiologist (A.B.H.). Because of the nature of this procedure, blinding was impossible. On follow-up, the consensus diagnosis could change on the basis of the clinical course, treatment results, or alternative diagnosis. In the results, the group referred to as "chronic gastrointestinal ischemia" contains those subjects with a final, unchanged diagnosis. The patients in whom the diagnosis was changed on follow-up will be reported separately.

Follow-up

Follow-up included assessment of complaints, physical examination, as well as yearly duplex ultrasound and/or angiography in patients who underwent a revascularization procedure. Symptom assessment was relatively simple; only those in whom symptoms disappeared after treatment were considered clinical successes.

For the follow-up of the presumed nonischemic patient group, the physicians of these patients were contacted by letter. The required information consisted of current health status, abdominal symptoms, the cause of death when the patient had died, and the presence of any signs, symptoms, or diagnostic procedures indicating gastrointestinal ischemia.

Statistics

Values are given as mean ± standard error of mean unless otherwise stated. P values $<.05$ were considered statistically significant. The Mann–Whitney test was used for comparing symptom scores between the groups with and without chronic gastrointestinal ischemia. For all baseline GET values the mean of the 2 consecutive measurements was taken. Interobserver variability for angiographic stenosis of CA and SMA and for GET results was determined by using the Cohen kappa test. Differences in GET variables between patients with and without stenosis and ischemia were calculated by using the unpaired Student t test. Association between GET result and the presence or absence of stenosis and ischemia was tested by using the Fisher exact test. The diagnostic accuracy of GET for chronic gastrointestinal ischemia was measured by receiver operator curve (ROC) analysis. The differences between curves were determined by comparison of the area under the curve and standard error. The sensitivity, specificity, positive and negative predictive values, as well as likelihood ratios were calculated. The outcome of patients treated for stenoses was determined by the life table analysis according to Kaplan–Meier by using a log-rank test.

Results

Patients and Symptoms

Between 1997 and 2000, 102 patients (67 female/35 male; median age, 52 years; range, 20–81 years) were evaluated. The clinical presentation (symptom scores) and demographic data of patients who were finally classified as having chronic gastrointestinal ischemia or no ischemia are summarized in Table 1. The presenting complaints were comparable; only postprandial pain was more pronounced in the ischemia group.

The complaints of the 38 patients with chronic gastrointestinal ischemia consisted of abdominal pain in 36 (95%), weight loss in 25 (66%), and diarrhea in 9 (24%). The abdominal pain was provoked by meals in 83%, by exercise in 60%, and occurred at rest in 67%. In chronic gastrointestinal ischemia more severe postprandial pain was reported: grade ≥2 in 71% of the ischemia patients compared to 42% in the nonischemic group ($P < .05$). No differences in body mass index (22.5 kg/m^2 in both groups), body mass index below 20 (34.2% vs 29.7%), and weight loss was seen between the ischemic and nonischemic groups. Gastric or duodenal ulcers, not explained by *Helicobacter pylori* infection, medication, or

Table 1. Demographics and Clinical Presentation (Diagnosis of Gastrointestinal Ischemia)

	All subjects (n = 102)	Chronic gastrointestinal ischemia[a] (n = 38)	No ischemia (n = 64)
Male/female	34/68	7/31	26/37[b]
Age, y (mean, range)	52 (20–81)	52 (24–75)	52 (20–81)
Abdominal pain, % (median score)	91% (0.8)	95% (0.8)	89% (0.8)
Pain after exercise, % (median score)	47% (0.7)	55% (0.9)	41% (0.7)
Pain after meal, % (median score)	72% (1.4)	82% (1.8)[c]	64% (1.2)
Weight loss, % (median score)	59% (1.3)	66% (1.5)	53% (1.2)
Diarrhea	18%	24%	14%
Ulcer, non-*H pylori*, non-NSAID	11%	13%	9%
Classic triad[d]	32%	42%	27%
Risk factors			
Other cardiovascular disorders	29%	46%	19%
Hypertension	22%	30%	18%
Smoking	63%	68%	60%
Diabetes	8%	13%	5%
Dyslipidemia	17%	20%	15%
Family history	56%	63%	53%
None	5%	0%	7%

Symptom scores ranged from 0–3 (see Methods).
[a]Patients diagnosed as chronic gastrointestinal ischemia, sustained during follow-up.
[b]$P < .05$ comparing ischemic and nonischemic patients (χ^2 test).
[c]$P < .05$ comparing ischemic and nonischemic patients (Mann–Whitney test).
[d]Classical triad is defined as postprandial pain, fear of eating, and weight loss.

Table 2. Vascular Involvement in Gastrointestinal Ischemia Patients

	Chronic gastrointestinal ischemia (n = 38)
Single vessel	20
CA	17
SMA	3
Multivessel	13
CA/SMA	10[a]
CA/IMA	0
CA/SMA/IMA	3
No stenosis	5[b]

IMA, inferior mesenteric artery.
[a]One subject had SMA stenosis >70% plus CA stenosis 50%–70%.
[b]5 subjects with suspected gastric vasospasm; in 2, spasms were seen during angiography. All responded to vasodilator treatment.

malignancy, were found in 12% in chronic splanchnic ischemia group versus 9% in the nonischemic group (not significant).

Splanchnic Angiography

In 47 of 102 patients 1 or more significant stenoses were found; in 42 of 47 the stenoses were >70%. Collateral vessels were found in 29 of the 47 patients with stenoses and in 11 of the 55 patients with normal vessels ($P < .0001$). The interobserver agreement for detection of a stenosis in the CA, the SMA, and the presence of collaterals was good with kappa values of 0.71, 0.77, and 0.63, respectively ($P < .001$ for all kappa values).

The vascular abnormalities of the 38 patients with a final diagnosis of chronic gastrointestinal ischemia are summarized in Table 2. In 2 of 5 patients without stenoses, abundant vasospasm was seen during angiography.

Gastric Exercise Tonometry

In 98 patients (96%) GET was interpretable. In 4 patients the level of exercise was above the goal range (BE decrease, ≥8). These 4 tests were excluded from analysis because we have previously shown false-positive tests in 45% of subjects at these exercise levels.[14]

The final diagnosis of gastrointestinal ischemia was made and sustained in 38 patients. Of these, 33 had splanchnic stenoses (CSS) and 5 had NOMI.[17] The $PgCO_2$ and PCO_2 gradient differed between patients with CSS, NOMI, and those without ischemia ($P < .0001$). The PCO_2 gradient in patients with CSS was higher compared to those without ischemia (1.2 ± 0.1 vs 0.3 ± 0.1 kPa, $P < .0005$), with similar exercise levels (BE decrease, 5.1 ± 0.3 vs 4.5 ± 0.2; not significant). The PCO_2 gradient in patients with NOMI was higher than in the nonischemic group (1.3 ± 0.1 vs 0.3 ± 0.1 kPa, $P < .01$) but not different from the CSS patients.

The diagnosis of NOMI was explained by pronounced vasospasm, seen on angiography in 2 patients. One patient had ischemia from cardiac failure, a condition known to cause NOMI.[18] In 2 others in whom vasospasm was suspected, nitrates were prescribed; both reported >50% reduction of pain on a visual analogue scale, sustained after >4-year follow-up.

Of the 38 patients with ischemia, 17 had no pain on exercise; 6 of these had a negative GET; 3 of 21 patients with pain on exercise had a negative GET ($P = .26$).

Gastric exercise tonometry criteria. We compared the maximum gastric PCO_2, the increase of gastric PCO_2, the PCO_2 gradient, and the area under the curve of the PCO_2 gradient. ROC analysis demonstrated that ΔPCO_2 and area under the curve were the best parameters for demonstrating ischemia (Figure 1) and proved better than the $PgCO_2$ ($P < .001$), but not different from the area under the curve of the PCO_2 gradient ($P = .71$). The area under the curve of the PCO_2 gradient was significantly better than the gastric PCO_2 ($P < .05$).

In 8 patients the increased PCO_2 gradient during exercise was based on a decreased arterial PCO_2 alone, without concomitant increase in gastric PCO_2. This was caused by exercise-induced hyperventilation. Only 1 of these 8 was diagnosed with chronic gastrointestinal ischemia. Our current data re-establish the previously estimated threshold value of 0.8 kPa as upper level of the normal PCO_2 gradient, with an optimal accuracy (Figure 2).

The GET is abnormal when 3 criteria are met: (1) increase in gastric PCO_2 over baseline, (2) PCO_2 gradient >0.8 kPa, and (3) BE decrease <8 mmol/L, during exercise. With these criteria, GET was abnormal in 29 of 38 patients with final consensus diagnosis of chronic gastrointestinal ischemia and in 5 of 64 patients without

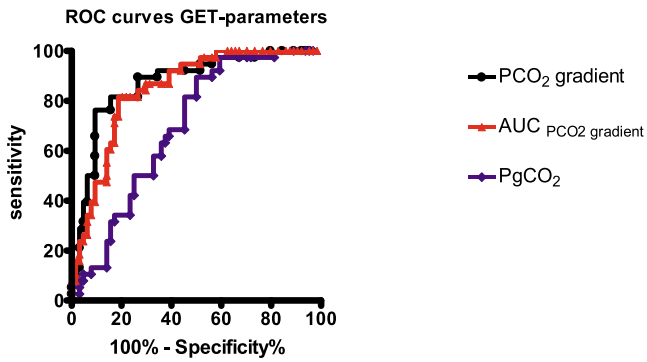

Figure 1. ROC of 3 tonometry parameters used in the diagnosis of splanchnic ischemia. *Circles,* maximum P_{CO_2} gradient during exercise; *triangles,* area under the curve (*AUC*) of the P_{CO_2} gradient; *diamonds,* gastric P_{CO_2} during exercise.

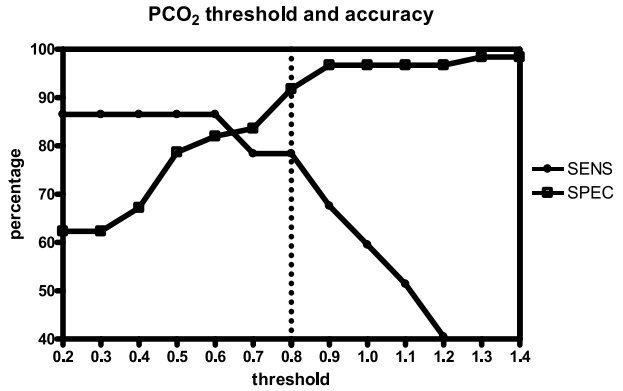

Figure 2. Relation between the threshold Pco_2 gradient, sensitivity (*SENS*), and specificity (*SPEC*) for detection of gastrointestinal ischemia.

(accuracy, 86%). The sensitivity and specificity of GET for chronic gastrointestinal ischemia were 78% and 92%, respectively; the positive and negative predictive values were 85% and 86%, respectively; the likelihood ratio for detection of gastrointestinal ischemia was 9.6.

Follow-up

Diagnosis on follow-up. Initially gastrointestinal ischemia was diagnosed in 43 patients; after a follow-up of mean 50 months (range, 33–81 months), the diagnosis was abandoned in 5 patients. The reasons were lack of even temporary improvement despite adequate stent placement or surgery, with normal vessel patency assessed with duplex and angiography 1 and 3 years after revascularization (n = 2) and development of complaints typical for irritable bowel syndrome and atypical for ischemia (relation to stool passage, bloating, and distended abdomen, n = 3). The latter patients presented with dyspepsia-like complaints (postprandial epigastric pain and fullness).

Of the 64 patients without ischemia, 59 with initial classification as nonischemic and 5 reassigned to this group during follow-up, follow-up data were available in 55 after mean 5.5 years (range, 3.8–7.7 years). None of these developed symptoms fitting acute or chronic splanchnic syndrome; 3 died of an unrelated cause. Nine were lost to follow-up.

Treatment results on follow-up. Of the 38 patients with chronic gastrointestinal ischemia, 33 had CSS and 5 had NOMI. Twenty-five CSS patients underwent vascular treatment. The 8 nontreated patients consisted of 3 patients with CA stenosis and mild complaints, who preferred conservative treatment with frequent small meals and proton pump inhibition over surgery. In 5 CSS patients a vascular procedure was indicated but not performed. Two of these died of bowel infarction within weeks after diagnosis, while waiting for surgery; all had multivessel involvement. Of the remaining 3, the operative risk was considered too high, the stenoses were unfitted for stent placement (n = 1), or they refused further treatment (n = 2).

Of the 25 treated patients, 19 were treated operatively, and 6 were treated by endovascular stent placement (n = 5) or percutaneous transluminal angioplasty (PTA) alone (n = 1). All 5 patients treated by PTA/stent placement showed good improvement. The patient treated by PTA alone had only a temporary response, but no further treatment was considered because of serious concomitant disease (metastatic lung cancer). Of the 19 operated patients, 3 died in the perioperative period from multiple organ failure. One was severely cachectic (body mass index, 16.0 kg/m^2), and 2 had prolonged periods of abdominal vascular rest pain indicating acute-on-chronic gastrointestinal ischemia. The remaining 16 had uneventful postoperative course, and improvement of symptoms was documented in all. Two multivessel CSS patients died on follow-up; one had a graft occlusion and subsequent bowel infarction 1.2 years after surgery, and the other died of unrelated cause 3 years later. We performed follow-up GET in 11 of 25 patients who were treated by revascularization. All had clinical improvement after treatment; GET normalized in 7 and improved in 4.

The outcome of the 12 treated single-vessel patients was quite different from the 13 multivessel CSS patients. None of the single-vessel patients died, and the 1-year success in this series was 100%, dropping to 79% after 4 years because of symptom recurrence from stent failure (n = 1) or restenosis of the autogenous reconstruction (n = 1) after >2 years. In the latter patient, endovascular dilatation relieved symptoms again. In the multivessel CSS patients 5 patients died, 3 perioperatively and 2 during follow-up. All surviving multivessel CSS patients were free of symptoms. Thus after 4 years of follow-up, all surviving multivessel CSS patients were symptom free, as well as 79% of the single-vessel patients. Taken together, 10 of 12 (83%) of patients alive at 4 years were free of symptoms.

Discussion

The current study was performed to establish the role of GET for detection of gastrointestinal ischemia in a cohort of patients with unexplained chronic abdominal symptoms and to establish its clinical impact for these patients. This study confirmed that GET test can indeed detect gastrointestinal ischemia, both CSS and NOMI. This is the first study to

show the clinical impact of GET, because the inclusion of GET results to standard clinical and anatomic data resulted in pain relief in 83% of patients sustained after 4 years of follow-up.

Tonometry has the unique capability that it can show actual ischemia, for whatever cause, and regardless of blood flow and metabolic activity.[17,19] During ischemia the tissue P_{CO_2} rises over the normal levels from reduced tissue CO_2 washout by the lowered blood flow and increased CO_2 production during anaerobic metabolism. Thus, an increased gastric-arterial P_{CO_2} level indicates local production and therefore ischemia in all shock and ischemia models.[19] The gastric P_{CO_2} can be measured conveniently by using air tonometry with small nasogastric catheters and a semiautomated capnograph. The use of test meal as provocative test seems more obvious, it proved unreliable,[20] and we therefore explored exercise as provocative test. In a pilot study, GET could successfully detect ischemia in 7 CSS patients[13] and was later validated by us in healthy volunteers.[14] The current study underscores the clinical usefulness and applicability of GET, with 96% interpretable tests, 86% accuracy, and no complications.

In 9 patients the GET was normal, despite gastrointestinal ischemia. Two of these patients were unfit to exercise because of underlying severe pulmonary emphysema. In 1 patient with isolated SMA stenosis, a second tonometer, placed in the jejunum as part of a feasibility test to small bowel tonometry, showed a peak jejunal P_{CO_2} gradient of 1.9 kPa, indicating small bowel ischemia. In another patient 24-hour tonometry, as part of another pilot study, showed repeated peaks in both gastric and jejunal P_{CO_2} gradients up to 8.0 kPa, correlating with abdominal pain episodes. Also, the higher frequency of false-negative tonometry among patients who did report exercise-induced pain indicates that measurement after meals still might be worthwhile. These findings all indicate that the accuracy of exercise tonometry testing might further improve with 24-hour measurements and small bowel tonometry.

In the current study most patients with CSS had single-vessel disease, whereas many others reported this syndrome predominantly in 2- or 3-vessel disease.[1] The 1- and 2- to 3-vessel involvements represent different clinical entities. In our series, approximately 50% of 1-vessel patients had CSS, compared to >90% of subjects with 2- to 3-vessel stenoses. Complications, especially bowel infarction, were common in 2- to 3-vessel patients and absent in those with 1-vessel stenosis. The symptomatic response to treatment, however, was comparable with disappearance of symptoms in both groups. This difference might have a major impact on diagnosis and treatment options. Diagnosing ischemia in patients with 2- to 3-vessel stenoses often will be right, even without a proper ischemia-specific test. In 1-vessel disease, diagnosing CSS without a test like GET can feel like tossing a coin, a 50% chance and no clue on how it will turn out. Thus, especially in this group, GET has additional value over angiography.

The perioperative mortality was rather high in this study, with 3 of 19 patients dying days to weeks after operation. Three factors could be identified to explain this mortality figure. First, 2 of 3 patients were operated for acute-on-chronic CSS, with prolonged and intensified bowel pain and increased lactate levels and leukocyte counts. During surgery a pale-bluish bowel was notably present in these patients; the procedure itself went well, but all died of multiple organ failure within 21 days after surgery. It could therefore be argued whether these are still chronic ischemia patients or already acute infarction or acute on chronic ischemia, known for its very high mortality of 80% or above.[21] Second, the third patient was extremely cachectic; she had an uneventful surgical procedure, but she died of multiple organ failure 2 weeks after the procedure. Probably the surgical procedures, which consisted of aortic clamping above the level of the splanchnic arteries, might just have been too much for this patient group. The third factor might thus be the procedure of choice. It is conceivable that less invasive procedures, like stent placement[22] or retrograde bypasses coming from the iliac vessels, could reduce this mortality figure in this high-risk patient group.

It seems unlikely, but cannot fully be excluded, that the patient group whom we considered asymptomatic might have benefited from vascular treatment as well. During follow-up we found no evidence of progressive gastrointestinal ischemia, although admittedly the observation period was relatively short in relation to such developments.[3] The fact that tonometry represents a physiologic test for gastrointestinal perfusion adequacy and most of the "non-ischemic" patients had normal tonometry seems a strong argument against treatment of these patients. Still, to rule out a beneficial effect of vascular treatment in these patients, randomized controlled trials would be needed, blinded to tonometry results. From an ethical viewpoint, ignoring physiologic data for choosing optimal treatment options in this disorder seems hardly defendable.

In 5 patients NOMI was diagnosed because the complaints fitted ischemia, tonometry was abnormal, and vessels on angiography were normal. It might be argued that these patients represent merely false-positive GET

results, but several arguments favor NOMI as diagnosis. NOMI is regularly observed in intensive care patients, in whom splanchnic vasoconstriction is an adaptive response to circulatory (pre)-shock.[17] This low-flow mechanism could explain findings in 1 patient with cardiac failure. In 2 others profound vasospasm of smaller branches of the CA during angiography coincided with abdominal pain, indicating NOMI.[1,19] We hypothesized that vascular spasm might be involved in the complaints of the other patients as well. In fact, in many vascular beds symptomatic vasospasms are known to cause symptoms, such as Prinzmetal's angina or syndrome X, Raynaud's disease, and hemiplegic migraine. Therefore, patients were treated with vasodilators (nitrates in 3, ketanserin in 1), and 3 of them showed remarkable improvement of symptoms with more than 50% reduction of pain within weeks, sustained during follow-up.

Conclusion

We have shown that GET is an accurate diagnostic test for chronic gastrointestinal ischemia in a large cohort of patients, with rigid diagnostic criteria and careful follow-up. The P_{CO_2} gradient during submaximal exercise enabled correct diagnosis in 86% of patients. GET enabled identification of patients with ischemia and normal vessels, caused by vascular spasm, which responded to vasodilator treatment.

The clinical impact of incorporating GET results in decision making was very significant, because 83% of patients treated for ischemia were free of symptoms after 4 years of follow-up.

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