Use of Visible Light Spectroscopy to Diagnose Chronic Gastrointestinal Ischemia and Predict Response to Treatment

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BACKGROUND & AIMS: **Chronic gastrointestinal ischemia (CGI) is more common than previously thought. Visible light spectroscopy (VLS) allows for noninvasive measurements of mucosal capillary hemoglobin oxygen saturation during endoscopy. We evaluated the response of patients with occlusive CGI to treatment after evaluation by radiologic imaging of the vasculature and VLS. We also identified factors associated with response to treatment in these patients.**

METHODS: **In a prospective study, we collected data from 212 patients referred for evaluation of suspected CGI from November 2008 through January 2011. Patients underwent an extensive evaluation that included visualization of gastrointestinal arteries and assessments of mucosal perfusion by means of VLS. Treatment response was evaluated in patients with occlusive CGI. Factors associated with response to therapy were assessed by using multivariate logistic regression analysis.**

RESULTS: **Occlusive CGI was diagnosed in 107 patients (50%); 96 were offered treatment (90%). After median follow-up period of 13 months, data on treatment response were available from 89 patients (93%); 62 patients had a sustained response (70%). Weight loss before treatment (odds ratio [OR], 1.93), presence of an abdominal bruit (OR, 2.36), and corpus mucosal saturation level <56% (OR, 4.84) were the strongest predictors of a positive response to treatment.**

CONCLUSIONS: **Treatment of CGI, diagnosed by a multimodal approach, provides a substantial long-term rate of response (70% in 13 months). Weight loss, abdominal bruit, and low corpus mucosal saturation identify patients most likely to respond to treatment. Multiple techniques should therefore be used to assess patients with CGI, including VLS measurements, to detect mucosal hypoxia.**

Keywords: Hypoxia; Gastrointestinal Mucosal Perfusion; Noninvasive Measurement.

Chronic abdominal symptoms are quite common, as are vascular stenoses of gastrointestinal (GI) arteries.[1–5] The diagnosis of chronic gastrointestinal ischemia (CGI) can therefore be challenging. Current diagnostic approaches include assessment of medical history, imaging of GI arteries, and assessment of GI mucosal perfusion by means of tonometry or visible light spectroscopy (VLS).[6,7]

We previously showed that medical history and physical examination were poor predictors for the presence of CGI. Addition of radiologic evaluation and in particular functional testing by means of tonometry substantially improved the accuracy of diagnosis.[8] VLS has recently been introduced as a new minimally invasive technique to detect mucosal hypoxia by means of measurement of mucosal capillary hemoglobin oxygen saturation during endoscopy in patients clinically suspected of CGI.[9–11]

The aim of this study was to evaluate the response to treatment, including response predictors, in a large, independent population of patients suspected of CGI and assessed by means of vascular imaging and VLS.

Methods

All consecutive patients with a clinical suspicion of CGI referred to the Erasmus MC were included after informed consent and prospectively followed. The Institutional Review Boards of the Erasmus MC University

Abbreviations used in this paper: **AIC, Akaike's Information Criterion; CA, celiac artery; CACS, celiac artery compression syndrome; CGI, chronic gastrointestinal ischemia; CI, confidence interval; CTA, computed tomography angiography; CVD, cardiovascular disease; GI, gastrointestinal; IQR, interquartile range; MRA, magnetic resonance angiography; OR, odds ratio; SMA, superior mesenteric artery; VLS, visible light spectroscopy.**

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Medical Center approved this study. The study accorded with STROBE guidelines.[12] In all patients, more common causes of upper abdominal complaints had been excluded. Patients were clinically defined as suspected for CGI if they had unexplained abdominal pain or unexplained weight loss (>5% of standard weight) and ≥70% stenosis of at least 1 of the main GI arteries on radiologic evaluation.

Standard Diagnostic Work-up

The diagnostic work-up included a medical and physical examination and an extensive questionnaire. The questionnaire focused on complaints, medical history, medication use, risk factors for cardiovascular disease (CVD), and comorbidities. Furthermore, all patients underwent radiologic visualization of GI arteries in combination with VLS measurement. This was first done by high-resolution computed tomography angiography (CTA) or magnetic resonance angiography (MRA) and if needed by further intra-arterial catheterization. The target arteries were, in particular, the celiac artery (CA) and superior mesenteric artery (SMA). A significant stenosis of GI arteries was defined as a luminal reduction >70%. Mucosal saturation was measured by using a fiberoptic catheter–based VLS oximeter during upper endoscopy as described earlier. The cutoff values for the descending duodenum, the duodenal bulb, and the gastric antrum were determined in our prior study. Mucosal ischemia was defined as detection of mucosal hypoxia at 1 or more of the above mentioned locations (Supplementary Figures 1 and 2).[9]

Consensus Diagnosis of Occlusive Chronic Gastrointestinal Ischemia

Medical history, complaints, and the results of all diagnostic procedures were discussed in a dedicated multidisciplinary team consisting of a vascular surgeon, intervention radiologist, and gastroenterologist, all who specialized in CGI. The discussion resulted in a consensus diagnosis of occlusive CGI or non-CGI. The consensus diagnosis of occlusive CGI was made in presence of (1) a clinical suspicion of CGI, (2) a significant stenosis in at least 1 of the GI arteries, and (3) detection of mucosal ischemia by means of VLS measurement. Occlusive CGI was classified as either due to single artery or multi-artery disease depending on the number of arteries involved. Patients diagnosed with occlusive CGI were offered surgical or endovascular revascularization.

Follow-up and Response

All patients diagnosed with CGI were prospectively followed at the outpatient clinic with scheduled visits at 6 weeks, 3 months, 6 months, and 1 year after treatment for assessment of clinical status and repeated duplex ultrasound scanning of the GI arteries. Thereafter, patients were assessed once yearly at our outpatient clinic or referred for yearly clinical assessment by their referring physician. Sustained response was defined as self-reported complete or >50% disappearance of postprandial pain, nausea, and other major complaints and persistent weight gain or stabilization during long-term follow-up of at least 6 months after the therapeutic intervention. Loss of response was defined as an initial positive response to treatment, but with loss of this response during follow-up despite patent GI arteries evaluated by renewed CTA. Primary non-responders were defined as patients who did not have any symptom improvement despite technically successful revascularization. Thus, we performed CTA at follow-up on patients with loss of response and on primary non-responders. Complete or >50% resolution of the major complaints and persistent weight gain were the main goals of treatment and therefore the most important criteria when considering follow-up CTA to investigate patency of the treated vessels. Long-term follow-up data of the latter patients were obtained by means of a survey that was conducted by contacting the primary care or referring physician and the patient. The survey focused on current health status, presence of any persisting symptoms, further diagnostic procedures, and events such as hospital admission or death.

Patients diagnosed as non-CGI were discharged from the outpatient clinic. Follow-up data of these patients were obtained by means of a survey that was conducted by contacting the primary care or referring physician and patient.

Statistical Analysis

Patients' characteristics were compared by using the Student t test, Mann–Whitney U test, or χ^2 test. For the univariate analysis the following patient characteristics were studied: age, gender, weight loss of any magnitude, weight loss per month (defined as the total amount of weight loss [in kg] a patient had from symptom onset divided by the period [in months]), postprandial pain, exercise-related pain, diarrhea, nausea, smoking, family history of CVD, known CVD, presence of abdominal bruit, body mass index after complaints, the classic triad, results of radiologic evaluation (single or multi-artery stenosis), and VLS measurements in duodenum, duodenal bulb, antrum, corpus, and esophagus.

With respect to VLS, test performances at different cutoff levels were investigated, and for each cutoff value the C statistic was estimated. The C statistic is a measure of discrimination, the ability to distinguish patients who had a persistent positive response to treatment vs those who did not. The C statistic is equal to the area under the receiver operating characteristic curve.

On the basis of literature and clinical knowledge, for multivariate analysis we used the factors with a P value