

Dynamic Color Doppler Sonography of Intestinal Wall in Patients with Crohn Disease Compared with Healthy Subjects

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ABSTRACT

Objective: Chronic inflammatory bowel diseases are characterized by inflammatory hyperperfusion of the intestinal wall in affected bowel segments. We applied a novel method to quantify color Doppler signals dynamically along a complete heart cycle inside the bowel wall. The aim was to describe bowel wall perfusion in Crohn disease patients in comparison with healthy probands and to compare a conventional activity index (Pediatric Crohn Disease Activity Index) with perfusion measurements as an indicator of inflammatory activity.

Method: Color Doppler sonographic videos of bowel wall perfusion from 34 healthy children (aged 5 to 18 years) and from 14 patients with Crohn disease (aged 8.2 to 15.9 years) were recorded under defined conditions. Perfusion signals (color hue, color area) were automatically measured inside the bowel wall. Specific tissue perfusion was calculated as mean flow velocity of a region of interest during one full heart cycle. Bowel wall perfusion was compared using the Pediatric Crohn Disease Activity Index in 12 patients.

Results: Specific bowel wall perfusion was significantly elevated in bowel segments of Crohn disease patients compared with healthy subjects ($P < 0.001$). Specific flow in small bowel was 0.025 cm/s in healthy probands and 0.095 cm/s in patients with Crohn disease, whereas large bowel wall perfusion of 0.012 cm/s in healthy probands clearly differed from 0.082 cm/s in patients with Crohn disease. No differences of perfusion between moderate and high Pediatric Crohn Disease Activity Index levels could be demonstrated despite a weak significant overall correlation.

Conclusion: The new method of dynamic, automatic non-invasive perfusion quantification is useful to describe local inflammatory activity in bowel segments affected by Crohn disease and adds new information to activity evaluation by Pediatric Crohn Disease Activity Index. Specific wall perfusion in intestines of Crohn patients is significantly elevated and reaches up to sevenfold intensity compared with healthy subjects. *JPGN* 39:524–528, 2004. **Key Words:** Bowel wall perfusion—Measurement—Color Doppler sonographic videos—Crohn disease—Healthy probands. © 2004 Lippincott Williams & Wilkins

INTRODUCTION

Inflammatory activity in Crohn disease can be evaluated by clinical, endoscopic, histologic, laboratory and sonographic investigations. Activity indices currently in use reflect disease activity according to general and rather unspecific terms (1–3). Color Doppler sonography allows depiction of inflammatory hyperperfusion and morphologic changes of the intestinal wall at the site of inflammation.

Imaging procedures can assign functional to morphologic information. They are therefore suitable to specifically correlate patient complaints with local changes in and around the bowel (4–6). Ultrasound has been used to

assess perfusion changes in the feeding arteries (7) as well as in the bowel wall itself (8,9).

Previously only still images have been evaluated and a rather coarse scoring system was applied. Velocity values of vessels or single pixels, their area and the change of these parameters with heartbeat had not been included. With a recently available software package (Pixelflux®; Chameleon-Software 2003, Leipzig, Germany) applied to renal and tumor perfusion measurement (10,11), it has become possible to include these measurements in intestinal wall segments. We investigated bowel wall perfusion with this new technique to determine whether the procedure is feasible and if a numerical discrepancy between healthy probands and Crohn disease patients would be detectable.

We sought to measure local perfusion inside intestinal wall segments by automatic, dynamic color Doppler signal quantification, to compare wall perfusion in Crohn disease patients with normal intestinal wall perfusion and to correlate the new method with conventional

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activity grading by a conventional index, the Pediatric Crohn Disease Activity Index.

Probands and Patients

We investigated 34 healthy subjects without anamnestic, clinical or laboratory signs of acute or chronic bowel disease (no history of recurrent diarrhea or acute diarrhea in the previous 4 weeks, no recurrent abdominal pain, no weight loss, normal weight for age and height, no fever, normal inflammatory signs as erythrocyte sedimentation rate, (5 to 18 years; mean, 12.5 years; median, 12.0 years) and 14 patients with endoscopically and histologically proven Crohn disease (8.2 to 15.9 years; mean value, 13.9 years; median, 15.7 years). Three hundred and forty videos with 14,875 single color Doppler sonographic images of healthy probands and 2345 videos of Crohn patients bowel segments encompassing 85,432 single color Doppler sonographic images have been quantitatively analyzed. Informed consent was achieved from probands, patients and their parents. Crohn disease patients were enrolled in the study without consideration of their actual disease activity.

METHODS

All patients and probands and parents gave informed consent for color Doppler sonography of the bowel. The bowel wall was depicted in a standardized manner in longitudinal and transverse sections. Longitudinal sections were set at midplane of intestinal tube, transsections perpendicular to the long axis.

The following segments were investigated separately: terminal ileum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum and small bowel loops in the right and left upper and lower quadrants. In patients with Crohn disease, affected intestinal segments had been determined by endoscopy and sonography. Typical sonographic signs of chronic transmural inflammation (thickening of the wall, loss of stratification, stenosis) made it easy to detect these segments in follow-up studies.

DICOM color Doppler sonographic videos were recorded with a Sequoia 512® ultrasound System (Acuson, Mountain View, CA). For all investigations the same transducer (8 MHz linear array; b-mode frequency, 8 MHz; color Doppler frequency, 7 MHz) and the same preset of the machine was used: focus at the depth of the bowel segment under investigation, color sensitivity with high spatial resolution (S1 grade of the manufacturer's denomination), edge delineation grade -1, delta value 5, post-processing scale 6, persistence 2. Videos with up to 3 seconds duration were recorded from all bowel segments in longitudinal and transverse sections. Mean values of perfusion signals (mean velocity value per area under investigation) for each bowel segment were calculated.

Videos were analyzed offline after transfer to a personal computer. A recently available software for blood flow intensity measurement (Pixelflux®, Chameleon-Software) was applied. This software, after calibration of velocity and distance, allows automatic quantification of Doppler data from a freely chosen region of interest. In each image of the video each color pixel

inside the region of interest was evaluated according to its velocity value and the area occupied by flow signals was determined. From these data the mean blood flow velocity was calculated during the complete heart cycle for the entire area under investigation. Blood flow intensity is proportional to flow velocity and to the area occupied by perfused vessels. This is the rationale for calculation of "specific flow." Specific flow is a measure of mean flow velocity encoded by color Doppler pixels as if the whole region of interest was perfused homogeneously with this velocity. In this manner mean blood flow intensity was evaluated for each segment of intestinal wall.

Differences of specific perfusion of the bowel wall in both groups were evaluated by means of the Mann-Whitney-*U* test. Correlation was calculated according to the Pearson coefficient. *P* values less than 0.05 were regarded as statistically significant.

RESULTS

Patients with Crohn disease had higher blood flow intensity compared with healthy probands irrespective of disease activity. We found a mean small bowel wall perfusion velocity of 0.025 cm/s in healthy probands and 0.095 cm/s in patients with Crohn disease and large bowel wall perfusion velocity of 0.012 cm/s in healthy probands and 0.082 cm/s in patients with Crohn disease. These differences were highly significant ($P < 0.001$) (Figs. 1 and 2). The Pediatric Crohn Disease Activity Index was calculated as normal in one, elevated (more than 150 but less than 220) in four patients and highly elevated (more than 220) in seven patients. No difference of perfusion was found between moderate and highly elevated Pediatric Crohn Disease Activity Index groups. A weak, significant correlation was demonstrated between bowel wall perfusion and Pediatric Crohn Disease Activity Index values ($r = 0.349$, $P = 0.001$) (Fig. 3).

DISCUSSION

Detection and exact evaluation of inflammation activity in Crohn disease is a basic question. Traditional pediatric measures of Crohn disease activity have drawbacks, including dependence on parameters that are un-specific measures of inflammation, inflammation-related changes in blood and physical sequelae of inflammation or malabsorption (2). Reservations have been expressed regarding these limitations (3,12-15). Other authors report on sufficient test sensitivity for clinical purposes and stress their value for scientific work (2,16-18). The sheer number of attempts to develop and adopt new indices and questionnaires clearly indicates that satisfactory results remain elusive (2,14,19-21).

Previously intestinal wall blood flow was quantified by counting color signals in a square centimeter of bowel wall section (8), detection of flow signals in diseased bowel wall (22), laser Doppler flowmetry (23) or observation of flow in splanchnic arteries (24). These methods

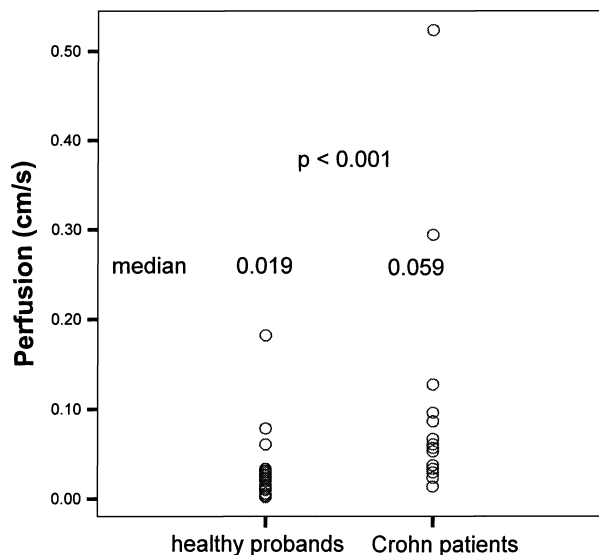


FIG. 1. Comparison of small bowel wall perfusion in healthy subjects and Crohn disease patients—the difference is significant.

have demonstrated value but remain limited in various ways. Simple counting of flow signals (i.e., vessel sections) is only a rough estimate of flow. Important characteristics such as flow velocity and diameter of intramural vessels, as well as relation of vessel area to wall area, are not considered by this method. Changes of signal intensity during the heart cycle may not be perceived. Laser Doppler flowmetry requires endoscopy and is thereby limited to endoscopically reachable parts of intestinal tract. Flowmetry in large splanchnic arteries

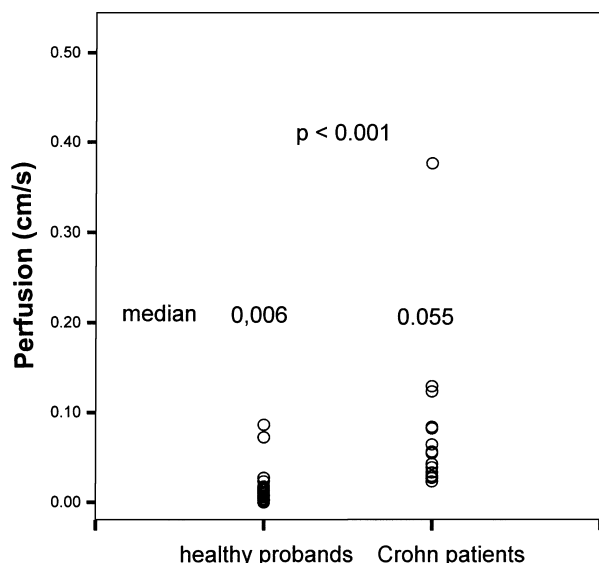


FIG. 2. Comparison of large bowel wall perfusion in healthy subjects and Crohn disease patients—the difference is significant.

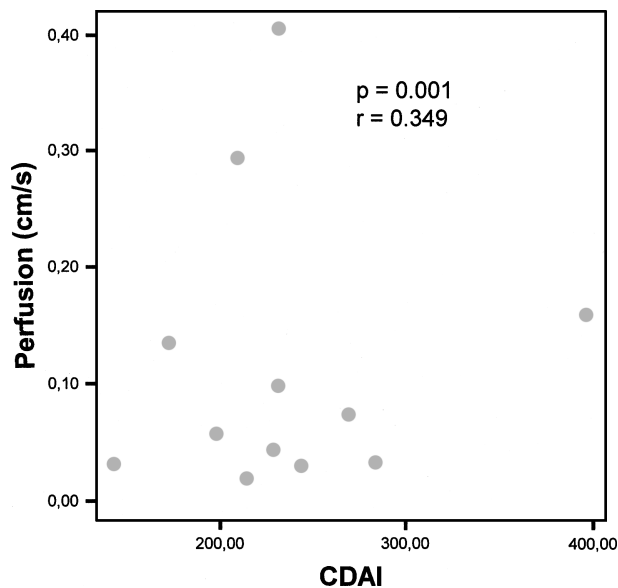


FIG. 3. Weak significant correlation (Pearson's correlation coefficient) between PDCAI score and bowel wall perfusion in Crohn disease patients.

refer to the whole bowel fed by these vessels. Local changes of flow in shorter segments may lead only to distinct changes of flow and could be missed with this method (25,26).

Our investigations are the first to describe bowel wall perfusion quantitatively throughout a complete heart cycle. We first measured intestinal perfusion in small and large intestines of healthy probands and found a low perfusion with significant differences between these segments of the intestinal tract. Patients with Crohn disease exhibit an enormous enhancement of blood flow intensity inside the swollen intestinal wall. Maximum flow exceeds normal flow 10-fold to 20-fold in single patients (results not shown). These changes of perfusion can be used diagnostically for follow-up studies and grading of disease activity. In clinical practice the use of activity indices is common. The combination of laboratory data and self-assessed criteria (stool frequency and consistency, abdominal pain) is problematic, especially in pediatric patients. We compared activity assessment by the Pediatric Crohn Disease Activity Index according to Harms et al. (1) with bowel wall perfusion measurement in 11 children. Nearly equal perfusion was found in both moderate and high activity groups (0.126 versus 0.121 cm/s). Correlation of both parameters was very weak but significant (Fig. 3). Despite the low number of patients a marked deviation between Pediatric Crohn Disease Activity Index and perfusion is obvious. We therefore hold the opinion that perfusion measurement is a valuable advancement over conventional scoring systems. This is especially important in a pediatric population in whom information regarding illness is always

given or at least modified by parents and other caregivers. A simple, noninvasive, quantitative, cheap measurement of local inflammatory activity is most welcome in this population. Discrepancies with scoring systems in use are not surprising considering that different parameters are evaluated. At inauguration of such systems the grading of the scores was arranged according to the common estimation of disease activity by an experienced physician (27). Because an independent standard of inflammation activity was missing a somewhat paradoxical situation arose. The combination of parameters selected attempted to describe disease activity better and more comparably. The parameters were summarized, but the decision, if there was a more or less active state of inflammation, was made according to general physician's evaluation. Modern imaging modalities overcome these limitations and add specific local information to the more general data of activity indices.

Even without consideration of actual disease activity or comparing affected and unaffected segments in detail, mean blood flow intensity of Crohn disease patients was up to seven times higher than perfusion of the intestinal wall in healthy probands. These findings indicate possible useful applications of the new technique of automatic color Doppler sonographic perfusion measurement in Crohn disease and its complications. Further studies should focus on monitoring therapeutic effects on local inflammation and application of this new technique on ulcerative colitis patients. The precise assessment of local inflammatory activity offers the chance for custom therapy according to individual patient states of inflammation.

CONCLUSION

Dynamic color Doppler measurement of intestinal wall perfusion can quantify inflammation in Crohn disease. It shows an up to sevenfold increase of perfusion intensity and significant differences from healthy probands and adds information to conventional activity grading. This tool could improve diagnostics and follow-up of chronic inflammatory bowel diseases.

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