CONTRAST-ENHANCED ULTRASONOGRAPHY OF THE SMALL BOWEL IN HEALTHY CATS

Alessia Diana, Swan Specchi, Marco Baron Toaldo, Roberto Chiocchetti, Andrea Laghi, Mario Cipone

We characterized the pattern of ultrasonographic contrast enhancement of the small intestinal wall using a commercial contrast medium (Sonovue®) in 10 healthy awake cats. Subjectively, a rapid intense enhancement of the serosal and submucosal layers was followed by gradual enhancement of the entire wall section during the early phase. At peak enhancement, there was a subjective loss of demarcation between intestinal wall layers. In the late phase, there was a gradual wash out of signal from the intestinal wall. Submucosal wash out occurred last. Time-intensity curves were generated for selected regions in the intestinal wall and multiple perfusion parameters were calculated for each cat. Perfusion parameters included arrival time (7.64 ± 2.23 s), baseline intensity (1.04 ± 0.04 a.u.), time to peak from injection (10.74 ± 2.08 s), time to peak from initial rise (3.1 ± 1.15), peak intensity (8.92 ± 3.72 a.u.), wash-in rate (2.06 ± 0.70 a.u./s) and wash-out rate (-1.07 ± 0.91 a.u./s). The perfusion pattern of normal feline small bowel may be useful for characterizing feline gastrointestinal disorders that involve the intestinal wall. © 2011 *Veterinary Radiology & Ultrasound, Vol. 52, No. 5, 2011, pp 555–559.*

Key words: cat, contrast-enhanced ultrasonography, small intestine.

Introduction

Contrast-enhanced ultrasonography has been used to evaluate perfusion of normal lymph nodes, liver, spleen, and kidney in the dog[1–5] and the normal pancreas and kidney in the cat.[6–8] This technique has also been used for the characterization of focal splenic,[9,10] hepatic[11–13] and renal lesions,[14] and for the diagnosis of congenital portosystemic shunts in small animals.[15]

In humans, contrast-enhanced ultrasonography was used to evaluate vascularity of the gastrointestinal wall in neoplastic[16–18] and inflammatory diseases.[19–23] Increased bowel vessel density, detected using a second generation ultrasound contrast medium, was associated with disease activity in patients with Crohn's disease.[21–23] In particular, different patterns of wall enhancement have been described in Crohn's disease patients on the basis of specific mural layer enhancement.[24] On the contrary, bowel ischemia is characterized by a decrease or lack of enhancement.[25]

In veterinary medicine, diagnostic ultrasonography has been used widely for the evaluation of the gastrointestinal wall both in normal and pathological conditions.[26] To our knowledge, there are only two reports concerning contrast-enhanced ultrasonography of the small intestine in the cat[8] and dog.[27] The first describes the quantitative contrast-enhanced ultrasonographic analysis of perfusion in abdominal organs of healthy cats, including small intestine[8] while the other describes intraoperative contrast-enhanced ultrasonography of normal canine jejunum.[27]

The first aim of this study was to assess the feasibility of contrast-enhanced ultrasonography in the feline small bowel. The second was to describe the pattern of sonographic contrast enhancement.

Materials and Methods

Ten healthy domestic short haired cats, volunteered by their owner, were studied. There were five males, four females and one neutered female. The mean age was 5.2 years (standard deviation [SD] ± 2 years) and mean bodyweight was 4 kg (SD ± 0.7 kg). The cats were healthy on the basis of physical findings and routine laboratory data. The cats were negative for feline leukemia virus antigen, feline immunodeficiency virus antibody, and feline coronavirus antibody. The cats were fasted overnight, for at least 12 h, before imaging. All procedures were conducted by the same sonographer (A.D.), using a real-time ultrasound machine.* Hair over the abdomen was clipped, the skin surface was cleaned with 70% isopropyl alcohol, and coupling gel was applied. The cats were awake and restrained manually during the examination.

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Received November 3, 2010; accepted for publication April 5, 2011.
doi: 10.1111/j.1740-8261.2011.01829.x

*iU22 ultrasound system, Philips Healthcare, Monza, Italy.

The abdomen was scanned by B-mode ultrasonography using a broadband curved array transducer (5–8 MHz). The gastrointestinal tract was also scanned with a broadband linear array transducer (3–9 MHz). With each cat in right recumbency, one superficial jejunal segment in the left middle abdominal region was selected for color Doppler evaluation and contrast-enhanced ultrasonography. The segment was scanned in a transverse section and the broadband linear array transducer was not moved subsequently. Color Doppler ultrasonography of the intestinal wall was performed using a low wall filter and 300 Hz pulse repetition frequency. Color gain was adjusted dynamically to maximize visualization of the blood vessels while avoiding artifactual color noise. Contrast-specific software (Pulse Inversion Harmonic and Power Modulation combined—PMPI) with a low mechanical index set (0.07) was activated. The gain setting was regulated to obtain an anechoic bowel wall, which was as complete as possible except for the hyperechoic serosal layer and the central hyperechoic line arising from the bowel lumen. Image acquisition was for 180 s from the time of onset of contrast medium administration. The contrast medium (Sonovue® †) was administrated manually through an indwelling cephalic venous 22 G catheter as a rapid bolus dose of 0.5 ml followed immediately by a rapid bolus of 4 ml saline The images were recorded as cine-segments in DICOM format and transferred to a personal computer.

Show Case software‡ was used to view the images and to export selected frames for analysis. Color Doppler images of the intestinal wall were evaluated subjectively for the distribution of mural vessels based on color Doppler signals within the intestinal wall.

The distribution of the contrast medium enhancement within the intestinal wall was evaluated subjectively as satisfactory or unsatisfactory based on the degree of jejunal mural enhancement and homogeneity of mural enhancement at peak intensity (PI). The pattern of contrast medium enhancement was also described.

To assess the degree of the enhancement of the intestinal wall, the E/W ratio was used,[24] where E is the major thickness of the enhanced layer and W is the width between the edge of the outer wall and the superficial mucosal interface measured in millimeters on gray-scale images (Fig. 1). The mean value of three measurements, obtained at three different points of the same ultrasonographic image, was used for analysis. The contrast-enhanced ultrasonography findings were evaluated during all three phases of wall perfusion (i.e. early, peak enhancement, and late phase).

A commercial software program§ was used for quantitative computerized analysis of the contrast medium blood pool phase. A region of interest (ROI), drawn to cover the wider portion of the intestinal section, was placed manually in the intestinal wall between the serosal layer and the mucosal interface. The ROI was maintained in the same position by the motion compensation tool of the QLAB software. This tool prevents the displacement of the ROI during respiratory motion. Furthermore, the ROI was adjusted manually on those frames affected severely by respiratory motion.

Artifactual data from adjacent tissue that moved into the ROI during respiratory motion or gas bubbles were removed manually from the final data set to reduce the influence of noise. The raw data obtained from each cat were plotted in time-intensity diagrams.

The following perfusion variables were recorded: arrival time (AT) defined as the time when contrast signal is increasing to greater than double the baseline value in the time-intensity curve, time to peak from injection (TTP_{inj}), time to peak from initial rise (TTP_{inr}), baseline intensity, PI, wash-in rate (W_i) and wash-out rate (W_o) (Fig. 2).

W_i and W_o were calculated as the maximal change rate, using data points 20% above baseline and 20% below peak to exclude variability at the toe and shoulder of the time-intensity curve. The data were then regressed for significance of linearity.¶ Significance for analysis was set at $P<0.05$. Data calculated for each variable, using a commercial software program,‖ include means and SD.

Results

There were no Doppler signals within the intestinal wall in any cat. Low Doppler signals were detected in the mesentery adjacent to the intestinal segment in five cats.

Contrast enhancement was judged subjectively to be satisfactory in nine cats. In one cat, inadequate concentration of contrast medium at the level of the intestinal wall was caused by incorrect positioning of the intravenous catheter. During contrast-enhanced ultrasonography, jejunal arteries were identified clearly and there was an initial rapid enhancement of serosal and submucosal layers, followed by a more gradual enhancement of the entire wall section (Fig. 3A). At peak enhancement, there was a subjective lack of demarcation between wall layers (Fig. 3B). In the late phase, there was a gradual wash out of signal from the intestinal wall. The wash out of the submucosal layer occurred last (Fig. 3C). This perfusion pattern of the intestinal wall was seen consistently in all cats. The mean E/W ratio was 0.92 (SD $\pm$ 0.09).

Quantitative computerized analysis of the intestinal wall enhancement was performed in nine cats (Table 1). Data of

†Bracco® diagnostic, Milano, Italy.
‡Trillium Technology, Ann Arbor, MI.
§QLAB quantification software, Philips Healthcare.
¶Prism 5®, GraphPad Software Inc., San Diego, CA.
‖Microsoft Excel, Microsoft Corporation, Redmond, WA.

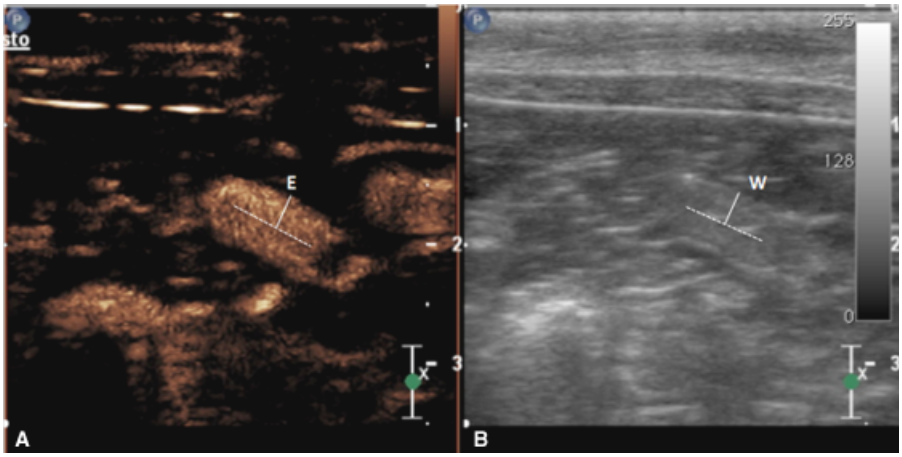

FIG. 1. An example of E/W ratio. Contrast enhancement image (A) and gray scale image (B) at peak enhancement. E is the major thickness of the enhanced layer under contrast-enhanced ultrasonography and W is the width between the edge of the outer wall and the superficial mucosal interface. The dotted lines represent the superficial mucosal interface.

W_i and W_o were characterized by a significant linear relationship ($P<0.01$). The correlation coefficient (r^2) of the regression lines ranged from 0.77 to 0.98.

Discussion

The microvascular architecture of the small intestinal wall is composed of two different parallel capillary beds: the mucous–submucous plexus and the muscular–serous plexus.[28–30] Under resting conditions, approximately 80% of the blood flow in the feline small intestinal wall is distributed to the mucosa–submucosa and 20% to the muscularis–serosa.[30–32] In particular, all of the main and large anastomotic vessels (30–80 μm in diameter) are located in the submucosal layer, whereas a plexus of smaller vessels is embedded in the *muscularis mucosae*.[30] The mucosal arteries divide in a stellate manner into branches which are ramified in the mucosal layer. Each villus is usually supplied by a single arterial vessel that runs in the central villous core. Close to the villous tip, the central vessel arborizes into a dense capillary network. The capillaries collect into veins at the villous base.[31–33]

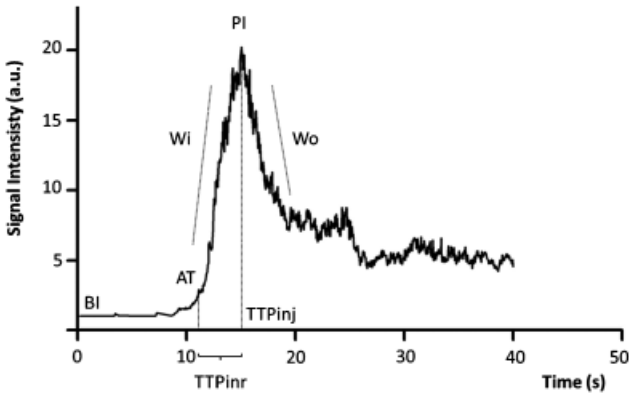

FIG. 2. Signal intensity in arbitrary units (a.u.) as a function of time in seconds (s) in a normal feline jejunal segment. Contrast enhancement increases until reaching peak intensity. AT, arrival time; BI, baseline intensity; TTP_{inj}, time to peak from injection; PI, peak intensity; TTP_{inr}, time to peak from initial rise; W_i, wash-in rate; W_o, wash-out rate.

We were unable to detect blood flow in intramural vessels in any cat using Doppler ultrasonography and only a few Doppler signals were found in the adjacent mesentery. In human medicine, color Doppler ultrasonography has been used to evaluate the vascularity of the intestinal wall in patients with Crohn's disease.[34–36] Affected intestinal segments have an increase in the number and caliber of intramural vessels.[34–36] Increased blood flow in the main splanchnic vessels has also been found in inflammatory bowel disease in both humans[34–36] and dogs.[37,38] Diameter and slow blood flow are limiting factors regarding detection of blood vessels in the normal feline bowel wall.[39]

The contrast-enhanced ultrasonography pattern, which was consistent across all cats, was associated strongly with the anatomic distribution of intramural vessels.[30,32] The intense and rapid enhancement of the submucosal layer depends on the presence of a rich plexus, draining 80% of the total intramural blood flow.[30,32,33] The slower wash out of the submucosal layer may be explained by the more tortuous capillary network in this layer that reduces blood flow through the submucosal vessels.

The mean E/W ratio was 0.92 indicating near complete enhancement of the entire intestinal wall from the mucosa to the serosa. Due to the small thickness of the normal feline small intestinal wall (2.41 ± 0.14 mm), a single ROI that included all mural layers was drawn. The results of the quantitative variables represent a mean value obtained from the entire intestinal wall rather than the different vascular distribution in each layer.

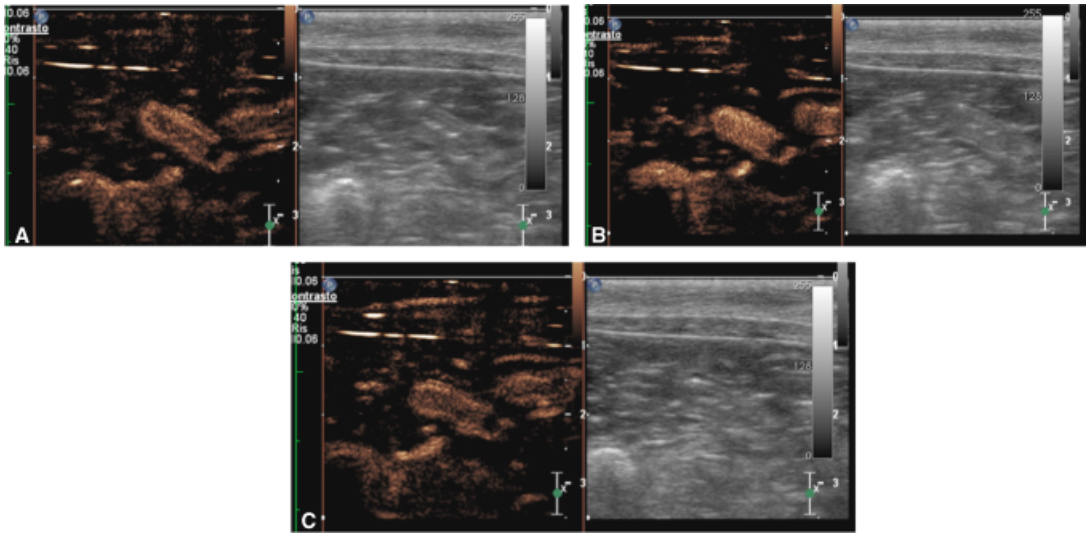

FIG. 3. A representative contrast-enhanced ultrasound sequence (A, B, and C) of a normal jejunal segment in a transverse plane after injection of Sonovue®. Each image illustrates contrast enhancement on the left and the gray scale image on the right. (A) The contrast medium is present predominantly in the serosal and submucosal layers. (B) Homogeneous enhancement of the entire intestinal wall at peak enhancement. (C) A gradual decrease of enhancement of the intestinal wall. Persistent enhancement is seen in the submucosal layer.

TABLE 1. Results (Mean ± SD) of Quantitative Contrast Enhanced Ultrasonography of Small Bowel in Nine Healthy Cats

Parameters	Mean ± SD
AT (s)	7.64 ± 2.23
BI (a.u.)	1.04 ± 0.04
TTP_{inj} (s)	10.74 ± 2.08
PI (a.u.)	8.92 ± 3.72
TTP_{inr} (s)	3.1 ± 1.15
W_i (a.u./s)	2.06 ± 0.70
W_o (a.u./s)	−1.07 ± 0.91

AT, arrival time; BI, baseline intensity; TTP_{inj}, time to peak from injection; PI, peak intensity; TTP_{inr}, time to peak from initial rise; W_i, wash in rate; W_o, wash out rate; a.u., arbitrary units.

Good quality time-intensity curves were obtained for nine cats. The upslope and downslope part of the curve was linear. A second small peak of enhancement due to reperfusion was observed later. These values were excluded from the measurement of W_o to examine only the first transit of the through the intestinal wall. Some parameters in our cats i.e. AT, TTP_{inj}, and TTP_{inr}, were slightly higher than others reported recently in healthy anesthetized cats.[8] Sedation and anesthesia were avoided purposely in our cats to obtain baseline values without iatrogenic changes in blood pressure and heart rate.[40–42] In feline spleen, anesthesia resulted in a longer AT compared with awake cats.[40] On the contrary, anesthesia resulted in a shorter time to peak enhancement of normal liver and kidney in the dog.[2,8] The impact of anesthesia on organ perfusion depends on the characteristics of anesthetic agent and on the different vascular structures and blood flow of each organ.[8] Several other factors, such as technical scanning variables, contrast medium characteristics, injection technique, and patient-related factors can influence quantitative variables.[2,5,8,43–46]

Peak intensity values were lower in comparison to those reported by others.[8] The use of different contrast media and different imaging system implies a different number of circulating microbubbles and, as a consequence, a different backscatter response from the tissue that influences the degree of contrast enhancement.[2,27,44,46] Differences in intensity-measuring units and scale among different modalities (dB vs. video-intensity units) can also complicate comparisons.[2,5] Furthermore, mechanical index influences the amount of microbubble destruction and also affects the amplitude of harmonic signals.[5,44,46] Because of these reasons, quantitative values obtained from different protocols are not entirely comparable.[2,5,8,43–46]

Fasting for at least 12 h before contrast-enhanced ultrasonography of the bowel is suggested to minimize the presence of gas and food particles[26] that create strong interference during the activation of the contrast-specific software. Furthermore, fasting is recommended to reduce the peristaltic activity[26] to avoid motion artefact that limits quantitative analysis.

In conclusion, we demonstrated that contrast-enhanced ultrasonography can be used for evaluation of intramural blood vessels of the feline small intestine. The perfusion pattern is distinctive. Contrast-enhanced ultrasonography may enable the characterization of bowel wall perfusion in cats affected by various gastrointestinal disorders.

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