Evaluation of computed tomographic enterography with an orally administered lactulose solution in clinically normal dogs

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OBJECTIVE
To determine optimal techniques for CT enterography in clinically normal dogs and to evaluate luminal distention after oral administration of lactulose solution as a contrast agent.

ANIMALS
15 healthy dogs.

PROCEDURES
CT was performed in a control group (2 dogs that underwent CT to evaluate metastasis and 5 other dogs). In a bolus administration group (5 dogs from the control group), lactulose solution (1.34 g/mL) was administered (60 mL/kg) rapidly via gastric tube to anesthetized dogs, and CT was performed every 10 minutes for 1 hour. In a continuous administration group of 8 other dogs, lactulose solution (60 mL/kg) was administered slowly via nasoesophageal tube over a period of 45 minutes. Then, 15 minutes after anesthetic induction, CT was performed every 10 minutes for 1 hour. Luminal distention of the small intestines was evaluated qualitatively by use of a 3-point scale.

RESULTS
All small intestinal segments had poor luminal distention in the control group. The terminal ileum had poor luminal distention for the bolus administration group. Nearly all segments had good luminal distention for the continuous administration group with mild adverse effects. Luminal distention scores from 0 to 20 minutes after lactulose administration were significantly higher than scores from 30 to 60 minutes. Interobserver reproducibility was high for all intestinal segments.

CONCLUSIONS AND CLINICAL RELEVANCE
CT performed between 0 and 20 minutes after continuous administration of lactulose solution (60 mL/kg) may reveal adequate luminal distention for examination of small intestinal segments in dogs. (Am J Vet Res 2016;77:367–373)
scribe and optimize the techniques for CT enterography in clinically normal dogs. We hypothesized that the degree of luminal distention of the small intestines of dogs could be affected by variations in the methods for administration of contrast medium.

Materials and Methods

Animals

Fifteen client-owned clinically normal adult dogs were enrolled in the study. This included 13 adult dogs (age range, 1 to 7 years; body weight range, 2.3 to 6 kg). Six of the dogs were male (5 neutered) and 7 were female (2 neutered). Breeds represented included Poodle (n = 5), mixed (5), Shih Tzu (1), Beagle (1), and Pomeranian (1). Two additional dogs that underwent abdominal CT for evaluation of metastasis of mammary gland tumor were also included (a 5-year-old neutered female Maltese that weighed 3.6 kg and a 6-year-old sexually intact female Cocker Spaniel that weighed 6 kg). All dogs were clinically normal as determined on the basis of results of a physical examination, CBC, serum biochemical analysis, and measurement of electrolyte concentrations. No dogs had evidence of gastrointestinal disease on the basis of the medical history or results for abdominal radiography, ultrasonography, or fecal testing.

Owner informed consent was obtained for all dogs. The protocol for this study was approved by the Institutional Animal Care and Use Committee at Seoul National University.

CT enterography

A control group comprised 7 dogs (the 2 dogs that underwent abdominal CT for evaluation of metastasis of mammary gland tumor and 5 other volunteered dogs). Those 5 volunteered dogs then comprised a bolus administration group. Finally, the 8 other volunteered dogs comprised a continuous administration group.

Food was withheld from all dogs for 12 hours before CT examination. For the control group, anesthesia was induced with diazepam (0.2 mg/kg, IV) and propofol (6 mg/kg, IV) and maintained with isoflurane in oxygen. Computed tomography without lactulose administration was performed on the anesthetized dogs. Dogs of the bolus administration group each received a bolus administration of lactulose solution. Dogs of the continuous administration group each received a nasoesophageal tube (3F to 5F). The lactulose solution was diluted at a ratio of 1:4 (1 part lactulose solution to 4 parts warm water) and was slowly administered (total volume of the diluted solution administered, 60 mL/kg) as a constant rate infusion via the nasoesophageal tube over a period of 45 minutes. Dogs were then anesthetized, butylscopolamine bromide (0.4 mg/kg, IV) was administered, and CT was performed beginning 15 minutes after completion of lactulose solution administration.

All CT images were acquired with dogs positioned in sternal recumbency, with the head slightly elevated to prevent reflux of contrast agent from the stomach during CT examination. All CT images were acquired by use of a 16-channel multidetector CT scanner. Images were acquired from the diaphragm to the pubic symphysis with the following settings: 120 kV, 200 mA, 1-second tube rotation time, 2.5-mm slice thickness, 1,375 pitch, and 200-mm field of view. Manual hyper-ventilation was performed during scanning to induce transient apnea and reduce motion artifacts. Adverse effects, including signs of nausea, vomiting, and diarrhea, were recorded.

Image analysis

The CT images were reconstructed at a thickness of 2.5 mm and evaluated with a soft tissue window (window width, 400 HUs; window level, 40 HUs) by 2 veterinary radiologists with ≥ 4 years of experience (SK and JS); the investigators were not aware of identifying information such as the group assignment or time at which the ST image was obtained. The small intestines were evaluated as the following 4 segments: descending duodenum, ascending duodenum, jejunum, and terminal ileum. The descending duodenum included the cranial duodenal flexure and descending portion of the duodenum. The ascending duodenum included the caudal duodenal flexure and ascending portion of the jejunal segment adequately distended (poor [A]), 40% to 70% of the jejunal segment adequately distended (good [B]), and > 70% of the jejunal segment adequately distended (optimal [C]).
the duodenum. The jejunum began at the duodenojejunal flexure and ended at the ileum. The terminal ileum was that portion of the ileum caudal to the ileocolic fold.

Luminal distention of each segment was qualitatively evaluated by use of a 3-point scale (0 = poor, 1 = good, and 2 = optimal) that had been modified from previous human enterography studies. The score was determined as the percentage of the small intestinal segment with adequate distention as follows: poor when < 40% of the segment was distended, good when 40% to 70% was distended, and optimal when > 70% was distended (Figure 1). During evaluation of the degree of luminal distention, the investigators attempted to examine the entire length of each given intestinal segment, if possible. The intestinal segment was considered to have adequate distention if the intestinal walls could be distinguished from the lumen.

Statistical analysis
Age and body weight of dogs in the control, bolus administration, and continuous administration groups were compared by use of a 1-way ANOVA. Luminal distention scores were expressed as mean ± SD. Analysis of reproducibility between reviewers was performed by use of the ICC test. Luminal distention scores over time for the continuous administration group were analyzed by use of the Mann-Whitney U test. Values of P < 0.05 were considered significant. Statistical analyses were performed with commercial software.

Results
Mean ± SD age of dogs did not differ significantly among the control (2.15 ± 2.71 years), bolus administration (3.63 ± 2.31 years), and continuous administration (3.11 ± 2.77 years) groups. Mean body weight did not differ among the control (4.04 ± 1.48 kg), bolus admin-

Table 1—Luminal distention score* and ICC for each intestinal segment for the bolus administration group (n = 5 dogs) on the basis of time after administration of lactulose solution.

<table>
<thead>
<tr>
<th>Intestinal segment</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descending duodenum</td>
<td>0.70 ± 0.67</td>
<td>1.20 ± 0.42</td>
<td>1.30 ± 0.48</td>
<td>1.20 ± 0.63</td>
<td>1.10 ± 0.73</td>
<td>1.10 ± 0.99</td>
<td>0.90 ± 0.87</td>
<td>0.955</td>
</tr>
<tr>
<td>Ascending duodenum</td>
<td>0.60 ± 0.84</td>
<td>1.10 ± 0.87</td>
<td>1.40 ± 0.51</td>
<td>1.50 ± 0.52</td>
<td>1.60 ± 0.51</td>
<td>1.40 ± 0.51</td>
<td>1.30 ± 0.82</td>
<td>0.943</td>
</tr>
<tr>
<td>Jejunum</td>
<td>0.10 ± 0.31</td>
<td>0.60 ± 0.51</td>
<td>0.70 ± 0.67</td>
<td>1.00 ± 0.94</td>
<td>1.00 ± 0.94</td>
<td>0.90 ± 0.73</td>
<td>0.90 ± 0.73</td>
<td>0.982</td>
</tr>
<tr>
<td>Terminal ileum</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0.40 ± 0.84</td>
</tr>
</tbody>
</table>

*Values reported represent the mean ± SD for 2 investigators who scored luminal distention by use of a 3-point scale (0, poor [< 40% of the jejunal segment adequately distended]; 1, good [40% to 70% of the jejunal segment adequately distended]; and 2, optimal [> 70% of the jejunal segment adequately distended]). †Oral administration of a bolus (60 mL/kg) of lactulose solution (1.34 g/mL) diluted 1:4 was designated as time 0. The descending duodenum included the cranial duodenal flexure and descending portion of the duodenum. The ascending duodenum included the caudal duodenal flexure and ascending portion of the duodenum. The jejunal segment was that portion of the ileum caudal to the ileocolic fold.
Table 1—Luminal distention scores* and ICC for each intestinal segment for the bolus administration group (n = 5 dogs) on the basis of time after administration of lactulose solution.

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<tr>
<th>Intestinal segment</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending duodenum</td>
<td>1.50 ± 0.51</td>
<td>1.56 ± 0.51</td>
<td>1.50 ± 0.51</td>
<td>1.13 ± 0.71</td>
<td>1.06 ± 0.68</td>
<td>1.25 ± 0.44</td>
<td>1.06 ± 0.44</td>
<td>0.951</td>
</tr>
<tr>
<td>Descending duodenum</td>
<td>1.38 ± 0.50</td>
<td>1.38 ± 0.50</td>
<td>1.44 ± 0.51</td>
<td>1.25 ± 0.57</td>
<td>1.19 ± 0.65</td>
<td>1.13 ± 0.61</td>
<td>1.06 ± 0.57</td>
<td>0.896</td>
</tr>
<tr>
<td>Jejunum</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>0.990</td>
</tr>
<tr>
<td>Terminal ileum</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>1.48 ± 0.50</td>
<td>0.990</td>
</tr>
</tbody>
</table>

*Oral administration of a bolus (60 mL/kg) of lactulose solution (1.34 g/mL) diluted 1:4 was designated as time 0 for the bolus group; time 0 for the continuous group was 15 minutes after completion of a continuous oral administration of the same total dose of lactulose solution, which was administered over a 45-minute period.

See Table 1 for remainder of key.

Table 2—Luminal distention scores* and ICC of the entire small intestinal tract for the bolus administration group (n = 5 dogs) and continuous administration group (8) on the basis of time after administration of lactulose solution.

<table>
<thead>
<tr>
<th>Administration group</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus</td>
<td>0.35 ± 0.62</td>
<td>0.73 ± 0.71</td>
<td>0.85 ± 0.73</td>
<td>0.93 ± 0.82</td>
<td>0.93 ± 0.85</td>
<td>0.85 ± 0.83</td>
<td>0.88 ± 0.85</td>
<td>0.953</td>
</tr>
<tr>
<td>Continuous</td>
<td>1.34 ± 0.78</td>
<td>1.38 ± 0.70</td>
<td>1.38 ± 0.74</td>
<td>1.25 ± 0.77</td>
<td>1.19 ± 0.77</td>
<td>1.19 ± 0.73</td>
<td>1.08 ± 0.71</td>
<td>0.927</td>
</tr>
</tbody>
</table>

†Time 0 was 15 minutes after completion of a continuous oral administration of lactulose solution (60 mL/kg), which was administered over a 45-minute period.

See Table 1 for remainder of key.

Discussion

In veterinary medicine, hydro-CT for stomach images14 or gastrointestinal CT images15 has been described. In a study14 involving hydro-CT, the stomach wall before administration of water was not appropriate for evaluation because the lumen was empty and collapsed. Computed tomographic evaluation of the gastric wall was performed after administration of various volumes of water via gastric tube, and it was proposed that oral administration of 30 mL of water/kg with IV administration of a contrast agent was adequate for uniform gastric distention and assessment of the stomach wall.14 In another CT study15 of 19 dogs without luminal distention, the gastrointestinal wall was identified from gastrointestinal segments in 77.7% of all gastrointestinal segments.

In the study reported here, the control group had poor distention of all small intestinal segments. General CT of the small intestines may not be appropriate for evaluating the intestinal wall because of poor distention of the lumen; adequate luminal distention is a requirement for CT examination of the small intestines of dogs, similar to the situation for humans.17 Results for the present study differed from those of a previous report15 in which there was a high rate for identification of the gastrointestinal wall without oral administration of contrast medium. We suspect that the lumen of certain intesti-
In the present study, we modified the human CT enterography technique for distending the small intestinal lumen. Our modifications accounted for noninvasiveness and feasibility. The protocol for CT enterography has not been standardized for humans. Various orally administered neutral contrast agents (eg, water, water and methylcellulose, lactulose solution, ultra–low-dose barium, polyethylene glycol, and milk) have been evaluated for their ability to improve small bowel distention for CT enterography of humans.19,21,22 Lactulose solution reportedly is an effective, orally administered neutral contrast agent for humans because it links unabsorbed, unfermented lactulose molecules with water.9 The volume of lactulose solution used in the present study (60 mL/kg) was determined on the basis of results for preliminary experiments in which we detected appropriate overall small intestinal distention. In 1 preliminary experiment, a lactulose solution (1.34 g/mL) diluted at a ratio of 1:4 (total dose administered, 30 mL/kg) that was continuously administered provided poor luminal distention in the duodenum, uneven luminal distention in the jejunum, and optimal luminal distention in the ileum. In another preliminary experiment, a lactulose solution (1.34 g/mL) diluted at a ratio of 1:4 (total dose administered, 70 mL/kg) that was continuously administered provided good luminal distention in the duodenum, uneven luminal distention in the jejunum, and optimal luminal distention in the ileum. Although adverse effects for CT enterography with lactulose in humans have been detected only in geriatric patients or in patients with malignancies, mild gastrointestinal signs were evident in healthy dogs in the continuous administration group in the study reported here. Overloading nonanesthetized dogs with a large volume of liquid over a relatively prolonged period was suspected to be the cause of the signs of nausea and vomiting, but more studies are needed to determine the optimal total volume and dilution rate for lactulose solution, and caution is needed to prevent aspiration pneumonia.

In humans, contrast agent is orally administered by voluntary drinking. The total volume is divided, and portions are ingested several times during a 30- to 75-minute period for a more even distribution throughout the intestinal tract.19,21-25 Two methods for oral administration of a large dose of contrast agent were used in the present study. Because it is not possible to induce voluntary drinking of contrast agent by dogs, a large volume of lactulose solution was administered as a bolus to anesthetized dogs. Although there was good luminal distention in the ascending duodenum, descending du-

![Figure 3](attachment:Figure3.png)

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**Figure 3**—Dorsal reconstructed CT images (window width, 400 HUs; window level, 40 HUs) of a representative dog of the bolus administration group obtained at 20 minutes for the descending duodenum (A), 40 minutes for the ascending duodenum (B), 40 minutes for the jejunum (C), and 60 minutes for the terminal ileum (D). The intestinal lumen (asterisk) had good distention in the descending duodenum, ascending duodenum, and jejunum but poor distention in the terminal ileum. See Figure 2 for remainder of key.
odenum, and jejunum during the first 60 minutes after bolus administration, the terminal ileum had poor luminal distention at all time points. For humans, continuous oral intake during a 15- to 20-minute period is required for successful intestinal distention, compared with discontinuous intake or intake over a more prolonged time frame. For more effective luminal distention of all small intestinal segments in the present study, the same total dose of lactulose solution was provided via continuous administration during a 45-minute period before induction of anesthesia. Examination of the CT image obtained 15 minutes after induction of anesthesia revealed that all small intestinal segments had good luminal distention during the first 60 minutes, except for the images of the terminal ileum obtained at 0 and 10 minutes. As a result, we concluded that continuous oral administration of contrast agent is required for a more even distribution in the intestinal lumen for CT enterography of dogs, similar to the situation for humans. The time at which the CT image with the greatest luminal distention was obtained for all small intestinal segments typically was 10 and 20 minutes for the continuous administration group.

The degree of distention of the small intestine differed between the 2 administration methods, which was in agreement with our hypothesis. Although the adverse effects were mild for the continuous administration group, care must be taken during anesthetic recovery.

Butylscopolamine bromide was administered immediately before CT in the present study. We anticipated that the butylscopolamine bromide would cause stagnation of luminal contents because of intestinal hypomotility. Although the spasmolytic effect of butylscopolamine bromide in dogs has been examined, the effect of butylscopolamine bromide on luminal distention is not clear and more studies are needed. Prokinetic agents such as glucagon, hyoscine-N-butylbromide, or metoclopramide are sometimes used in conjunction with oral administration of contrast agents to humans for maximizing bowel distention with a minimum amount of contrast intake, but the usefulness of these drugs has not been clearly identified.

In the present study, the CT enterography technique of administering a lactulose solution (1.34 g/mL) diluted at a ratio of 1:4 (total dose administered, 60 mL/kg) via continuous oral administration over a 45-minute period through a nasoesophageal tube provided good distention of all small intestinal segments, with the greatest luminal distention detected between 0 and 20 minutes after lactulose administration was completed. These data can be used for additional CT enterography studies on bowel disease of dogs. Computed tomographic enterography can be used in the evaluation of small bowel disease (eg, inflammatory or neoplastic disease) for detection of mural thickening, symmetry of small bowel thickening, and mucosal hyperenhancement after IV administration of contrast agent. To standardize CT enterography protocols for use on dogs, further studies are needed regarding the technique of continuous oral administration of a large volume of contrast agent. Additionally, factors that can affect the degree of luminal distention and quality of images; the types, amounts, and dilution rates of contrast agents; the use of prokinetic agents; and CT imaging time and image-acquisition intervals need to be further evaluated.

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Footnotes
a. Merodex, Dong Wha Pharm Corp, Seoul, Korea.
References


