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Clinical Case Report

Contrast-enhanced computed tomography characterization of canine rectal neoplasms

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Abstract

Differential diagnosis of rectal neoplasms is necessary to determine an appropriate treatment plan. In humans, computed tomography (CT) is used to evaluate colorectal neoplasms. This retrospective study assessed the CT features of canine rectal neoplasms, including seventeen inflammatory polyps, six adenocarcinomas, three B-cell lymphomas and four leiomyomas on triple-phase CT. A mass lesion was observed in all seventeen cases of inflammatory polyps (100%), two of six adenocarcinomas (33%), and all four cases of leiomyoma (100%). Wall thickening was observed in four of six (67%) adenocarcinoma cases and all three (100%) lymphoma cases. The leiomyoma was more likely to show obstruction than inflammatory polyps, adenocarcinomas, and lymphomas. Homogeneous enhancement was detected in zero of seventeen (0%) inflammatory polyp cases, two of six (33%) adenocarcinoma cases, all three (100%) lymphoma cases, and all four (100%) leiomyoma cases in all post contrast phases. Lymphadenopathy was detected in three adenocarcinoma cases (50%) and three lymphoma cases (100%). Inflammatory polyps indicated a heterogeneous radial-enhancement mass. Leiomyomas indicated a homogeneous enhancement mass with bowel obstruction. In wall thickening lesions, adenocarcinoma indicated twolayer thickened annular lesions and lymphoma indicated homogeneous thickened annular lesions but less enhancement than the mucosa. These findings may help confirm the diagnosis and reduce the use of invasive biopsy procedures.

Key Words: Adenocarcinoma, Inflammatory polyp, Leiomyoma, Lymphoma, Miniature Dachshunds

Introduction

In dogs, nearly 60% of rectal neoplasms are malignant, with adenocarcinoma being the most common^{5,25)}. Other types of malignant neoplasms include lymphoma and leiomyosarcoma^{9,25)}, while benign neoplasms include adenomatous polyps and

leiomyoma^{18,36)}. In Japan, inflammatory polyps are commonly observed in miniature dachshunds²⁹⁾.

The diagnosis of rectal neoplasms is challenging because of the inherent inaccessibility of the rectum¹⁾. Several treatments for rectal neoplasms have been reported. Surgical resection is the most common treatment for canine rectal

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Laboratory of Veterinary Surgery, Division of Veterinary Science, Graduate School of Life and Environmental Sciences, Osaka Prefecture University, 1-58 Rinku, Ohrai-kita, Izumisano, Osaka 598-8531, Japan Fax: +81-72-463-5463, Tel: +81-72-463-5476; E-mail: akiyoshi@vet.osakafu-u.ac.jp doi: 10.14943/jjvr.69.3.163 adenocarcinoma^{2,21,27)}. Large, primary intestinal lymphomas treated with chemotherapy, with or without additional local therapy including surgery or radiation, have a very good prognosis^{9,37)}. Immunosuppressive therapy and endoscopic polypectomy are effective in treating inflammatory polyps²⁹⁾. Thus, the differentiation of rectal neoplasms is critical for determining an effective treatment plan.

Ultrasonography is used to detect wall abnormalities and changes in the motility of the gastrointestinal tract³⁶⁾. However, acoustic shadowing from intraluminal air, feces, and pelvic bones can make detection of colorectal lesions challenging^{7,35)}. Proctoscopy and colonoscopy are essential for complete assessment of the extent of rectal neoplasms⁵⁾. A gross examination is poorly predictive of tumor type²⁸⁾, and histopathological examination is necessary to confirm the endoscopic findings³⁸⁾. Endoscopic biopsy is a minimally invasive procedure used to collect tissue³⁴⁾. Histopathological results from endoscopic biopsies are not always representative of the lesion because of the possibility of very small and superficial tissues¹⁸⁾. If a minimally invasive biopsy fails to confirm the diagnosis, exploratory laparotomy is typically performed³⁴⁾. Therefore, an imaging modality that can differentiate rectal neoplasms may help confirm the diagnosis and reduce the use of invasive procedures.

In humans, computed tomography (CT) is used to evaluate colorectal neoplasms¹⁴⁾. CT is the most effective method for detecting metastasis, regional tumor extension, and complications such as obstructions, perforations, and fistulas¹⁴⁾. Even when colon preparation is poor, intravenous contrasts can enhance the neoplasms and make their presence more conspicuous in the presence of non-enhanced stool or copious fluid²⁶⁾. To the best of our knowledge, there is limited published information on the CT characteristics of rectal neoplasms in dogs. This study aimed to assess the CT findings of canine rectal neoplasms.

Materials and Methods

This was a retrospective case series. The owners of the dogs described in this study provided their informed consent for the diagnostic procedures, treatment, and use of clinical data, such as medical history, imaging studies, and histopathological findings for research and publication purposes. As all diagnostic studies and initiated treatments were part of daily clinical activities, the study did not reach the threshold for submission to the local ethics and welfare committee. We reviewed the records of all dogs with suspected rectal neoplasms upon rectal examination and had undergone CT examinations at Osaka Prefecture University and Kinki Animal Medical Training Institute & Veterinary Clinic between 2014 and 2020. The inclusion criterion was the presence of concurrent histopathologically diagnosed rectal neoplasms. The exclusion criterion was the documentation of metastatic lymphadenopathy from another origin tumor or multiple tumors.

CT technique

All dogs were fasted for 24 h and received saline enema before the CT examination. CT examinations were performed using a SOMATOM Scope (Siemens AG, Munich, Germany) or Activion 16 (Canon Medical Systems Corporation, Tochigi, Japan) multidetector 16-slice CT scanner in helical scan mode following the usual protocol. All dogs were induced with 7 mg/kg of propofol (Propofol 1%; MSD Animal Health K.K., Tokyo, Japan) and maintained with isoflurane (2%) and oxygen with an endotracheal tube. The dogs were placed in the dorsal recumbency position and ventilated during the CT procedure. Apnea was induced during acquisition by stopping the ventilator. A total body scan was performed for all the dogs. The CT acquisition protocols were standardized. With the SOMATOM Scope, CT was performed with a pitch of 0.65, scan thickness of 1.2 mm, 100 mAs, 120 kV, and a patient sizeadjusted display field of view (FOV). The images



Fig. 1.

Images were reformatted in sagittal (A), dorsal (B), and cross-sectional (C) planes. Cross-sectional plane was used to measure total wall thickness of lesion.

were reconstructed at 2-mm slice thickness using soft-tissue and lung reconstruction algorithm. With Activion 16, CT was performed with a pitch of 0.9, scan thickness of 0.5 mm, 100 mAs, 120 kV, and patient size-adjusted display FOV. The images were reconstructed at 2-mm slice thickness with soft-tissue and lung reconstruction algorithm (FC03 and FC53, respectively). For contrastenhanced imaging, all dogs were administered 2 mL/kg of iohexol (300 mgI/mL) (Ioverin 300; Teva Pharma Japan, Inc., Aichi, Japan) via an indwelling intravenous cannula placed in the cephalic vein. The injection duration was 20 s. Contrast-enhanced studies were performed during the arterial-phase (20 s after the injection of contrast medium), the portal -phase (60 s), and equilibrium-phase (180 s).

Image analysis

CT images were displayed in an abdominal window setting (window level = 35 HU, window width = 360 HU) to assess rectal neoplasms on a computer workstation using digital imaging and communications in medicine (DICOM) image viewing software (Horos software ver. 2.4.1, Horos Project, Minneapolis, MA, USA). CT images were displayed in a pulmonary window to assess pulmonary metastasis (window level, -600 HU; window width, 1500 HU). All images were reviewed by two experienced veterinary radiologists, and the CT features were determined by consensus. Images were assessed in random order in three different readout sessions with at least a 2-week interval between each session to minimize potential bias.

The following CT features were recorded: lesion shape (mass lesion or wall thickening), the presence or absence of bowel obstruction, spreading of the lesion outside the wall (presence or absence), patterns of contrast enhancement (homogeneous or heterogeneous) of the lesion on arterial-phase, portal-phase and equilibriumphase, presence or absence of lymphadenopathy, location of lymphadenopathy, and presence or absence of pulmonary metastasis.

With respect to lesion shape, a mass lesion was defined as a soft tissue mass protruding into the lumen from the bowel wall. According to the literature¹³⁾, a minimum diameter of 3 mm was defined as a thickened wall lesion. The total wall thickness of the lesion was measured in the cross-sectional plane (Fig. 1). Bowel obstruction is defined as severe dilatation with feces of the proximal colon of the lesions²⁰. According to the literature, we defined the spreading of the lesion outside the intestinal wall as an irregular outer margin of the bowel wall as well as to perirectal adipose tissues²³⁾. The enhancement patterns of the lesion on the arterial-phase, portal-phase, and equilibrium-phase were classified as less (homogeneous) or more (heterogeneous) than 10 HU of difference in enhancement present⁴⁰. In the medial iliac, internal iliac, sacral, ileocolic, and colic lymph nodes, lymphadenopathy was considered present when the length, width, or thickness of the lymph nodes was greater than the mean size of normal lymph nodes³⁾. The reported lengths, widths, and thicknesses of each normal canine lymph node are summarized in Table 1^{3} .

The maximum short-axis (SA) diameter (mm) and maximum long-axis (LA) diameter (mm) of

Lymph node	Length(range)	Width(range)	thickness(range)
medial iliac	22.8 (3.0-56.0)	6.7 (2.4–11.2)	4.6 (1.2–9.6)
internal iliac and sacral	10.3 (4.5–16.0)	4.8 (2.0–9.2)	3.7 (2.0–7.1)
ileocolic	9.7 (3.0–19.0)	6.1 (2.7–14.0)	4.9 (2.7–10.6)
colic	No detect	No detect	No detect

Table 1. Previously published length, width and thickness of each normal canine lymph nodes.

Mean size (mm) were measured in each lymph nodes.

Table 2. CT features of each group of dogs with rectal neoplas	ms.
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	Inflammatory polyp	Adenocarcinoma	Lymphoma	Leiomyoma
	N = 17	N = 6	N = 3	N = 4
CT features				
Lesion shape				
Mass	17/17 (100%)	2/6 (33%)	0/3 (0%)	4/4 (100%)
Wall thickening	0/17 (0%)	4/6 (67%)	3/3 (100%)	0/4 (0%)
Obstruction				
Presence	0/17 (0%)	2/6 (33%)	0/3 (0%)	4/4 (100%)
Absence	17/17 (100%)	4/6 (67%)	3/3 (100%)	0/4 (0%)
Spreading outside the wall				
Presence	0/17 (0%)	3/6 (50%)	1/3 (33%)	0/4 (0%)
Absence	17/17 (100%)	3/6 (50%)	2/3 (67%)	4/4 (100%)
Enhancement pattern				
Arterial-phase				
Homogeneous	0/17 (0%)	2/6 (33%)	3/3 (100%)	4/4 (100%)
Heterogeneous	17/17 (100%) †	4/6 (67%)	0/3 (0%)	0/4 (0%)
Portal-phase				
Homogeneous	0/17 (0%)	2/6 (33%)	3/3 (100%)	4/4 (100%)
Heterogeneous	17/17 (100%) †	4/6 (67%)	0/3 (0%)	0/4 (0%)
Equilibrium-phase				
Homogeneous	0/17 (0%)	2/6 (33%)	3/3 (100%)	4/4 (100%)
Heterogeneous	17/17 (100%) †	4/6 (67%)	0/3 (0%)	0/4 (0%)
Lymphadenopathy				
Presence	0/17 (0%)	3/6 (50%)	3/3 (100%)	0/4 (0%)
Absence	17/17 (100%)	3/6 (50%)	0/3 (0%)	4/4 (100%)

CT, Computed tomography, †, radial enhancement; non-contrast-enhanced inner layer and contrasted outer layer as a point.

the enlarged lymph nodes were measured in any reformatted plane (transverse, sagittal, or dorsal) as per a previous study⁸⁾. The median diameters of SA and LA were calculated. Pulmonary metastasis was defined as a soft-tissue density nodule detected in a pulmonary window.

Statistical analyses

Statistical analyses were performed using commercially available software (R version 2.12.1;

R Foundation for Statistical Computing, Vienna, Austria). The normality of the data was assessed using the Shapiro-Wilk test, which indicated nonnormal distribution.

Results

Of the 50 dogs that met the inclusion criterion, 20 met the exclusion criterion. Rectal

neoplasms were diagnosed as inflammatory polyps (n = 17, 57%), adenocarcinoma (n = 6, 20%), B-cell lymphoma (n = 3, 10%), or leiomyoma (n = 4, 13%). All inflammatory polyps and lymphoma diagnoses were based on endoscopic biopsies, while the adenocarcinoma and leiomyoma diagnoses were based on surgery with excisional biopsy.

The inflammatory polyp group consisted of four neutered and one intact male dog as well as eight spayed and four intact female dogs. The median age of the dogs with inflammatory polyps was 10 years (range, 7–14 years). The dog breeds included sixteen Miniature dachshunds and one Toy poodle.

The adenocarcinoma group consisted of three neutered male dogs and three spayed female dogs. The median age of the dogs with adenocarcinoma was 12 years (range, 10–14 years). The dog breeds included one each of Miniature dachshund, Toy poodle, Labrador retriever, French bulldog, American cocker spaniel, and Shiba inu.

The lymphoma group consisted of one intact male dog, one spayed, and one intact female dog. The median age of the dogs with lymphoma was 11 years (range, 9–11 years). The dog breeds included one each of Pug, Chihuahua, and Miniature schnauzer.

The leiomyoma group consisted of three neutered and one intact male dog. The median age of the dogs with leiomyoma was 12.5 years (range: 10–14 years). The dog breeds included one each of Yorkshire terrier, Labrador retriever, Chihuahua, and Golden retriever.

CT features

The CT features are summarized in Table 2. A mass lesion was observed in all seventeen (100%) inflammatory polyp cases, two of six (33%) adenocarcinoma cases, and all four (100%) leiomyoma cases. Wall thickening was observed in four of six (67%) adenocarcinoma cases and all three (100%) lymphoma cases.

Bowel obstruction was present in zero of seventeen (0%) inflammatory polyp cases, two of six (33%) adenocarcinoma cases, zero of three (0%) lymphoma cases, and all four (100%) leiomyoma cases. The leiomyomas were more likely to show obstruction than inflammatory polyps, adenocarcinomas, and lymphomas. Spreading of the lesion outside the wall was observed in zero of seventeen (0%) inflammatory polyp cases, three of six (50%) adenocarcinoma, one of three (33%) leiomyoma cases, and zero of four (0%) leiomyoma cases. Spreading of the lesion outside the wall was not detected in any mass lesion.

The enhancement pattern was classified as homogeneous in zero of seventeen (0%) inflammatory polyp cases, two of six (33%) adenocarcinoma cases, all three (100%) lymphoma cases, and all four (100%) leiomyoma cases in the arterial-, portal-, and equilibrium-phases. Inflammatory polyps and adenocarcinomas were more likely to show heterogeneous enhancement than lymphomas and leiomyomas in all postcontrast phases.

Heterogeneous enhancement of the inflammatory polyp indicated radial enhancement. Inflammatory polyps form a intraluminal mass. The inner layer of these masses included a noncontrast-enhanced area, with the outer layer of the mass contrasted as a point. The masses were equally enhanced compared to the mucosa. Mass lesions of adenocarcinomas showed a intraluminal mass. These masses showed homogeneous enhancement but were slightly less enhanced than the mucosa. Wall thickening lesions of adenocarcinomas showed a two-layered thickened annular bowel wall with heterogeneous enhancement. The inner layer showed an annular lesion with equal enhancement compared to the mucosa in all post-contrast phases. Lymphomas showed a thickened annular bowel wall with homogeneous enhancement but less enhancement than the mucosa in all post-contrast phases. Leiomyomas formed a homogeneous and less enhanced mass outside the mucosa with obstruction. Representative images of the mass lesions of inflammatory polyps, adenocarcinomas, and leiomyomas are shown in Fig. 2. Representative images of wall thickening lesions,







Representative CT images of rectal neoplasms forming a wall thickening lesion. CT images of adenocarcinoma in precontrast (A), arterial-phase post-contrast (B), portal-phase post-contrast (C), and equilibrium-phase post-contrast (D) images; and CT images of lymphomas in pre-contrast (E), arterial-phase post-contrast (F), portal-phase post-contrast (G), and equilibrium-phase post-contrast (H) images. Adenocarcinomas show a two-layered thickened annular bowel wall with heterogeneous enhancement (arrowhead). Lymphomas show a thickened annular bowel wall with homogeneous enhancement (arrow).

Fig. 2.

Representative CT images of rectal neoplasms forming a mass lesion. CT images of inflammatory polyps in precontrast (A), arterial-phase post-contrast (B), portal-phase post-contrast (C), and equilibrium-phase post-contrast (D) images; CT images of adenocarcinoma in pre-contrast (E), arterial-phase post-contrast (F), portal-phase post-contrast (G), and equilibrium-phase post-contrast (H) images; and CT images of leiomyomas in pre-contrast (I), arterial-phase post-contrast (J), portal-phase post-contrast (K), equilibriumphase post-contrast (L), and a reformatted dorsal plane (M) images. The inflammatory polyps show radial enhancement (arrowhead). The adenocarcinomas show slightly less enhancement than the mucosa (arrow). The leiomyomas show homogeneous and less enhancement outside the mucosa (black arrow) with obstruction. *: Dilatation of the proximal colon.

including adenocarcinomas and lymphomas, are shown in Fig. 3.

Lymphadenopathy was not detected in dogs with inflammatory polyps or leiomyomas, but was diagnosed in dogs with adenocarcinomas and lymphomas (Table 2). Three of six (50%) adenocarcinoma cases were detected as having lymphadenopathy based on the CT results. In dogs with adenocarcinomas, the medial iliac lymph node, internal iliac lymph nodes, and colic lymph nodes were affected in all cases (100%), two cases (67%), and two cases (67%), respectively. There were no other suspected metastatic lesions. Based on the CT results, all three lymphoma cases were diagnosed as lymphadenopathy. In these dogs, the medial iliac, internal iliac, sacral, ileocolic, and colic lymph nodes were affected in two cases (67%), all cases (100%), one case (33%), one case (33%), and two cases (67%), respectively (Table 3). The LA and SA of each enlarged lymph node in the adenocarcinoma and lymphoma cases are shown in Table 3.

None of the rectal neoplasm cases showed findings suggestive of pulmonary metastasis.

Discussion

In Japan, miniature dachshunds are reported to be predisposed to developing colorectal inflammatory polyps²⁹⁾. Inflammatory polyps in miniature dachshunds consist of granulated-like tissue that forms polypoid protrusions from the tip

Adenocarcinoma	Lymphoma	
N = 3	N = 3	
30 (22–34) (100%) #	26.5 (16–37) (67%)	
9 (8–22) (100%)	16 (8–24) (67%)	
16 (14–18) (67%)	15 (14–59) (100%)	
9 (6–12) (67%)	6 (5-21) (100%)	

 Table 3. Computed tomographic measurements and features of lymphadenopathy in dogs with adenocarcinoma and lymphoma.

18 (12-24) (67%)

10 (9-11) (67%)

LA, long-axis; SA, short-axis

Medial iliac lymph nodes LA (mm) SA (mm)

Internal iliac lymph nodes LA (mm) SA (mm)

Sacral lymph nodes LA (mm)

Ileocolic lymph nodes LA (mm)

SA (mm)

SA (mm)

SA (mm)

Colic lymph nodes LA (mm)

Median (range) (% of detected cases).

of the mucosa to the lumen³²⁾. Histopathologically, inflammatory polyps in miniature dachshunds consist of hyperplastic mucosal epithelium and increased goblet cells with dilated crypts filled with abundant mucinous material^{29,32)}. In humans, mucinous colorectal carcinoma exhibits heterogeneous enhancement due to poor enhancement of mucinous materials^{22,39}. In this study, inflammatory polyps showed heterogeneous enhancement, such as radial enhancement, without a contrast-enhanced area of the inner layer. On the other hand, adenocarcinomas that formed intraluminal mass showed homogeneous enhancement in this study. In dogs, massforming rectal adenocarcinoma transits from villose and consist of adenomatous structure with proliferating epithelial cells or increased goblet cells^{30,33)}. The enhancement pattern of inflammatory polyps may be influenced by the abundance of mucinous materials. On CT, mass lesions with radial enhancement may help in the diagnosis of inflammatory polyps.

In this study, the thickening lesions of adenocarcinomas were indicated as a two-layered annular mass with a strongly heterogeneous enhanced inner layer at the all post-contrast phases. Annular adenocarcinomas spread diffusely into the mucosal epithelium and invade the submucosa³¹⁾. The invasion of adenocarcinoma may be reflected as two-layered annular mass. Enhancement of the thickened bowel wall in adenocarcinomas is influenced by ischemia, necrosis, and fibrosis^{4,22)}. In humans, heterogeneous enhancement of colorectal carcinoma is dependent on mucinous materials and fibrous stroma¹¹⁾. The mucinous materials and fibrous stroma indicate a hypoattenuated area on CT²²⁾. In dogs, infiltrated adenocarcinoma occasionally exhibit changes that include bone spicules, fibrosis, and mucin production¹⁷⁾. Heterogeneous enhancement may depend on histopathological findings of the tumors.

64 (33%)

27 (33%)

15 (33%)

9 (33%)

48.5 (32-65) (67%)

25.5 (23-28) (67%)

In this study, the leiomyomas formed a homogeneous and less contrast-enhanced

extraluminal mass, similar to those reported in humans^{15,16,28)}. Leiomyomas arise from smooth muscle cells¹⁹⁾. In contrast-enhanced CT of canine intestinal wall, the mucosal surface shows a stronger enhancement compared to submucosal layer¹⁰⁾. Therefore, less enhancement of leiomyomas compared to mucosa may indicate arising layer of leiomyomas. In this study, all cases of leiomyoma indicated bowel obstruction. In a case report of dog, leiomyoma is diagnosed at the time of luminal obstruction by the mass in the rectum because of its non-invasive, slow-growing nature¹⁹⁾. Therefore, a homogeneous enhancement of mass lesions arising in the submucosa with bowel obstruction may help diagnose leiomyoma on CT.

On the CT scan images, the lymphomas showed homogeneous enhancement but less enhancement than the mucosa. In dogs, lymphoma diffusely infiltrates the submucosa, lamina propria, and serosa, causing diffuse thickening of the intestinal wall^{24,28,34)}. Contrast-enhanced CT makes it possible to identify the layer structure of the intestinal wall. Less enhancement than the mucosa may indicate infiltrated layer of lymphomas. The enhancement pattern is influenced by histologic characteristics²²⁾. In dogs, colorectal lymphomas are most commonly of B-cell origin, and the neoplastic cells infiltrate like a solid sheet^{6,9)}. In this study, all lymphoma cases were B cell origin. The homogeneous enhancement may be influenced by the solid infiltration of neoplastic cells.

None of the mass lesions spread outside the wall of the lesion. Spreading is caused by lesions in the mucosa and typically spreads progressively to the deeper layers of the bowel wall²³⁾. Inflammatory polyps and mass-forming rectal adenocarcinoma spread toward the lumen^{30,32)}. Although leiomyomas arise from smooth muscle cells between the serosa and submucosa, leiomyomas have a non-invasive nature¹⁹⁾. Therefore, spreading may not be detected in mass lesions. However, mass-forming rectal adenocarcinoma infiltrate into the submucosa and muscularis³⁰⁾. Further studies with larger sample sizes are needed to examine the association between the spread of the lesion outside the wall of the intestines in each type of rectal neoplasm.

Lymphadenopathy was diagnosed at the regional lymph nodes in adenocarcinomas and lymphomas. In this study, the LA and SA of lymphomas tended to be larger than those of adenocarcinomas. In humans, gastrointestinal lymphoma indicates bulky lymphadenopathy¹². Further studies with larger sample sizes are needed to examine the difference in the size of enlarged nodes between lymphoma and other rectal tumors.

Our study had several limitations. First, it was based on a relatively small number of dogs with a limited distribution of tumor types, and we were not able to investigate other types of rectal neoplasms, such as adenomatous polyps or leiomyosarcomas. Second, we used a retrospective design. CT findings of each rectal neoplasm were not compared with histopathological findings. Adenocarcinomas were not assessed for histologic variants. Enlarged lymph nodes were not confirmed by cytological or histopathological examinations.

In conclusion, contrast-enhanced CT allows for more accurate characterization of rectal neoplasms. A heterogeneous radial enhancement mass and homogeneous enhancement mass with bowel obstruction may indicate inflammatory polyps and leiomyomas, respectively. Two-layered thickened annular lesions and homogeneous thickened annular lesions, but with less enhancement than the mucosa, may indicate adenocarcinomas and lymphomas, respectively. These findings may help confirm the diagnosis and reduce the use of invasive biopsy procedures.

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Conflict of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, and/ or publication of this article.

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