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Colon Wall Thickness at the Cross Roads of Gastroentero-Dermatology Among Diseased Dogs: Clinical Research

Hasta Köpeklerde Gastroentero-Dermatoloji Kavşağında Kolon Duvar Kalınlığı: Klinik Araştırma

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ABSTRACT Objective: Utilization for bowel ultrasonography (USG) in humans has been thoroughly recognized, whereas less bull's eye has been concentrated on specifical USG analytes on colon during disease state among dogs. Lack of literature and the evidence of proof for 'gut-brain-skin axis' prompted us to focus on patterns of colon wall architectural alterations during disease activity among dogs with gastroentero-dermatological involvement. Out of the classical pictorial essay interpretations composed of normal bowel wall architecture detailed elsewhere, the present study prospectively involved dogs with inflammatory bowel disease (IBD) and co-morbidity (with evidence of dermatological disorder). **Material and Methods:** The colon wall thickness (coWt) of 8 dogs with gastroentero-dermatological disease, as measured by ultrasonography, was compared with apparently healthy dogs with proposed normal values. Complete dermatological and gastroenterological laboratory analysis (relevant and necessary ones) were deemed available. **Results:** In dogs with IBD increased coWt were evident in contrast to healthy ones, reflected as 3.66±1.28 vs. 2.07±0.44 (p=0.012). Although ultrasonographic intestinal wall measurements do not appear to be capable of establishing a diagnosis of intestinal inflammation, it should not be unwise to draw preliminary conclusion that coWt might alter in gastroentero-dermatological diseases. **Conclusion:** The same 'grey zone' of between 1 and 2.6 mm adapted in healthy dogs could be used in the canine colon to distinguish the reference range, reserving the term 'abnormal' for a coWt of greater than 3.1 mm in the colon, at least for dogs with IBD.

Keywords: Canine intestine; gastro-dermal axis; inflammatory bowel disease; ultrasonography

ÖZET Amaç: Bağırsak ultrasonografisi (USG), insanlarda tüm kompartmanlarda bakılırken, hasta köpeklerde kolonun spesifik USG analizleri daha az hedef alınarak yoğunlaşılır. "Bağırsak-beyin-deri ekseni" üzerine literatür ve teşhisi için bulguların eksikliği, aktif gastroentero-dermatolojik tutulumu olan hasta köpeklerde kolon duvarının yapısal değişim paternlerine odaklanmamızı sağlar. Daha ayrıntılı bir şekilde, normal bağırsak duvarı yapısından oluşan klasik girişimsel görüntüleme yorumları, bu çalışmada prospektif olarak inflamatuar bağırsak hastalığı (İBD) ve komorbidite hastalığı (dermatolojik hastalık bulgulu) olan köpeklerden yapılacaktır. **Gereç ve Yöntemler:** Kolon duvar kalınlığı [colon wall thickness (coWt)], ultrasonografik ölçüm yapılarak gastroentero-dermatolojik hastalıklı 8 köpeğin ölçümleri, önerilen normal değer aralığında sağlıklı görünüşe sahip köpeklerle karşılaştırıldı. Tamamlanan dermatolojik ve gastroenterolojik laboratuvar analizleri (ilgili ve gerekli olanlar) yeterli kabul edildi. **Bulgular:** Köpeklerde İBD bulunanlarda 3,66±1,28 ile sağlıklı olanların 2,07±0,44 aksine coWt değerlerinde artış belirgindi (p=0,012). Ultrasonografik bağırsak duvarı ölçümü, bağırsak inflamasyonunun teşhisi için yeterli gibi görünmese de coWt'nin değişiminin gastroentero-dermatolojik hastalıklarda güç bulunduğu ön tanısını çıkarmak amaca uygun değildir. **Sonuç:** Sağlıklı köpeklerde kullanılan 1-2,6 mm aralığındaki 'gri zon' köpeklerde kolonun referans aralığının ayrımında kullanılabilmekle birlikte, en azından İBD bulunan köpeklerde coWt 3,1 mm'den daha büyük olması 'anormal' olarak değerlendirilebilir.

Anahtar Kelimeler: Köpek bağırsak; gastro-dermal eksen; inflamatuar bağırsak hastalığı; ultrasonografi

Inflammatory bowel diseases (IBD), which should be denoted and abbreviated as IBD throughout the whole manuscript, has been well recognized gastrointestinal issue both in humans and animals, which was weel described in a prior review.[1,2] In human being IBD described both Crohn's disease [with frequent involvement of ileum/colon along with granuloma formation composed of the entire intestinal wall] and ulcerative colitis (UC)].[3-5] Dogs, similarly, could also exist IBD, ever if continuing

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more than three weeks Washabau and Holt, with histological involvement of mucosal inflammation.[6-9]

Given pathogenesis of IBD among dogs; i) decontrol of mucosal immunity, ii) deprivation of antigenic tolerance (nutritional, intestinal bacteria, etc.), iii) respond to immunomodulant drugs; iv) hypersensitivity reactions [elevated IgE positive cells in diseased dogs], v) discontinuity of the mucosal barrier [antigenic exposure].[8,10-14] In an attempt to diagnose IBD, 3 frequently used techniques [radiology, ultrasonography and endoscopy] are available worldwide.[2] Specifically ultrasound is capable of detecting gut layering and wall thickness which could exclude other relevant etiological reasons, as because the significance of intestinal wall thickening in dogs with IBD has regained attention.[15-17]

Colon, to the best of our knowledge and approach, the chief of the intestinal environment, has been well recognized as the longest section of the large intestine. It discrete food material into required materials and stools. Colon wall thickness (coWt) is generally not a routine part of ultrasonography (USG) through national veterinary surgeons (as evidenced by large oral survey) as it is not thought as a concern, whereas might denote disease status. Figure 1 depicts dogs enrolled at this study and also denoted healthy reference ranges for coWt detected by USG. Therefore, the purpose of the present study reported herein was to measure the thickness of individual wall layers of the colon of dogs with both gastroenterological and dermatological disease. Our hypotheses was that there might exist a significant difference in the thickness of the mucosal layer of the colon among diseased dogs.

MATERIAL AND METHODS

Relevant terminology was as follows, which is thought to be useful as shown below at Table 1.

ULTRASONOGRAPHIC PROCEDURES

Ultrasonographic examination (Figure 2) was performed with an ultrasound system (Mylab30 CV, Esaote, Italy) and a curvilinear or linear-array transducer. All abdominal USG examinations were

Gastrointestinal segment	Canine species (mm) coWT	Dogs (diseased) enrolled at the present study with coWT	Dogs (healthy) enrolled at the present study with coWT
Colon 	1.0-2.6* 2.0-3.0^	1.7-5.6	1.6-3.1

FIGURE 1: : Provided the reference ranges of normal wall thickness of colon among healthy dogs as detected previously (*Larson and Biller, Gladwin et al, ^Penninck and d'Anjou,) along with results obtained at our study.[18,20,21]
coWt: Colon wall thickness.

TABLE 1: Relevant terminology were as follows, which is thought to be useful adopted by Strobel.[25]

Wall layering of the gastrointestinal tract subclassified in to 5 distinct layers:	Appearance at ultrasonography	Sonoanatomy of the intestinal wall along with layer echogenicity
Lumen-	(synonym; luminal-mucosal interface) Its presence could be variable depending on its luminal contents (if empty, exhibits a mucous pattern with a hyperechoic line)	Hypoechoic or hyperechoic
Mucosa-	Hypoechoic in silhouette, its width is variable depending on the section of gastrointestinal tract	Hypoechoic
Submucosa-	In the vast majority of the gastrointestinal system appearing relatively narrow/hyperechoic	Hyperechoic
Muscularis	Hypoechoic in appearance with variable thickness	Hypoechoic
Serosa	A thin hyperechoic layer, not easy to clearly determine	Hyperechoic

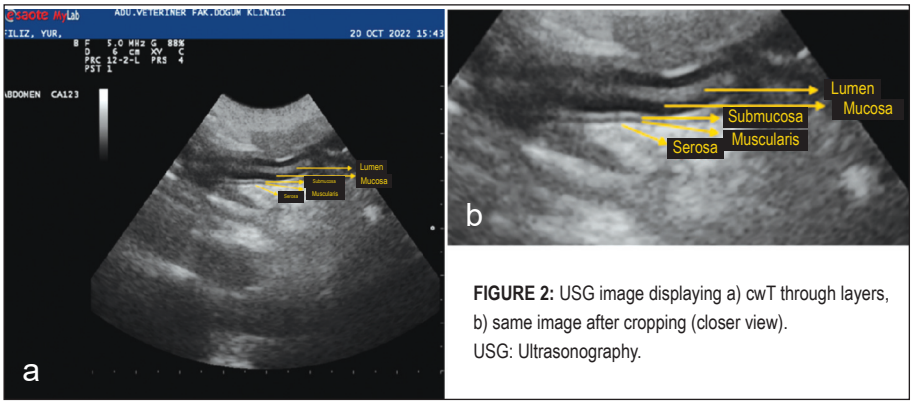

FIGURE 2: USG image displaying a) cwT through layers, b) same image after cropping (closer view).
USG: Ultrasonography.

performed by attendance of all researchers. Hair was removed on the abdomen and relevant necessary coupling gel was applied thereof. As a brief explanation each diseased dog was positioned in dorsal recumbency. A transverse image of the descending portion of the colon was deemed available as a target application.[18] Entire locations of the colon are completely visualized via initiating at the level of the ileocolic junction in all dogs and the transducer sweeped cranially through the ascending colon (short segment of large intestine). This was followed by detection of the transverse colon and final step of scanning the descending colon (by use of the urinary bladder as a landmark for determining descending colon).[19]

Measurements of wall layers were firstly obtained 2 of the researchers, separately and individually, by use of electronic calipers on a computerized system. Calculations were deemed available from a single transverse image of the colon composing coWt along with a sum of thickness of the mucosa, submucosa, muscularis, and serosa.[18,19] All measurements were inspected on an academical hierarchy involving secondary audition by 2 relevant researchers, which were finally approved for evidence of proof by first eye opinion. This system was established for several years as hierarchy of norms for USG examination, reducing the margin of error to zero. Finally, bulls-eye interpretation was deemed available.

STATISTICAL ANALYSIS

CoWt measurements were expressed as mean±standard deviation. Data were compared using the Mann-Whitney U-test and p-value <0.05 was considered statistically significant. All analysis and graphical presentation were performed using the GraphPad Prism® 9.0 (GraphPad Software Inc., La Jolla, CA, USA).

ETHICAL APPROVAL

This study was performed according to The Declaration of Helsinki, ethical principles and approved by the Animal Experiments Local Ethics Committee of Aydın Adnan Menderes University (date: August 18, 2022, no:64583101/2022/86).

RESULTS

Demographic data and coWt of all diseased dogs were shown on Table 2. Dogs were weighing 4.9 to 31 kg (medium to large breeds as was shown on Table 2), at the age of 2.5 to 11 years, and of both sexes. Photographic records were shown on Figure 3, Figure 4, Figure 5, along with boxplot analytes and statistical analysis (Figure 6, Table 3).

DISCUSSION

Colon has been sub-classified into 3 parts: i) ascending, ii) transverse, and iii) descending. Among entire intestinal segments, the colon uniquely exhibited the thinnest wall, to those of its layering is normally alike due to gas and feces distension. An empty colon might exist rippling with distinguishable layers.[19] In the present study as shown in Figure 5, one case (1 year old dog) exhibited gas artefact, in which coWt could not be detected whereas the day after initial diagnosis and calculation of coWt was 4.8

TABLE 2: Demographic data and coWt of all diseased dogs.

Dogs enrolled at the present study	Demographic data	coWt (mm) diseased dogs	coWt healthy dogs
Case I	11 years old Collie with dermatomyositis and IBD	5.6	1.6
Case II	3 years old male French Bulldog with IBD and food allergy	4.2	2.4
Case III	4 years old female with IBD, SIBO and food allergy	3.1	2.0
Case IV	2.5 years old female Golden retriever with IBD and atopic dermatitis	4.0	3.1
Case V	4 years old male cross-bred with IBD and demodectic mange	1.9	3.0
Case VI	3 years old female English Bulldog with IBD and sarcoptic mange	1.7	2.2
Case VII	6 years old male Terrier with IBD and atopic dermatitis	3.6	1.9
Case VIII	2 years old male French Bulldog with IBD and hypothyroidism	3.9	1.6
Case IX	3 years old male Terrier with IBD and sarcoptic mange	4.9	1.8

IBD: Inflammatory bowel disease; coWt: Colon wall thickness.

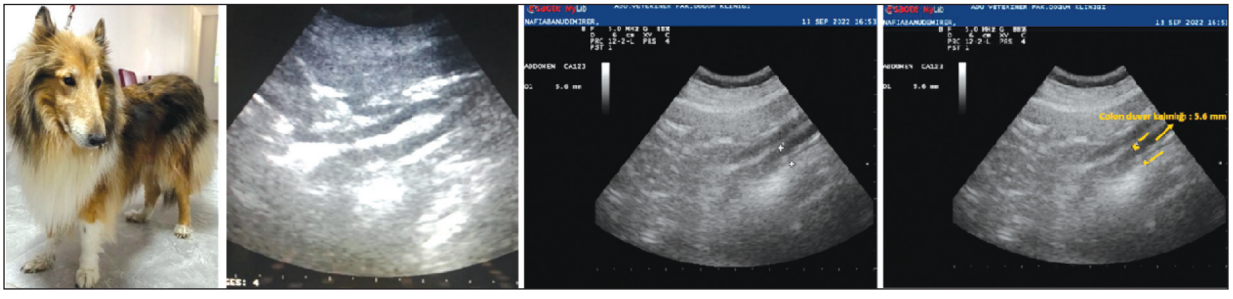

FIGURE 3: Collie breed dog at the age 11 years with a presumptive diagnosis of **a)** IBD and dermatomyositis, **b)** basic USG at initial referral, **c)** calibers were marked for detecting coWt, and **d)** coWt was detected as 5.6 mm.
IBD: Inflammatory bowel disease; USG: Ultrasonography; coWt: Colon wall thickness.

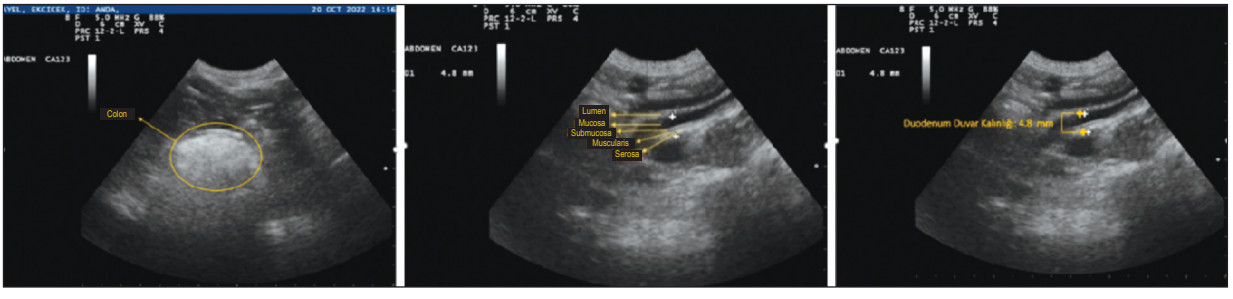

FIGURE 4: A Golden Retriever at the age of …with a coWt of 4 mm.
coWt: Colon wall thickness.

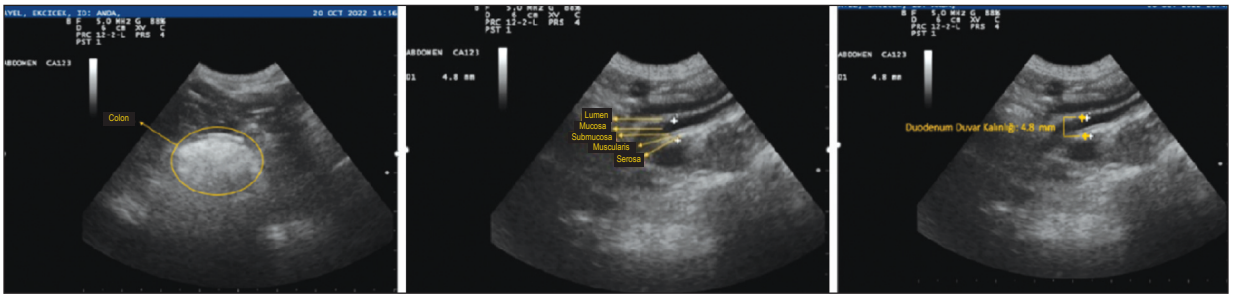

FIGURE 5: A 1 year old dog with a sudden onset of waxing and wanning clinical signs of gastroentero-dermatology. a) the day before coWt detection because of gas artefact, b) the day after initial diagnosis and calculation of coWt, c) as 4.8 mm.
coWt: Colon wall thickness.

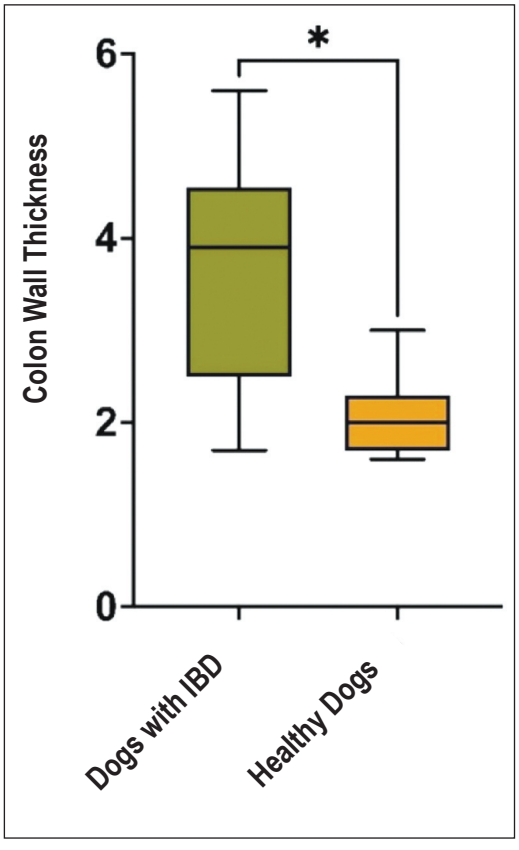

FIGURE 6: coWt among dogs with IBD and healthy ones (cross matched for comparative interpretation) enrolled herein as box plot analytes.
IBD: Inflammatory bowel disease; coWt: Colon wall thickness.

TABLE 3: Colon wall thickness of both in diseased (in dogs with IBD) and to those of healthy ones.

Colon wall thickness		p value
Dogs with IBD	Healthy dogs	
3.66±1.28	2.07±0.44	0.012

IBD: Inflammatory bowel disease.

mm (Figure 5). It should not be unwise to draw preliminary conclusion that whether if gas artefact was severe, USG examination might have helped better understanding and interpretation at least 24 hours later.

Among dogs reported ranges for normal coWt is around 1.0-2.6 mm and 2.0-3.0 mm.[18,20,21] Provided the reference ranges of normal coWt among healthy dogs as detected previously 1.0-2.6 usually accepted appropriate.[18,20] In a prior study ultrasonographically measuring the thickness of the individual wall layers of the duodenum, jejunum, and colon of small, medium and large dogs, total coWt (mean±SD) were 1.5±0.3 mm, 1.4±0.5 mm, and 1.6±0.4 mm, respectively.[18] In the present study in dogs with various gastroentero-dermatological diseases coWt varied between 1.7 to 5.6 mm. Although it is not very easy to draw preliminary suggestions, it should not be unwise to draw conclusion that coWt values (>3.1 mm) might debug diseased (gastoentero-dermatological cases) from healthy dogs. Cut-off value as 3 mm was based on findings of prior highest value of description.[21] Somebody might criticize this preliminary finding, whereas our subsequent study would be directed to larger surveys of coWt among dogs at the cross-roads of gastroentero-dermatology.

Expolarated data from the present study must be discussed briefly and comparatively to what have been described previously. In prior research claiming that food allergy could have relationship with impaired intestinal barrier, authors attempted to detect bowel wall thickening ultrasonographically for identification of the latter condition. Eight infants with food allergy presented wall thickening only in the jejunum (>2 mm), suggesting it as a useful marker for interpretation.[22] In agreement another study investigated the macroscopic/histological alterations of the large intestine in patients with atopic dermatitis. Out of 15 patients with atopic dermatitis, 4 presented melanosis coli, in which authors concluded that atopic dermatitis patients were prone to exist chronic inflammation of the large intestine.[23] In the present study 2 dogs with atopic dermatitis and other 2 dogs with food allergy presented gastrointestinal issues as co-morbidity, each might be mimicking gut-brain-skin axis involvement.

The vast majority of disorders invading the colon is the IBD with major phenotypes of Crohn's disease and UC among humans.[3,24,25] The latter disease with gastrointestinal involvement also presented in dogs, as an integral part of the chronic enteropathy even if lasting more than 3 weeks.[6,7] On the other hand transabdominal USG has been well recognized beneficial tool for determination of bowel wall thickening and the distribution of composed segments in several types of IBD. Furthermore,

interpretation of complications and disease activity along with guidance of treatment selections are probable via USG.[26-29] In a total of 9 dogs involved herein at the present study were diagnosed with IBD, presented coWt of 1.7-5.6 mm, to those of 7 out 9 showed coWt of >3 mm all were above according to selected literature.[21]

CONCLUSION

In conclusion it should not be unwise to offer 'grey zone' of between 1 and 2.6 mm adapted in healthy dogs could be used in the canine colon to distinguish the reference range, reserving the term 'abnormal' for a coWt of greater than 3.1 mm in the colon, at least for dogs with IBD.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Kerem Ural;* ***Design:*** *Kerem Ural, Hasan Erdoğam;* ***Control/Supervision:*** *Kerem Ural;* ***Data Collection and/or Processing:*** *Kerem Ural, Hasan Erdoğan, Songül Erdoğan, Gamze Gökçay, Cansu Balıkçı;* ***Analysis and/or Interpretation:*** *Kerem Ural;* ***Literature Review:*** *Kerem Ural, Hasan Erdoğan, Songül Erdoğan, Gamze Gökçay, Cansu Balıkçı;* ***Writing the Article:*** *Kerem Ural;* ***Critical Review:*** *Kerem Ural, Hasan Erdoğan, Songül Erdoğan;* ***References and Fundings:*** *Kerem Ural, Hasan Erdoğan, Songül Erdoğan, Gamze Gökçay, Cansu Balıkçı;* ***Materials:*** *Kerem Ural, Hasan Erdoğan, Songül Erdoğan, Gamze Gökçay, Cansu Balıkçı.*

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