DIAGNOSTIC UTILITY OF ABDOMINAL ULTRASOUND FOR DETECTING NON-PERFORATED GASTRODUODENAL ULCERS IN DOGS

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Summary

* Background: Abdominal ultrasound is frequently used to detect non-perforated gastroduodenal ulcers in dogs. Studies assessing the diagnostic utility of abdominal ultrasound for the detection of non-perforated gastroduodenal ulcers have yielded mixed results. No studies to date have investigated the effects of patient bodyweight, breed, sex, age, ulcer aetiology (neoplastic or inflammatory) or location, on the diagnostic accuracy of abdominal ultrasound.
* Methods: Retrospective, multicentre study to evaluate the diagnostic utility of abdominal ultrasonography for the diagnosis of non-perforated gastroduodenal ulceration in dogs.
* Results: Sixty-one dogs met the inclusion criteria. Ulcers were detected during ultrasound examination in 18/61 dogs, yielding a sensitivity of 29.5% (95% CI 18.8-42.7%). Ulcers in the pyloric region were detected more frequently than those in the duodenum, however, location was not significantly associated with the ability of ultrasound to detect lesions (P=0.41). No associations were identified between the ability of ultrasound to detect an ulcer and patient bodyweight (P=0.45), breed (P=0.98), sex (P=0.90), age (P=0.94), and neoplastic versus inflammatory nature of ulcerative lesions (P=0.93).
* Conclusion: The diagnostic utility of ultrasound as the sole modality for the detection of non-perforated gastroduodenal mucosal ulceration is poor. The authors therefore recommend the use of additional modalities when ulcerative lesions are suspected.

Keywords: Gastric ulcer; duodenal ulcer, stomach ulcer, ulceration, ultrasound

**Introduction**

Gastroduodenal ulceration occurs when the mechanisms governing physiological homeostasis of the gastrointestinal tract are impaired, resulting in exposure of the submucosa and deeper layers due to disruption of the mucosal lining1. Ulceration can occur following the administration of certain drugs or as a complication of systemic disease. In dogs, the most common causes of gastroduodenal ulceration are non-steroidal anti-inflammatory drugs (NSAIDs)8 and corticosteroids9,1, although systemic hypovolaemia1, inflammatory bowel disease2,3, hepatic disease4, primary gastrointestinal neoplasia5,6 and mastocytosis7, are all potentially ulcerogenic. Less commonly, uraemia10, exercise-induced hyperthermia11,12, gastric dilation and volvulus (GDV)13, gastrointestinal foreign bodies14 and intervertebral disc disease15,16 have also been associated with gastroduodenal ulceration.

Dogs with non-perforated gastroduodenal ulceration often present with largely non-specific clinical signs17. A swift diagnosis enables treatment to be rapidly implemented, thereby reducing the likelihood of spontaneous perforation requiring emergency surgery. This is of particular importance because of the high post-surgical mortality rates of 20-80% that have been reported in animals with gastrointestinal perforation as a consequence of systemic inflammatory response, shock and multiple organ dysfunction18,19.

Endoscopy is currently considered to be the most reliable yet minimally invasive modality for the diagnosis of gastroduodenal ulceration in small animals20. Nonetheless, there is an inherent risk of iatrogenic rupture during the procedure and thus ultrasound is typically used in the first instance21. Furthermore, abdominal ultrasonography is arguably more widely available and similarly non-invasive, and may also enable the early detection of lesions thus facilitating rapid case management.

The ultrasonographic appearance of both neoplastic and non-neoplastic gastroduodenal ulcers has been well-documented in dogs20,22, 23 Typically, a gastroduodenal ulcer appears on ultrasound as a focal area of mucosal thickening with a central, crater-shaped mucosal defect containing accumulations of hyperechoic microbubbles20. The reported usefulness of ultrasound in the detection of ulceration in dogs has yielded mixed results. In one study, despite having only a limited diagnostic utility in the investigation of chronic vomiting in dogs, abdominal ultrasound was determined to be useful in the detection of severe gastrointestinal ulceration in three cases24. In a separate retrospective review of both dogs and cats undergoing exploratory laparotomy, gastrointestinal ulceration or perforation were identified as the lesions most likely to be missed during pre-operative abdominal ultrasonography25. Interestingly, ultrasound performed better in a much later study of 82 dogs, in which the authors reported sensitivities of 65% and 86% for the detection of non-perforated and perforated ulcers respectively23, a difference that may be attributable to improvements in ultrasound technology in the intervening time period. It should be noted that many of the dogs in this last study underwent assessment by multiple imaging modalities and hence the diagnostic utility of ultrasound alone for non-perforated ulcers was only ascertained in a relatively small patient sample size.

Patient bodyweight may significantly affect the diagnostic utility of ultrasound for detecting abdominal lesions, such that Computed Tomography (CT) is recommended for larger dogs26. To date, the relationship of patient breed and bodyweight on the diagnostic utility of ultrasound for the detection of gastroduodenal ulceration has not been investigated in dogs.

The first objective of this retrospective, multicentre study was to ascertain the diagnostic utility of abdominal ultrasonography for the diagnosis of non-perforated gastroduodenal ulceration in referral populations of dogs. The second objective was to investigate the effect of patient signalment including patient bodyweight, breed, sex, age, the location of the gastroduodenal ulcer and the inflammatory versus neoplastic nature of the ulcerative lesions.

**Materials and methods**

Ethical approval for this study was granted by the University of Liverpool’s Veterinary Research and Ethics Committee. Electronic medical records at the University of Liverpool’s Small Animal Teaching Hospital, Willows Veterinary Centre and Referral Service, Anderson Moores Veterinary Specialists and Southern Counties Veterinary Specialists were retrospectively searched for dogs diagnosed between January 2013 and May 2017 with gastric or duodenal ulceration. Specifically, medical, ultrasound, endoscopy and surgical reports were searched using the key words ‘gastric ulcer, stomach ulcer, duodenal ulcer and ulceration’. Animals were included in the study if they had an abdominal ultrasound performed in the referral hospital, followed by endoscopic or surgical confirmation of non-perforated gastric and/or duodenal ulceration within 48 hours of the ultrasound exam. Endoscopies, exploratory laparotomies and abdominal ultrasound had to have been performed by a board-certified medic, surgeon or radiologist respectively, or a resident under direct supervision. Cases were excluded if the confirmation of gastroduodenal ulceration by endoscopic examination or exploratory laparotomy was not achieved, if perforation of the gastroduodenal ulcer was suspected, or if medical records were incomplete.

Patient bodyweight, breed, sex and age were recorded from medical records. From the imaging reports, the ultrasonographic features recorded included the presence of gastric and/or duodenal ulceration and the location of the ulcer (i.e. pylorus or pyloric antrum, gastric fundus, lesser or greater curvature of the stomach, duodenum). Each study was recorded as positive if gastric and/or duodenal ulceration was specifically documented in the conclusion of the imaging report, with or without further lesion description. Where identified, additional sonographic features recorded included the presence of gastric or duodenal distention with gas or fluid, focal gastrointestinal wall thickening or thinning and/or loss of wall layering, the presence of a gastrointestinal foreign body, evidence of pancreatic inflammation, abdominal lymphadenopathy and the evidence of free abdominal fluid. The presence and location of any gastric or duodenal masses associated with the area of ulceration were also documented.

Ulcer presence was confirmed with either endoscopy, or exploratory laparotomy and gastro-enterotomy. For all methods, the presence and location of ulcerative lesions were documented (pylorus or pyloric antrum, fundus, lesser curvature, greater curvature, or duodenum).

Statistical analyses were performed using dedicated statistical software packages; SPSS 22.0 (SPSS Inc, Chicago, Illinois, USA) and R (R version 3.2.0, The R Foundation for Statistical Computing). Independent variables were generated from signalment data, surgical or endoscopy records and ultrasound reports. Variables examined were those related to the animal (bodyweight, breed, sex, age), nature of ulceration (neoplastic or inflammatory) and reported ulcer location at surgery or endoscopy.

Descriptive statistics were calculated for all variables; continuous data summarised as medians with interquartile ranges (IQR), and categorical data as frequencies with 95% confidence intervals (95% CI). For categorical variables with excessive categories and/or categories containing only small numbers of animals, merging into appropriate groups was performed. Normality of distribution for continuous variables was assessed with graphical analysis, probability plots and the Kolmogorov-Smirnov test. For continuous variables (age and weight), the functional form (shape) of the variable with respect to the outcome was assessed using generalised additive models (GAM). GAM models were fitted using cubic spline smoothers and tested for departure from linear trend to determine whether an assumption of linear association was valid.

The dependent (outcome) variable considered was the detection or failure to detect an ulcer on ultrasound, with associations between this and independent variables examined via multivariable logistic regression. All variables that showed some association with detection on ultrasound on initial univariable analysis (a *P*-value <0.25) were considered for incorporation into the multivariable model.

**Results**

Sixty-one dogs with non-perforated gastroduodenal ulceration were included; they had a median age of 97.5 months (IQR 72.0-124.3 months) and a median weight of 23.3kg (IQR 11.8-29.4kg). Breeds included Labrador retrievers (12), Staffordshire bull terriers (9), Golden retrievers (5), terrier-types (5), Border collies (3), crossbreeds (4) and 23 other breeds represented by one dog each. There were 31 female dogs (two entire) and 30 male dogs (11 entire).

Across all centres, three different ultrasound machines including General Electric Logiq 8 (34 dogs), General Electric Logiq 5 (14 dogs) and General Electric 9 Milwaukee (13 dogs) were utilised with a variety of ultrasound transducers from 2 to 6 MHz curvilinear, 5 to 8 MHz curvilinear and 5 to 14 MHz linear transducers. Ultrasonography was performed with the dogs restrained either manually or under sedation or general anaesthesia. Variable sedative and anaesthetic protocols were selected by the consulting anaesthetist at the time of scanning. All ultrasounds were performed by a board-certified veterinary radiologist, or a radiology resident under direct supervision of a veterinary radiologist.

Overall, ulcers were detected by ultrasound in 18/61 dogs, giving a sensitivity of 29.5% (95% CI 18.8-42.7%).

A total of 51 dogs underwent endoscopy and ten dogs underwent exploratory laparotomy and gastro-enterotomy. Three dogs had both endoscopy and surgery. The location of all 18 ulcerative lesions detected on ultrasonography agreed with the surgical and/or endoscopic findings. Three cases were excluded from statistical analysis as the location was not specified in ultrasound reports.

Ulcers were present in the duodenum in 16/58 (27.5%), and stomach of 42/58 (72.4%) of dogs. Of these, lesions were identified ultrasonographically in 3/16 (18.8%) and 19/46 (41.3%) patients respectively. The location of the ulcers and proportion of those detected by ultrasound at each location is detailed in Table 1. Surgically or endoscopically confirmed ulcerative lesions were located at the gastric fundus in 3/58 (5.1%) cases, greater curvature of the gastric body in 2/58 (3.4%) cases, lesser curvature of the gastric body in 9/58 (15.5%) cases and at the pyloric antrum or pylorus in 24/58 (41.4%) cases. Of these confirmed lesions, ultrasound detected ulcers at the greater curvature 1/2 (50.0%), lesser curvature 1/9 (11.1%), pyloric antrum or pylorus 11/24 (45.8%), but did not detect any lesions in the gastric fundus (0/3 (0.0%)). Gastric ulcers with no specified origin were recorded in 4/58 (6.9%) cases, half of which 2/4 (50.0%) were identified on ultrasound exam. In all 18 cases identified by ultrasound, a crater-like thinning of the mucosal wall was described, as demonstrated in Figures 1 and 2.

In all 61 dogs, further gastroduodenal changes reported on ultrasound, aside from gastroduodenal ulceration, included focal or diffuse thickening of the gastric or duodenal wall in 14/61 (22.9%) and 12/61 (19.7%) cases respectively. There was partial or complete loss of wall layering in 10/61 (16.3%) cases, gastroduodenal hypomotility in 3/61 (4.9%) cases, gastric distention with fluid in 7/61 (11.5%) cases and gastric distention with gas in 2/61 (3.3%) cases. Gastric pneumatosis was noted in a single case 1/61 (1.6%).

Although a mild abdominal effusion was observed in 4/61 (6.6%) cases, abdominocentesis was unattainable in these cases, as the volume of fluid was too small. Despite this, no evidence of perforation was detected at either surgery in three of the cases or during endoscopy in the remaining case. Free peritoneal gas was identified in one (1.6%) patient that had undergone exploratory laparotomy within seven days prior to the ultrasound exam, but no gastrointestinal perforation was identified at surgery.

Abdominal lymphadenomegaly was recorded in 10/61 (16.4%) dogs, involving the gastric 6/10 (60.0%), mesenteric 3/10 (30.0%), and pancreaticoduodenal 1/10 (10.0%) lymph nodes. Lymphadenopathy occurred in association with gastroduodenal neoplasia in 2/10 (20.0%) of these cases. Additional abdominal abnormalities included pancreatitis 1/61 (1.6%) and cranial mesenteric thrombosis 1/61 (1.6%).

Ulcerative lesions associated with gastrointestinal masses were seen in 12/61 (19.7%) dogs, and example of which is demonstrated in Figure 1. Ulcerated mass-like lesions were located at the pylorus or pyloric antrum 6/12 (50.0%) (all adenocarcinoma), lesser curvature 4/12 (33.3%), duodenum 1/12 (8.3%), and greater curvature 1/12 (8.3%). Results of histopathology were available in 8/12 (66.7%) dogs with ulcerated mass-like lesions. Gastric adenocarcinoma was confirmed in 7/12 (58.3%) dogs and 1/12 (8.3%) dog had gastric lymphoma. The diagnoses of the remaining four masses remains unknown at the time of writing since neither cytology nor histopathology were performed in these cases.

There were no associations identified between the ability of ultrasound to detect an ulcer and patient bodyweight (P=0.45), breed (P=0.98), sex (P=0.90), age (P=0.94), or the underlying aetiology of the ulcer (neoplastic versus inflammatory) (P=0.93). Ulcers located in the pyloric region were detected more frequently than those in the duodenum (see Table 1), but overall location was not significantly associated with the ability of ultrasound to detect lesions (P=0.41). As no variables showed an association of P<0.25, no multivariable analysis was performed.

**Discussion**

The overall diagnostic utility of ultrasound for the detection of gastroduodenal ulceration in this patient population was poor. The location of the ulceration, patient signalment including both breed and body weight, and the association or lack thereof with neoplasia, did not significantly affect the sensitivity of ultrasound for the detection of ulceration.

In our study, ulcers were detected by ultrasound in just 18/61 dogs, giving rise to a sensitivity of 29.5% (95% CI 18.8-42.7%). In support of our findings and as mentioned earlier, poor utility of ultrasound for detecting gastroduodenal ulceration has been previously documented20. However, unlike our study, these studies lacked either surgical or endoscopic confirmation. It is notable that the sensitivity of ultrasound in our study was substantially lower than that reported by Fitzgerald et al 2017 for non-perforated ulcers. As expected, their study also demonstrated an improved sensitivity when perforated ulcers were assessed23. All cases included in our study were non-perforated, which may in part may help to explain the lower sensitivity, at least compared with the detection rate for perforated ulcers. Furthermore, Fitzgerald et al used broader criteria compared to that employed in our study, such that a positive result for detection was reported not only if direct visualisation of a mural defect was recorded as in our study, but also if secondary features such as peritoneal fluid or gas, were identified. This in all likelihood contributed significantly to the higher sensitivity than that reported here.

Accompanying ultrasonographic features including focal wall thickening and partial or complete loss of wall layering, were occasionally observed in this patient population. Gastric distention with fluid and gastroduodenal hypomotility were also observed in a small number of cases. These are non-specific findings that have been previously documented in both benign and malignant gastroduodenal ulceration20,23. Free abdominal fluid was also observed in 7/69 (10.1%) cases, although in these animals, gastrointestinal perforation was not documented on surgical or endoscopic examination. The authors hypothesise that this fluid likely represented an aseptic peritoneal effusion associated with focal peritonitis adjacent to the gastrointestinal wall lesion. Unfortunately, it was not possible to test this hypothesis on account of the retrospective nature of this study.

# An uncommon complication that has occasionally been reported in animals with gastrointestinal ulceration is the presence of intra-mural gas, known as gastric or intestinal pneumatosis27. The condition can result secondary to wall necrosis allowing the subsequent introduction of gas-producing bacteria into the intestinal wall (more specifically known as emphysematous gastritis) and is the most likely explanation for the presence of gas identified within the gastric wall in one dog in our study. Gastric pneumatosis has also been described in dogs with GDV28 and can be idiopathic27 and has been reported in association with gastric ulceration in cats29,30.

In this study, thrombosis of the cranial mesenteric artery was observed during ultrasound in one dog. The CT features of arterial mesenteric thrombosis have been described in dogs with mucosal necrosis31, and ulcerative lesions associated with mesenteric thrombosis and intestinal ischaemia have been documented in cats using grey scale32 and contrast-enhanced ultrasound33. However in this patient, it is unlikely that thrombosis of the cranial mesenteric artery alone would be sufficient to cause duodenal ischaemia, as the duodenum receives mostly dual arterial supply from the cranial pancreaticoduodenal artery, a branch of the celiac artery, and the caudal pancreaticoduodenal artery, a branch of the caudal mesenteric artery34. Further evaluation of the mesenteric vasculature to identify any additional mesenteric thrombi would have been useful in this patient.

In this study population, confirmed gastroduodenal ulceration occurred most frequently within the pyloroantral region, followed in order of descending frequency by the duodenum, lesser curvature, and greater curvature of the stomach. Previous studies in dogs have shown that NSAID-associated ulceration most commonly affects the pyloroantral and duodenal regions35. Similarly, ulceration associated with gastric adenocarcinoma typically arises along the lesser curvature or pyloroantral regions of the stomach5,36-39 since these are predilection sites for this particular tumour type, and ulceration resulting from liver disease most commonly occurs in the duodenum40. Despite the relatively high frequency of pyloroantral ulcers in the present study, only 11/24 (45.8%) pyloroantral lesions were detected during ultrasound examination. Ultrasound also performed poorly when detecting ulcers within the duodenum, fundus, lesser curvature and greater curvature, with only 18.8%, 0.0%, 11.1% and 50.0% lesions being detected respectively. Limitations of abdominal ultrasound of these regions is likely to be due to a combination of patient-related and anatomical factors, including intercostal location, body habitus, intraluminal gas distribution and the presence of ulcerative lesions within rugal folds, which can be easily missed.

Malignant gastroduodenal ulceration has been well documented in dogs. In dogs, malignant ulceration is frequently associated with gastrointestinal adenocarcinoma, most likely due to tumour necrosis41. Gastric adenocarcinoma is the most common gastric tumour in dogs and as mentioned above, typically located along the lesser curvature and pyloroantral regions of the stomach5,37,38,42,43. Our data support these findings; 7/8 canine masses undergoing histopathology were confirmed as being gastric adenocarcinoma. Half of all canine tumours were located within the pyloroantral region, a further 33.3% being identified along the lesser curvature.

No breed or sex predilection was identified in our patient population, although Rottweilers were overrepresented in one study of 16 dogs with spontaneous gastroduodenal perforation44, and an increased prevalence in middle-aged, male patients has been suggested17.

This study is limited by its small sample size and retrospective methodology. Consequently, a standardised protocol was not established for the ultrasonographic assessment of ulcerative lesions. Due to the retrospective nature across multiple institutions, there is a variability in the use of ultrasound machinery and operator experience. The primary objective of this study was to assess the detection of ulcers in a clinical setting, hence still ultrasound images were not reviewed, and operators may not have been blinded to the clinical history and presentation. This unavoidably introduces the potential for intra-observer variability and observer bias. This study is further limited by the lack of histopathology and as such, the presence or absence of neoplasia cannot be confirmed in all patients. Future prospective studies with available histopathology are warranted to explore the accuracy of abdominal ultrasound with histopathologically-confirmed, ulcerative neoplastic or inflammatory lesions.

**Conclusions and clinical relevance**

The diagnostic utility of abdominal ultrasound as a sole modality for the detection of non-perforated gastroduodenal mucosal ulceration is poor, regardless of patient breed or bodyweight. Lesions may be more easily detected if located within the pyloroantral region, although this finding was not statistically significant in our study population. Non-specific accompanying ultrasonographic features of focal wall thickening, loss of layering and the presence of gastroduodenal neoplasia alert the clinician to the possible presence of an ulcerative lesion. Ultrasound may be useful for first line investigation, however, due to its limited diagnostic utility, it cannot be relied upon to definitively exclude the presence of gastroduodenal ulceration. The authors recommend the use of additional modalities such as CT and endoscopy should ulcerative lesions be suspected but not identified on ultrasound.

**Funding and competing interests statement**

None of the authors have a conflict of interest regarding this study.

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Figure 1: Confirmed gastric ulceration in an 11-year-old, female neutered, German Shorthaired Pointer with a gastric adenocarcinoma. Note the thickening and homogeneous hypoechogenicity of the gastric wall, with associated loss of layering. A focal, crater-like wall defect consistent with gastric ulceration is present in the mucosa of the gastric fundus (white arrow). The image was acquired with a 12MHz Linear Array probe.

Figure 2: Confirmed gastric ulceration in A) 6-year-old, male neutered Lhasa Apso, and B) 12-year-old male neutered Labrador retriever both with severe ulcerative gastritis. In both cases, focal, crater like defects containing gaseous microbubbles are present (white arrows) within the mucosa of the gastric body. There is moderate to marked thickening and loss of layering of the gastric wall in both images and in (B), diffuse hyperechogencity of the wall is also noted (asterisk). The images were acquired with a 14MHz linear array probe (A), and 10 MHz macro-convex probe (B).

 Table 1: The location of ulcers and proportion of those detected by ultrasound at each location.

|  |  |  |
| --- | --- | --- |
| **Ulcer location** | **Ulcer detected** | **Total** |
| **No** | **Yes** |
| **Duodenum** | 13 | 3 | **16** |
| (81.3%) | (18.8%) |
| **Fundus** | 3 | 0 | **3** |
| (100%) | (0%) |
| **Greater curvature** | 1 | 1 | **2** |
| (50.0%) | (50.0%) |
| **Lesser curvature** | 8 | 1 | **9** |
| (88.9%) | (11.1%) |
| **Pylorus/pyloric antrum** | 13 | 11 | **24** |
| (54.2%) | (45.8%) |
| **Unspecified stomach** | 2 | 2 | **4** |
| (50.0%) | (50.0%) |
| **Total** | 40 | 18 | **58** |
| (69.0%) | (31.0%) |