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# Evaluating acidic gastroesophageal reflux with wireless pH monitoring in French bulldogs with sliding hiatal herniation

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## Abstract

**Background:** Sliding hiatal herniation (SHH) and gastroesophageal reflux (GER) commonly occur in French bulldogs. Wireless pH monitoring can quantitatively assess acidic GER in dogs affected by SHH.

**Hypothesis/Objectives:** Measure acidic GER in French bulldogs with SHH, pre- and post-brachycephalic obstructive airway syndrome (BOAS) surgery, utilizing a wireless pH capsule (Bravo Calibration-free, Medtronic, Minnesota), and correlate with owners' observations of regurgitation.

**Animals:** Eleven French bulldogs diagnosed with SHH via swallowing fluoroscopy.

**Methods:** Prospective cohort study. A pH capsule was endoscopically placed in the esophagus. Up to 96 hours of data were acquired as the owner logged clinical signs. Spearman's correlation and Wilcoxon rank-sum tests evaluated factors correlated with acid exposure time (AET), defined by the % time pH < 4. In 4/11 dogs, Bravo monitoring was repeated 2-4 months after BOAS surgery.

**Results:** Medians (Q1-Q3) for age and weight were 21 months (17-35.5) and 10.0 kg (8.9-11.5). BOAS severity was mild (3), moderate (4), or severe (4). Medians (Q1-Q3) for AET and reflux events were 3.3% (2.6-6.4) and 70 (34-173). Clinical score ( $P = .82$ ) and BOAS severity ( $P = .60$ ) were not correlated with AET, but age was negatively correlated ( $\rho = -.66$ ,  $P = .03$ ). Median probability (Q1-Q3) that regurgitation was associated with a reflux event was 72.5% (0-99). Percent AET numerically improved in all 4 dogs that underwent BOAS surgery although not statistically assessed.

**Conclusions and Clinical Importance:** Wireless pH monitoring documented acidic GER in French bulldogs with SHH, captured subclinical events, and showed improvements after BOAS surgery.

## KEYWORDS

acid exposure time, brachycephalic, brachycephalic obstructive airway syndrome, bravo capsule, GERD

**Abbreviations:** AET, % acid exposure time; BCS, body condition score; BOAS, brachycephalic obstructive airway syndrome; DogSAT, Dog Swallowing Assessment Tool; GER, gastroesophageal reflux; GERD, gastroesophageal reflux disease; SAP, symptom association probability; SHH, sliding hiatal hernia.

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## 1 | INTRODUCTION

Sliding hiatal herniation (SHH), or type I hiatal herniation, and subsequent gastroesophageal reflux disease (GERD) commonly afflict brachycephalic breeds and can cause severe weight loss, esophagitis, and recurrent aspiration pneumonia.<sup>1-7</sup> The prevalence of this condition has increased with the rising popularity of brachycephalic breeds, especially the French bulldog, the current most popular breed in the United States,<sup>8</sup> and warrants improving the diagnosis and treatment of SHH and GERD.<sup>9</sup> Sliding hiatal herniation can be noninvasively diagnosed using swallowing fluoroscopy to identify the intermittent displacement of the gastroesophageal junction through the diaphragmatic esophageal hiatus, but fluoroscopy can yield false negative results and cannot assess the nature or frequency of GERD.<sup>2,5-7</sup> Management of SHH and GERD involves acid suppressant and prokinetic medications or in some cases, surgical correction of the brachycephalic obstructive airway syndrome (BOAS) or hiatal laxity. However, response to medical therapy or surgery can be variable and challenging to objectively assess when relying upon clinical signs or observations by pet owners.<sup>1,3,4,10-12</sup>

Clinical signs of SHH and GERD in dogs can vary from subtle signs of lip smacking or hard swallowing<sup>6,7</sup> to more pronounced signs such as overt regurgitation, dysphagia,<sup>2,4-7</sup> or recurrent episodes of coughing secondary to aspiration of food and water.<sup>7</sup> Clinical signs can also be misinterpreted by pet owners who might perceive signs as normal for the breed<sup>13,14</sup> or incorrectly classify regurgitation as vomiting. To overcome the subjectivity, an objective diagnostic tool such as pH monitoring might be useful to assess GERD in brachycephalic dogs with SHH, correlate reflux events to owner-reported clinical signs, and evaluate response to treatment.

Catheter-based pH monitoring has been used to quantify reflux in a prior cohort of brachycephalic dogs, but a workup to definitively diagnose SHH was not performed.<sup>15</sup> There are also several inherent limitations to catheter-based pH monitoring that can compromise the assessment of GERD. Catheter retention requires that dogs are hospitalized during data collection, which limits study durations to 1-2 days in stressful hospital environments. The intranasal catheter can also occlude stenotic nares to further exacerbate patient discomfort and BOAS. Catheter-free, wireless pH monitoring using a Bravo pH capsule is the preferred method to assess GERD in human patients and can continuously monitor acidic reflux for up to 96 hours after placement.<sup>16-18</sup>

Primary objectives of this study were to utilize wireless Bravo pH monitoring to evaluate acidic reflux and the association with owner-reported clinical signs of regurgitation in a cohort of French bulldogs diagnosed with SHH. A secondary objective was to evaluate acidic reflux after BOAS surgery in a subset of dogs. We hypothesized that acidic reflux would be considered pathologic according to human definitions of GERD<sup>18</sup> and that reflux events would variably correlate with regurgitation observed by pet owners. We also expected improvement in acidic reflux after corrective BOAS surgery.

## 2 | MATERIALS AND METHODS

A prospective cohort study was conducted to enroll French bulldogs that were presented to the University of California Davis Veterinary Medical Teaching Hospital between January 2021 and December 2022 and were diagnosed with a type I hiatal hernia. Dogs with 1 or more signs of gastroesophageal reflux (GER) such as regurgitation, lip smacking, air licking, hard swallowing, retching, and gagging or hacking often after eating drinking, increased activity or excitement were considered for inclusion. Cases were then enrolled if diagnostic imaging with thoracic radiographs, swallowing fluoroscopy, or abdominal ultrasound confirmed a sliding hiatal hernia. Administration of acid suppressants, antacids, or prokinetic medications within 2 weeks before Bravo pH capsule (Bravo Calibration-free, Medtronic Inc., Minnesota) placement was a criterion for exclusion. A clinical history and signs of uncontrolled gastrointestinal or pancreatic disease such as daily vomiting, diarrhea, or inappetence was an exclusion criterion. Concurrent esophageal disorders such as megaesophagus or esophageal stricture, or comorbidities such as renal, hepatic, cardiac, respiratory, and uncontrolled endocrine disease were also causes for exclusion. Prior hiatal hernia surgery was an exclusion criterion. Prior BOAS surgery that resulted in improved clinical signs of BOAS or GERD was an exclusion criterion.

Clinical history related to the hiatal hernia and respiratory signs such as stertor, exercise intolerance, and cyanosis were recorded for each dog. Owners of each dog were asked to fill out a questionnaire, the Dog Swallowing Assessment Tool (DogSAT; Figure S1), at baseline and 2-4 months after BOAS surgery if the surgery was performed. The DogSAT is in the process of being validated and a manuscript describing it in detail is in preparation. The questionnaire is comprised of 17 questions pertinent to the dog's clinical history and signs relating to swallow function. The scores from each question were totaled to calculate a cumulative score. Owners were not allowed to review previous responses from the baseline form when filling out the questionnaire post-BOAS surgery.

All dogs underwent a complete physical examination including an assessment of body condition using the Purina body condition scoring system,<sup>19</sup> nares stenosis, and a grading of their BOAS as described and validated (Methods in Supporting Information).<sup>20,21</sup>

Complete blood count and chemistry panels were performed to ensure all dogs were in good health. All dogs were fasted for at least 12 hours before performing diagnostic imaging. Radiographs performed included 3-view thoracic radiographs and a right lateral cervical view using an available digital radiography system (Sound Eklin, Carlsbad, California). All dogs then underwent a swallowing fluoroscopy procedure in lateral recumbency or standing and were fed in 3 phases: 60% wt/vol liquid barium sulfate, canned food mixed with barium, and kibble mixed with barium.<sup>3,4</sup> Images were obtained using a standard fluoroscopy unit (EasyDiagnost Eleva, Philips Medical Systems, Bothell, Washington). Acepromazine 0.01 to 0.03 mg/kg was administered IV for mild tranquilization to facilitate the study if needed. If a hiatal hernia was not detected on swallowing fluoroscopy, a diagnosis via thoracic radiographs or abdominal ultrasound was

required for inclusion. Once a hiatal hernia was diagnosed, the dog returned within 2 weeks of and at least 48 hours after the date of videofluoroscopic imaging to undergo Bravo pH capsule placement.

All dogs were fasted for at least 12 hours before capsule placement. The anesthetic protocol was tailored to each dog and conducted by anesthesiologists and anesthetists of the University of California, Davis Veterinary Medical Teaching Hospital Anesthesia Service. Proton pump inhibitors and prokinetics were not permitted during anesthesia nor during the first 96 hours after capsule placement. After induction of anesthesia, the esophagus and stomach were evaluated with a flexible endoscope (EVIS EXERA III Video Colonoscope PCF-PH190L/I, Olympus America Inc., Pennsylvania) for mucosal lesions such as erosions or ulcerations, erythema, granularity, gastric follicular hyperplasia and any evidence of foreign material, masses, or polyps. The gastroesophageal junction was examined antegrade to evaluate the opening of the lower esophageal sphincter and to look for evidence of a hiatal hernia. A hiatal hernia was confirmed antegrade when gastric rugal folds were seen everting cranially above the hiatus into the distal esophagus (Figure S2A). The stomach was then insufflated with air and the endoscope was retroflexed in a J-manuever to view the cardia and assess the hiatus retrograde. A wide hiatus was diagnosed on retroflexed view when the aperture of the esophageal hiatus was loose rather than snugly fit around the scope according to human definitions (Figure S2B).<sup>22</sup> Esophageal and gastric biopsies were not obtained and duodenal evaluation was not performed to minimize procedure time. However, the pyloric sphincter was evaluated for any evidence of stenosis or hypertrophy.

All capsule placements were performed by 2 of the study investigators (Tarini Ullal and Stanley Marks). The calibration-free Bravo capsule was activated and paired to the recording device. The vacuum flow was attached to the Bravo pH deployment catheter and tested. The site of capsule attachment was selected by measuring 6-cm proximal to the squamocolumnar junction (see Figure S2A). The capsule delivery device was then inserted transorally and advanced into the esophagus to the pre-measured site. The capsule was released and tethered to the esophageal mucosa as previously described.<sup>23</sup> Appropriate capsule placement was confirmed with endoscopic visualization (Figure 1). After placement, the capsule began detecting and sampling pH data in 6 second intervals.

After placement of the capsule, the anesthetist assisted in recovery of the dog, which included extubation and post-anesthesia monitoring in the recovery ward. Dogs were discharged after normalization of their vital signs and return to ambulatory status. Upon discharge, 1 of the study investigators (Tarini Ullal) provided verbal and written instructions to guide owners on monitoring and recording of clinical signs. Visual aids including video examples of lip smacking, hard swallowing, and regurgitation compared to vomiting were provided to each owner. For the next 4 days, the owner kept a written log of clinical signs observed during daytime periods and simultaneously pressed buttons corresponding to each clinical sign on the recording device that was secured to the dog with a Holter vest. Meal and drink periods as well as the period during which the dog was asleep overnight were logged by the owner. Dogs continued their normal daily routines during data collection but were fed a liquefied slurry version of their usual diet to prevent early detachment of the capsule from



**FIGURE 1** The Bravo pH capsule is seen tethered to the esophageal mucosa following placement with the deployment device (not pictured).

the esophageal mucosa. After 96 hours, the owner returned the logbook and recording device and the pH data was uploaded and analyzed using a computerized software program (Reflux Reader 6.1). Logbook data were manually entered into the computer software and merged with the uploaded pH data. Measurements before discharge from the post-anesthesia recovery ward and meal or drink periods were excluded from data analysis. If the data showed an acidic pH for a prolonged duration of several hours followed by a rise to an alkaline pH, it was presumed that the capsule had detached from the esophagus and passed into the stomach and intestinal tract. Data collected after capsule detachment was also excluded from analysis. Owners confirmed capsule detachment and passage by monitoring the stool for elimination of the capsule.

The computerized software calculated Bravo pH metrics such as analysis time (hours), % acid exposure time (AET), number of reflux events, number of long reflux events, longest reflux episode (minutes), and the DeMeester Score.<sup>24,25</sup> The % AET was defined by the percentage of time during the study that the pH was < 4. As previously defined in Bravo monitoring studies in humans<sup>26-28</sup> and dogs,<sup>23</sup> a reflux event was defined as a drop in pH < 4. A long reflux event was defined by a duration of > 5 minutes. Percent AET and the rate of reflux events per hour of analysis time were calculated separately for day and nighttime periods. A daytime period was defined as the time in between the dog waking up in the morning and going to sleep at night. The nighttime period was defined by the span of time during which the dog was sleeping at night. Percent AET was also calculated independently for each day of the study. The DeMeester score<sup>25</sup> was automatically calculated by the software as a composite score of 6 different variables: AET overall, AET during the awake day, AET when

asleep at night, number of reflux events, number of long reflux events, and longest reflux episode. The DeMeester score and AET are the most useful Bravo metrics to examine GERD in human patients.<sup>29</sup> Symptom association probability (SAP) was also calculated by the computer software using a Fisher's exact test to examine the correlation between clinical signs observed by the owner and reflux events documented by the pH capsule. A repeat Bravo pH capsule placement procedure was performed 2-4 months post-operatively in a subset of dogs that underwent corrective BOAS surgery. Corrective BOAS surgery entailed staphelectomy or folded flap palatoplasty, alarplasty, with or without tonsillectomy and laryngeal sacculotomy as decided by the surgeon.

## 2.1 | Statistical analysis

Statistical analysis was performed using R Statistical Computing Software Version 4.3.0. Categorical variables such as sex (male/female) and endoscopic findings of a hiatal hernia observed antegrade (yes/no), wide hiatal aperture observed retrograde (yes/no), and presence or absence of esophageal mucosal erosions or ulcerations, erythema, and granularity were summarized as counts. Medians and interquartile ranges were calculated because Shapiro-Wilk testing showed that data was not normally distributed for continuous variables such as age, weight (kg), DogSAT scores, BOAS grade, and pH metrics (eg, analysis time, AET, number of reflux events, number of long reflux events, longest reflux event, DeMeester score, and SAP). Analysis time was defined as the total number of hours available for analysis. Spearman's correlation and Wilcoxon rank-sum tests were used to evaluate correlations between a subset of continuous and categorical variables and AET. The subset of variables included age, sex, weight, BCS, DogSAT scores, BOAS grade, and endoscopic findings consistent with a hiatal hernia antegrade and wide hiatal aperture retrograde. Wilcoxon rank-sum tests were used to compare AET between the following groups: male and female, hiatal hernia visualized or not visualized endoscopically, and a wide hiatal aperture visualized or not visualized via endoscopy. Repeated measure ANOVA tests were used to compare AET between Days 1, 2, and 3. Wilcoxon signed-rank tests were used to assess AET and DeMeester scores before and after exclusion of the post-anesthetic recovery period. Wilcoxon signed-rank tests were also used to compare analysis time, AET, and rate of reflux events between day and nighttime periods. In the subset of dogs undergoing corrective BOAS surgery, descriptive statistics were reported on the DogSAT scores, BOAS grades, and AET, measured pre- and post-operatively. All hypothesis tests were 2-sided and evaluated at a significance level of 0.05.

## 3 | RESULTS

### 3.1 | Signalment, clinical signs, BOAS assessment, and diagnostic imaging results

Eleven French bulldogs were enrolled, comprising of 5 female spayed, 4 male castrated, and 2 male intact dogs. A 12th dog was initially enrolled and then excluded because gastric heterotopia was

diagnosed histopathologically from endoscopic biopsies obtained of the distal esophagus. Three dogs had previously undergone staphelectomy (2) or alarplasty (1) by the referring veterinarian before enrollment. Surgery did not improve clinical signs of BOAS (2) or exacerbated signs of regurgitation (1). Medians and interquartile ranges (Q1-Q3) for age was 21 months (17-35.5) and for weight was 10.0 kg (8.9-11.5). All 11 dogs presented for clinical signs of regurgitation. Six dogs were reported to have signs of hacking or gagging while eating. Three dogs had signs of hacking or coughing separate from eating and drinking. Four dogs had a history of hard swallowing or repeated attempts to swallow. One dog had a history of lip smacking and another had a history of difficulty prehending suspected from macroglossia. One dog had a history of reverse sneezing after regurgitating. Four dogs had a history of intermittent vomiting. Six dogs were reported to have stertor and a history of reported exercise intolerance, difficulty breathing while sleeping, or both. One dog had a history of 2 collapse episodes after eating. None had a history of cyanosis. Median (Q1-Q3) for DogSAT scores were 22.5 (17-32).

On physical examination, median (Q1-Q3) for BCS was 4 (3.5-5.5). BOAS severity was graded as mild in 3, moderate in 4, and severe in 4 dogs. Nasal stenosis was noted in 10/11 dogs and graded as mild (3), mild to moderate (1), moderate (5), or severe (1). Stertor was noted on physical exam in all dogs and graded as mild (5), moderate (3), or severe (3). After an exercise test, stertor increased in severity from mild to moderate for 3 dogs and moderate to severe for 1 dog. Mild stridor was ausculted pre-exercise test in 1 dog. Mild inspiratory effort was observed in 3 dogs before the exercise test, which progressed to moderate effort in 2 dogs after the exercise test. Inspiratory effort was not observed in 3 dogs until after the exercise test, which revealed mild inspiratory effort. No dog experienced cyanosis or syncope during the exercise test.

Thoracic radiographs diagnosed a hiatal hernia in 3 of 11 dogs. All 11 dogs had evidence of BOAS on a lateral cervical radiograph based on 1 or more findings of an elongated thickened soft palate, pharyngeal collapse, or straightening of the hyoid apparatus with caudal retraction of the larynx. Ten of 11 dogs had a bronchial or bronchointerstitial pattern on thoracic radiographs. No dog had an alveolar pattern.

Videofluoroscopic swallow study was performed in lateral recumbency in 8 dogs and in standing or dorsoventral recumbency in 3 dogs. Six dogs required tranquilization with 0.01 to 0.03 mg/kg IV acepromazine. The swallowing fluoroscopy study confirmed a hiatal hernia in 10/11 dogs and all 11 dogs had GER. The 1 dog not diagnosed with a hiatal hernia on swallowing fluoroscopy was diagnosed on thoracic radiographs and abdominal ultrasound. Four dogs had a redundant esophagus, which caused a mild delay in bolus transit in 1 dog, moderate delay with retrograde bolus movement in the second dog, and no appreciable delays in the other 2 dogs. Esophageal dysmotility was noted in 6 additional dogs and localized to the thoracic esophagus (2), caudal esophagus (2), or both (2). Six dogs experienced mild tracheal aspiration of liquid barium during the study after which the study was discontinued and the dog was permitted to stand upright and walk. Light coupage was performed and the dog was re-examined with fluoroscopy, which confirmed clearance of aspirated material in all 6 dogs.



Abdominal ultrasound was performed in 10/11 dogs. In 4/10 dogs, a hiatal hernia was visualized on ultrasound by identifying cranial movement of the lower esophageal sphincter above the diaphragmatic margin.

### 3.2 | Endoscopic findings

Esophagoscopy identified a hiatal hernia on antegrade view (Figure S2A) in 2/11 dogs and a wide hiatal aperture (Figure S2B) in 7/11 dogs. All 11 dogs had evidence of esophagitis based on presence of either esophageal erythema or granularity in 10/11 dogs and 7/11 dogs, respectively. Erythema was assessed to be mild (5) or mild to moderate (5). Granularity was assessed to be mild (4) or moderate (3). Only 1/4 dogs showed resolution of esophageal erythema and granularity after BOAS surgery. No esophageal erosions or ulcerations were observed in any of the dogs. All 4 dogs that underwent BOAS surgery had a wide hiatal aperture identified on maximally insufflated and retroflexed view both before and after BOAS surgery. No gastric erosive lesions, masses, foreign material, polyps, or pyloric hypertrophy were observed in any dog.

### 3.3 | Bravo capsule placement and data collection

A total of 16 procedures were performed including 11 baseline, 4 after BOAS surgery, and 1 after hiatal hernia surgery. Capsule placement was successful in 14/16 procedures. In 2 procedures, the capsule did not release from the deployment device. A second attempt immediately thereafter with a new deployment device was successful. The capsule was placed at a median (Q1-Q3) distance of 26 cm (25-27.3) from the maxillary incisor. Median (Q1-Q3) duration of the procedure was 31.5 (25-41) minutes, including close inspection of the esophageal mucosa and esophageal hiatus upon retroflexion of the endoscope. Capsule detachment from the esophagus and passage into the stool was confirmed in all cases by owner observation (14/16) or a lateral thoracic radiograph (2/16).

### 3.4 | Bravo pH monitoring results at baseline

Median (Q1-Q3) for analysis time was 67.6 (59.4-89.5) hours. Medians (Q1-Q3) for AET and number of reflux events were 3.3% (2.6-6.4) and 70 (34-173) events, respectively. Medians (Q1-Q3) for number of long reflux events and longest reflux events were 6 (4-15) events and 23 (19-30) minutes, respectively. Median (Q1-Q3) for DeMeester Score and SAP for regurgitation were 13.6 (10.8-24.5) and 72.5% (0-99), respectively. According to human definitions,<sup>30</sup> %AET > 6% and DeMeester scores > 14.7 were reflective of elevated acid exposure in 4/11 and 5/11 dogs, respectively (Table S1). However, only 3/11 dogs met the human criteria for a definitive diagnosis of GERD (AET > 6% for ≥ 2 days).<sup>18</sup>

**TABLE 1** Association of variables with % acid exposure time in French bulldogs with sliding hiatal herniation.

	Rho	P-value
Age	−.66	<b>.03</b>
Sex		.25
Weight	−.46	.15
BCS	−.22	.51
BOAS severity score	.18	.60
DogSAT score	.09	.82
Hiatal hernia on antegrade view		.44
Wide hiatal aperture on retrograde view		.65

Note: P value <.05 designated in bold. Cells are grayed because Wilcoxon rank sum tests were performed to assess these variables.

Age was negatively associated with AET ( $\rho = -.66$ ,  $P = .03$ ), but sex, BCS, DogSAT score, BOAS grade, visualizing a hiatal hernia antegrade, and a wide hiatal aperture viewed retrograde via endoscopy were not associated with AET (Table 1). Median (Q1-Q3) AET before and after exclusion of pH data from the post-anesthetic recovery period was 5.8 (3-6.5) and 3.3 (2.6-6.4), respectively. Median (Q1-Q3) DeMeester score before and after exclusion of the data from the same period was 19.4 (11.8-24.8) and 13.6 (10.8-24.5). There were no significant differences between AET ( $P = .23$ ) and DeMeester scores ( $P = .48$ ) before and after exclusion of pH data from the post-anesthetic recovery period. The total number of hours of analysis time was significantly higher in the day compared to the night ( $P = .002$ ), but pH metrics such as AET ( $P = .01$ ) and rate of reflux events per hour ( $P = .002$ ) that were referenced to number of analysis hours were both significantly higher in the day compared to the night (Table 2). Medians and interquartile ranges for analysis time, AET, and rate of reflux events between day and night are presented in Table 2. Percent AET did not significantly differ between Days 1, 2, and 3 ( $P = .11$ ) of data collection.

### 3.5 | Bravo pH monitoring results after surgical intervention

Four dogs underwent BOAS surgery, which comprised of staphylectomy and alarplasty (1) or combination alarplasty, folded flap palatoplasty, and tonsillectomy (3). Two dogs also underwent bilateral laryngeal saccullectomy. All 4 dogs showed numerical improvements in AET (Table S2) after BOAS surgery of which a subset showed improved DogSAT scores (3) and BOAS grades (2). One dog showed improved AET but neither DogSAT score nor BOAS grade improved after staphylectomy and alarplasty. This dog later underwent hiatal hernia reduction surgery consisting of esophagopexy, gastropexy, and phrenoplasty which improved the DogSAT score and minimally changed AET from 1.7% to 1.6%.

**TABLE 2** Bravo analysis variables between day and night in French bulldogs with sliding hiatal herniation.

	Day	Night	
	Median (Q1-Q3)	Median (Q1-Q3)	P-value
Analysis time (hours)	37.7 (35.3-52.0)	29.4 (21.6-35.9)	.002
AET (%)	4.4 (0.9-3.5)	1.1 (0.7-2.1)	.01
Reflux events per hour	1.5 (0.8-2.6)	0.4 (0.3-0.7)	.002

Abbreviations: AET, acid exposure time; Q1, first quartile, 25th percentile; Q3, third quartile, 75% percentile.

## 4 | DISCUSSION

Wireless pH monitoring Bravo capsule technology successfully documented acidic reflux episodes in French bulldogs with SHH in this study. Capsules were placed without complication and acquired data for a median of 3 days, enabling data collection for longer durations compared to catheter-based pH studies. Although capsule placement required general anesthesia, there were no differences in pH data across Days 1-3 of data collection. Acid exposure time was higher in younger dogs and during the day compared to the night. Only 3 dogs had elevated AET and DeMeester scores consistent with GERD according to human criteria.<sup>18</sup> Although AET was not correlated with BOAS grade, AET did numerically improve in all 4 dogs after BOAS surgery. Regurgitation observed by owners was variably correlated with capsule detected reflux events, underscoring the challenges of relying on owner observations and highlighting the benefits of using an objective tool such as Bravo capsule technology to quantify reflux.

Bravo capsule technology was safe and straightforward to implement and provided objective, quantitative information regarding acidic reflux in this study. It also allowed the dog to be comfortable in a home environment during data collection, minimizing stress and discomfort associated with transnasal pH catheter probes as has been observed in human patients.<sup>31</sup> Wireless pH monitoring also permitted extended data collection of >48 hours in this study. This was beneficial in collecting data beyond the initial day of capsule placement because the anesthesia and hospital visit required for capsule placement could have transiently exacerbated GERD. However, interestingly, there were no significant differences in AET and DeMeester scores after excluding the post-anesthetic recovery period. Additionally, there were no significant differences in pH data on Days 1, 2, and 3 of the study after capsule placement. Thus, it is plausible that the effects of anesthesia on GERD after a brief endoscopic capsule placement are minimal.

Extended monitoring, apart from compensating for the potential effects of anesthesia, has proven valuable in human patients to increase the diagnostic sensitivity of GERD,<sup>16,32</sup> identify symptom-reflux associations, and account for day-to-day variability in activity and meals that can affect GER physiology and acid exposure.<sup>33</sup> Extended monitoring can also assist in making therapeutic decisions that reduce healthcare burden and costs. For example, prolonged pH

monitoring >48 hours better predicts human patients that are unlikely to respond to proton pump inhibitor therapy.<sup>17,34</sup> Currently, Bravo pH monitoring is not affordable, available, or feasible for many veterinary practices. However, Bravo pH monitoring could be beneficial to improve the diagnosis of GERD and tailor treatment plans that prioritize BOAS or hiatal hernia surgery over medical management in affected brachycephalic dogs.

Acid exposure time and DeMeester scores are the 2 most valuable variables evaluated in human patients with GERD<sup>29</sup> of which AET is the more reproducible metric.<sup>35</sup> When AET > 6% for ≥ 2 days, GERD is confirmed in human patients.<sup>17,18</sup> Notably, even though all dogs had SHH and clinical signs of GERD, none of the dogs in this study had erosive or ulcerative esophagitis and only 3/11 (27%) met the human criteria for GERD. This could be because the normative reference intervals for AET in healthy dogs are lower compared to those of healthy human controls. In 2 studies that performed pH monitoring in healthy non-brachycephalic dogs, median (range) AET was only 0.3% (0-3.1)<sup>23</sup> and 0.1% (0-3.6%), 95th percentile of 1.8%<sup>36</sup> compared to 2.3% (95th percentile, 5.9%) in healthy humans.<sup>28</sup>

In a study evaluating brachycephalic dogs using transnasally placed pH catheters, the authors differentiated between dogs with abnormal and normal AET based on a median (range) of 6.4% (2.5-36.1) and 0.3% (0-2.4), respectively. However, none of these dogs underwent diagnostic testing for hiatal herniation and dogs comprised of a mix of different brachycephalic breeds in contrast to the present study, which only included French bulldogs. In addition to breed, numerous other factors including the presence and severity of the hiatal hernia, BOAS, esophagitis, obesity, diet, stress, and activity could increase GERD and contribute to considerable variation in AET. The present study evaluated some of these variables in association with AET and only found a significant negative correlation between age and AET perhaps because younger dogs have more severe congenital BOAS or hiatal anomalies. Percent AET was also significantly higher during the day compared to night. This was a unique finding that contradicted a study in non-brachycephalic dogs with clinical signs of GERD.<sup>23</sup> A potential hypothesis for the difference in results between the 2 studies is that brachycephalic dogs might be more affected by increased activity, higher temperatures, and frequent eating and drinking throughout the day, that can exacerbate BOAS, increase respiratory and abdominal effort, and cause gastric distension that predispose to SHH and reflux events. The present study did not identify significant associations between AET and clinical scores from the DogSAT questionnaire, BOAS grade, or endoscopic findings supportive of SHH.

Three of 4 dogs that underwent BOAS surgery in this study showed numerical improvements in clinical DogSAT scores and AET after surgery. However, the small number of dogs precluded statistical analysis to support any conclusions regarding the benefit of BOAS surgery in dogs with SHH. Surgical correction of BOAS can ameliorate negative intrathoracic airway pressure to treat SHH and GERD.<sup>1,10,15</sup> However, videofluoroscopic swallow assessments of dogs after BOAS surgery have not shown improved SHH or GERD.<sup>10</sup> The 1 dog in the present study that did not clinically improve after BOAS surgery did

improve after hiatal hernia surgery although there was minimal change in AET from 1.7% to 1.6%. The result of this 1 dog indicates that numerical improvements in AET might not correspond to clinical improvements and that some dogs might require both BOAS and hiatal surgical correction.

Another reason AET and DogSAT scores might not have corresponded is because of the subjectivity and potential unreliability of owner observations as demonstrated by the SAP results in this study. The SAP for regurgitation was highly variable, with an IQR from 0% to 99% and a median of 72% likely because of differing levels of owner compliance, attentiveness, documentation, and frequency of clinical signs. Bravo pH capsule technology can capture clinically silent or subtle reflux events and provide a more objective assessment of GERD that an owner cannot always provide. For example, Bravo pH monitoring could help identify silent reflux events in dogs with recurrent aspiration pneumonia. Interestingly, none of the dogs in this study had radiographic evidence of aspiration pneumonia although 3/11 had clinical signs of cough and 10/11 had bronchial or bronchointerstitial patterns radiographically perhaps from chronic microaspiration.<sup>7,37</sup>

There are limitations of the Bravo pH capsule technology that were potential weaknesses of the study. For example, weakly acidic or alkaline reflux could not be detected, which would have required impedance technology. Capsule placement also required anesthesia, which could have increased GERD and introduced variability because the anesthetic protocol was not standardized. Although esophagogastroscopy was performed in conjunction with capsule placement, gastointestinal biopsies were not performed during endoscopy to rule out underlying gastrointestinal disease. However, dogs with inappetence, chronic diarrhea, and frequent vomiting were excluded to try to address this limitation. Diet and activity regimen were not standardized and the 4 dogs that underwent BOAS corrective surgery did not undergo the same surgical approach by the same surgeon, which might have introduced variability in pH results and post-surgical outcome. Additionally, feeding a liquefied diet to prevent early detachment of the capsule could have improved esophageal clearance and gastric emptying.<sup>38,39</sup> This could have reduced clinical signs of reflux observed and GERD events detected by the capsule. However, no owners reported clinical improvement during Bravo pH data collection. Finally, a potential bias of this study design was its selection of owners that permitted enrollment of their dogs in a clinical trial involving an anesthetic procedure and intensive daily monitoring for up to 96 hours. This might have selected for more motivated dog owners and dogs at lower risk for anesthetic complications, skewing toward dogs with milder BOAS and SHH and a lower acidic reflux burden.<sup>12</sup>

## 5 | CONCLUSION

In conclusion, Bravo pH capsule technology proved to be a successful tool in documenting and quantifying acidic reflux in French bulldogs with SHH. Higher esophageal acid exposure was found in

younger dogs and during the day compared to the night. Results also showed an improvement in acidic reflux in a subset of dogs that underwent corrective BOAS surgery although the sample size was small. Despite the cost and expertise required, Bravo pH capsule technology could more objectively assess and help manage GERD in brachycephalic dogs with SHH, as utilized in human patients.<sup>30,34</sup>

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## CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

## OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

## INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Approved by University of California, Davis IACUC protocol 22047.

## HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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