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Strongly acidic gastroesophageal reflux and esophageal lumen pH before and after esophageal lavage with water or two bicarbonate concentrations in anesthetized dogs

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OBJECTIVE
To increase acidic esophageal lumen pH in dogs that developed gastroesophageal reflux (GER) during anesthesia. We compared water and 2 different bicarbonate concentrations.

ANIMALS
112 healthy, nonbrachycephalic dogs presented for ovariectomy.

PROCEDURES
Following standard anesthesia and surgery protocols for ovariectomy in all dogs, esophageal lumen impedance and pH were monitored using a dedicated probe. Esophageal impedance indicates the presence of GER whereas pH indicates the acidity level. Dogs with strongly acidic GER and an esophageal lumen pH value < 4.0 were included in the study, and lavage was performed with either tap water, bicarbonate 1%, or bicarbonate 2% until the pH increased to > 4.0. The effect of lavage on esophageal pH was compared using the Kruskal–Wallis and Wilcoxon 2 sample tests. Associations between lavage and pH changes were determined.

RESULTS
Of 48/112 dogs with strongly acidic GER, 33% neutralized their esophageal pH during surgery. For the 32 dogs that maintained an esophageal lumen pH value < 4, esophageal lavage with water increased the lumen pH to > 4 in 78.6% of dogs, whereas both bicarbonate concentrations increased it in 100% of the dogs to a more neutral pH ($P < .0001$). The dogs in the water group were more likely to regurgitate after anesthesia (36% vs 0% in both bicarbonate groups, $P = .028$).

CLINICAL RELEVANCE
Bicarbonate 1% and 2% increased esophageal lumen pH to more than 4 after strongly acidic GER. Lavage with water was mildly effective, but required large volumes and predisposed to further regurgitation after anesthesia.

The incidence of gastroesophageal reflux (GER) in anesthetized dogs is high. Prevalence is reported to occur between 12.5% and- 60% of anesthesia events.[1–5] When GER occurs, complications can develop, such as esophagitis, esophageal stricture formation, or nasopharyngeal stenosis. The incidence for these complications is unknown. Not all dogs with GER will develop inflammation, and not all inflammation will result in stricture formation. Although only a small percentage of patients will develop esophagitis resulting in stricture formation, when it occurs the prognosis is guarded. Stricture formation is reported to be a serious complication from general anesthesia and GER.[6] In one study,[7] 65% of dogs that presented with esophageal stricture had a recent anesthesia event within 2 weeks of presentation. Esophageal strictures are difficult to manage, and have prolonged and expensive treatment protocols that can lead to a 20% mortality rate.[7–9]

Gastroesophageal reflux is defined as retrograde passage of gastric contents into the esophagus.[10] Lower esophageal sphincter relaxation during anesthesia is thought to be the primary predisposing factor. Reflux coupled with the absence of esophageal clearance, duration of reflux contact time, and reflux character (acidity and enzymes such as pepsin) are considered responsible for esophageal inflammation and ultimately progression to stricture formation in some cases.[11–14] Gastroesophageal reflux with a pH < 4 is considered strongly acidic and thought to be involved in the pathogenesis of inflammation and stricture.[11–14]

Studies to prevent GER in anesthetized dogs have been unrewarding. Antiemetic drugs such as metoclopramide and maropitant at recommended doses did not reduce the incidence of GER during anesthesia (metoclopramide 0.4 mg/kg IV, followed by 0.3 mg/kg/h IV[15] or maropitant 1 mg/kg IV and PO[16,17]). Gastroprotectant therapy studies reducing gastric pH prior to anesthesia had variable results.[5] For these reasons, our study objective was to identify and test different lavage solutions to increase esophageal lumen pH after GER in anesthetized dogs with a pH < 4. The study aim was to compare the use of water and 2 bicarbonate concentration solutions to increase esophageal lumen pH to minimize potential esophageal damage.

Materials and Methods

The study was approved by the Institution Animal Care and Use Committee (protocol 16-6873A) and the Hospital Clinical Research Board. In addition, signed consent from owners was obtained for all dogs that participated in the study.

In this prospective, randomized clinical trial, the inclusion criteria consisted of healthy dogs determined by history, physical examination, hematocrit, total plasma protein, and no history of regurgitation or vomiting. At the beginning of each study day, dogs were randomized to a lavage treatment protocol—water, bicarbonate 1%, or bicarbonate 2%—using a random generator. Dogs requiring lavage received the predetermined treatment. All dogs were American Society of Anesthesiologists physical status classification I that presented for elective ovariectomy. Dogs were excluded from the study if they had received any medication during the previous 7 days, had brachycephalic head conformation, received anticholinergic drugs during anesthesia, encountered intraoperative complications (eg, excessive bleeding, previous ovariectomy, unresponsive hypotension with a mean arterial pressure < 60 mm Hg) or had a body weight < 10 kg. Dogs weighing < 10 kg were considered too small to place both an endoscope, and esophageal impedance and pH probe safely in the esophagus.

Anesthesia and surgery

All dogs received the same standardized anesthesia and surgery protocols. Hydromorphone 0.1 mg/kg SC (Hydromorphone HCl, Westward Pharmaceutical) was administered 20 to 30 minutes before anesthesia induction. Four to 8 mg/kg propofol IV (PropoFlo, Abbott Laboratories) was titrated to induce anesthesia and place a properly sized endotracheal tube. Anesthesia was maintained with isoflurane. The anesthesia plane or depth was similar for all dogs, with the isoflurane vaporizer concentration set at 1.5% before surgery and adjusted depending on the dog's requirements. If a dog responded to surgical stimulation (movement or increase in heart rate > 20%, increase in blood pressure > 20%, or increase in respiratory rate > 20%), the vaporizer was increased in stepwise increments of 0.25% each time and the oxygen flow rate increased to 4 L/minute for 5 minutes to accelerate the anesthesia plane change. If a dog became hypotensive (mean arterial pressure < 60 mm Hg), the vaporizer was decreased in a stepwise fashion by 0.25% each time and the oxygen flow rate increased to 4 L/minute for 5 minutes to accelerate the anesthesia plane change. All dogs received IV fluid therapy of Lactated Ringers solution at 5 mL/kg/hour.

Vital signs under anesthesia were monitored using an ECG for heart rate and rhythm, capnography for respiratory rate and end-tidal carbon dioxide (CO_2), rectal thermometer for body temperature, and noninvasive oscillometric blood pressure for systolic, mean, and diastolic arterial blood pressures (Model V plus, VetTrends). Dogs were allowed to breath spontaneously. However, if end-tidal CO_2 increased to > 60 mm Hg, assisted hand ventilation was performed until CO_2 decreased to < 60 mm Hg.

Ovariectomies were performed via midline laparotomy in dorsal recumbency by a fourth-year veterinary student under direct supervision of an experienced veterinarian. All surgeries followed the same standard surgical protocol. At the end of surgery, all dogs received carprofen 2.2 mg/kg SC (Rimadyl, Zoetis).

GER assessment and lavage

A flexible, minimally invasive esophageal impedance and pH probe with measurement marks every centimeter (model #ZIN-BS-45E, SandHill Scientific) was used to determine GER incidence, GER pH, and esophageal lumen pH. The esophageal probe was inserted orally with the aid of an endoscope immediately after endotracheal tube placement. The distal end of the probe was positioned 3 cm proximal to the lower esophageal sphincter to prevent contact with it. The pH probe was secured to the endotracheal tube with tape, and centimeter markings were recorded to ensure there was no movement of the probe. The impedance and pH probe contains 6 impedance electrodes spaced 2 cm apart, starting 2 cm from the probe's distal end. The pH sensor is located 3 cm from the probe's distal end. The impedance electrodes measure the presence of fluid in the esophageal lumen as well as fluid movement and direction (eg, GER) throughout the esophagus. The pH electrode measures the esophageal lumen and fluid pH with an accuracy of 0.1 pH unit. Esophageal pH and impedance data were recorded continuously using an external recording device (ZepHr Impedance/pH reflux recorder, SandHill Scientific) until completion of anesthesia, when the probe was removed. The pH electrode was calibrated in buffer solutions of pH 4 and 7 according to the manufacturer's instructions.

Gastroesophageal reflux was defined when fluid entered the esophagus from the stomach and moved rostrally toward the oral cavity. This was observed by a continuous decrease of impedance (at least a 50% decrement in ohms) across 2 or more of the most distal impedance electrodes, as reported in previously published guidelines.[18] Reflux was

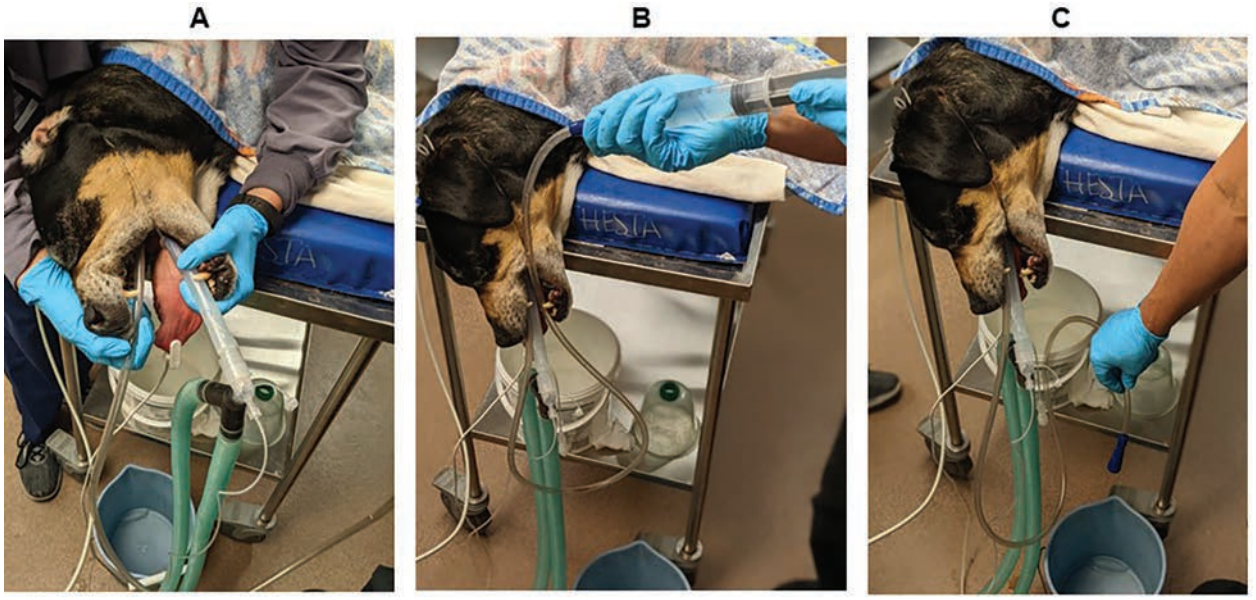

Figure 1—Pictures depicting esophageal lavage. A—An esophageal tube (18 F or 6 mm, or 27 F or 9 mm outside diameter) was inserted to the level of the fourth to fifth intercostal space. Syringe suction and gravity are used to remove gastroesophageal reflux material. B—Lavage aliquots were administered by syringe through the esophageal tube using gravity by raising the proximal end of the tube above the dog and moving the distal end back and forth to spread the lavage throughout esophageal lumen. The patient's head is angled downward to allow the lavage solution to exit via the mouth and nose. C—Lavage solution is aspirated using the syringe and using gravity, placing the tube below the dog's level.

classified depending on GER pH as strongly acidic GER (pH < 4.0), weakly acidic GER (pH ≥ 4.0 and < 7.0) or non-acidic GER (pH ≥ 7.0).[19–21] The GER pH is reported as the average from data points obtained every 5 seconds during each GER event using Sandhill BioVIEW Analysis software (version 5.5.4.1) and Sandhill pH Analysis software (version 4.0.1). Esophageal lumen pH is reported as the average pH obtained every 5 seconds (from the time of probe insertion to probe removal) using the same computer software.

Gastroesophageal reflux was defined when reflux material was not observed exiting the mouth or nostrils. If reflux material was clinically observed exiting the mouth and nostrils, it was considered regurgitation.

Esophageal lavage was performed in dogs with strongly acidic GER and having an esophageal lumen pH value of < 4.0 at the completion of surgery. Esophageal pH was monitored continuously before and after lavage, and until the end of anesthesia, which was approximately 10 to 15 minutes after surgery. Dogs were randomized to receive aliquots of either tap water, 1% bicarbonate, or 2% bicarbonate solution. Injectable 8.4% sodium bicarbonate (VetOne Sodium Bicarbonate™, Nova-Tech) was diluted in tap water to make either a 1% or 2% solution. Specifically, 2.5 mL or 5 mL of bicarbonate was diluted with tap water to a total volume aliquot of 20 mL, making a 1% or 2% solution, respectively. Lavage volumes were 20 mL for bicarbonate solutions or 60 mL for tap water according to previously published guidelines.[22] The measured pH values for lavage tap water, 1% bicarbonate, and 2% bicarbonate were 7.4 ± 0.2, 8.4 ± 0.3, and 8.6 ± 0.1 respectively.

The lavage technique consisted of the oral placement (18 F or 6 mm, or 27 F or 9mm outside diameter) of an esophageal tube to the level of the fourth to fifth intercostal space and applying syringe suction to remove any GER material from the esophageal lumen. Lavage aliquots were administered by syringe through the esophageal tube using gravity by raising the proximal end of the tube above the dog and moving the distal end back and forth to spread the lavage throughout the esophageal lumen **(Figure 1)**. The patient's head was angle downward, below the level of the body, to allow lavage solution to exit the mouth and nose. Lavage solution was aspirated using the same syringe to remove any remaining solution, and then by gravity by placing the tube's proximal end below the level of the dog. pH was measured for 2 minutes to ensure a stable luminal pH. Esophageal lavage was repeated until the esophageal lumen pH value increased to > 4.0. Lavage failure was considered when the lumen pH did not increase to > 4.0 after 5 aliquots or when the lumen pH decreased further from the starting value. The study consort flow diagram depicting study events is presented in **Figure 2**.

Statistical analysis

A power analysis to detect Student *t* test pH differences before and after lavage using a power of 80% and an alpha value of 5%, assuming esophageal lumen pH differences of at least 2 units after lavage, indicated 6 dogs per group were sufficient to identify differences in esophageal lumen pH. Data from

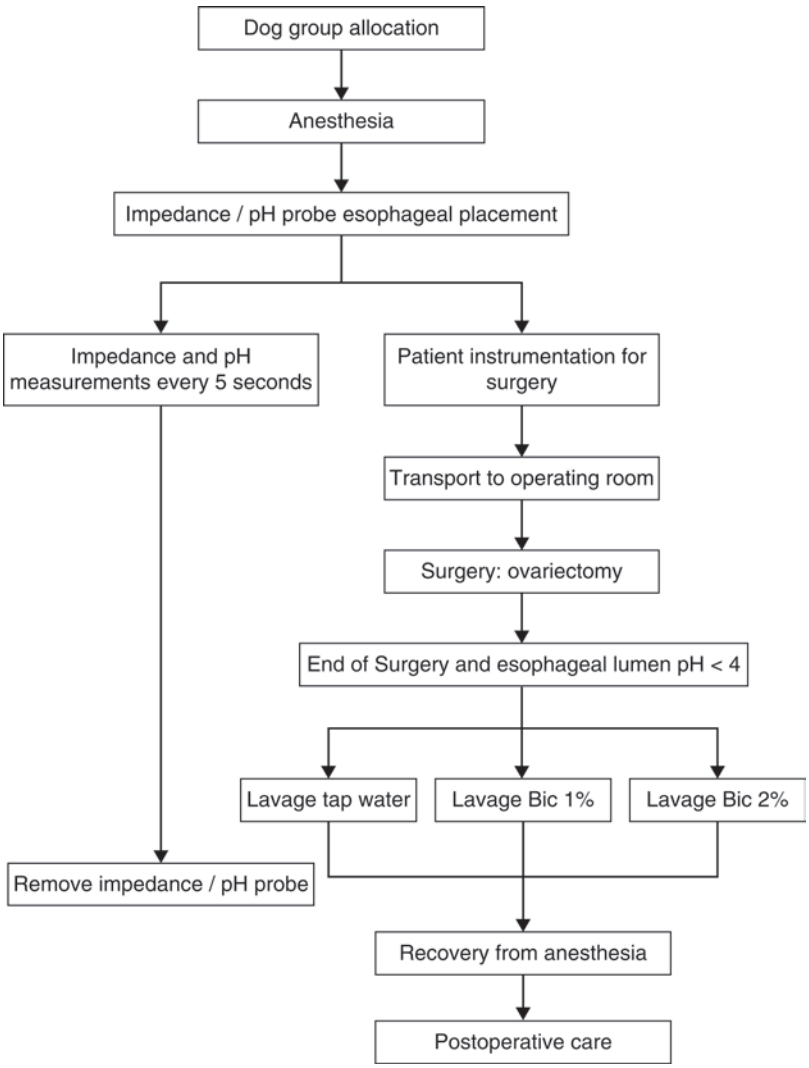

Figure 2—Consort flow diagram depicting study sequence of events. Bic = Bicarbonate.

Wilson and Evans[22] were used to perform the power calculation.

Continuous data were evaluated for normality assumption using the Shapiro–Wilk test. Age, body weight, and anesthesia duration were normally distributed and compared using 1-way ANOVA. Data are presented as mean ± SD. Normality was not met for the rest of the data; the nonparametric Kruskal–Wallis test was used when comparing 3 groups, and the Wilcoxon 2 sample test was used when comparing 2 groups to evaluate differences among groups. A nonparametric post hoc test (the Dwass, Steel, Critchlow–Fligner method) was used to perform pairwise comparisons. The Fisher exact test was used to evaluate the association between 2 categorical variables. pH data are presented as median (range). We report the mean ± SD for lavage volumes used and some pH data for comparison with other studies. Spearman's rank was used to identify correlations between volumes of lavage solution with esophageal lumen pH changes. A *P* value < .05 was used to determine statistical difference. SAS v9.4 (SAS Institute Inc) and GraphPad Prism v9.0.0 (GraphPad Software) were used for statistical analyses.

Results

Of the 112 dogs studied, 64 dogs developed GER but only 48 had strongly acidic GER with a pH < 4.0. Of the 48 dogs with strongly acidic GER, 32 maintained an esophageal lumen pH at < 4 at the end of surgery and were included in the study for esophageal lavage. Dogs were assigned randomly to receive lavage with either water (n = 14), 1% bicarbonate (n = 8), and 2% bicarbonate (n = 10). Dog mean age, body weight, anesthesia duration, and breed distribution were similar among groups **(Table 1)**, with no difference among groups.

Esophageal lumen pH values at the end of surgery but before lavage were 3.35 (range, 1.5 to 3.9) for the water group, 2.75 (range, 1.8 to 3.8) for the 1% bicarbonate group, and 3.8 (range, 1.9 to 3.9) for 2% bicarbonate group **(Table 2)**. Esophageal lumen prelavage pH comparison among groups had a *P* value of .05. However, the post hoc pairwise comparison among groups had a *P* value of .62 for water vs bicarbonate 1%, *P* = .13 for water vs bicarbonate 2%, and *P* = .08 for bicarbonate 1% vs bicarbonate 2%.

The water group pH increased to > 4.0 after lavage in 11/14 dogs (78.6%). The remaining 3 dogs were considered to have lavage failure (pH < 4.0). The esophageal lumen pH value increased to > 4.0 in all dogs with bicarbonate lavage after the first 20-mL aliquot. The esophageal lumen pH values postlavage for each group were 4.2 (range, 2.4 to 5.6) for the water group, 7.65 (range, 5.8 to 8.5) for the 1% bicarbonate group, and 8.45 (range, 7.1 to 8.9) for the 2% bicarbonate group (Table 2). The pH increase in both bicarbonate groups was significantly greater when compared to the water group (*P* = .000 for 1% bicarbonate and *P* = .000 for 2% bicarbonate). No difference was observed between bicarbonate groups (*P* = .98). Water lavage required an average of 298 ± 155 mL water to increase the esophageal lumen pH value by 1.16 ± 1.14 (15.8 ± 10.7 mL/kg body weight). In both bicarbonate groups, only one 20-mL aliquot of bicarbonate increased the pH value by 4.76 ± 0.83 for the 1% solution and by 4.8 ± 0.85 for the 2% solution. The index lavage volume for bicarbonate 1% was 1.1 ± 0.3 mL/kg, and for bicarbonate 2% was 1.1 ± 0.3 mL/kg. The volume of water used for lavage did not correlate with changes in esophageal lumen pH (*r* = 0.27,

Table 1—Group characteristics for tap water, bicarbonate 1%, and bicarbonate 2% groups. Mean ± SD for age, body weight, and anesthesia duration.

Characteristic	Tap water (n = 14)	Bic 1% (n = 8)	Bic 2% (n = 10)	*P* value
Age (months), mean ± SD	17.1 ± 8.5	16.3 ± 8.8	15.7 ± 8.8	.92
Body weight (kg), mean ± SD	21 ± 6.1	19.8 ± 5.9	20 ± 6.3	.89
Anesthesia (minutes) mean ± SD	178 ± 32	176 ± 20	175 ± 46	.97
Breed	Mixed (n = 5), American Staffordshire Terrier (n = 4), Dalmatian (n = 1), Australian Shepherd (n = 2), Golden Retriever (n = 1), Labrador Retriever (n = 1)	Mixed (n = 2), American Staffordshire Terrier (n = 3), Australian Heeler (n = 2), Dalmatian (n = 1)	Mixed (n = 3), Australian Heeler (n = 1), Dalmatian (n = 2), American Staffordshire Terrier (n = 2), Australian Shepherd (n = 1), Labrador Retriever (n = 1)	—

Dog breed distribution per group. Data compared using 1-way ANOVA.

Table 2—Data comparison between groups.

Variable	Tap water (n = 14)	Bic 1% (n = 8)	Bic 2% (n = 10)	*P* value
Bic (mL):water[a] (mL)	—	2.5:17.5	5:15	—
Lavage success[b] (%)	78.6	100	100	.23
Prelavage pH, median (range)	3.35 (1.5–3.9)	2.75 (1.8–3.8)	3.8 (1.9–3.9)	.05
Postlavage pH, median (range)	4.2 (2.4–5.6) a,b	7.65 (5.8–8.5) a	8.45 (7.1–8.9) b	< .0001
Recovery Regurg[c] (%)	36 a,b	0 a	0 b	.028
Lavage volume (mL), mean ± SD	298 ± 155 a,b	20 a	20 b	< .0001

Bic = Bicarbonate. Bic 1% = Bicarbonate 1%. Bic 2% = Bicarbonate 2%.

[a]The volume of commercial bicarbonate 8.4% and the volume of tap water necessary to make Bic 1% and Bic 2% solutions. [b]The percentage of dogs with esophageal lumen pH > 4.0 postlavage. [c]The percentage of dogs with regurgitation during or within 10 minutes of anesthesia extubation.

Letters within columns indicate statistical differences between groups. The Kruskal-Wallis test and nonparametric post hoc test were used to compare data between groups.

P = .34). In the 3 dogs in which water lavage did not increase the pH value to > 4.0, the prelavage esophageal lumen pH value was 2 (range, 1.5 to 3.5) and the postlavage pH value was 2.4 (range, 2.4 to 2.6).

A complication observed in the water lavage group was that 5/14 dogs (36%) regurgitated esophageal fluid within the first 10 minutes after endotracheal extubation. No dog from the 1% or 2% bicarbonate group regurgitated during the recovery period. The regurgitation incidence during recovery was different among groups (*P* = .028). Water volume used for lavage was not associated significantly with regurgitation incidence during recovery (*P* = .10). However, the 5 dogs with recovery regurgitation received greater lavage volumes (396 ± 173 mL) when compared to the 9 dogs from the same group with no regurgitation (243 ± 121 mL).

Of the 48 dogs with strongly acidic GER, only 32 maintained an esophageal lumen pH value of < 4.0 at the end of surgery. Meaning, 16 dogs (33%) were able to either clear or neutralize their esophageal lumen pH during surgery. These 16 dogs increased the esophageal lumen pH value from 2.1 ± 0.8 to 5.4 ± 0.9 (*P* < .000) during surgery. Furthermore, of the 64 dogs with GER in the study, none was observed to regurgitate through the mouth or nose.

Discussion

Forty-two percent of dogs undergoing anesthesia and surgery in this study developed strongly acidic GER. We show for the first time that 33% were capable of neutralizing or clearing the strongly acidic pH without treatment. Lavage using water for an esophageal lumen pH of < 4.0 at the end of surgery was less successful in increasing pH to > 4.0, and predisposed some dogs to regurgitation. Bicarbonate 1% or 2% lavage increased esophageal pH in all dogs.

We were unable to determine why some dogs were able to clear or neutralize esophageal lumen pH after GER when others could not. The intrinsic ability to neutralize acidic luminal pH may explain why most dogs are considered to have silent reflux.[23] Further studies are necessary to understand GER, esophageal clearance mechanisms, and stricture pathophysiology more fully.

American Animal Hospital Association guidelines[24] suggest esophageal lavage when GER is observed in anesthetized patients. Lavage with tap water is often a common approach to dilute and remove GER material as well as to neutralize acidic GER and lumen pH.[25,26] However, similar to our study, a short communication reported that regular tap

water barely increased esophageal lumen pH in dogs with acidic GER. Wilson and Evans[22] showed that 60% of dogs failed to increase esophageal lumen pH to > 4 after water lavage, with a mean overall lumen pH increase of 2.2. Allison et al[26] also showed a pH increase of 1.61 after water lavage. Thus, the use of tap water for esophageal lavage may not always increase the luminal pH value to > 4. Results from our study found that large volumes of water and repeated lavage attempts were required to increase luminal pH, and predisposed patients to regurgitation during recovery. Allison et al[26] did not report postlavage regurgitation during recovery, but a smaller volume of water (3.1 mL/kg) was used to increase the esophageal lumen pH value from 3.8 to 5.7. Although no correlation between water volume and pH change was identified in our study, a smaller water volume would have resulted in a greater incidence of lavage failure, similar to the findings by Wilson and Evans.[22]

In contrast to water, the use of dilute bicarbonate changed esophageal lumen pH immediately, and only 20 mL was necessary to increase the pH value by 4.8 units. The luminal pH remained at > 4 for at least 10 to 15 minutes, at which time it was necessary to remove the impedance and pH probe as the dogs recovered from anesthesia. It is unknown whether or for how long the esophageal lumen pH remained at > 4 after recovery. Wilson and Evans[22] did show that esophageal lavage with a 20-mL aliquot of bicarbonate 4.2% increased lumen pH to 7 for a median of 89 minutes and, in some dogs, for up to 180 minutes.

Both Wilson and Evans[22] and Allison et al[26] used 4.2% bicarbonate. We chose more dilute concentrations of 1% and 2%, with the thought of minimizing potential bicarbonate mucosal damage,[27] neutralizing but not alkalinizing luminal pH, and making the dilution recipe easy for clinical practice. Further studies are necessary to determine the ideal concentration, dilution method, and lavage volumes to neutralize GER and esophageal pH most effectively. The ideal lavage solution may depend on GER pH, GER volume, and other intrinsic characteristics. For example, studies have shown different GER predisposing factors that can possibly impact GER characteristics: surgery type,[1,28] brachycephalic breeds,[29] laryngeal paralysis,[30] use of anticholinergic or opioid drugs,[2,3] food withholding,[4,31] and patient position.[28]

In summary, 67% of dogs with strongly acidic GER during surgery maintained a strongly acidic esophageal environment and may require lavage. Bicarbonate 1% or 2% was found to increase the esophageal lumen pH to > 4. Lavage with water may fail to increase pH and predispose to further regurgitation when large volumes are used. Bicarbonate lavage as described herein is easy to perform and appears to be effective in neutralizing acidic esophageal lumen.

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