EFFECT OF PRE-ANESTHETIC FASTING TIME ON GASTROESOPHAGEAL REFLUX AND STOMACH SIZE

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EFFECT OF PRE-ANESTHETIC FASTING TIME ON GASTROESOPHAGEAL REFLUX AND STOMACH SIZE

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Abstract: Many small animal patients at some point in their life will undergo general anesthesia. Gastroesophageal regurgitation (GER) is a complication that can be encountered during this time and could potentially lead to severe esophageal ulcers or stricture formation. To help reduce this risk, it has been recommended that patients not be fed for a specific period of time before their anesthesia. However, the best length of fasting time to reduce gastroesophageal regurgitation has been poorly identified. The effect of pre-anesthetic fasting time on the incidence of gastroesophageal regurgitation was evaluated. The null hypothesis states that pre-anesthetic fasting time will have no significant effect on the incidence of gastroesophageal regurgitation. Eight healthy, adult purpose-breed Beagles were randomly assigned to a fasting period of three, six, nine, or 12 hours. Following induction of anesthesia, esophagoscopy and abdominal radiographs were performed. A visual analog scale was used to determine the amount of ingesta present in the stomach, reported as a percentage representing stomach fullness. Esophageal pH and GER events were recorded using esophageal pH/impedance monitoring and endoscopic visualization of reflux. Recording for a GER event was performed for one hour. No premedication was utilized during the study. A wash out period of 14 days occurred between anesthetic episodes and all dogs rotated through each fasting treatment group once. Data was analyzed for acidity of reflux, time of reflux, evidence of esophageal pathology, and size of stomach. Our results failed to reject the null hypothesis. However, results did indicate that a shorter fasting time was significantly associated with a larger stomach size. For each 1% increase in stomach size, the odds that a dog would have a GER event increased by 17%. Results of this study indicate that stomach size, rather than pre-anesthetic fasting time, is directly associated with an increased risk of GER.
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Post-anesthetic esophagitis, esophageal stricture, and aspiration pneumonia are rare but potentially serious consequences of gastroesophageal reflux (GER) during anesthesia. Reported post-operative incidence estimates of esophagitis and stricture are 0.07%-0.96%, with aspiration pneumonia estimated to occur in 0.17% of dogs.\textsuperscript{1,3} Estimates of GER during anesthesia are dramatically higher and have been reported to occur in 16-60% of dogs.\textsuperscript{4-6} To reduce the risk of gastroesophageal regurgitation, fasting guidelines have been developed for veterinary patients, which state that solid food be withheld for at least six hours prior to anesthesia, but liquids may be allowed up until anesthesia.\textsuperscript{7} Unfortunately, in the authors’ experience, many practices do not adopt this newer guideline due to fear of regurgitation and/or aspiration and continue to adopt a 12-hour fasting period even though little evidence supports that it is superior to shorter fasting periods. In fact, a greater risk of gastroesophageal regurgitation was found in patients who were fasted over a 12-hour period.\textsuperscript{5} Purported advantages of a shorter solid food fasting in human medicine include reduction in patient thirst, hunger, anxiety, and decreased surgery-induced immunosuppression.\textsuperscript{8-11} To the author’s knowledge, there have been no previous studies solely evaluating pre-anesthetic fasting time and its effect on gastroesophageal regurgitation. The studies that are available have all had compounding factors, which have included pre-medications or anesthetic induction drugs that are no longer available. The objective of this investigation
is to determine the effect of pre-anesthetic fasting time on gastroesophageal regurgitation in the absence of pre-medication. Our null hypothesis states that pre-anesthetic fasting time will have no significant effect on the incidence of gastroesophageal regurgitation.
CHAPTER II

REVIEW OF LITERATURE

ANATOMY OF THE ESOPHAGUS

The esophagus is a hollow tube that connects the oral cavity to the stomach, allowing transfer of liquids or solid food from one area to the other. In veterinary patients, the esophagus in the dog is comprised of skeletal muscle; whereas the distal third of the esophagus in the cat is comprised of smooth muscle. The mucosa of the esophagus is lined by stratified squamous epithelium. The outer two layers of the esophagus include the submucosa and muscularis. At either end of the esophagus are ill-defined esophageal sphincters. The upper esophageal sphincter functions to prevent movement of air into the esophagus when not eating by contraction of the cricothyroideus and cricopharyngeus muscles. The lower esophageal sphincter (LES) provides protection against reflux, or backward movement, of stomach contents into the lower esophagus. The LES is not an easily identified valve-like structure; instead it is comprised of thickening of the muscularis layer and several other anatomic contributors (diaphragmatic crural muscles, the angle at which the esophagus and stomach meet, and the folds of the gastroesophageal mucosa) that add to LES resting tone.
PATHOPHYSIOLOGY OF GASTROESOPHAGEAL REGURGITATION

Damage to the esophageal mucosa and submucosa can be severe. As a result of this, many animals will have pain during eating resulting in anorexia, weight-loss, and in extreme cases, death. The most common cause of esophagitis and esophageal stricture formation in veterinary medicine is due to development of gastroesophageal reflux during general anesthesia.

Gastroesophageal reflux contains gastric acid, pepsin, bile salts, and trypsin, which cause direct damage to the esophageal mucosa. A study completed by Tobey et. al. suggested that pepsin resulted in an irreversible lesion to the mucosa, making pepsin the most potent irritator of the four agents. In response to acid erosion, numerous changes occur at the level of the esophageal mucosa. First, an increase in paracellular permeability occurs which allows acid to penetrate into the basolateral membrane leading to inflammation and irritation of the esophagus.  

As inflammation worsens, a viscous cyclical cycle is produced. Proinflammatory cytokines (IL-1β, IL-6, and IL-8) are released by a variety of cells including esophageal epithelium, neutrophils, and macrophages. Interleukin-8, released by the esophageal epithelium, is a potent chemoattractant of neutrophils. Several studies have demonstrated that as the severity of disease increases, so does the production of IL-8. Cellular damage succeeds with the recruitment of more neutrophils and release of reactive oxygen species occurs. Another cytokine, interleukin-6 allows for production of platelet-activating factor (PAF) and initiation of the production of prostaglandin E2 (PGE2), and thromboxane. These end-products are responsible for recruitment of more neutrophils and the release of hydrogen peroxide (H2O2). As H2O2 is released, continued cellular damage, necrosis and apoptosis occurs to the esophagus.

Esophageal motility and tone of the LES will also be affected by PAF, IL-6, and PGE2. The altered motility is a consequence of inhibition of acetylcholine release from esophageal...
cholinergic neurons. This decreased tone of the lower esophageal sphincter will allow for continued gastric reflux and caustic damage.

PREVALENCE OF GASTROESOPHAGEAL REGURGITATION IN ANESTHETIZED VETERINARY PATIENTS

Post-anesthetic esophagitis, esophageal stricture, and aspiration pneumonia are potential sequelae to gastroesophageal reflux during anesthesia. Reported incidence of the three is rare with recent studies estimating esophagitis and stricture formation to occur in 0.07%-0.96% and aspiration pneumonia in 0.17% of dogs. Although the reported post-operative incidence is rare, the incidence of gastroesophageal reflux occurring during surgery is dramatically higher. Studies have documented an incidence of 16-60% in dogs. A recent paper, utilizing an impedance probe similar to the esophageal pH/impedance probe utilized in this study reported an incidence of GER in 38% of dogs in their control group.

Multiple variables have been investigated to determine their effect on GER. Esomprazole and cisapride when used in combination or omeprazole alone have documented a decrease in GER during surgery. Other studies have illustrated an increased risk of GER for patients undergoing orthopedic surgery and weighing more than 40 kg. A decrease in lower esophageal pressure has been reported with the use of anticholinergics, thiopental, opioids, and isoflurane, which are many drugs used during anesthesia. But perhaps the most controversial is the pre-operative fasting time.
It is believed that animals who have recently ingested a meal have an increased risk of GER and its sequelae due to anesthetic relaxation of the lower esophageal sphincter.

CURRENT FASTING GUIDELINES

In veterinary medicine, current guidelines recommend solids be withheld for at least 6 hours prior to anesthesia, but liquids may be allowed just until anesthesia. Unfortunately, in the author’s experience, many practices do not adopt this guideline due to fear of regurgitation and aspiration. Most practices still recommend no food for 12 hours prior to surgery. An older study investigated the effect of preoperative fasting time in dogs. In this study, no increased risk of GER was found in patients with a 2-4 hours fast period. Ironically, an increased risk of GER was found in patients fasted over 12 hours. Unfortunately, this study has several limitations. Anesthetics that were used in the study are unavailable now and premedication was a variable that may have compounded the findings, as some of the medications used could have lowered the lower esophageal pressure.
CHAPTER III

METHODOLOGY

Eight healthy, young adult (1-3 years of age), purpose bred beagles were obtained for the purpose of the study. The study was approved by the Oklahoma State University Institutional Animal Care and Use Committee prior to commencement. Dogs were randomly assigned a number through the use of a random numbers generator. Twenty-four hours prior to the day of anesthesia, the dogs were assigned a randomized fasting period of either three, six, nine, or 12 hours. The 12 hour fasting period served as the control for each dog. All dogs were assigned to each fasting period once. A 14-day break was provided between anesthetic episodes to allow for complete patient recovery and to monitor for development of post-procedural complications. The last meal before anesthesia was a commercially available canned dog food which contained half of the subject’s resting energy requirement. Water was allowed until two hours before the anesthesia.

INDUCTION OF ANESTHESIA

On the day of anesthesia, a cephalic intravenous catheter was placed without the use of premedication. Induction of anesthesia was performed by administering an injection of propofol (6-8 mg/kg [2.7-3.6 mg/lb], intravenous) to effect to allow for endotracheal tube intubation. Subjects were intubated with an appropriately sized endotracheal tube and anesthesia was
maintained with isoflurane (1-2%). Anesthetic monitoring included heart rate, respiratory rate, pulse oximetry, electrocardiography, capnography, oscillometric non-invasive blood pressure, and rectal thermometry. Measurements were recorded every five minutes for the duration of the procedure. A forced-air warming device and intravenous fluid warmer were used to maintain normothermia.

**ESOPHAGOSCOPY AND STOMACH SIZE RECORDING**

Immediately following induction, dogs were positioned in left lateral recumbency and a flexible gastroscope was used to assess the esophagus and lower esophageal sphincter. Any evidence of esophageal pathology was graded (none=0, mild=1, moderate=2, severe=3). All endoscopy and grading was performed by a single board-certified small animal internist who was blinded to the dog’s fasting period. The patient was then transported to the radiology department where three-view (right lateral, left lateral and ventrodorsal) abdominal radiographs were obtained and be used to assess stomach size by a board certified veterinary radiologist. Intravenous propofol boluses were used as needed to maintain unconsciousness. Following acquisition of the radiographs, subjects were transported back to the anesthesia induction/preparation room and repositioned in left lateral recumbency. Intermittent positive pressure ventilation was used for the rest of the anesthetic procedure.

**GASTROESOPHAGEAL REGURGITATION DETECTION**

A single-use pH/impedance probe was attached to an external reference pad placed on the right lateral thorax. The probe had six impedance rings, spaced 2 cm apart, and one pH sensor placed 2 cm from the distal end of the probe. The pH electrode was calibrated according to manufacturer’s instructions with 4.0 and 7.0 pH buffer solutions. The pH/impedance probe was then placed five centimeters orad to the lower esophageal sphincter (LES) with the use of endoscopic guidance and a snare loop. Care was taken not to penetrate the LES. Any evidence of GER was recorded
when placing the probe. The probe was then attached to a multi-use recording device and continuous recording of pH and impedance occurred for 60 minutes.

A reflux episode was defined as a 50% decrease in ohms seen in two consecutive channels in the distal esophagus for >2 seconds from pre-episodic esophageal baseline. The reflux was then identified as either acidic (pH <4.0), weakly acidic (4.0 ≤ pH < 7.0), or non-acidic (pH ≥ 7.0). Baseline esophageal pH was determined as the pH of the esophagus within the first 10 minutes of data collection.

ASSESSMENT OF STOMACH SIZE
Stomach size was assessed by a single board certified veterinary radiologist who was blinded to the dog’s fasting period. A visual analog scale measuring 10 cm was created. The bar was labeled “empty” at one end and “could not be any fuller” at the other end. A hash mark was made on the line to indicate how distended the stomach appeared to be after examination of all three views. No attempt was made to quantify the amount of ingesta versus the amount of intraluminal gas. The distance between the hash mark and the “completely empty” bar was measured in centimeters. Because the scale length was 10 cm, the distance of the hash mark to the “empty” bar was recorded as a percent of the total 10 cm distance.

STATISTICAL ANALYSIS
Fasting period and presence of regurgitation were statistically analyzed with a McNemar’s test to determine if a cause-effect relationship existed. The McNemar’s test allowed for comparison of each pair of times (i.e. three hour to six hour, three hour to nine hour, etc.). Analysis of variance was then performed on stomach size and baseline esophageal pH for each fasting. A binary response model, with regurgitation as the response, and stomach size (in percent) as the
explanatory variable was used to determine an odds ratio of stomach size and presence of a GER event. A p-value of < 0.05 was defined as a significant.
CHAPTER IV

FINDINGS

INDICENCE OF GASTROESOPHAGEAL REGURGITATION

Three of the eight (37.5%) dogs had at least one episode of GER. Five dogs had no evidence of regurgitation during any anesthetic episode. Two dogs had a GER event during two fasting groups while they were under general anesthesia. One dog had one GER event during one fasting group. Of the dogs that had two GER events, one had its event during the three and 12 hour fasting periods, while the other had a GER event during the six and 12 hour fasting period. The dog with only one episode of GER experienced that episode when it was fasted for three hours.

A total of five GER events were recorded by observers, making the overall incidence of GER to be 15.6%. Reflux was observed via endoscopy in four events and one episode of reflux was documented based on pH/impedance monitoring. Results of the number of dogs that had a GER event in each fasting group are summarized in Figure 1. Of the GER events observed, it was interesting to note that they all occurred within 20 minutes of induction. Two reflux events were observed on endoscopy immediately after induction, whereas the other two visible events occurred following completion of abdominal radiographs. Dog 3 regained consciousness 17 minutes into the procedure. Endoscopy was repeated and the small amount of regurgitation
observed previously was unchanged. A new pH/impedance probe was placed after the subject was re-anesthetized. Another GER event was documented by impedance nine minutes into anesthesia. There was no significant difference between fasting groups with regard to observation of a GER event ($p = 0.4795$). A summary of the dogs that had regurgitation and when it was detected can be found below in Table 1. During the study, no dogs had evidence of esophageal pathology (i.e. erosion, ulcers) based on endoscopic examination and no episodes of continued regurgitation after anesthesia were reported to the authors by the animal care takers.

**Figure 1.** Summary of dogs that had GER events and when they occurred during the procedure.

![Figure 1](image)

**Table 1.** Summary of GER events observed in each fasting group. (*) Represents one dog that woke during the procedure. This dog had two episodes of GER in the same anesthetic period.

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<tr>
<td><strong>Stomach size (%)</strong></td>
<td>33</td>
<td>51</td>
<td>27</td>
</tr>
<tr>
<td><strong>Fasting group (hr)</strong></td>
<td>3</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td><strong>Regurgitation Time (after induction, minutes)</strong></td>
<td>20</td>
<td>9</td>
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RELATIONSHIP OF STOMACH SIZE AND GASTROESOPHAGEAL REGURGITATION

As expected, stomach size was significantly larger in the three hour fasting group than all other fasting groups (p < 0.05). Average stomach size for the three hour fasting period was 27.9%. The average stomach size was smallest for the nine hour fasting group, with a mean of 8%. The average stomach size for the six hour fasting period was 16% and 11% for the twelve hour fasting period. A significant relationship was observed for stomach size and presence of a GER event (p < 0.05), with the larger stomach size having more GER events. For every 1% increase in stomach size, the odds that a dog would regurgitate increased by 17% (OR = 1.17).

ESOPHAGEAL pH

Baseline esophageal pH did not differ significantly amongst the fasting groups (p > 0.07). One dog that regurgitated in the three hour fasting period had an initial esophageal pH of 3.0, but within 10 minutes of data collection the esophageal pH increased to 4.5. Baseline esophageal pH was weakly acidic (4.0 < pH < 7.0) in 26 of 32 (87.5%) anesthetic episodes. Baseline pH was nonacidic (pH ≥ 7.0) in 6 of 32 (18.7%) anesthetic episodes. Mean and median baseline esophageal pH for each fasting group was 5.5/5.4 (3 hour), 6.5/6.4 (6 hour), 5.9/5.7 (8 hour), and 6.3/6.2 (12 hour).
CHAPTER V

CONCLUSIONS

Results of the current study demonstrate that fasting time was unrelated to the presence of a GER event; therefore, the null hypothesis could not be rejected. This supports that long pre-anesthetic fasting times 12 hours or greater may not be necessary. It is interesting to note the three and 12 hour fasting periods had two animals with two episodes, or four of the five GER events. As mentioned previously, a study completed by Galatos in 1995 found that a longer fasting time increased the risk of GER.\(^5\) Lower esophageal sphincter (LES) pressure can respond to increased acidity through relaxation.\(^19\) The study completed by Galatos demonstrated that dogs with a prolonged fasting time had acidic gastric contents.\(^5\) This may explain why they found, and our study also supported, prolonged fasting times (12 hours or greater) to have a higher incidence of GER. Gastric pH levels were not measured in the current study because intubation of the LES may have resulted in its relaxation and increased risk of GER.

The current study found an association between increased stomach volume and increased risk of regurgitation. As expected, the average stomach size was largest in the three hour fasting group. Of the dogs that had a GER event, stomach size was greater than or equal to 23%. However, there were several dogs with stomach sizes larger than 23% that did not exhibit a GER event. Of the dogs that did have a GER event, there are times when similar stomach size for other fasting times
were observed, but no regurgitation occurred. These data indicate that anesthetic GER is a complex event and dependent on more factors than pre-procedural fasting times and stomach size.

There are multiple factors that can affect the gastric emptying time and consequently the volume of the gastric contents at the time of surgery, including dietary nutrients, health, current medications, and type of food (i.e. liquid vs. solid).\textsuperscript{20} It has been purported that lipids have the slowest gastric emptying time, while carbohydrates are intermediate and protein rich meals have the fastest emptying time.\textsuperscript{20} A canned adult maintenance food was chosen for this study for its availability and palatability. Ingestion of the entire meal at specific time was needed to accurately measure fasting times in this study. A canned diet was selected to entice the subject to consume the entire meal when offered. A recent study illustrated that when half of the resting energy requirement was provided, gastric content volume was not significantly increased in dogs being fed a canned dog food, when compared to a dry dog food.\textsuperscript{21} Another study completed by Hardy and colleges revealed that gastric volume and incidence of GER were not correlated in humans.\textsuperscript{22} To the authors’ knowledge, this is the only veterinary study to report that a relationship between stomach size and incidence of GER may exist in healthy, young adult dogs. Further investigation into pre-procedural gastric volume and risk of GER is warranted.

Premedications were not included in the current study, as they can affect gastrointestinal motility. A decrease in lower esophageal pressure has been reported with the use of anticholinergics, thiopental, opioids, and isoflurane.\textsuperscript{23-25} However, premedications have been shown to aid induction in multiple ways, including restraint and relaxation of the patient.\textsuperscript{18} This may translate into a better and more even anesthetic plane. In the authors’ experience, the use of premedication allows for easier restraint for intravenous catheter placement and patients have less risk of regaining consciousness as they are transported through the hospital. In this study, two of the
three subjects that had a GER event had more difficult intravenous catheter placement and required additional propofol during transportation. No regurgitation was observed on initial endoscopic examination prior to abdominal radiographs; however, during endoscopic pH/impedance probe placement, reflux was observed within the esophagus. It is possible that these subjects had their regurgitation event during the period when they were regaining consciousness. This may be a risk factor for patients that develop esophagitis after anesthesia. A light plane of anesthesia has been reported to be a risk factor for GER in human surgery. For this reason, it is recommended that patient’s level of anesthesia be monitored frequently. Keeping a patient adequately anesthetized during movement from one area of the hospital to another could be challenging, but if done appropriately, may decrease the risk of GER.

Propofol was utilized as the induction agent in the current study as it is widely available and thiopentone, which was utilized in previous fasting period studies, is no longer available. It is important to note that when comparing thiopentone and propofol, a higher risk of GER was observed with propofol. At our hospital, sevoflurane and isoflurane inhalants are available. Due to widespread use of isoflurane in private practice, isoflurane was chosen as the inhalant. A recent study by Wilson and colleagues found that there was a similar risk of GER in dogs undergoing a surgical procedure using both sevoflurane and isoflurane inhalants.

LIMITATIONS
The current study has several limitations including population size, homogeneity of the subjects, and type of dog food fed. Ideally, a larger study population would have been used; however, given the potential for serious complications with short fasting times, the authors’ felt that client-owned patients should not be enrolled until it could be determined if a risk of increase GER occurred with shorter fasting times. A larger sample size may have resulted in a different incidence of GER. A cross-over study design was implemented to increase the power of the study
with the number of available subjects. The small number of subjects in our study could increase the risk for a Type II statistical error. Two subjects had evidence of GER in two separate anesthetic events. This could be indicative of other, undiagnosed factors in these subjects that predisposed them to GER. The subjects used were purpose-bred beagles and where of similar size and age. With a more heterogeneous population of subjects, the results of the study could be extrapolated to a more diverse population as would be present in a clinical population of dogs. Finally, canned dog food was used in order to encourage the dogs to eat when food was available. Use of a dry food may have had a different effect on GER incidence.

CONCLUSION

The results of this study indicate that stomach size, rather than pre-anesthetic fasting time, was associated with an increased risk of GER. For every 1% increase in stomach size, the odds that a dog would regurgitate increased by 17%. This study was intended to serve as a pilot study in which the risk of gurgitation could be identified. It is intended that future studies with the addition of anesthetic pre-medication at different fasting times will be performed.
REFERENCES


34. Raptopoulos D, Galatos AD. Gastro-oesophageal reflux during anaesthesia induced with either thiopentone or propofol in the dog. Vet Anaesth Analg 1997;24:20-22.

APPENDICES

ABBREVIATIONS

GER: Gastroesophageal regurgitation

LES: Lower esophageal sphincter

PAF: Platelet activating factor

FOOTNOTES

a. Adult Science Diet, Turkey Flavor, Hill’s Pet Nutrition, Topeka, KS

b. PropoFlo, Abbott, Chicago, IL

c. Isothesia, Henry Schein, Dublin, OH

d. Bair Hugger, 3M Animal Health, Maplewood, MN

e. i-Warm, Midmark, Versailles, OH

f. Olympus Veterinary Scope VET-PQ140, Center Valley, PA

g. Esophageal pH/impedance probes, model # ZPN-BS-01E, Sandhill Scientific, Inc, Denver, CO

h. Rotator Snare, REF #00711120, US Endoscopy, Mentor, OH

i. ZypHr recording device, Sandhill Scientific, Inc, Denver, CO
VITA

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