Effect of changes in intra-abdominal pressure on diameter, cross-sectional area, and distensibility of the lower esophageal sphincter of healthy dogs as determined by use of an endoscopic functional luminal imaging probe

Philipp D. Mayhew BVM&S

Kathryn A. Pitt DVM, MS

Michele A. Steffey DVM

William T.N. Culp VMD

Philip H. Kass DVM, MPVM, PhD

Stanley L. Marks BVSc, PhD

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From the Departments of Surgical and Radiological Sciences (Mayhew, Pitt, Steffey, Culp), Population Health and Reproduction (Kass), and Medicine and Epidemiology (Marks), School of Veterinary Medicine, University of California-Davis, Davis, CA 95616.

Address correspondence to Dr. Mayhew (philmayhew@gmail.com).

OBJECTIVE
To evaluate the effect of intra-abdominal pressure (IAP) on morphology and compliance of the lower esophageal sphincter (LES) by use of impedance planimetry in healthy dogs and to quantify the effect of changes in IAP.

ANIMALS
7 healthy, purpose-bred sexually intact male hound-cross dogs.

PROCEDURES
Dogs were anesthetized, and cross-sectional area (CSA), minimal diameter (MD), LES length, LES volume, and distensibility index (DI) of the LES were evaluated by use of an endoscopic functional luminal imaging probe. For each dog, measurements were obtained before (baseline) and after creation of a pneumoperitoneum at an IAP of 4, 8, and 15 mm Hg. Order of the IAPs was determined by use of a randomization software program.

RESULTS
CSA and MD at 4 and 8 mm Hg were not significantly different from baseline measurements; however, CSA and MD at 15 mm Hg were both significantly greater than baseline measurements. The LES length and LES volume did not differ significantly from baseline measurements at any IAP. The DI differed inconsistently from the baseline measurement but was not substantially affected by IAP.

CONCLUSIONS AND CLINICAL RELEVANCE
Pneumoperitoneum created with an IAP of 4 or 8 mm Hg did not significantly alter LES morphology in healthy dogs. Pneumoperitoneum at an IAP of 15 mm Hg caused a significant increase in CSA and MD of the LES. Compliance of the LES as measured by the DI was not greatly altered by pneumoperitoneum at an IAP of up to 15 mm Hg. (*Am J Vet Res* 2016;77:799–804)

Surgical management of GERD and hiatal herniation in humans has evolved over the past half century. Commonly used fundoplication techniques involve wrapping a portion of the stomach around the distal portion of the esophagus to increase pressure at the gastroesophageal junction and discourage hiatal herniation and GERD. When laparoscopic Nissen fundoplication was introduced in human medicine in 1991, a new set of challenges was created for surgeons. To ensure that crural repair and any stomach wraps created would approximate normal gastroesophageal junction anatomy and function, it was necessary to estimate the dimensions of the LES intraoperatively before and after a wrap was created.[1] This has historically been performed by use of 54F to 60F bougie dilators placed intraoperatively at the time of wrap suturing.[2] The 360° Nissen procedure has undergone many modifications, incorporating a variety of partial wraps such as the Toupet, anterior 90° fundoplication, and anterior 180° fundoplication[3,4] as well as incisionless transoral techniques.[5] Although open fundoplication techniques have been used in a small number of dogs with hiatal hernias,[6] the surgical procedure reported most frequently is a combination of phrenoplasty, esophagopexy, and left-sided gastropexy performed through a celiotomy.[6–9] Despite substantial advancements in veterinary laparoscopic surgery in recent years,[10] minimally invasive manage-

ABBREVIATIONS

CSA	Cross-sectional area
DI	Distensibility index
GERD	Gastroesophageal reflux disease
IAP	Intra-abdominal pressure
IBP	Intraballoon pressure
LES	Lower esophageal sphincter
MD	Minimal diameter

ment of hiatal herniation has not been reported in clinical canine or feline patients. Similar to use in human clinical patients, a modality for intraoperative assessment of the geometry of the LES would be beneficial to provide an objective measure of the tightness of a repair, especially if a laparoscopic approach is used and manual palpation of the area is precluded.

A new device, an endoscopic functional luminal imaging probe, has been developed. It consists of a balloon-tipped catheter that incorporates a pair of electrodes at each end of the balloon and is used to measure the CSA, MD, and DI within luminal organs of the gastrointestinal tract. This device has been termed a smart bougie,[11,12] and it involves the use of impedance planimetry. Impedance planimetry uses an alternating current generated by electrodes at the ends of a cylindrical bag filled with a solution of known conductivity to calculate multiple CSA, volume, and diameter measurements. The device has been used for monitoring LES morphology and distensibility in both preclinical[11,13] and clinical settings.[5,14–17]

Effects of pneumoperitoneum on morphology of the LES have received little attention in the literature and are relevant given that laparoscopic fundoplication techniques have largely superseded open fundoplication for treatment of hiatal hernia and severe GERD in humans. Information on the effects of pneumoperitoneum would be relevant to laparoscopic hiatal hernia repair in veterinary patients. In human medicine, it has been suggested that efforts should be made to standardize intraoperative goals for LES dimensions and distensibility, and attempts have been made to achieve this through the use of impedance planimetry techniques.[12] Such standardization in veterinary patients would be more challenging given the wide variability in size, body weight, and body shape among species and breeds. However, it is important to account for factors that may affect these measurements, such as the effects of pneumoperitoneum.

The objectives of the study reported here were to evaluate by use of an endoscopic functional luminal imaging probe the effects of IAP on morphology and compliance of the LES in healthy dogs and to quantify the effects of changes in IAP. The null hypothesis was that increases in IAP would not have a significant effect on CSA, MD, LES length, LES volume, and DI.

Materials and Methods

Animals

Seven healthy purpose-bred sexually intact male hound-cross research colony dogs were included in the study. Body weight of the dogs ranged from 20.2 to 24.3 kg (median, 21.2 kg). The study was approved by an institutional animal care and use committee.

Anesthesia and analgesia

Dogs were anesthetized in accordance with a standardized protocol. Dogs were premedicated with morphine (0.3 mg/kg, SC) and atropine (0.02 mg/kg, SC). Anesthesia was induced with propofol (5 mg/kg, IV, to effect), and maintained with isoflurane in oxygen. Buprenorphine (0.01 mg/kg, SC, q 6 to 8 h, as needed) and carprofen (2 mg/kg, SC, once) were administered for postoperative analgesia.

Surgical procedures

Hair was clipped from the ventral aspect of the abdomen of each dog, and the area was aseptically prepared in accordance with standard protocols. A 5-mm-long skin incision was made on the ventral midline distal to the umbilicus. A modified Hasson approach[18] was used to introduce a 6-mm threaded laparoscopic cannula[a] through the linea alba into the abdomen. Pneumoperitoneum at various IAPs was induced by administration of CO_2 via a mechanical insufflator.[b]

Impedance planimetry measurements

An endoscopic functional luminal imaging probe[c] was used to obtain intraoperative measurements of the LES in each dog. After anesthesia was induced in the dogs, the catheter of the imaging probe was purged of air by use of an automated purge sequence. The catheter was then advanced through the mouth into the esophagus and into the stomach without endoscopic guidance. The balloon on the catheter was inflated with 20 to 30 mL of fluid of known conductivity that was supplied by the manufacturer. The catheter was partially withdrawn until the outline of the LES was clearly visible as an hourglass shape on the generator display **(Figure 1)**. This confirmed the balloon was correctly positioned. The balloon was deflated, and the pressure sensor was calibrated to an intragastric pressure of 0 mm Hg prior to each measurement.

Baseline measurements (0 mm Hg) as well as measurements at IAPs of 4, 8, and 15 mm Hg were recorded. The baseline measurement was recorded first, followed by measurements at each of the 3 IAPs; order of the IAPs was determined by use of a randomization software program.[d] At each IAP, the catheter balloon was sequentially inflated with 30, 40, and 50 mL of the conductive fluid. Measurements of CSA, MD, LES length, LES volume, and IBP were recorded. A measure of LES compliance, the DI, was calculated as CSA/IBP, as reported previously.[15,19] Pneumoperitoneum was removed by opening the valve on the laparoscopic cannula while applying manual pressure to the abdomen to ensure that as much CO_2 as possible was expelled. The balloon was completely deflated between subsequent changes in IAP. After measurements were completed, the catheter was withdrawn, and CO_2 was evacuated from the peritoneal cavity through the cannula. The incision was closed in a routine manner, and all dogs were allowed to recover from anesthesia.

Statistical analysis

A mixed-effects linear regression model was used to evaluate the fixed effects of IAP and balloon volume on CSA, MD, IBP, LES length, LES volume, and

DI. Each dog was treated as a random effect. Residuals were evaluated to verify model assumptions. Post hoc multiple comparisons were adjusted by use of a Bonferroni correction. Commercial statistical software[e] was used for all analyses. Values of $P < 0.05$ were considered significant.

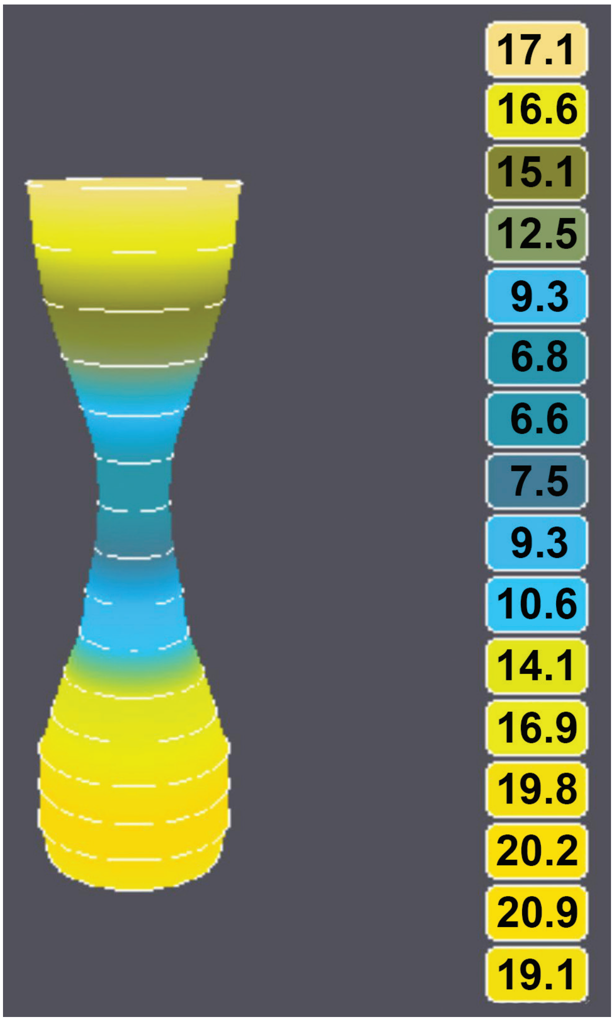

Figure 1—Real-time depiction of results obtained by use of an endoscopic functional luminal imaging probe for a representative healthy sexually intact male adult hound-cross dog. Notice the hour-glass shape of the image. The constriction represents the LES. Values on the right side represent the estimated diameter (in mm) of the various regions.

Results

The experimental procedures were completed in all 7 dogs without complication. The linear regression model allowed each variable tested (CSA, MD, IBP, LES length, LES volume, and DI) to be compared between baseline (0 mm Hg) and the 3 IAPs (4, 8, and 15 mm Hg) while adjusting for balloon volume. Similarly, the model also allowed the variables to be evaluated at the different balloon volumes when adjusted for IAP.

Data could not be recorded at a balloon volume of 50 mL and IAP of 15 mm Hg because the hourglass shape was lost, which made it impossible to definitively identify the LES. Results were summarized **(Table 1)**.

The CSA was significantly ($P < 0.001$) greater at an IAP of 15 mm Hg, compared with the baseline measurement. However, CSA at an IAP of 4 or 8 mm Hg was not significantly different from the baseline measurement. After data were adjusted on the basis of IAP, CSA was significantly ($P < 0.001$) greater at a balloon volume of 40 mL than at 30 mL, at 50 mL than at 30 mL, and at 50 mL than at 40 mL.

The MD was significantly ($P < 0.001$) greater at an IAP of 15 mm Hg, compared with the baseline measurement, but MD at an IAP of 4 or 8 mm Hg was not significantly different from the baseline measurement. After data were adjusted on the basis of IAP, MD was significantly ($P < 0.001$) greater at a balloon volume of 40 mL than at 30 mL, at 50 mL than at 30 mL, and at 50 mL than at 40 mL. The IBP was significantly greater at 4 mm Hg ($P = 0.03$), 8 mm Hg ($P < 0.001$), and 15 mm Hg ($P < 0.001$), compared with the baseline measurement. After data were adjusted on the basis of IAP, IBP was significantly greater at a balloon volume of 40 mL than at 30 mL ($P = 0.007$), at 50 mL than at 30 mL ($P < 0.001$), and at 50 mL than at 40 mL ($P < 0.001$).

Values for LES length and LES volume did not differ significantly between baseline measurements and measurements obtained at an IAP of 4, 8, and 15 mm Hg. After data were adjusted on the basis of IAP, LES length was significantly ($P < 0.001$) shorter at a balloon volume of 40 mL than at 30 mL, at 50 mL than at 30 mL, and at 50 mL than at 40 mL. After data were adjusted on the basis of IAP, LES volume

Table 1—Mean ± SD values of variables for an endoscopic functional luminal imaging probe at various IAPs and balloon volumes.

	0 mm Hg IAP			4 mm Hg IAP			8 mm Hg IAP			15 mm Hg IAP		
Variable	30 mL	40 mL	50 mL	30 mL	40 mL	50 mL	30 mL	40 mL	50 mL	30 mL	40 mL	50 mL
CSA (mm²)	58 ± 36	139 ± 65*	283 ± 74*†	87 ± 36	158 ± 56*	313 ± 82*†	76 ± 59	161 ± 90*	301 ± 84*†	123 ± 68‡	244 ± 42*‡	NA
MD (mm)	8.2 ± 2.6	14.3 ± 6.5*	18.4 ± 2.6*†	10.3 ± 2.3	14.3 ± 3.0*	20.0 ± 2.8*†	9.2 ± 3.9	14.1 ± 3.8*	30.2 ± 3.0*†	12.2 ± 3.4‡	18.5 ± 2.4*‡	NA
IBP (mm Hg)	4.4 ± 1.7	7.3 ± 13.4*	16 ± 3.8*†	6.1 ± 2.2‡	8.1 ± 2.8*‡	19.2 ± 3.2*†‡	10.6 ± 2.7‡	12.1 ± 3.1*‡	22.2 ± 2.8*†‡	15.3 ± 8.1‡	16.3 ± 4.8*‡	NA
LES length (mm)	36.4 ± 3.8	27.9 ± 4.9*	17 ± 2.7*†	35.0 ± 6.5	29.3 ± 3.5*	17.5 ± 2.7*†	38.6 ± 7	29.3 ± 4.5*	11.7 ± 6.1*†	43.3 ± 2.9	21.0 ± 10.8*	NA
LES volume (mm³)	5.2 ± 0.7	6.3 ± 1.9*	5.8 ± 1.5†	5.4 ± 1.4	7.1 ± 1.7*	6.3 ± 0.8†	5.3 ± 1.5	7.0 ± 1.4*	4.1 ± 1.7†	7.4 ± 1.8	6.6 ± 2.8*	NA
DI	14 ± 10	22 ± 13*	19 ± 7*	17 ± 12	22 ± 12*	17 ± 6*	8 ± 7[a]	15 ± 11*‡	16 ± 6*‡	12 ± 12	18 ± 8*	NA

An IAP of 0 mm Hg was considered the baseline measurement.

*Within an IAP within a row, value differs significantly ($P < 0.05$) from the value at a balloon volume of 30 mL. †Within an IAP within a row, value differs significantly ($P < 0.05$) from the value at a balloon volume of 40 mL. ‡Within a row, value differs significantly ($P < 0.05$) from the value for the corresponding balloon volume at baseline.

NA = Not available.

was greater at a balloon volume of 40 mL than at 30 mL ($P = 0.02$) and at 50 mL than at 40 mL ($P = 0.03$); however, there was not a significant difference in LES volume between balloon volumes of 50 and 30 mL

The DI was significantly ($P = 0.005$) lower at an IAP of 8 mm Hg, compared with the baseline measurement; however, there were no significant differences between baseline measurements and measurements obtained at an IAP of 4 or 15 mm Hg. After data were adjusted on the basis of IAP, DI was significantly greater at a balloon volume of 40 mL than at 30 mL ($P = 0.007$) and at 50 mL than at 30 mL ($P = 0.04$); however, there was not a significant difference in DI between balloon volumes of 50 and 40 mL.

Discussion

Impedance planimetry is being increasingly used in humans to improve functional assessment of the LES in patients with esophageal dysphagias, provide intraoperative guidance during procedures, and document preoperative and postoperative outcomes for a variety of esophageal interventions.[5,12–17] Few studies[13,15] of anesthetized clinically normal human subjects or animals with experimentally created conditions have been conducted to analyze in detail the effects of various IAPs on variables obtained with an endoscopic functional luminal imaging probe. In 1 study[15] of human patients who did not have a history of GERD symptoms or had not had previous surgery for GERD or hiatal herniation but who were undergoing a variety of laparoscopic procedures, significant effects of pneumoperitoneum were detected. In that study,[15] pneumoperitoneum with an IAP of 13 mm Hg induced a decrease in CSA and MD with minimal changes in DI. This has led to the conclusion that researchers and clinicians must take into account the effect of pneumoperitoneum on variables measured by use of impedance planimetry and the recommendation that pneumoperitoneum be standardized among patients to allow appropriate comparisons to be made across studies.[12]

The main objective of the study reported here was to evaluate the effect of IAP on morphology and compliance (as measured by DI) of the LES. The data may aid clinicians who are planning to use intraoperative impedance planimetry to guide surgical decisions when considering laparoscopic hiatal herniorrhaphy procedures. The principal findings of the present study were that pneumoperitoneum did not significantly affect CSA or MD at an IAP of 4 or 8 mm Hg; however, CSA and MD at an IAP of 15 mm Hg were both significantly greater than baseline measurements. These findings have clinical importance because many laparoscopic interventions are performed at an IAP > 8 mm Hg. In addition, a recent multi-institutional focus group of human medical clinicians who used the endoscopic functional luminal imaging probe recommended standardization of pneumoperitoneum (when it is used) at an IAP of 12 mm Hg during laparoscopic procedures.[12]

The finding that CSA and MD increased at higher IAPs is in contrast to results of a clinical study[15] of human patients without GERD who underwent laparoscopic interventions. In that study,[15] CSA and MD at an IAP of 13 mm Hg were both significantly lower than baseline values. The authors hypothesized that cranial displacement of the diaphragm as a result of increased intraperitoneal pressure may have exerted a tractional effect on the hiatal crura that acted to narrow the LES. There may be several explanations for the morphological changes to the LES during higher-pressure pneumoperitoneum in the healthy dogs of the present study. Manometric studies[20,21] of humans have revealed varying effects of increasing IAPs on LES pressures. In a small number of patients who underwent laparoscopic treatment for achalasia or cholecystectomy, pneumoperitoneum was not found to significantly affect LES pressure or LES length.[20] A study[21] conducted to manometrically evaluate the effect of pneumoperitoneum on LES pressure revealed that increasing IAP was associated with a progressive increase in LES pressure. In the study reported here, IBP, which is not an indication of manometric esophageal wall pressure, steadily increased with increases in IAP, which suggested that a decrease in LES pressure alone was unlikely to be the cause of the increases in CSA and MD. Unfortunately, high-resolution manometry was not performed on these dogs to enable us to compare LES pressure profiles to impedance planimetry variables. It may be more likely that an alteration of the morphology of the diaphragmatic crura, hiatus, or LES may have been responsible for the increases in CSA and MD in this study; however, it is challenging to elucidate the exact mechanism for these changes without detailed evaluation of the complex changes in this area under conditions of increased IAP.

The LES of dogs and humans differs anatomically, which may contribute to some of the differences between impedance planimetry results obtained in the present study and those reported for human subjects. The LES of humans is composed of semicircular clasp fibers and sling fibers that make up an incomplete U-shaped ring of muscle, whereas the LES of dogs is circular muscle that forms a complete ring.[22] Minor gastroesophageal reflux is not considered an abnormal finding in dogs, and the LES of dogs is considered to be a more lax structure, compared with the laxness of its human counterpart.[23] However, it was interesting that the mean ± SD value for MD at a balloon volume of 30 mL was 8.2 ± 2.6 mm in the dogs of the present study, which was identical to the weighted mean for a cohort of 154 clinically normal human subjects.[12] It should be mentioned that the dogs in the present study were anesthetized, whereas human subjects in the aforementioned report[12] were awake or conscious but sedated. For clinically normal human subjects who are conscious but sedated, the median CSA reported[24] at balloon volumes of 30 mL is 94 mm^2, which was not greatly dissimilar from the median of 58 ± 36 mm^2 for the dogs of the study reported here. Mean ± SD IBP (4.4 ± 1.7 mm Hg) for the 7 dogs of the present study was distinctly less than that reported[24] for clinically normal human subjects (25 mm Hg). Because DI is a function of CSA and IBP, it is markedly higher in dogs than in humans. This provides further evidence that although the dimensions of the canine LES (for hound-cross dogs of the size and body conformation in the present study) are extremely similar to those of clinically normal human subjects, the LES is a laxer and more distensible structure in dogs than in humans.

It has been hypothesized that DI determined by use of an endoscopic functional luminal imaging probe device can provide a unique qualitative assessment of the compliance of the LES. Compliance cannot be easily measured by any other means, including endoscopy or manometry, because it inherently depends on a response of the tissues to a distention force. In studies of GERD patients, investigators have attempted to use DI to differentiate clinically relevant subsets of patients. Contradictory evidence has been published that suggests GERD patients have higher DI values than do control subjects,[24] whereas this was not found in another study.[17] The DI has been used to differentiate clinical patients with esophageal achalasia from control subjects and to gauge effects of laparoscopic Heller myotomy and newer endoluminal approaches.[19,25] In the study reported here, DI of the 7 healthy dogs was significantly greater at a balloon volume of 40 mL than at 30 mL. However, there were relatively small differences between the baseline value and measurements at the various IAPs. Lack of a profound effect of pneumoperitoneum on DI of humans has been reported previously.[15]

In the study reported here, 3 balloon volumes were used, which is similar to numerous other studies conducted with an endoscopic functional luminal imaging probe. There is a paucity of information on use of this device for dogs,[13] and the authors believed that it was important to evaluate a range of balloon volumes. In these research hound-cross dogs with a median body weight of 21 kg, a balloon volume of 50 mL often caused loss of the hour-glass shape of the LES, which resulted in a uniform cylindrical shape and an inability to collect data, especially at high IAPs. It appeared that balloon volumes of 30 or 40 mL would be more appropriate in dogs of this size for measurement of endoscopic functional luminal imaging probe variables. It has been recommended that all studies of humans should include a standardized balloon volume of 30 mL so that results can be accurately compared among studies.[12] It was perhaps unsurprising that increasing the balloon volume generally increased CSA, MD, IBP, and DI but shortened LES length. Similar findings have been reported for asymptomatic human patients as well as human patients with GERD.[15,24]

In the present study, pneumoperitoneum at an IAP of 4 or 8 mm Hg was not associated with a significant alteration of CSA or MD in healthy dogs. At higher IAPs, significant differences were detected, and personnel who use an endoscopic functional luminal imaging probe in clinical or research settings should be aware that there may be alterations in these variables attributable to the effect of IAP alone. Compliance of the LES as measured by the DI appeared to be less significantly affected by increases in IAP; thus, DI may represent a relatively stable variable during investigations performed with pneumoperitoneum. Useful comparative information for translational research purposes was obtained, and data on clinically normal dogs were provided for a potentially useful intraoperative monitoring tool that could facilitate the development of minimally invasive interventions for GERD and hiatal herniation in small animal patients.

Footnotes

a. EndoTIP, Karl Storz Veterinary Endoscopy, Goleta, Calif.
b. Endoflator, Karl Storz Veterinary Endoscopy, Goleta, Calif.
c. EndoFLIP, Crospon Inc, Galway, Ireland.
d. Randomizer.org. Available at: www.randomizer.org Accessed Feb 1, 2012.
e. STATA/IC, version 13.1, StataCorp LP, College Station, Tex.

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