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Assessment of laparoscopic working space in guinea pigs (*Cavia porcellus*) undergoing carbon dioxide insufflation at different intra-abdominal pressures

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OBJECTIVE
To evaluate pneumoperitoneal volumes (laparoscopic working space) in guinea pigs (*Cavia porcellus*) undergoing pneumoperitoneum via carbon dioxide insufflation at different intra-abdominal pressures (IAPs) (4, 6, and 8 mm Hg) and recumbencies (dorsal, right lateral, and left lateral).

ANIMALS
Six 3- to 4-month-old sexually intact female Hartley guinea pigs.

PROCEDURES
Guinea pigs were anesthetized, intubated, and had an abdominal insufflation catheter placed. A baseline abdominal CT scan was performed. Guinea pigs underwent insufflation, with each IAP given in a random order for 10 to 15 minutes with a washout period of 5 minutes between pressures. Abdominal CT scans were acquired at each IAP and at each recumbency. Pneumoperitoneal volumes were calculated using software.

RESULTS
Increases in IAP increased working space significantly (*P* < .001). The 6- and 8-mm Hg pressures increased working space from 4 mm Hg by 7.3% and 19.8%, respectively. Recumbent positioning (*P* = .60) and body weight (*P* = .73) did not affect working space. Order of IAP had a significant (*P* = .006) effect on working space. One of the guinea pigs experienced oxygen desaturation and bradycardia at 6- and 8-mm Hg IAP.

CLINICAL RELEVANCE
Although an increased working space occurred at 6 and 8 mm Hg compared to 4 mm Hg, further research is needed concerning the cardiovascular effects of pneumoperitoneum in guinea pigs to determine whether those higher IAPs are safe in this species. An IAP of 6 mm Hg can be considered for laparoscopic cannula placement, followed by a lower IAP for laparoscopic procedures.

Minimally invasive surgery has been found to have several benefits over open surgery in small animals. The possibility of reduced postoperative pain makes minimally invasive surgery an attractive option in small exotic companion mammals, as pain can lead to gastrointestinal stasis and other complications. *Guinea pigs (Cavia porcellus)* are prone to reproductive disorders, particularly ovarian cysts, and laparoscopic ovariectomy could be used prophylactically to prevent this condition. In addition, the development of uterine leiomyomas may be associated with ovarian cysts in guinea pigs, and laparoscopic ovariectomy could prevent such uterine disorders theoretically if performed at a young age.

Laparoscopic working space, or pneumoperitoneal volume, is space in the abdominal cavity created through gas insufflation to allow for the manipulation of endoscopic instruments. The most commonly used gas for this purpose is carbon dioxide (CO$_2$). Working space is typically measured via CT, although other methods are available, such as the use of a tape measure and calipers. In rabbits (*Oryctolagus cuniculus*) undergoing abdominal CO$_2$ insufflation, working space volume was found to increase from 4 to 8 mm Hg and from 8 to 12 mm Hg. However, there was a smaller increase in working space when increasing the intra-abdominal pressure (IAP) from 8 to 12 mm Hg compared to 4 to 8 mm Hg. The authors concluded that the increase in working space of more than 8 mm Hg may not provide a clinically important benefit when performing laparoscopy in rabbits.
Laparoscopic surgery has been described in nonintubated guinea pigs in an experimental setting with an IAP of 5 mm Hg; however, anesthetic parameters were not described in that study.\(^1\) Laparoscopic ovariectomy has been described in guinea pigs with a 3-port technique and an IAP of 6 to 8 mm Hg\(^2\) as well as with a 2-port technique and an IAP of 5 mm Hg.\(^2\) Aside from these clinical reports and other experimental studies, literature on the clinical use of laparoscopy in guinea pigs is limited. In a study\(^2\) that used a pressure of 6 to 8 mm Hg for laparoscopic ovarioectomy in guinea pigs, the working space was judged to be satisfactory for the procedure. However, bradycardia and hypercapnia were encountered secondary to the pneumoperitoneum. Therefore, it is necessary to balance the need for adequate working space to carry out the laparoscopic procedure safely with the need to prevent anesthetic complications from the elevated IAP. Therefore, the objective of this study was to evaluate the pneumoperitoneal volumes (laparoscopic working space) via CT in guinea pigs undergoing pneumoperitoneum via CO\(_2\) insufflation at 3 different IAPs (4, 6, and 8 mm Hg) and in 3 different recumbencies (dorsal, right lateral, left lateral).

**Materials and Methods**

**Animals**

The study was approved by the Animal Care Committee of the University of Guelph. Six specific pathogen-free intact female Hartley guinea pigs were obtained from a commercial vendor (Charles River Laboratories). They were group-housed in a large pen with a variety of hides and enrichment items. The diet consisted of autoclaved timothy and alfalfa hay, and guinea pig pellets (Teklad Global High Fiber Guinea Pig Diet 2041; Envigo). The guinea pigs were approximately 3 to 4 months of age at the time of the study (October 5 to 9, 2020). The animals were determined to be healthy on the basis of a physical examination. Hematologic and plasma biochemical analyses were also performed on a subset of animals prior to the study. The animals had been used previously in a study on determining reference intervals for adrenal parameters in guinea pigs, but it had been at least 4 weeks since any procedures had been performed on them.

**Anesthesia**

The animals were fasted at least 3 hours prior to sedation. Each guinea pig was sedated with midazolam (1 to 2 mg/kg; midazolam, 5 mg/mL; Sandoz) and buprenorphine hydrochloride (0.2 mg/kg; Vetgesic Multidose, 0.3 mg/mL; Champion Alstoe) IM. A 26-gauge IV catheter (Abbocath-T, ICU Medical) was placed in a lateral saphenous or cephalic vein. Each guinea pig was then induced with 6 to 10 mg/kg propofol (propofol injection 10 mg/mL; Fresenius Kabi Canada) administered IV to effect, as well as supplemental isoflurane 2% to 5% (vaporizer setting) in oxygen delivered via facemask to maintain an adequate anesthetic plane for intubation. The animal was placed on a tabletop rabbit and rodent dentistry table (Sontec Instruments) and intubated endoscopically with a 16-gauge IV catheter without the stylet using a previously described technique.\(^2\) Anesthesia was maintained with isoflurane at 2% to 4% (vaporizer setting) in oxygen at 1 to 1.5 L/min. Respiration was controlled with a ventilator (Mark 4 Anesthesia Assistor/Controller and Mark 8 Ventilator; Bird Corporation). Anesthetic monitoring equipment included a pulse oximeter probe on a forelimb or hind limb (model 2500A Vet, Nonin Medical) and capnograph (Nellcor Portable Bedside Capnograph/Pulse Oximeter, Covidien). IV crystalloid fluids (PlasmaLyte-A, Baxter) were provided at a preset rate of 5 mL/hour (7.2 to 8.3 mL/kg/h) using a spring-loaded syringe infusion pump (Springfusor 10, Go Medical Industries). A rectal temperature was taken prior to sedation and at the conclusion of the procedure. Heat support was provided with a forced-air warming system (Bair Hugger Warming Unit model 505, 3M).

**Insufflation cannula placement**

The ventral abdomen was shaved and prepared in a sterile environment. A 0.5 to 1-cm preumbilical skin incision was made, and the abdomen was entered using a modified Hasson technique as described previously.\(^2\) An 18-gauge IV catheter was placed for insufflation because plastic cannulas smaller than 5 mm were not available and a metal cannula would interfere with the CT scans. The catheter was secured with sutures and a transparent film dressing (Tegaderm Film, 3M Health Care).

**CT and abdominal insufflation**

A baseline abdominal CT scan (slice thickness, 0.625 mm; 120 kVp; 140 mA; pitch, 0.938:1; rotation time, 1 second) was performed in dorsal recumbency, using a 16-slice helical CT scanner (GE Bright Speed, GE Healthcare). Then, the abdomen was insufflated to 1 of 3 IAPs (4, 6, or 8 mm Hg) in a random order for the initial and subsequent IAPs. The order was determined using a balanced cross-over repeated Latin square design. After the insufflation cannula was placed, capnoperitoneum was created with a mechanical CO\(_2\) insufflator (Highflow 40L Insufflator, Stryker) at a flow rate of 1 L/minute. The pressure generated was indicated by the insufflator, which has an accurate pressure sensor. The pressure was held for 10 to 15 minutes, and then an abdominal CT was performed in dorsal recumbency, followed by right lateral and then left lateral recumbency. The order of the recumbencies was not randomized for practical reasons. The animals were placed in complete lateral recumbency, rather than an oblique position, as complete lateral recumbency was found previously to be necessary to visualize the ovaries adequately during laparoscopic ovarioectomy.\(^2\) The insufflation was then discontinued. After a washout period of 5 minutes, the procedure was repeated for the next IAP. After the CT scans were completed, the insufflation catheter was removed. The skin was closed with 5-0 polydioxanone suture in a simple interrupted pattern.
Postoperative care

After the surgery was completed, anesthesia was discontinued and the animal was extubated after it was breathing spontaneously. Flumazenil (0.05 mg/kg; flumazenil, 0.1 mg/mL injectable; Sandoz) was given IV, IM, or SC to reverse the benzodiazepine. Flumazenil was repeated as needed based on the animal’s recovery from sedation. Meloxicam (1.5 mg/kg) was given SC after the procedure for analgesia. An additional dose of buprenorphine (0.2 mg/kg) was given IM as needed for additional analgesia 7 to 10 hours after the initial dose. Meloxicam was continued (1.5 mg/kg, SC or PO, q 12 h) for 2 to 3 days after the procedure. Additional supportive care included subcutaneous fluids (43 to 50 mL/kg) and syringe-feeding a liquid diet (15 to 25 mL/kg; Critical Care, Oxbow Animal Health) as needed to maintain hydration and gastrointestinal motility. Each guinea pig was kept in an individual cage separate from the other guinea pigs for at least 24 hours after the procedure to ensure appropriate recovery and to monitor the appetite and fecal production. The guinea pig’s attitude, weight, vital parameters, and incision were monitored for at least 2 days after the procedure. After this study, guinea pigs were used in another study investigating pneumoperitoneum in guinea pigs. They were then spayed and placed for adoption.

Laparoscopic working space (pneumoperitoneal volume) calculation

The segmentations were performed using a software package. The pneumoperitoneal gas was segmented with a Hounsfield threshold unit range of –1,024 HU to a high of –910 HU. The pneumoperitoneal volume was created from the segmented slices and calculated by the software in milliliters. The study was evaluated in cross-sectional slices to ensure the gastrointestinal gas was not selected. Gastrointestinal gas was excluded because it was not contiguous with the free peritoneal gas during segmentation. For each IAP evaluated, we planned to obtain 18 measurements of pneumoperitoneal volume (1 measurement for each of the 6 animals positioned in each of the 3 recumbencies [dorsal, right lateral, and left lateral]).

Statistical analysis

The effects of the various pneumoperitoneal pressures and recumbencies on working space were assessed using linear mixed models. Working space volume (measured in milliliters) was the outcome variable; pneumoperitoneal pressures, recumbencies, order, weight, and interactions were used as fixed effects; and individual guinea pigs were used as the random effect. Residual plots were used to assess linearity, homogeneity of variances, normality, and outliers. Quantile plots were also performed on the residuals by treatment groups for normality assessment. Residuals resulting from the fitted model were verified to be normally distributed and had no evidence of heteroskedasticity. A compound correlation matrix structure was used for modeling dependence. Assumptions of the models were met and no outliers were detected. An analysis of variance was performed on the fixed effects, and post hoc comparisons for the different pressures were performed using a Tukey adjustment. An alpha of 0.05 was used for statistical significance. Statistical analysis and graphing was performed with available software.

Results

Prior to the study, both a CBC and a plasma biochemical profile were performed in 1 animal and a biochemical profile only was performed in an additional 3 animals. Complete bloodwork was unable to be performed in all animals because of difficulties in sample collection from peripheral blood vessels. The median body weight at the initiation of the study was 673 g (range, 606 to 692 g). All 6 of the guinea pigs were intubated successfully during the study. One of the guinea pigs was unable to be intubated when it was first attempted; the procedure was aborted that day and the animal was intubated successfully 4 days later. An IV catheter was unable to be placed in 1 of the guinea pigs, so the animal was induced with isoflurane (5% isoflurane in oxygen via a facemask) alone rather than propofol. It was also given subcutaneous fluids (30 mL/kg) rather than IV fluids during the procedure. All the guinea pigs recovered uneventfully from anesthesia and survived the postoperative monitoring period. Two guinea pigs were given additional doses of buprenorphine 7 to 10 hours after the initial dose.

Baseline CT scans were available for 5 of the 6 guinea pigs, and no abnormalities were identified. The baseline CT scan was, inadvertently, not performed in 1 guinea pig.

Mean intra-abdominal working space volume was significantly (P < .001) increased with increases in IAP applied, controlling for other variables in the model. All IAPs resulted in significantly different mean working space volumes (Figure 1). The mean intra-abdominal working space volumes for 6- and 8-mm Hg IAP were significantly (P < .05) greater than that for 4 mm Hg (Figure 2). The 6- and 8-mm Hg IAPs increased working space by 7.3% and 19.8%, respectively, from that of the 4-mm Hg IAP.

Recumbent positioning did not have an influence on working space (P = .60), nor did the body weight (P = .73). However, order of pressure inflation had a significant (P = .006) effect on working space. Pressures given first in the sequence led to significantly (P < .027) less working space than when given second or third (Figure 3). No interaction between IAP and order was detected (P = .76; Supplementary Figure 1).

Eighteen measurements were completed for the 4-mm Hg IAP (3 different recumbent positions per each of the 6 guinea pigs), with a mean ± SD pneumoperitoneal volume of 191 ± 19.2 mL (range, 160 to 217 mL). For the 6-mm Hg IAP, 15 measurements were completed, with a mean ± SD
pneumoperitoneal volume of 207 ± 9.8 mL (range, 193 to 228 mL); CT at the 6-mm Hg IAP was not completed for 1 guinea pig because of cardiovascular instability (poor oxygen saturation and bradycardia) at this pressure. For the 8-mm Hg IAP, 17 measurements were completed (mean ± SD, 230 ± 11.6 mL; range, 202 to 245 mL). The CT in left lateral recumbency was not performed for the same guinea pig, likewise because of cardiovascular instability. As a result of the oxygen desaturation and bradycardia encountered in this animal, insufflation had to be discontinued earlier than planned, because it was considered unsafe for the animal to continue, resulting in these data being missing for this individual (CT in left lateral recumbency at 8 mm Hg and all 3 recumbencies at 6 mm Hg).

A challenge encountered during the study was related to the ability of the mechanical insufflator to regulate IAP, and generating a greater IAP than the one entered. This required the IAP input to be adjusted to deliver the desired IAP. In 1 guinea pig, the abdominal catheter had to be replaced because...
of kinking of the catheter, which resulted in very high readouts for IAP (22 mm Hg).

One of the guinea pigs had dehiscence of the skin incision noted 3 days after the procedure. The incision was repaired and 3 days of meloxicam were administered. No other surgical complications were noted.

**Discussion**

In our study, an increase in pneumoperitoneal volume occurred with increasing IAP in a proportional manner. In cats undergoing pneumoperitoneum, abdominal circumference and height were significantly greater at 8 mm Hg than at 4 mm Hg. Increasing the pressure to 15 mm Hg increased the circumference further, but not the height, and the mild increase in abdominal circumference was unlikely to be clinically relevant. Given the cardiorespiratory alterations at 15 mm Hg, the authors of that study did not think the mild improvement in working space at 15 mm Hg was sufficient to justify its use and recommended against an IAP > 8 mm Hg in cats. Similarly, in rabbits, the mean working space increased by 19% from 4 to 6 mm Hg, but only by 6.9% from 8 to 12 mm Hg. Therefore, given the proportional increase in pneumoperitoneal volumes with increasing IAP in the guinea pigs in our study, compared with the more modest increase in working space in rabbits at greater pressures, it is possible that guinea pig abdomens may be more compliant than rabbit abdomens. Because partial pressure of CO₂ and end-tidal CO₂ increase—and cardiac output decreases—with increasing IAP in rabbits, the authors recommended that IAP be limited to 4 to 8 mm Hg when performing laparoscopic procedures in rabbits.

The guinea pigs in our study were much smaller than the rabbits used in the aforementioned working space study (median weight, 0.673 kg vs 3.39 kg). Because of their small size, they may be more susceptible to adverse effects from greater IAPs. The negative cardiovascular impacts of pneumoperitoneum can be exacerbated at greater IAPs. In dogs undergoing pneumoperitoneum, cardiac output may increase or be maintained at relatively low pressures, but experience a decrease at high IAPs.
than the IAP inputted. The small size of the insufflation catheters was thought to contribute to this problem. Unfortunately, the IAP was not measured directly via manometry in this study. In cats, IAP readings from the mechanical insufflator were not significantly different from manometry at 4 mm Hg, but at 8 and 15 mm Hg, manometry IAPs were found to be significantly greater than those measured with the insufflator. The gas flow rate used in our study (1 L/min) was the lowest possible with the available equipment. However, animals of this small size may benefit from insufflators able to generate lower flow rates and potentially produce more accurately small changes in IAP. We are unaware of whether such equipment exists, but as human pediatric laparoscopy expands, such equipment may become available. Other limitations of our study include the small number of animals as well as missing data resulting from the adverse effects encountered.

In conclusion, an IAP of 4 to 6 mm Hg should be explored further for guinea pigs undergoing laparoscopic surgery. Although IAPs of 6 and 8 mm Hg increased working space, the negative cardiovascular effects may not justify their use. Because of the adverse effects encountered in 1 guinea pig at an increased IAP, efforts should be made to minimize the IAP during clinical procedures in guinea pigs. Given that the animals in this study were apparently healthy, the negative effects of capnoperitoneum could be further pronounced in guinea pigs with underlying cardiorespiratory disease. Additional research is needed concerning the ability to perform various diagnostic and therapeutic procedures in guinea pigs at an IAP of 4 to 6 mm Hg.

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References


Supplementary Material

Supplementary materials are posted online at the journal website: avmajournals.avma.org