Incidence of and risk factors for postoperative regurgitation and vomiting in dogs: 244 cases (2000–2012)

John A. Davies, DVM; Boel A. Fransson, DVM, PhD; Anastacia M. Davis, BSc; Aaron M. Gilbertsen, DVM; John M. Gay, DVM, PhD

Objective—To determine the incidence of and risk factors for postoperative regurgitation and vomiting (PORV) in dogs.

Design—Retrospective cohort study.

Animals—244 client-owned dogs.

Procedures—Dogs referred for nonelective surgery in the first 3 months of 2000 and 2012 were included. Breed; sex; age; weight; body condition score; emergency status; food withholding status; history of vomiting or regurgitation; American Society of Anesthesiologists score; presence of diabetes or hypothyroidism; preoperative PCV and total solids concentration; anesthesia protocol; corticosteroid, opioid, neuromuscular blocking agent, and nitrous oxide usage; anesthesia time; surgery time; type of surgery; and occurrence of vomiting or regurgitation within 24 hours after recovery from anesthesia were recorded. Data were analyzed by means of the Fisher exact test, Wilcoxon rank sum test, and logistic regression.

Results—30 of 244 (12.3%) dogs meeting study inclusion criteria developed PORV. There was no significant difference in the incidence of PORV between the 2000 (12/111 [10.8%]) and 2012 (18/133 [13.5%]) cohorts, although the incidence of regurgitation was higher in 2012. Univariate logistic regression identified the most significant risk factors as gastrointestinal surgery (OR, 11.15; 95% confidence interval [CI], 3.11 to 40.03), premedication without strong sedatives including either an α2-adrenoceptor agonist or acepromazine (OR, 5.36; 95% CI, 1.89 to 15.17), American Society of Anesthesiologists score of 4 (OR, 5.25; 95% CI, 1.05 to 26.15), history of vomiting or regurgitation (OR, 5.12; 95% CI, 1.83 to 14.31), emergency surgery (OR, 4.08; 95% CI, 1.29 to 12.90), neurologic surgery (OR, 3.18; 95% CI, 1.02 to 9.92), sevoflurane inhalation anesthesia (OR, 2.78; 95% CI, 1.25 to 6.13), and being sexually intact (OR, 2.37; 95% CI, 1.07 to 5.27). Multivariate analysis was not clinically useful owing to the low sensitivity and specificity of the model.

Conclusions and Clinical Relevance—Between 2000 and 2012, there was no change in the incidence of PORV for dogs undergoing neurologic, orthopedic, and soft tissue surgical procedures; however, the proportion of dogs that regurgitated increased significantly in 2012. Preoperative antiemetic prophylaxis should be considered in dogs undergoing gastrointestinal surgery and in those in which other risk factors are present. (J Am Vet Med Assoc 2015;246:327–335)

Postoperative regurgitation and vomiting negatively affects the comfort level of veterinary patients and can lead to multiple adverse outcomes, including aspiration pneumonia, esophagitis, esophageal strictures, esophageal perforation, and increased tension on suture lines.1,2 The resultant postoperative morbidity can result in prolonged hospitalization and dramatically increased treatment costs. In human patients, PONV is a syndrome that is defined as nausea, vomiting, or both, occurring in the 24-hour period following surgery.3,4 It is a common complication, affecting between 20% and 30% of patients.5–7 The incidence of PORV and complications in dogs is not known, but in our clinical experience and as reported by others,8 it appears to have increased in recent years. Possible reasons for this may include longer anesthetic and surgical times with the increased use of advanced imaging, advent of more complex procedures such as those in the field of minimally invasive surgery, and interventional radiology, and evolving perianesthetic drug choices.

Postoperative nausea and vomiting has been extensively investigated in the human medical literature,1,9 and meta-analysis has identified being female, history of PONV or motion sickness, nonsmoking, being...
< 50 years old, duration of volatile gas anesthesia, and postoperative opioid usage as independent risk factors for this syndrome.3-5 The high prevalence of PONV in human patients and the risk for potentially life-threatening complications have led to the development of a scoring system by Apfel et al.,10 designed to identify high-risk patients who would benefit from prophylactic treatment. A similar scoring system does not exist in veterinary medicine.

Although there are numerous investigations of PONV in people, this is not mirrored in the veterinary literature. Studies11–18 evaluating gastroesophageal reflux during general anesthesia in dogs have found high rates of gastroesophageal reflux (10% to 55%). However, the reported rate of overt regurgitation in one study13 of dogs undergoing anesthesia was low (414/4,271 anesthetic events [0.96%]). A 2012 study19 found a postoperative regurgitation rate of 1.7% (1/58 patients) for a study of PORV in dogs after elective cranial cruciate ligament surgery with hydromorphone analgesia. Others have evaluated the risk of PORV, or its complications, in canine patients with specific surgical procedures or medications.8,11,19,20 However, to our knowledge, no studies have been conducted to evaluate the overall incidence of PORV in dogs or have attempted to identify risk factors for PORV.

The purpose of the study reported here was to determine the incidence of PORV in dogs at our institution, both recently and 12 years earlier. We hypothesized that the incidence of PORV would be greater in 2012 than 2000. Further, we hypothesized that this increase would be associated with longer anesthesia and surgery times because of a larger number of more complicated procedures.

Materials and Methods

Study design and case selection—Surgery reports for canine patients having nonelective surgery during two 3-month periods (January 1 to March 31, 2000, and January 1 to March 31, 2012) at the Veterinary Teaching Hospital, Washington State University, were included in the study. Exclusion criteria were reports for patients that had undergone elective procedures (ie, ovariohysterectomy and neutering) and noncanine surgeries. Medical records were obtained for the remaining cases. Incomplete or missing medical records were excluded. When multiple surgeries were performed on the same dog during the study period, only the first surgical procedure was included in the study.

Data collection—Data collected from the medical records included the date of surgery, breed, sex, age, weight, body condition score, whether the surgery was performed on an emergency basis, food withholding status, history of vomiting or regurgitation (within the week prior to surgery or as a chronic condition), ASA score, presence of concurrent diabetes or hypothyroidism, preoperative PCV and serum total solids concentration, history of corticosteroid usage (≤ 1 week prior to surgery), premedications, anesthetic induction agents, inhalation anesthetic agents (including nitrous oxide), intraoperative and postoperative opioid use, use of neuromuscular blocking agents, length of anesthesia, length of surgery, type of surgery, and vomiting or regurgitation within 24 hours after recovery from anesthesia.

Statistical analysis—A power analysis performed prior to data collection found that a sample size of at least 100 would be needed to detect risk factors with a relative risk of at least 4 with an α of 0.05 and a power of 80% when the prevalence of PORV is 4% in the unexposed group21 (ie, when evaluating the risk of PORV among sexually intact dogs, the unexposed group would be gonadectomized dogs). For continuous predictor variables (eg, weight), OR is the change in log odds associated with a 1-unit change in the predictor variable (eg, 1 kg).

Dichotomous and continuous variables were compared by means of the Fisher exact test, and ranked variables were compared by means of the Wilcoxon rank sum test. Median and range were used to describe continuous variables with ranked variables presented as percentage and whole number. Differences in risk factor distributions between the 2 cohorts were evaluated by means of logistic regression models. Data were pooled from both cohorts (ie, 2000 and 2012), and univariate logistic regression was performed on each variable. Variables with a value of P ≤ 0.25 were entered into a multiple logistic regression model. Variables were removed by backward elimination to generate the final model (P ≤ 0.05 for all variables). Residuals of this model were assessed graphically for outliers, and the effect of the outliers on the model was evaluated by removing them. Significance was set at P ≤ 0.05 for all analyses. No adjustment was made for multiplicity. Statistical analysis was performed with commercially available software.a

Results

A total of 244 dogs met the inclusion criteria and were evaluated (Table 1). Although some risk factors were distributed differently between the 2 cohorts, no risk factors were significantly different.

Seventy breeds were included in the study. In 2000, the 3 most common breeds were Labrador Retriever (n = 16), Dachshund (14), and Golden Retriever (10). In 2012, the 3 most common breeds were Labrador Retriever (n = 30) mixed breed (18), and German Short Haired Pointer (7). Seventy-four of the 111 (66.7%) dogs in the 2000 cohort and 100 of the 133 (75.2%) dogs in the 2012 cohort were classified as medium- to large-breed dogs; 37 of the 111 (33.3%) dogs in the 2000 cohort and 33 of the 133 (24.8%) dogs in the 2012 cohort were classified as small- or toy-breed dogs. The number of small- and large-breed dogs was not significantly different (P = 0.156) different between cohorts. Dachshunds were significantly (P = 0.003) more likely to vomit than other breeds, but they did not have more PORV events (P = 0.081). The majority of Dachshunds (15/20 [75.0%]) in the study had neurologic surgery for intervertebral disk disease. The types and incidence of neurologic surgeries were summarized (Table 2). The overall incidence of PORV was 12.3% (30/244), with 5.7% (14/244) vomiting, 5.7% (14/244) regurgitating, and 0.8% (2/244) both vomiting and regurgitating (Table 1).
Surgery type—Surgeries were initially grouped into either soft tissue, orthopedic, or neurologic procedures. Compared with the dogs in the other categories, the incidence of PORV was significantly (P = 0.023) higher in dogs undergoing soft tissue surgery (16/83 [19.3%]), significantly (P = 0.003) lower in dogs undergoing orthopedic surgery (8/127 [6.3%]), and not significantly (P = 0.395) different in dogs undergoing neurologic surgery (6/34 [17.6%]).

Fourteen of the 83 (16.9%) soft tissue surgeries were classified as primary gastrointestinal surgery involving disease of the esophagus, stomach, small or large intestines, or pancreas. Of the 69 dogs undergoing soft tissue surgery not involving gastrointestinal disease, 10 (14.5%) developed PORV, whereas 6 of 14 dogs receiving gastrointestinal surgery developed PORV. Thus, among dogs undergoing soft tissue surgery, those undergoing gastrointestinal surgery had a PORV episode more frequently (P = 0.024).

When the dogs undergoing gastrointestinal surgery were removed from the soft tissue surgery group, the incidence of PORV among the remaining dogs was not different from that among dogs undergoing orthopedic (P = 0.071) or neurologic (P = 0.774) surgery. Of all 30 dogs developing PORV, 6 (20.0%) had gastrointestinal surgery, whereas 8 of 214 (3.7%) dogs without PORV had gastrointestinal surgery (P = 0.003).

Risk factors for PORV—Given that there was not a significant difference in the incidence of PORV or risk factor distribution between the 2 cohorts, risk factor analysis was conducted on pooled data (Table 3). In addition, we found that even though corticosteroid usage was not significantly (P = 0.278) higher in PORV dogs, compared with dogs without PORV, significantly (P = 0.024) more dogs that received corticosteroids vomited. This was not observed in regurgitating dogs (P = 0.479). Acepromazine premedication was not associated with a reduced incidence of PORV, compared with other premedicants (P = 0.174).
Significantly ($P = 0.006$) more dogs received an opioid as part of their premedication in 2012, compared with 2000. However, similar to the use of $\alpha_2$-adrenoceptor agonists, this was not significantly ($P = 0.616$) different between dogs with and without PORV. Interestingly, there was a significant ($P = 0.008$) increase in the incidence of regurgitation among dogs receiving propofol, although this was not observed among the dogs that vomited ($P = 0.796$).

Significantly ($P = 0.001$) more dogs that had anesthestia maintained with sevoflurane regurgitated, compared with dogs that had anesthesia maintained with isoflurane. Sevoflurane did not appear to affect the incidence of vomiting ($P = 1.000$). The ASA scores of dogs that were given sevoflurane were significantly ($P < 0.001$) increased, compared with ASA scores of those given isoflurane. Of the 14 dogs regurgitating, 5 received isoflurane and 9 received sevoflurane. Use of hydromorphone as a postoperative analgesic did not result in a higher incidence of PORV ($P = 1.000$).

Univariate logistic regression (Table 3) identified being sexually intact, emergency surgery, history of vomiting or regurgitation, PCV, total solids concentration, ASA score of 4, type of inhalation anesthetic, and type of surgery as significant ($P < 0.05$) risk factors. When multivariate logistic regression was performed, only age, type of inhalation anesthetic, and type of surgery were significant ($P < 0.05$). Based on the receiver operating characteristic curve, the Youden index was used to select a cutoff point maximizing the correct classification of PORV. At this optimal point (0.11), the model was able to correctly predict PORV 67.1% of the time, with a sensitivity of 66.7%, specificity of 67.1%, positive predictive value of 22.2%, and negative predic-
tive value of 93.5%. There were no significant outliers in the model.

**Discussion**

In our study population of dogs, we found the incidence of PORV to be 12.3% (30/244) on the basis of pooled data obtained for patients undergoing nonelective neurologic, orthopedic, or soft tissue surgery in January 1 to March 31, 2000, and January 1 to March 31, 2012. Of the 244 dogs, vomiting occurred in 16 (6.6%) and regurgitation in 16 (6.6%), together comprising the 30 cases of PORV. Because the incidence of PORV was not significantly different between the 2 years, we rejected our primary hypothesis. However, compared with the 2000 cohort, there was a significant increase in the number of dogs that regurgitated in 2012. Correspondingly, there was a marked decrease in the number of dogs that vomited. The incidence of postoperative regurgitation in this study (6.6%) contrasts with that previously reported of 1% to 2%.13,19

Classically, regurgitation is considered a passive expulsion of food from the gastrointestinal tract orad to the small intestine and is not associated with nausea. Conversely, nausea and regurgitation are important components of gastroesophageal reflux disease in people. Unfortunately, nausea without vomiting is challenging to assess in veterinary patients.22 The retrospective nature of this study precluded us from determining the characteristics of the postoperative regurgitation episodes. However, the dogs regurgitating in this study often regurgitated small amounts of serosanguineous to bile-tinged fluid, rather than nondigested food. In addition, most were concurrently inappetant. We speculate that the observed postoperative regurgitation in our patient population may be associated with nausea and possibly gastroesophageal reflux.

In addition to the increased regurgitation and decreased vomiting noted in this study, the 2000 and 2012 cohorts differed in respect to weight, emergency status, ASA status, prior corticosteroid administration, premedications, anesthetic induction agents, anesthetic maintenance agents, use of nitrous oxide, intraoperative and postoperative opioid usage, use of neuromuscular blocking agents, and number of neurologic surgeries performed. Thus, 1 or more of these factors may be associated with the results reported for regurgitation and vomiting.

In human patients, being female is an independent risk factor and females are reportedly23–25 3 times as likely to develop PONV. This increased risk is not observed until after puberty and is apparently not correlated with the menstrual cycle. To date, the exact cause has not been elucidated, although a hormonal cause is suspected on the basis of the fact that the increased risk occurs after the onset of puberty.23 Although sex was not found to be a significant risk factor for PORV in the present study, significantly more sexually intact dogs developed PORV than gonadectomized dogs. We found that sexually intact dogs were 2.37 times as likely to develop PORV (93% CI, 1.07 to 5.27). Similar to the studies in human patients, we suspect this may be due to the influence of gonadal hormones. Our study did not find a link between female sex and PORV, but it is possible that this may have been observed had early elective gonadectomy not been so prevalent in our population of dogs. Further prospective studies would be needed to evaluate this.

Dachshund was the only breed in this study with a significant increase in vomiting, compared with other breeds, although the incidence of PORV was not greater in Dachshunds. The previously established increased risk for vomiting associated with intervertebral disk disease5 is likely the cause, given that most Dachshunds had surgery for intervertebral disk disease.

When we compared the 2 cohorts, we found that dogs were significantly heavier in 2012. A contributing factor may have been the slightly greater proportion of large-breed dogs in 2012 (100/133 [75.2%]) versus in 2000 (74/111 [66.7%]). However, breed type was not significantly different between the cohorts. Within the most common breed (Labrador Retrievers [46/244]), we noted an increase in median body weight (33 kg [72.6 lb; range, 17.7 to 47 kg [38.9 to 103.4 lb]) in 2000 vs 34.95 kg [76.9 lb; range, 22 to 49 kg [48.4 to 107.8 lb]) in 2012), which was not significant (P = 0.136). This was not surprising, considering that body weight of dogs has been found to correlate with the weight of their owners26 and the CDC27 has tracked a progressive increase in the weight of the US population during the cohort interval for this study.

Dogs undergoing emergency procedures had a significantly higher incidence of PORV (OR, 4.08; 95% CI, 1.29 to 12.90). To our knowledge, emergency procedures in human patients are not associated with increased rates of PONV.26 Lower rates of PONV after emergency open cholecystectomy have been reported.29 We speculate that this observed increase in the risk of PORV with emergency procedures is due to the high number of gastrointestinal surgeries performed on an emergency basis in dogs. Of the 15 dogs having emergency surgery in the present study, 6 underwent gastrointestinal surgery.

In people, a history of motion sickness or prior PONV is an independent risk factor for PONV. Although the exact mechanism is not yet understood, people with a history of motion sickness or PONV are thought to be susceptible individuals. A genetic basis for this is suspected, in view of the fact that first-degree relatives have also been found to be susceptible.4 The concept of susceptible individuals in dogs is supported by the significant increase in dogs that develop PORV if they have a history of vomiting or regurgitation. We found that dogs with a history of PORV were 5.12 times as likely to have a PORV event, especially regurgitation (95% CI, 1.83 to 14.31). This predisposition may also be attributable to a genetic basis in dogs; however, further studies would be needed to confirm this.

American Society of Anesthesiologists scores were significantly lower in the 2012 cohort, reflecting that anesthesia procedures performed in this cohort were not overall considered to be as high risk as those in the earlier cohort. Although ASA scores are subjective assessments of overall patient health, they have been found to closely relate to the incidence of perioperative complications in human patients.30 We found that dogs with PORV had higher ASA scores than those that
Hemoconcentration secondary to fasting is believed to exacerbate PONV in human patients, and the incidence of PONV has been reported to decrease when supplemental crystalloid fluid therapy is given after the procedure. In contrast, we found that significantly more PORV events occurred in dogs that were hemodiluted (lower PCV and total solids concentration). This is supported by our regression analysis showing that for every 1-unit decrease in the PCV or total solids concentration, there was a 1.05 (95% CI, 1.01 to 1.09) and 1.51 (95% CI, 1.04 to 2.22) times increase (corresponding to a 0.95 [95% CI, 0.91 to 0.99] and 0.66 [95% CI, 0.45 to 0.96] decrease with every 1 unit increase of the PCV or total solids) in the odds of a PORV event.

Interestingly, as ASA score increased in our data set, the PCV and total solids concentration decreased. This relationship may be explained by causes of anemia other than blood loss, such as anemia of inflammatory disease.32 These conditions may occur more often in systemically compromised dogs with high ASA scores. Additionally, these higher risk dogs may have received IV fluids prior to surgery, reducing the PCV and total solids concentration of these samples that are routinely obtained a few hours prior to anesthesia.

Corticosteroid usage decreased significantly for the 2012 cohort, compared with the 2000 cohort, which was attributed to a change in clinical practice. This was particularly relevant for neurologic surgeries, which accounted for 29 of the 38 (76.3%) dogs that received steroids. In human patients, perioperative dexamethasone administration has been found to significantly reduce the incidence of PONV.31 Other glucocorticoids may also have a dose-dependent antiemetic effect.34 A protective effect was not observed in this study. This could be due to the timing of steroid administration, given that they were not necessarily given during the perioperative period. Alternatively, the antiemetic effect may not be as strong in dogs. Of note, 4 of 27 (14.8%) dogs receiving steroids in 2000 vomited, compared with 2 of 7 in 2012. This increase was attributed to a type I statistical error, considering that this was only 2 dogs, 1 of which had an insulinoma and the other pyometra.

Use of α2-adrenoceptor agonists increased significantly in the 2012 cohort. This was attributed to the widespread availability of newer generation α2-adrenoceptor agonists with wider therapeutic ranges (eg, dexmedetomidine). Interestingly, α2-adrenoceptor agonists have been shown to significantly reduce lower esophageal sphincter tone35 and increase the rate of gastroesophageal reflux in dogs.18 Although significantly high rates of regurgitation were seen in the 2012 cohort where the use of α2-adrenoceptor agonists was common, neither the incidence of PORV nor regurgitation was significantly higher among those dogs receiving these medications, compared with those not receiving these medications. Logistic regression also failed to find an association between PORV and the use of α2-adrenoceptor agonists. On the basis of results of this study, the use of α2-adrenoceptor agonists does not appear to have an effect on the incidence of PORV.

Interestingly, when regression analysis was performed, dogs that did not receive a strong sedative (either an α2-adrenoceptor agonist or acepromazine) as a premedicant were 5.36 (95% CI, 1.89 to 15.17) times as likely to develop PORV, as were dogs receiving acepromazine. Studies30,37 have shown acepromazine to have a protective effect on vomiting from opioids administration, and it is possible this protective effect may extend to the postoperative period. However, we attributed this increase in the risk of PORV to systemically compromised dogs with high ASA scores not requiring strong sedatives as part of their anesthetic protocol.

When comparing the anesthetic induction agents used between the 2 cohorts, the marked increase in propofol usage and decrease in thiopental usage in 2012 was conspicuous. This marked shift was attributed to the inability to obtain thiopental and the decreased cost of propofol that occurred during the intervening 12 years. Propofol has been reported to have a protective effect for human patients at risk for PONV,19,38; however, conflicting reports39,40 exist that describe this effect as only being observed when propofol is administered as a CRI. Interestingly, the reduction in PONV appears to be primarily due to a reduction in the incidence of vomiting.40 The exact mechanism of action is unknown; it is thought to be due to its psychological anxiolytic effect.9 Conversely, others have postulated that the observed protective effect may have less to do with an innate antiemetic property of propofol than with the elimination of the volatile anesthetic, a known independent risk factor.31 An early study16 in the use of propofol on dogs found that propofol decreases the lower esophageal sphincter tone significantly more than thiopental and is associated with a higher incidence of gastroesophageal reflux. Our study did not find a significant change in PORV associated with the use of propofol. However, when we evaluated for vomiting and regurgitation separately, the incidence of regurgitation in the pooled cohorts was significantly higher among dogs in which anesthesia was induced with propofol. Even though propofol usage was not found to be a risk factor for PORV, our data suggest that it may be a significant risk factor for regurgitation. This further strengthens our suspicion that postoperative regurgitation represents gastroesophageal reflux. We are not aware of any studies evaluating a possible antiemetic effect of propofol in dogs. However, is it interesting that propofol was used significantly more in the 2012 cohort, and we suggest

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that further studies are needed to determine the risk of regurgitation and vomiting associated with propofol usage in small animal patients.

There was a significant increase in the use of sevoflurane in 2012. Although sevoflurane was available in 2000, it was not being clinically used at our institution, resulting in the significant increase observed. Sevoflurane has been associated with a 17% higher risk of gastroesophageal reflux in dogs, compared with isoflurane, which may in part explain the increased rate of postoperative regurgitation noted in the later cohort. In fact, we found that PORV in 2012 was significantly higher in dogs receiving sevoflurane than in dogs receiving isoflurane. Of note, sevoflurane was associated with a significant increase in the incidence of regurgitation, and regression analysis found a 2.78 times increase in the odds of developing PORV (95% CI, 1.25 to 6.13), compared with dogs receiving isoflurane. These findings suggest that the use of sevoflurane may be an important risk factor in predicting PORV and regurgitation in particular. However, when the ASA scores of the dogs on sevoflurane and isoflurane in 2012 were compared, the dogs receiving sevoflurane also had significantly higher ASA scores. Given that patients with higher ASA scores may be expected to be associated with increased risk for complications, the association between PORV and sevoflurane may instead reflect the anesthesiologist’s choice to use a maintenance agent with a lower solubility in these more critically ill patients. Sevoflurane may contribute to higher rates of regurgitation; however, further study would be needed to determine its contribution.

Use of nitrous oxide during anesthesia was markedly lower in the 2012 cohort, which was attributed to the changing clinical preferences of our anesthesiology department, but this did not affect the incidence or risk of developing PORV. Interestingly, use of both intraoperative and postoperative opioids increased significantly in the 2012 cohort. We believe this increase reflects our profession’s increased awareness of pain and its undesirable effects on patients.

In human patients, postoperative opioid usage is an independent risk factor for PONV. Although an increase in the incidence of PORV attributable to intraoperative opioid usage was not found, we did find an increase, although not significant ($P = 0.081$), in the incidence of PORV among dogs that received postoperative opioids, compared with those that did not. However, on further evaluation, the anesthetic and surgery times of dogs that did not receive postoperative opioids were significantly shorter and included procedures such as plate removals. This suggests that these findings may reflect that postoperative opioids are typically not given for shorter and less invasive procedures. Consistent with a previous study, the use of hydromorphone as a postoperative analgesic did not result in a significantly higher rate of PORV. Neuromuscular blocking agents were not used in the 2012 cohort but were used in 6 cases in the 2000 cohort. This resulted in a significant decrease in their usage. We attributed this to a type I statistical error because they are used in our hospital but not frequently. No association between the use of neuromuscular blocking agents and PORV was identified.

Our secondary hypothesis that anesthesia and surgery times would be longer in the 2012 cohort was rejected, given that both anesthesia and surgery times were shorter. These differences were not significant. Anesthesia times are an independent risk factor for PONV in humans. However, our study did not find a significant ($P = 0.304$) difference in anesthetic times between dogs with and without PORV. Determining the exact cause of this difference between dogs and humans was beyond the scope of this study. We suggest that this is likely due to differences between the species in their response to inhalation anesthetics.

In humans, lower esophageal sphincter tone has been found to decrease in a dose-dependent manner as the concentration of the inhalation anesthetic increases. To our knowledge, a similar effect in dogs has not been reported. It is possible that the lower esophageal sphincter in humans undergoes considerably more relaxation under surgical depths of inhalation anesthetic concentrations than that of dogs and the longer this relaxation is present, the greater the risk of gastroesophageal reflux and subsequent PONV. In contrast, Hashim et al. found that although lower esophageal sphincter pressures dropped with increased duration of anesthesia in dogs, the effect was offset by surgical stimulation.

Duration of surgery is not an independent risk factor for PONV in human patients; similarly, a significant difference was not found between the surgery times of dogs with and without PORV. This has previously been explained by the anesthesia-related relaxation of the lower esophageal sphincter being counteracted by the stimulation of the surgical procedure. In the present study, orthopedic procedures were associated with a lower incidence of PORV, compared with neurologic and soft tissue procedures. Dogs undergoing soft tissue or neurologic procedures, compared with dogs undergoing orthopedic procedures, had an OR of 3.55 (95% CI, 1.44 to 8.74) and 3.18 (95% CI, 1.02 to 9.92), respectively. We attributed the low rate of PORV among dogs undergoing orthopedic procedures to the fact that these procedures were typically elective and dogs were otherwise healthy. Consequently, they have lower ASA scores and are less likely to have a history of vomiting, another important factor in predicting PORV in dogs. In contrast, dogs undergoing soft tissue procedures included the majority (12/19) of the dogs with a history of vomiting, those having gastrointestinal surgery, and those with neoplasia or trauma with associated metabolic instability resulting in higher ASA scores. Specifically, significantly more dogs undergoing gastrointestinal surgery had a PORV episode than those undergoing soft tissue surgery not involving gastrointestinal disease. Compared with dogs undergoing orthopedic procedures, dogs undergoing gastrointestinal surgery had an OR of 11.15 (95% CI, 3.11 to 40.03). Dogs undergoing soft tissue surgery not involving gastrointestinal disease had an OR of 2.52 (95% CI, 0.95 to 6.72), which was nonsignificant. We suggest that both disease of and surgical trauma to the gastrointestinal tract may decrease normal function and stimulate local receptors producing emesis.

Finally, the increased risk of PORV among dogs having neurologic surgery appears to be an inherent risk of neurologic surgery and is consistent with pre-
vious reports. A multiple logistic regression model was developed in an attempt to predict dogs that would be at increased risk of PORV. The model that best predicted PORV was one that contained age, type of inhalation anesthesia, and type of surgical procedure. Because of the potentially fatal consequences of aspiration pneumonia, the probability cutoff was chosen to optimize the sensitivity and specificity while minimizing the number of false-negative results. Even though this model was the most useful of those tested, the sensitivity (66.7%) and specificity (67.1%) were not considered high enough to support a clinically useful scoring system similar to the Apfel simplified risk scoring system for humans.

Limitations of the present study include its retrospective nature and its reliance on preexisting data that varied in its level of detail. Further, the dogs were not all in our intensive care unit under continuous observation during the first 24 hours. It is possible that some dogs’ regurgitation or vomiting remained undetected.

This study did not attempt to elucidate the effects of prophylactic gastrointestinal protective treatment. We considered such investigations beyond the scope of this already comprehensive study. Subjectively, our awareness of PORV has greatly increased since 2000, which has affected our use of prophylactic treatments. Nonetheless, we cannot rule out that prophylactic treatments affected the incidence of PORV in the 2012 cohort. For example, introduction of effective antiemetics such as maropitant citrate may have influenced the rate of vomiting in the later cohort. We hope that our findings will be useful in the design of future prospective randomized case-control studies evaluating the efficacy of various therapeutic measures. Given the potentially fatal outcome, the ability to identify surgical patients at high risk for PORV and administer specific prophylactic treatment would be of great value. Antiemetic prophylaxis should be considered by clinicians treating patients with an identified risk factor.

References


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**From this month’s AJVR**

**Pharmacokinetics of pergolide after intravenous administration to horses**

David I. Rendle et al

**Objective**—To determine the pharmacokinetics of pergolide after IV administration to horses.

**Animals**—8 healthy adult horses.

**Procedures**—Pergolide mesylate was administered IV at a dose of 20 µg/kg (equivalent to 15.2 µg of pergolide/kg) to each horse, and blood samples were collected over 48 hours. Pergolide concentrations in plasma were determined by means of high-performance liquid chromatography–tandem mass spectrometry, and pharmacokinetic parameters were determined on the basis of noncompartmental methods.

**Results**—After IV administration of pergolide, mean ± SD clearance, elimination half-life, and initial volume of distribution were 959 ± 492 mL/h/kg, 5.64 ± 2.36 hours, and 0.79 ± 0.32 L/kg, respectively.

**Conclusions and Clinical Relevance**—With an elimination half-life of approximately 6 hours, twice-daily dosing may be more appropriate than once-daily dosing to reduce peak-trough fluctuation in pergolide concentrations. Further pharmacodynamic and pharmacokinetic studies of pergolide and its metabolites will be necessary to determine plasma concentrations that correlate with clinical effectiveness to determine the therapeutic range for the treatment of pituitary pars intermedia dysfunction. (*Am J Vet Res* 2015;76:155–160)