

Parvovirus Enteritis and Other Risk Factors Associated With Persistent Gastrointestinal Signs in Dogs Later in Life: a Retrospective Cohort Study

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Abstract

Background: Parvoviral enteritis is a viral gastrointestinal (GI) infection of dogs. Recovery from PE has been associated with persistent GI signs. The objectives of this study were: (i) To determine whether dogs that have recovered from PE (post-parvo dogs) had an increased risk of persistent GI signs compared to uninfected controls. (ii) To investigate the lifestyle and clinicopathologic factors that are associated with persistent GI signs in post-parvo dogs.

Methods: Eighty-six post-parvo dogs and 52 age-matched control dogs were enrolled in this retrospective cohort study. The owners were interviewed about the health and habits of their dogs using a questionnaire. We used logistic regression to test whether parvovirus enteritis and other risk factors are associated with general health problems in all dogs and with persistent GI signs in post-parvo dogs.

Results: The prevalence of persistent GI signs was significantly higher in post-parvo dogs compared to control dogs (57% vs 25%, $P < 0.001$). Markers of disease severity such as neutropenia, low body temperature, and treatment with an antiemetic medication (metoclopramide) were significant risk factors for persistent GI signs in post-parvo dogs. Persistent GI signs in post-parvo dogs was a risk factor for health problems in other organ systems.

Conclusions: Parvovirus enteritis is a significant risk factor for persistent GI signs in dogs highlighting the importance of prevention. The risk factors identified in the present study may guide future investigations on the mechanisms that link parvovirus enteritis to chronic health problems in dogs.

Background

Canine parvovirus type 2 (CPV-2) is a non-enveloped, single-stranded DNA virus that is highly contagious among canines. CPV-2 causes parvoviral enteritis (PE), which is characterized by severe gastroenteritis in dogs, usually puppies (1). The signs of PE include lethargy, vomiting, fever, diarrhea, and neutropenia. These signs are caused by the viral destruction of rapidly dividing cells, including intestinal crypt cells and neutrophils (2). CPV-2 infects a variety of organs including the small intestine, tonsils, lymph nodes, thymus, spleen, heart, liver, and kidneys (3). In untreated dogs, PE has a mortality rate of 10–20% (1), but it can be successfully managed by in-hospital or outpatient treatment.

Dogs that recover from parvovirus infection have increased risk of long-term gastrointestinal (GI) signs compared to uninfected control dogs (4, 5), but the factors underlying this increased risk have not been investigated (4, 5). Microbiome studies on dogs infected with CPV-2 have shown perturbed fecal microbiota (6), and have isolated enterotoxigenic bacteria (*Clostridium perfringens* and *C. difficile*). Dogs with PE are frequently treated with antimicrobials to combat secondary bacterial infections, and these treatments will also perturb the gut microbiome (as shown in mice and humans (7, 8)) with unknown consequences for long-term health. Thus, perturbations in the gut microbiome of the dog caused by CPV-2 and/or by antimicrobial treatments during hospitalization might be linked with the development of long-term GI signs.

In humans, there are conflicting results about the long-term consequences of severe diarrhea in early childhood (9–12). Children infected with non-typhoid *Salmonella* and/or exposed to farms (considered unhygienic environments) were less likely to develop autoimmune diseases (e.g. allergic rhinoconjunctivitis, asthma) later in life (9). Infants that had diarrhea in their first year of life, mounted a more vigorous immune response to vaccination during adolescence (13). In contrast, other studies have shown that severe enteritis in infants interferes with their immune systems and may result in food allergies and inflammatory bowel disease (10, 11). Severe diarrhea in childhood has been associated with physical and cognitive deficits in older children (12). Bacterial gastroenteritis in adults has been associated with gastrointestinal disorders such as irritable bowel syndrome (14). Potential mechanisms underlying these long-term consequences of severe diarrhea include changes in GI permeability (15) and perturbations in the gut microbiome (7, 8).

The first aim of our study was to confirm whether dogs that have recovered from parvovirus enteritis (post-parvo dogs) are more likely to suffer from long-term GI signs compared to uninfected control dogs. The second aim was to identify the risk factors associated with long-term GI signs in post-parvo dogs. We hypothesized that clinicopathological surrogate markers of disease severity (e.g. degree of neutropenia, treatment with anti-emetics or antibiotics) would be associated with long-term GI signs. Identifying the risk factors that predict whether post-parvo dogs will develop long-term GI signs will improve our treatment of this important disease and enhance our understanding of how acute viral infections during development influence lifetime health.

Results

Comparison of explanatory variables between control dogs and post-parvo dogs: The percentage of female dogs was similar between the control group (48.1%; 25/52) and the post-parvo group (47.6%; 41/86). The percentage of purebred dogs was similar between the control group (50.0%; 26/52) and the post-parvo group (47.6%; 41/86). The mean age at admission was similar between the control dogs (mean = 27.0 weeks; range 9.6–124.9 weeks) and the post-parvo dogs (mean = 30.6 weeks; range 6.0–192 weeks). The mean time to follow up for control dogs (mean = 7.66 years; range 3.09–12.42 years) was longer than the post-parvo dogs (mean = 5.27 years; range 0.48–12.40 years). The mean age at follow up for control dogs (mean = 8.18 years; range = 3.57–13.59 years) was older than the post-parvo dogs (mean = 5.86 years; range = 0.75–12.61 years). This difference in the mean time to follow up and the mean age at follow up was caused by the second sample of post-parvo dogs, which did not have age-matched control dogs. For this reason, we included the age at admission and the time to follow up as covariates in all statistical analyses.

The prevalence of persistent GI signs at follow up in post-parvo dogs (57.0% = 49/86) was significantly (2.3x) higher compared to the control dogs (25.0% = 13/52; $\chi^2 = 12.13$, $df = 1$, $P < 0.001$). However, this simple comparison does not consider the many other factors that can influence the probability of persistent GI signs at follow up (see below).

Analysis of factors that influence general organ signs in control dogs and post-parvo dogs: After model simplification, 8 of the 11 explanatory variables remained in the model, of which 6 were significant (Fig. 1; Sect. 3 of the supplementary material). Post-parvo dogs were significantly more likely to have signs at follow up than control dogs (Fig. 1; $P < 0.001$). Compared to other organs, dogs had significantly more signs at follow up in the GI tract (Fig. 1; $P < 0.001$) and significantly fewer signs at follow up in the urinary system (Fig. 1; $P = 0.001$). The probability of signs at follow up was positively associated with the time of follow up (Fig. 1; $P < 0.001$). Purebred dogs had significantly fewer signs at follow up than mixed breed dogs (Fig. 1; $P = 0.023$). Dogs with a medical history had significantly more signs at follow up than dogs with no medical history (Fig. 1; $P = 0.035$). Indoor dogs had significantly more signs at follow up than outdoor dogs (Fig. 1; $P = 0.009$).

Analysis of the factors that influence persistent GI signs at follow up in post-parvo dogs: The PE-affected dogs that were included in the analysis ($n = 60$) received the following treatments during their hospitalization: 23.3% (14/60) were given metoclopramide, 35.0% (21/60) were given antiemetics (mean = 0.50; range = 0–3 antiemetics per dog), 25.0% (15/60) were given antacids (mean = 0.27; range = 0–2 antacids per dog), and 98.3% (59/60) were given antimicrobials (mean = 1.53; range = 0–4 antimicrobials per dog), with ampicillin being the most common type of antimicrobial.

After model simplification, 8 of the 24 explanatory variables remained in the model, of which 5 were significant (Fig. 2; Sect. 5 of the supplementary material). Dogs treated with metoclopramide during hospitalization were significantly more likely to have persistent GI signs than dogs not treated with metoclopramide (Fig. 2, $P = 0.027$). The probability of persistent GI signs was negatively associated with the body temperature of the dog at hospital admission (Fig. 2, $P = 0.019$). According to Fig. 2, the probability of having persistent GI signs at the time of follow up was 7 times higher in PE-affected dogs with a body temperature of 37.5 °C (~ 0.875) compared to PE-affected dogs with a body temperature of 40.0 °C (~ 0.125). Thus, PE-affected dogs with higher body temperature (fever) at admission were less likely to have persistent GI signs at the time of follow up. Total white blood cell count was positively associated with persistent GI signs (Fig. 2, $P = 0.037$), whereas segmented neutrophils (Fig. 2, $P = 0.023$) and band neutrophils (Fig. 2, $P = 0.031$) were negatively associated with persistent GI signs. Thus, dogs with more severe neutropenia (i.e. low counts of neutrophils) at admission were more likely to have persistent GI signs.

The three explanatory variables that were not statistically significant are mentioned here because they were significant in another analysis with a larger sample size ($n = 79$), but that did not include the CBC variables (see Sect. 4 of the supplementary material). The probability of persistent GI signs was positively associated with the time of follow up (Fig. 2, $P = 0.054$). Purebred dogs were less likely to have persistent GI signs than mixed breed dogs (Fig. 2, $P = 0.108$). Dogs with a medical history were more likely to have persistent GI signs than dogs with no medical history (Fig. 2, $P = 0.064$).

Comparison of general signs between post-parvo dogs with or without persistent GI signs: The prevalence of signs in the other 5 organs was 1.7 times higher in post-parvo dogs with persistent GI signs (22.2% =

50/225) compared to post-parvo dogs without GI signs (Fig. 3; 13.1% = 23/175). A GLMM with binomial errors that analyzed the prevalence of signs in the other 5 organs as a function of 17 explanatory variables confirmed that this difference between dogs with versus without persistent GI signs was significant (see Sect. 6 of the supplementary material).

Discussion

Parvovirus enteritis is a risk factor for persistent GI signs in dogs: Our study confirmed that dogs that recover from parvovirus enteritis are more likely to suffer from persistent GI signs compared to control dogs. The prevalence of persistent GI signs at the time of follow up in the post-parvo dogs was 57%, which was 2.3 times higher than the prevalence in the age-matched controls (25%). Our results are consistent with two other studies that found an association between PE and the presence of persistent GI signs in post-parvo dogs (4, 5). Our study found a higher prevalence of persistent GI signs (57%) in post-parvo dogs compared to a recent study by another research group (42%) (5). This discrepancy may arise from differences in the questionnaire (e.g. number and types of questions), differences in how the responses of the owners are converted to whether the dog has signs or not, and differences in the time of follow up. Both studies show that a high percentage of dogs have persistent GI signs after recovery from parvovirus infection, and it is therefore important to identify the underlying risk factors for these chronic GI health problems.

Risk factors that influence organ signs in control and post-parvo dogs: There were numerous risk factors that influenced the probability of whether the control dogs and post-parvo dogs had signs at the time of follow up in the 6 organ systems surveyed by the questionnaire. The probability of signs in the 6 organ systems was significantly associated with the time of follow up. The time of follow up ranged from 0.5 to 12.4 years, where the maximum represents a significant fraction of the lifespan of the average dog. This result was expected because a longer time to follow up means that the dog is older at the time of the questionnaire and has therefore had more time to develop the diseases and signs associated with old age (16–18). Our study shows the importance of controlling for the time of follow up by including it as a covariate in the statistical analysis. The shorter time of follow up for the post-parvo dogs compared to the control dogs, suggests that our study underestimates the effect of PE on the future health problems (i.e. because the post-parvo dogs were younger and therefore expected to be healthier at the time of follow up compared to the control dogs).

At follow up we found that owners were significantly more likely to report signs for the GI tract and significantly less likely to report signs for the urinary system compared to other organ systems. Parvovirus enteritis is foremost a disease of the GI tract and so we expect GI signs to be more common at follow up compared to signs in other organ systems. Another explanation is that our questionnaire asked more questions about the GI tract (6 questions) compared to the other 5 organ systems (2–3 questions per system). All else being equal, the probability of detecting at least one symptom for a given organ system increases with the number and types of questions targeting that particular organ system. Thus, it is not surprising that a questionnaire found a higher prevalence of signs for the GI tract compared to the

other 5 organ systems. Differences in the number and types of questions (essentially a measure of sampling effort) may also explain why the prevalence of signs was lower in the urinary system compared to the other five organ systems.

Dogs with a medical history (i.e. treatment with other medications at any point in time during the period of follow up) were significantly more likely to have signs in the 6 organ systems at follow up compared to dogs with no medical history. This result is expected because dogs with health problems are more likely to be treated with medication, and their owners are more likely to report these dogs as having signs on the questionnaire. Due to the variety of medications prescribed for different health problems, we did not investigate whether any particular medication was associated with signs in the 6 organ systems. In summary, dogs that are treated with medication during the time of follow up are more likely to be reported by their owners as having signs at the time of follow up.

Our study found that indoor dogs had significantly more signs in the 6 organ systems at follow up compared to outdoor dogs. One explanation is a human monitoring effect; owners may have more opportunities to monitor the health of indoor dogs compared to outdoor dogs. An interesting alternative explanation is the hygiene hypothesis, which was developed to explain the proliferation of autoimmune diseases (allergies, asthma, etc.) in human populations of the developed world. Numerous studies have found that children that spend more time in the outdoors and/or in unhygienic environments are less likely to develop allergies and autoimmune diseases (9, 13). Our observation that an indoor lifestyle is a risk factor for persistent health problems in dogs (as recognized by the dog owners) suggests that the hygiene hypothesis may also be true for canids.

Purebred dogs were significantly less likely to have signs in the 6 organ systems at follow up compared to mixed breed dogs. This effect was unexpected because purebred dogs, which are more inbred, tend to have more health problems than mixed breed dogs, which are outbred (19, 20). One explanation is an owner effect; owners might be more attentive about reporting signs in expensive purebred dogs compared to mixed breed dogs.

Risk factors that influence persistent GI signs in post-parvo dogs: Some of the results of our study suggest that dogs more severely ill with PE are at greater risk of persistent GI signs. There was a significant negative association between the body temperature of the PE-affected dog at hospital admission and persistent GI signs at the time of follow up. The probability of post-parvo dogs having persistent GI signs at the time of follow up was 7 times higher for hypothermic dogs (body temperature of 37.5 °C) compared to hyperthermic dogs (body temperature of 40.0 °C). Previous studies on PE in dogs have suggested that hypothermia at the time of hospital admission indicates severe metabolic disease or shock (2, 21, 22). Hypothermia in PE-affected dogs at the time of admission may be a marker of disease severity and more severe disease may be a risk factor for persistent GI signs later in life.

Our study also found that neutropenia during hospital admission was significantly associated with a higher probability of persistent GI signs at follow up (Fig. 2). Neutropenia (low neutrophil count in blood) is a known sign of PE, and is consistent with the pathology of PE. Canine parvovirus-2 targets the rapidly

dividing precursor cells in the bone marrow that produce neutrophils, which results in neutropenia (2, 23). Our observation that neutropenia is a risk factor for persistent GI signs, suggest that low neutrophil counts are a marker of severe PE. In contrast, total WBC counts during hospitalization for PE were positively associated with persistent GI signs at follow up. Besides neutrophils, the total WBC count includes leucocytes such as lymphocytes, eosinophils, basophils, and monocytes. The reason for this finding is uncertain as it cannot be attributed to a consistent increase in another leukocyte given the lack of significance found when the individual leukocyte values were analyzed.

In the analysis of the signs in the 6 organ systems for the control dogs and the post-parvo dogs, the explanatory variables of the time of follow up, breed, and medical history were all significant (Fig. 1). The same result was found in an analysis of the prevalence of persistent GI signs for a larger sample of post-parvo dogs (n = 79), which did not include the explanatory variables from the CBC panel (Sect. 3 of the supplementary material). However, when the explanatory variables from the CBC panel were included, the sample size decreased (n = 60), and these 3 explanatory variables were no longer statistically significant (Fig. 2). The explanations as to why time of follow up, breed, and medical history are risk factors for persistent GI signs in post-parvo dogs are probably the same explanations as to why these three explanatory variables are risk factors for signs in the 6 organ systems in all dogs (control and post-parvo).

Metoclopramide treatment is associated with persistent GI signs in post-parvo dogs: The only treatment associated with an increased risk of persistent GI signs was the use of metoclopramide. The reason for this is speculative. Although metoclopramide is an antiemetic, in our practice we do not consider it a very effective treatment and rarely use it for this purpose. This medication was likely used in our practice when ileus is considered a major component of vomiting. Of course, it is not possible to retrospectively ascertain the reasons clinicians used metoclopramide. Ileus severe enough to require intervention may also be a marker of disease severity, though this too is speculative. In critically ill children, secondary ileus can lead to bacterial overgrowth (24), and in canine PE patients, gut bacterial translocation is linked with septic complications (2).

Our study found no evidence that the use of multiple antiemetics was a risk factor for persistent GI signs. We expected that dogs with severe vomiting during their hospitalization for PE would be given more antiemetics and therefore that the use of multiple antiemetics would be a marker for disease severity. This type of bias is common in retrospective studies where sicker patients get more treatments than less sick patients, which results in the treatments being associated with poorer outcomes. In a retrospective study on parvovirus treatment, dogs given antiemetics had longer hospitalization times than dogs that were not given antiemetics (25). The reason why our study did not find the expected positive association between the number of antiemetics prescribed and the probability of persistent GI sign is unclear. It would likely require a well-defined prospective study to assess the association between vomiting and ileus with regard to severity of disease.

Use of multiple antimicrobials are not a risk factor for persistent GI signs in post-parvo dogs: The use of multiple antimicrobials during hospital admission was not associated with persistent GI signs in post-parvo dogs at the time of follow up. This result was surprising because in our institution, multiple antimicrobials are routinely used in dogs that are assessed as being more severely affected, whereas a single agent such as ampicillin is generally used in those dogs that are less ill. This result is also surprising because we expected that the use of multiple antimicrobials would be more likely to perturb the gut microbiota than the use of a single antimicrobial. In mice and humans, the use of antimicrobials has been shown to alter the intestinal microbiota with lasting consequences such as changes in metabolism or increased enterocolitis (7, 26). One limitation of our study was that we simply counted the number of antimicrobials that were prescribed, which meant that we did not investigate whether different types of antimicrobials are risk factors for persistent GI signs. Studies on human patients have shown that the alteration of the gut microbiota depends on the type of antimicrobial used (8). The effects of various antimicrobials on the microbiome in dogs generally remains unknown.

Persistent GI signs is a risk factor for other health problems in post-parvo dogs: Post-parvo dogs with persistent GI signs were significantly more likely to have signs in the other 5 organ systems (ear, orthopedic, respiratory, skin, and urinary systems) that we assessed. Previous studies on humans have found that severe diarrhea experienced in childhood is a risk factor for health problems in other organ systems during adulthood (10–12, 14). Our study suggests that PE during puppyhood is a risk factor for a variety of health problems for dogs later in life.

Limitations of the study: The present retrospective study has several limitations. One limitation is that treatment protocols were not standardized and at the discretion of the attending clinician and therefore we do not know the decisions underlying the various treatment regimens. Standardized management plans for dogs with PE do not exist at our institution. Similarly, there were no objective measures by the clinician of the severity of PE in the dogs. Another limitation is the subjectivity of the owners in assessing the health status of their dogs at the time of follow up. However, a strong defense of our study is that hospital measures of disease severity (e.g. body temperature, neutrophil count, and metoclopramide treatment), of which the owners were not aware, were strongly associated with owner assessments of dog health, which occurred an average of 5 to 8 years after hospitalization for PE. To create such associations through bias, the owners would have to somehow know that their dog had a severe case of PE and then remember to exaggerate the health symptoms of their dog 5 to 8 years later in a follow up interview. We therefore conclude that the risk factors for persistent GI symptoms in post-parvo dogs identified in this study are biologically real rather than imagined by their owners.

Conclusion

More than half of the dogs that recovered from PE suffered from persistent GI signs later in life. Some clinical factors in post-parvo dogs such as time to follow up, indoor lifestyle, body temperature at hospital admission, use of metoclopramide, WBC counts, and neutrophil counts were risk factors for persistent GI signs. Persistent GI signs in post-parvo dogs are common, and it is therefore important to investigate the

underlying mechanisms. Our study shows the importance of owner education and preventive vaccination against CPV-2 to protect puppies from developing chronic GI problems.

Methods

Study aims: (i) To determine whether dogs that have recovered from PE (post-parvo dogs) had an increased risk of persistent GI signs compared to uninfected controls. (ii) To investigate the lifestyle and clinicopathologic factors that are associated with persistent GI signs in post-parvo dogs.

Study design: This is a retrospective cohort study. Client-owned dogs that had been diagnosed and treated for PE at the teaching hospital of the Western College of Veterinary Medicine at the University of Saskatchewan from April 1999 to December 2018 were identified using the medical record system. The diagnosis of PE was based on appropriate history and clinical signs, and a positive point-of-care (POC) ELISA kit test for canine parvovirus antigen (SNAP® Canine Parvovirus Antigen Test Kit, IDEXX Laboratories, Inc., Westbrook, Maine, USA). Control dogs were selected using the same medical record system and were matched to PE-affected dogs using two criteria: (i) the control dog was presented for vaccination within 2 weeks of admission of the PE-affected dog and (ii) the control dog was within 6 months of the age of a PE-affected dog. These two criteria prevented us from matching the dog breed between the control dogs and the PE-affected dogs.

Several years after hospital admission, the owners of the dogs (control and PE-affected) were contacted by phone to complete our questionnaire, which included basic questions about the lifestyle and health of the dog. Owners were asked to report only on signs that occurred after the PE hospitalization and during the follow up period. Dogs with completed questionnaires were included in our retrospective study, and the duration between hospital admission and the phone interview was recorded as the follow up time period. We completed questionnaires for 52 control dogs and 41 post-parvo dogs in 2011. To increase the sample size, we completed a second sample of questionnaires for 45 post-parvo dogs in 2019.

Questionnaire: The questionnaire is available in Sect. 1 of the supplementary material and it contained 31 questions regarding the current health status of the dog. The questionnaire addressed the following health conditions: presence of persistent GI signs, vomiting, diarrhea, owners' perception of "sensitive stomach", clinical signs consistent with pruritus of skin or ear, ear infection, respiratory signs, orthopedic signs, urinary tract disease signs, weight loss or gain, polyuria-polydipsia, vaccination status, and deworming status. The questionnaire also included information on the diet history, length of the feeding period for the current diet, lifestyle (indoor, outdoor), and medical history other than parvoviral enteritis, which was defined as the dog being treated with medications in the follow up time period between the original hospital admission (for PE or vaccination) and the questionnaire interviews.

Whenever appropriate, owners were asked to assess the degree of clinical signs. We used the information from the questionnaire to classify dogs (control and post-parvo) as having GI signs (yes versus no) depending on whether the owners recognized the signs of vomiting and/or diarrhea (at least 1 sign

versus 0 signs). Similarly, we used the questionnaire to classify the dogs as having clinical signs for the 5 other organ systems: ear, orthopedic, respiratory, skin, and urinary (supplementary material, Sect. 1).

Clinicopathological data: Clinicopathological data were extracted from electronic medical records and included hospitalization data, in-hospital management data, and laboratory data. The hospitalization data included age at admission (weeks), breed, and gender. The in-hospital management data included use and type of antiemetics (e.g. maropitant, ondansetron, metoclopramide, etc.), use and type of antimicrobials (e.g. ampicillin, amikacin, enrofloxacin, etc.), and use and type of antacids (e.g. H₂ blocker, proton-pump inhibitor). The laboratory data included complete blood count (CBC) panel with blood smear evaluation by clinical pathologists. For dogs where the CBC panel was performed more than once, the replicate panel with the lowest leukocyte count was selected for the statistical analysis. The timing of the blood sampling in relation to admission and treatment is summarized in the supplementary material (Table S10).

Statistical analysis: All the statistical analyses were done using R version 1.3.959. The details of the statistical methods are given in Sect. 2 of the supplementary material. A *P* value of less than 0.05 is considered statistically significant.

Analysis of factors that influence general organ signs in control dogs and post-parvo dogs: We used a generalized linear mixed effects model (GLMM) with binomial errors to analyze whether an individual dog experienced signs at follow up for a given organ system (0 = no signs, 1 = signs; see Sect. 3 of the supplementary material for details). The identity of the dog was modelled as a random factor to account for non-independence of different organs for the same dog. There were 11 explanatory variables: (1) parvoviral infection history (control, post-parvo), (2) organ system (ear, GI, orthopedic, respiratory, skin, and urinary system), (3) sex (female, male), (4) purebred (no, yes), (5) lifestyle (indoors only, indoors and outdoors, outdoors only), (6) up-to-date vaccination (no, yes), (7) deworming treatment given (no, yes), (8) medical history (no, yes), (9) age of the dog at admission (days), (10) time of follow up (days), and (11) dog weight at admission (kg). The continuous variables were transformed to z-scores (mean of zero, units of standard deviations) to facilitate model convergence and comparison of the effect size between variables measured in different units. We simplified the model by sequentially removing explanatory variables with a *p*-value > 0.10. For this analysis, there were 52 control dogs and 86 post-parvo dogs (total of 138 dogs).

Analysis of the factors that influence persistent GI signs at follow up in post-parvo dogs: We used a generalized linear model (GLM) with binomial errors to investigate the variables associated with persistent GI signs in the post-parvo dogs (see Sect. 5 of the supplementary material for details). There were 15 explanatory variables from the questionnaire and in-hospital management: (1) sex (female, male), (2) purebred (no, yes), (3) lifestyle (indoors only, indoors and outdoors, outdoors only), (4) up-to-date vaccination (no, yes), (5) deworming treatment given (no, yes), (6) medical history (no, yes), (7) metoclopramide treatment (no, yes), (8) number of prescribed antiemetics (0–4), (9) number of prescribed antacids (0–3), (10) number of prescribed antimicrobials (0–10), (11) age of the dog at

admission (days), (12) time of follow up (days), (13) duration of hospitalization (hours), (14) dog weight at admission (kg), and (15) dog body temperature at admission (°C). There were another 9 explanatory variables from the CBC panel: (1) total WBC, (2) segmented neutrophils, (3) band neutrophils, (4) lymphocytes, (5) eosinophils, (6) basophils, (7) monocytes, (8) hematocrit, and (9) toxic change. As before, the continuous variables were transformed to z-scores and we simplified the model by sequentially removing explanatory variables with a p-value > 0.10. For this analysis, there were 31 and 29 post-parvo dogs with and without persistent GI signs, respectively (total of 60 post-parvo dogs).

Abbreviations

CBC: complete blood count

CPV-2: Canine parvovirus type-2

GI: gastrointestinal

PE: parvoviral enteritis

POC: point-of-care

GLMM: generalized linear mixed effects model

GLM: generalized linear model

Declarations

Ethics approval and consent to participate

The University of Saskatchewan Behavioural Research Ethics Board (USask Beh-REB) is constituted and operates in accordance with the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TPCS 2 2018). The USask Beh-REB reviewed this study (application ID = 2716), and the proposal was found to be acceptable on ethical grounds. The USask Beh-REB evaluated the behavioural application form, the consent form, and the questionnaire, and they issued a certificate of approval. All pet owners involved in this study provided verbal informed consent to participate in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request. Requests for the data should be directed to Maarten J. Voordouw

(maarten.voordouw@usask.ca).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KT, APC, and AMF designed the study. KT and AMF collected and interpreted the data. KT and MJV analysed the data. KT, APC, and MJV wrote the manuscript. All authors read and approved the final manuscript.

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Figures

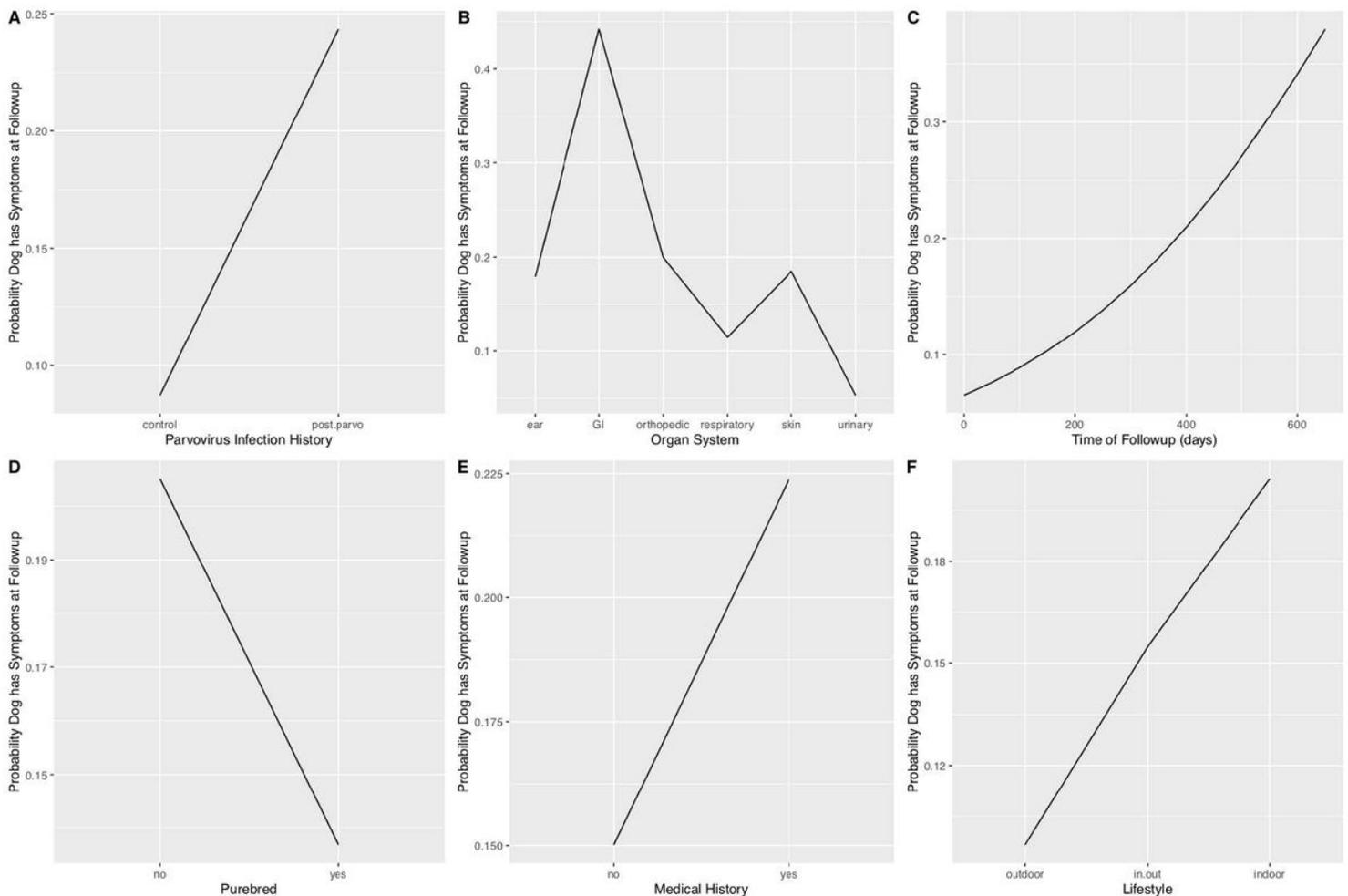


Figure 1

Risk factors for persistent health problems for control and post-parvo dogs. Effects of six explanatory variables on the probability that the dogs have signs in the 6 organ systems at the time of follow up. The

six explanatory variables are as follows: (A) parvovirus infection status (control, post-parvo), (B) organ system (ear, GI, orthopedic, respiratory, skin, urinary), (C) time of follow up with owners, (D) purebred (no, yes), (E) medical history (no, yes), and (F) lifestyle (outdoor, indoor and outdoor, indoor). The sample size included 52 control dogs and 86 post-parvo dogs (total of 138 dogs). The y-axis shows the probability that the dogs will develop signs in the 6 organ systems at the time of follow up. To facilitate interpretation, the continuous variables are shown on the x-axis in their original units rather than in units of standard deviation.

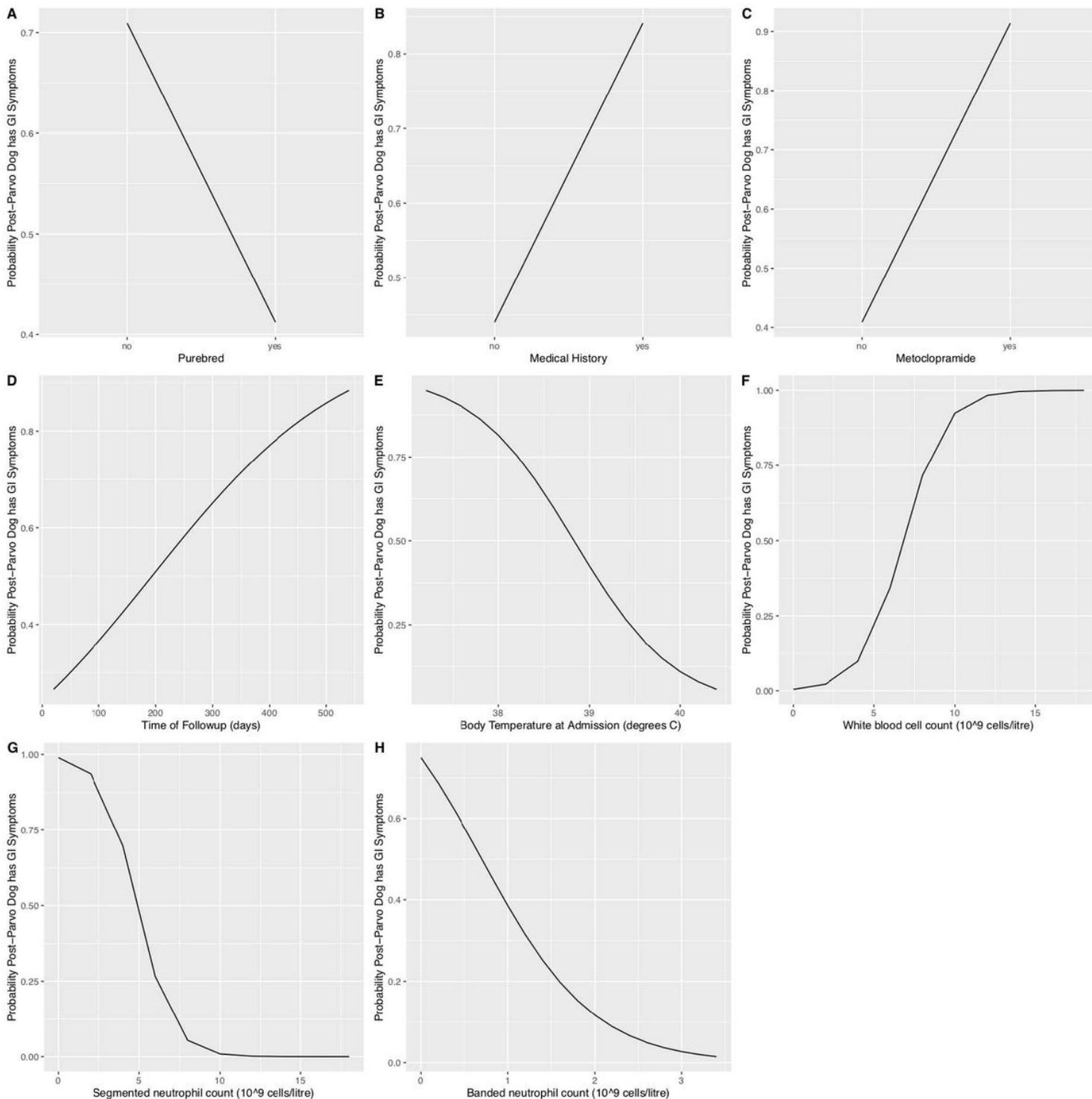


Figure 2

Risk factors for persistent GI signs in post-parvo dogs. Effects of eight explanatory variables on the probability that the post-parvo dogs had persistent GI symptoms at follow up. The eight explanatory variables are as follows: (A) purebred (no, yes), (B) medical history (no, yes), (C) metoclopramide treatment (no, yes), (D) time of follow up with owners, (E) body temperature at admission, (F) white blood cell count, (G) segmented neutrophil count, and (H) band neutrophil count. The sample size included 31 and 29 post-parvo dogs with and without persistent GI signs, respectively (total of 60 post-parvo dogs). The y-axis shows the probability that the post-parvo dogs will develop persistent GI signs. To facilitate interpretation, the continuous variables are shown on the x-axis in their original units rather than in units of standard deviation.

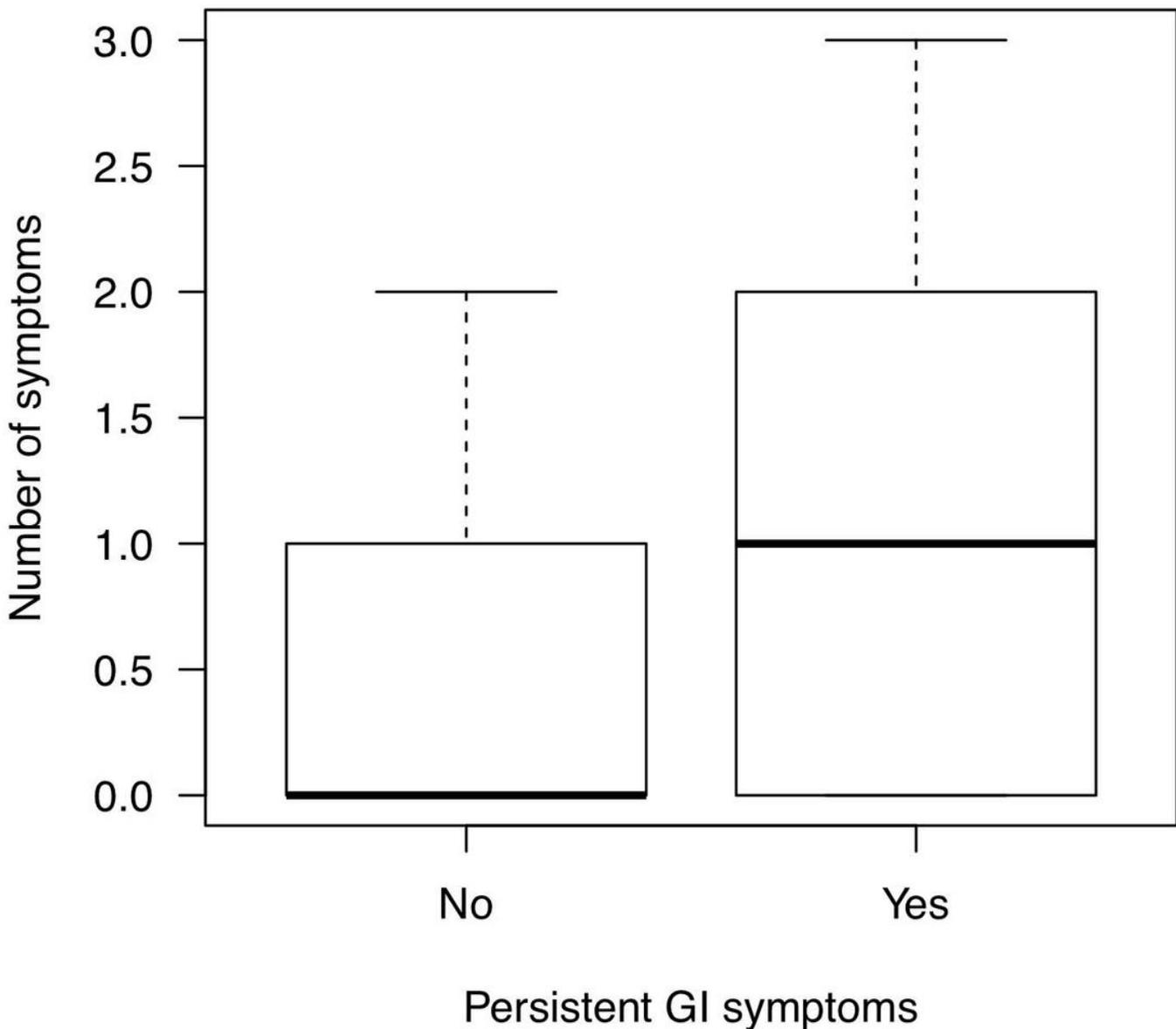


Figure 3

Post-parvo dogs with persistent GI signs have other health problems. Post-parvo dogs with persistent GI symptoms have more symptoms in the other 5 organ systems compared to post-parvo dogs with no persistent GI symptoms. The 5 organ systems include ear, orthopedic, respiratory, skin, and urinary system. The y-axis shows the number of organ systems with signs at the time of follow up. The boxplots show the median (black line), 25th and 75th percentiles (edges of the box), and minimum and maximum values (whiskers).

Supplementary Files

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