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Operative factors associated with short-term outcome in horses with large colon volvulus: 47 cases from 2006 to 2013

L. M. Gonzalez¹, C. A. Fogle^{1,*}, W. T. Baker², F. E. Hughes³, J. M. Law¹, A. A. Motsinger-Reif⁴, and A. T. Blikslager¹

¹North Carolina State University, College of Veterinary Medicine, 1060 William Moore Drive, Raleigh, NC 27607, USA

²Woodford Equine Hospital 3550 Lexington Rd, Versailles, KY 40383, USA

³Peterson and Smith Equine Hospital 4747 Southwest 60th Avenue Ocala, FL 34474, USA

⁴North Carolina State University, Statistics Department, 2311 Stinson Drive, Raleigh, NC 27695, USA

Summary

Reasons for performing the study—There is an important need for objective parameters that accurately predict the outcome of horses with large colon volvulus.

Objectives—To evaluate the predictive value of a series of histomorphometric parameters on short-term outcome, as well as the impact of colonic resection on horses with large colon volvulus.

Study Design—Retrospective cohort study

Methods—Adult horses admitted to the Equine and Farm Animal Veterinary Center at North Carolina State University, Peterson & Smith and Chino Valley Equine Hospitals between 2006–2013 undergoing an exploratory celiotomy, diagnosed with large colon volvulus of 360 degrees, where a pelvic flexure biopsy was obtained, and that recovered from general anaesthesia, were selected for inclusion in the study. Logistic regression was used to determine associations between signalment, histomorphometric measurements of interstitial: crypt ratio, degree of haemorrhage, percentage loss of luminal and glandular epithelium, as well as colonic resection with short-term outcome (discharge from the hospital).

*Corresponding author callie_fogle@ncsu.edu.

Authors' declaration of interests

No competing interests have been declared

Ethical Animal Research

Mucosal biopsies were obtained with the consent of the owners, and biopsy procedures were approved by the NC State University Institutional Care and Use Committee.

Authorship

L.M. Gonzalez contributed to the study design, study execution, data analysis and interpretation, preparation and final approval of the manuscript. C.A. Fogle contributed to the study design, study execution, data analysis and interpretation, preparation and final approval of the manuscript. W.T. Baker and F.E. Hughes contributed to the acquisition of data and final approval of the manuscript. J.M. Law contributed to the study design, study execution and final approval of the manuscript. A.A. Motsinger-Reif is a statistician who contributed to the data analysis and interpretation. A.T. Blikslager contributed to the study design, study execution, data analysis and interpretation, preparation and final approval of the manuscript.

Results—Pelvic flexure biopsies from 47 horses with large colon volvulus were evaluated. Factors that were significantly associated with short-term outcome on univariate logistic regression were Thoroughbred breed ($P = 0.04$), interstitial: crypt ratio >1 ($P = 0.02$) and haemorrhage score ≥ 3 ($P = 0.005$). Resection ($P = 0.92$) was not found to be significantly associated with short-term outcome. No combined factors increased the likelihood of death in forward stepwise logistic regression modelling. A digitally quantified haemorrhage area measurement strengthened the association of haemorrhage with non-survival in cases of large colon volvulus.

Conclusions—Histomorphometric measurements of interstitial: crypt ratio and degree of haemorrhage predict short-term outcome in cases of large colon volvulus. Resection was not associated with short-term outcome in horses selected for this study. Accurate quantification of mucosal haemorrhage at the time of surgery may improve veterinary surgeons' prognostic capabilities in horses with large colon volvulus.

Keywords

horse; large colon volvulus; strangulation; pelvic flexure; surgery

Introduction

Large colon volvulus is an acute, severe abdominal crisis in the horse. Large colon volvulus accounts for 10–20% of horses presented for colic that undergo exploratory laparotomy.

Reported short-term survival rates for horses with large colon volvulus vary markedly, with reported ranges of 35–86% [1–9]. Long-term survival of horses with large colon volvulus is the lowest amongst surgical causes of colic, with a recent report of 48.3% and 33.7% survival following one and 2 years, respectively [7]. The accurate prediction of survival of horses with large colon volvulus has been an ongoing area of interest for many years but remains elusive. Indicators used for prognosis have included preoperative parameters such as plasma lactate levels and abdominal ultrasound findings, operative findings including colonic luminal pressure and surface oximetry, and histomorphometric measurements obtained from pelvic flexure biopsies [4, 6, 8, 10–13]. However, the accuracy of pelvic flexure biopsies to predict short-term survival in cases of large colon volvulus has recently been called into question [4]. Consequently, the most common basis for prognosis continues to be the surgeon's clinical impression of colonic viability based on the appearance of the bowel and the mucosa at the time of surgery [8, 10]. Therefore, there is an important need for objective parameters that accurately predict survival of horses with large colon volvulus. Resection and anastomosis of the large colon is one available treatment option recommended by some surgeons to improve survival outcomes, but recent studies suggest resection has a limited impact on survival [11]. For example, reported short-term survival for horses treated by resecting the large colon are not significantly different than for horses treated by manual replacement of the large colon alone [1, 2, 11]. It is not possible to resect the entire large colon because of its attachment to the base of the cecum and a short area of the dorsal body wall, leading proponents of resection to propose that 'de-bulking' severely injured colon may enhance survival [14]. However, resection of the large colon is time-consuming and expensive. Therefore, in addition to overall evaluation of prognostic

indicators, there is a need to determine if resection and anastomosis improves survival in horses with large colon volvulus so that more informed operative decisions can be made. The aim of this study was to evaluate the potential predictive value of a series of histomorphometric parameters on short-term outcome (discharge from the hospital), as well as the impact of colonic resection on horses with large colon volvulus.

Materials and methods

Study population and inclusion criteria

Adult horses admitted to the Equine and Farm Animal Veterinary Center at North Carolina State University, as well as Peterson & Smith and Chino Valley Equine Hospitals between February 2006 and March 2013 undergoing an exploratory celiotomy, diagnosed with large colon volvulus of 360 degrees where a pelvic flexure mucosal biopsy was obtained, and that recovered from general anaesthesia were selected for inclusion in the study. Pelvic flexure biopsy samples from cases of large colon volvulus were banked for future studies at these institutions during this time. Medical records from these cases were retrospectively reviewed. Perioperative data and survival information were obtained for each horse included in the study, including survival from surgery, and survival until discharge (short-term outcome). However, statistical analyses to identify factors associated with short-term outcome were only performed on cases that fully recovered from general anaesthesia following surgical correction of volvulus. This was done to avoid analysis of horses euthanised at surgery for economic reasons. Mucosal biopsies were obtained from a control group of horses that had pelvic flexure enterotomies for non-strangulating lesions, and used to establish baseline histomorphometric parameters.

Surgical and Perioperative Management

The decision for manual correction of the volvulus alone or correction with large colon resection and anastomosis was based on clinical assessment of large colon viability by the surgeon. The wishes of the owner, based on discussion of surgical assessment, were honoured in all cases, including the decision to perform euthanasia on economic grounds. Factors used to assess colon viability have been previously published and included serosal colour, wall thickness, friability, motility and a palpable pulse [2]. In all cases of large colon volvulus, complete evacuation of colonic contents was based on the degree of colonic distension but was performed in the majority of cases. Pre-operative antibiotics and analgesics therapy for all cases included potassium penicillin G (22,000 U/kg intravenously (i.v.) every 6 h), gentamicin (6.6 mg/kg i.v. every 24 h) and flunixin meglumine (1.1 mg/kg i.v. every 12 h). Post-operative antibiotics and analgesics were continued for at least 5 days and further administration was determined on a per case basis as indicated by evaluation of the patient and results of laboratory tests. Abdominal drains were routinely placed at surgery if a resection and anastomosis was performed and postoperative abdominal lavage was performed. The administration of lidocaine (bolus 1.3 mg/kg i.v. followed by constant rate infusion of 0.05 mg/kg/min i.v.) was based on clinical assessment and presence of ileus. Intravenous fluids were administered as needed postoperatively. Polymyxin B (6000 U/kg i.v. every 12 h) and plasma were administered as needed for treatment of clinical evidence of endotoxemia and hypoproteinemia. The decision to euthanise select horses in the

postoperative period was made on the basis of clinical assessment and further discussion with the owner.

Specimen preparation

All mucosal biopsies were collected at the time of enterotomy and immediately placed in 10% neutral buffered formalin solution. Tissues were routinely processed, embedded in paraffin, sectioned at 5 µm, and stained with hematoxylin and eosin by the same histopathology laboratory (NC State University, College of Veterinary Medicine).

Histomorphometric Measurements

Morphologic changes were evaluated and graded (in the case of epithelial loss) or scored (in the case of haemorrhage) based on established criteria [15] by 2 of the authors (L.M.G., C.A.F.). The evaluators performed histological evaluations independently and were blinded to horse and short-term outcome data. Evaluation by light microscopy (10X and 40X objective lenses) of at least 4 visual fields was performed. The interstitial: crypt ratio was defined as the ratio of the measured lamina propria space occupied by the interstitium and the space occupied by the crypts (Fig 1A). A normal value for the interstitial: crypt ratio was considered to be 1 [15]. The percentage loss of luminal epithelium was based on visual estimation of the percentage of luminal epithelium that was separated from the basement membrane [15]. A grade of 1 to 4 was assigned to estimated ranges of epithelial loss (grade 1, 0–25%; grade 2, 25–50%; grade 3, 50–75%; grade 4, 75–100%). In addition, the percentage of glandular epithelial loss was calculated by measuring the distance from the crypt base to the point of glandular epithelial loss or separation from the basement membrane divided by the total length of the crypt. A haemorrhage score within the lamina propria of the mucosal biopsy was assigned a score of 0 to 4 (score 0, no haemorrhage; score 1, few individual red blood cells (RBCs) within the lamina propria; score 2, increased number of individual RBCs; score 3, appearance of clumps of RBCs; score 4, confluent RBCs obscuring the demarcation of the lamina propria) (Fig 1B).

Digital quantification of haemorrhage

Degree of haemorrhage was digitally quantified by measuring the area taken up by RBCs within a discrete space in an image using a software program (Adobe Photoshop v. 10.0)^a. More specifically, each digital image was imported into a graphic software package (Adobe Photoshop v. 10.0)^a, and the resolution was set to 118 pixels/cm. A 6.4 cm × 6.4 cm square, abutting the muscularis mucosa and centred on the image was selected and transferred into a new canvas. The processed image was then loaded into an image analysis package (ImageJ [a public domain, Java-based image processing program developed at the National Institutes of Health and available as freeware from <http://rsbweb.nih.gov/ij>]^b and the settings were adjusted in order to accurately identify the red blood cells (hue 232/255, saturation 0/255 and brightness 178/255) using the Huang thresholding method [16]. The haemorrhage area was subsequently acquired (Fig 1C). Three images obtained from each evaluating author (L.M.G., C.A.F.) were assessed using the software.

^aAdobe

^bNational Institutes of Health, Bethesda, Maryland, USA.

Data Analysis

Short-term outcome was defined as horses that were discharged from the hospital. Chi square analysis was used to determine if an association existed between institution (NCSU vs. other) and short-term outcome as well as between breed distribution and institution. Age, breed, gender, interstitial: crypt ratio, crypt length, % luminal epithelial loss, % glandular epithelial loss, haemorrhage score, haemorrhage area and whether or not a resection was performed were evaluated for association with short-term outcome. The cut off points for dichotomising the quantitative variables entered in the logistic regression model were determined from measurements obtained from control cases and from previous studies [8, 15]. The normal value for crypt length (392 μ m) was determined by averaging the measurements obtained from the control cases as a normal value has not been previously published. The interstitial: crypt ratio cut off point of ≤ 1 as normal and >1 abnormal, % luminal epithelium loss $<50\%$ as normal and $\geq 50\%$ abnormal, and %glandular epithelial loss $<50\%$ as normal and $\geq 50\%$ as abnormal have been previously described as indicators of severity of injury [8, 15]. The haemorrhage scoring system has also been previously described and a score associated with moderate to severe haemorrhage (≥ 3) was selected as the cutoff for logistic regression analyses [8, 15]. A raw $P<0.05$ was considered statistically significant. To test for potential multivariable models that might be significant, forward selection, using a Bayesian information criteria was performed to build a potential multivariable association model. Using this Bayesian information criteria selection criteria, a null model was built. Modelling was performed in Stata V11^c. To test for concerns of potential confounding variables for the one statistically significant variable after multiple comparisons, multiple logistic regression modelling was performed, where these variables were entered to test for the significance of each of these variables after correcting for the other. While true estimates of predictive values are not possible in the current retrospective study, contingency table measures of model fit (including sensitivity, specificity, and a contingency table estimate of negative and positive predictive value) were calculated.

The sensitivity (the probability that a truly affected individual would test positive), specificity (the probability of a surviving horse having a negative test result) and accuracy (the sum of the number of true positives and true negatives divided by the sum of the number of true positives, false positives, false negatives and true negatives) of haemorrhage score and area for prediction of death and short-term outcome in horses with large colon volvulus were calculated. Haemorrhage area calculations were used to generate a probability of death curve. The probability of death was calculated by counting the number of deaths as haemorrhage area incrementally increased and dividing by the total number of individuals with haemorrhage area measurements equal to or less than each measurement. A standard error of mean was calculated and represented graphically for each measured haemorrhage area by averaging all of the measured areas for a single case (6 measurements per case; 3 images per case from each author; L.M.G., C.A.F.).

A Fisher's exact test was used to test for an association between surgical resection and haemorrhage score.

^cStataCorpLP, College Station, Texas, USA.

Results

Pelvic flexure biopsies from 71 cases of large colon volvulus were obtained. Twenty-seven cases with biopsies from NCSU, 43 from Peterson and Smith Equine Hospital and one from Chino Valley Equine Hospital were evaluated. Of all horses admitted for surgery, 36 of 71 (51%) survived until discharge. Of the 71 large colon volvulus cases taken to surgery, 24 horses were not recovered from anaesthesia, 5 having intra-operative colon rupture, 5 due to owner declining further intervention despite the surgeon's recommendation and 14 because the surgeon's prognosis was grave and the owner elected euthanasia. Forty-seven horses with large colon volvulus met the inclusion criteria for further analyses. Of cases with large colon volvulus, the breeds were Thoroughbred (n = 22), Quarter Horse (n = 10), Warmblood (n = 9), Arabian (n = 2), Paso Fino (n = 2), Tennessee Walking Horse (n = 1), and American Paint Horse (n = 1). The breed distribution for each of the hospitals was Warmbloods (23%), Quarter Horses (59%), and other breeds (10%) from NCSU and Thoroughbreds (73%), Warmbloods (17%), Quarter Horses (3%) and other breeds (7%) from the 2 other contributing hospitals. The mean age was 9 years (range, 2–23 years), with 3 horses of unknown age. There were 35 mares, 10 geldings and 2 stallions. Thirty-six of 47 (76.6%) survived until discharge from the hospital. Nineteen of 25 (76%) horses that had manual reduction alone survived, whereas 17 of 22 (77%) that had a resection and anastomosis following correction of large colon volvulus survived. All horses in which a large colon resection and anastomosis was performed that recovered from general anaesthesia were from Peterson and Smith Equine Hospital except for one performed at Chino Valley Equine Hospital. Two large colon resections were performed at NCSU, one was ultimately euthanised intra-operatively due to systemic deterioration under general anaesthesia and another was unable to recover and was humanely euthanised upon the owner's request. All anastomoses were performed as end-to-end as described [2].

Fourteen horses that underwent exploratory celiotomy necessitating pelvic flexure enterotomy for reasons other than a strangulating lesion were used as controls. Of the group of control horses, the breeds were Thoroughbreds (n = 4), Quarter Horses (n = 3), Morgans (n = 2), Warmbloods (n = 2), draught horse (n = 1), Tennessee Walking Horse (n = 1) and a pony (n = 1). The mean age was 11 years (range, 1–27 years). There were 6 mares and 8 geldings. The average crypt length in control horses was 392 μ m. The mean interstitial: crypt ratio was 0.9 (standard deviation $\pm$ 0.3). The median percent glandular epithelial loss and grade of luminal epithelial loss were 0 (inter-quartile range, 0–0.478), and 1 (IQR 1–2.5) respectively. The average haemorrhage score was a score of 1 and the average haemorrhage area was 0.2 ± 0.2 ppi.

Factors that were nominally significantly associated with short-term outcome on univariate logistic regression were Thoroughbred breed (P = 0.042), interstitial: crypt ratio >1 (P = 0.022) and haemorrhage score ≥ 3 (P = 0.005) (Table 1). Twenty-one of 21 (100%) cases of large colon volvulus with luminal epithelium loss <50% survived, whereas 15 of 26 (58%) of horses with luminal epithelium loss $\geq 50\%$ survived. Of cases of large colon volvulus with glandular epithelial loss <50%, 35 of 44 (80%) survived. Two of 3 (67%) of large colon volvulus cases with $\geq 50\%$ glandular epithelia loss survived. The interstitial: crypt ratio >1 and haemorrhage score ≥ 3 were strongly associated with non-survival (Table 1).

Haemorrhage score was accurate for prediction of death and survival in horses with large colon volvulus in that 7 horses were accurately predicted to die out of 13 horses with a haemorrhage score ≥ 3 , (sensitivity, 64%; 95% CI, 0.354–0.848; positive predictive value (PPV), 54%), and 30 horses were accurately predicted to survive out of 34 with a haemorrhage score <3 , (specificity, 83%; 95% CI, 0.681–0.921; negative predictive value (NPV), 88%). Thoroughbred breed was slightly protective (Table 1). In the univariate logistic regression model, resection was not found to significantly impact short-term outcome (Table 1). However, in cases with haemorrhage score <3 , 18 of 22 (82%) without resection survived and all 12 horses (100%) with resection survived. When the haemorrhage score was ≥ 3 , one of 3 (33%) horses without resection survived and 5 of 10 (50%) horses with resection survived. A Fisher's exact test for association of haemorrhage score with survival was not found to be statistically significant ($P = 1.00$). In a forward stepwise logistic regression model, no combined factors increased the likelihood of death.

In multivariable analysis testing for potential confounding and collinearity amongst the 3 nominally associated variables: Thoroughbred breed, interstitial: crypt ratio >1 , and haemorrhage score, results indicated that the haemorrhage score had the strongest association, and the only statistically significant association. When controlling for interstitial: crypt ratio and breed, haemorrhage score was still significant ($p < 0.03$), and the other 2 variables were no longer significant when haemorrhage score was included in the model ($p > 0.05$ in all cases).

The statistical strength of the haemorrhage score and its strong association with death led us to pursue a more objective means to measure the amount of haemorrhage within the lamina propria. Haemorrhage score was 79% accurate for prediction of death and short-term outcome. Digital quantification of haemorrhage severity was therefore calculated to address the subjectivity of the haemorrhage grading system. A haemorrhage area ≥ 0.84 ppi was associated with a 26-fold increased likelihood of non-survival (OR 26; CI 2.9 – 230.3; $P = 0.003$). Haemorrhage area was 79% accurate for prediction of death and short-term outcome in horses with large colon volvulus with 10 horses predicted to die out of 19 with a haemorrhage area ≥ 0.84 (sensitivity, 91%; 95%CI, 0.623–0.984; PPV, 53%), and 27 horses predicted to survive out of 28 with a haemorrhage area <0.84 ppi, (specificity, 75%; 95%CI, 0.589–0.863; NPV, 96%). No horses died with a haemorrhage area measurement <0.2 ppi. Only one horse died with a haemorrhage area measurement <0.84 ppi (Fig 2). When the haemorrhage area measurement was ≥ 0.84 ppi, 10 of 19 (53%) animals died.

Discussion

There is a need for objective parameters that associate the severity of colonic injury with survival in horses with large colon volvulus. Since the information gained from histomorphometric assessment is limited to the post-operative period in most practices, the more readily available pre and intraoperative parameters such as heart rate, packed cell volume, and plasma lactate have remained commonly utilised prognostic tools despite their indirect indication of colonic compromise. We therefore reasoned that more in depth histological evaluation, including objective measurement of mucosal haemorrhage, may provide a more accurate assessment of the likelihood of short-term outcome in the

postoperative period. In addition, no study has performed risk analyses to evaluate if large colon resection improves short-term outcome in cases of large colon volvulus.

Histomorphometric analysis of colonic tissue has long been considered the gold standard for assessing tissue viability [8, 15]. The observation that the histologic changes observed at the pelvic flexure are uniformly distributed throughout all colonic tissue involved in the volvulus further contributed to the perceived value of histologic assessment in grading tissue damage [17]. Specific histomorphometric parameters found to be associated with loss of intestinal viability and death in cases of large colon volvulus are interstitial: crypt ratio ≥ 3 and glandular epithelial loss $>50\%$ [8]. The basis for increased interstitial: crypt ratio in cases of severe injury has been attributed to increased haemorrhage that causes architectural damage as the interstitium expands and glandular epithelium is compressed [10, 17]. The association of the degree of glandular epithelial loss with loss of tissue viability has been attributed to the integral role of the glandular epithelium in the renewal of the mucosal lining [8, 10]. Recently, though, the reliability of histomorphometric grading of tissues derived from pelvic flexure biopsies in cases of large colon volvulus has been questioned [4]. Levi *et. al.* determined that short-term survival could not be accurately predicted by histopathologic evaluation, whereas heart rate at admission, as well as heart rate and packed cell volume 24 hours postoperatively were significantly associated with survival [4]. However, in that study, histopathologic measures were not assessed individually, but were grouped and then assigned a numerical score [4]. We found that luminal epithelium loss and glandular epithelial loss were difficult to measure accurately and seemed to be susceptible to processing artifact. Therefore our overall impression was that luminal epithelium loss and glandular epithelial loss were not consistent measures of tissue damage. Additionally, within our study population, a small number of cases had an interstitial: crypt ratio of ≥ 3 . Since an interstitial: crypt ratio measurement ≤ 1 is accepted as normal, and the mean measurement of the control cases was <1 , we used >1 as a cut-off value. This led to the finding that horses with an interstitial: crypt ratio >1 were 12-fold more likely to be non-survivors during hospitalisation. However, interstitial: crypt ratio did not further increase the likelihood of non-survival when combined with other factors when performing multiple logistic regression.

Interestingly, the degree of haemorrhage (as assessed by haemorrhage score), a parameter not associated with death in any other study, was found to have a strong statistical association with non-survival. This was of particular interest since determining haemorrhage within tissue would seem to have a greater potential for use in clinical practice in the absence of a pathologist at the time of surgery. The accuracy of the haemorrhage score in predicting survival or non-survival was 79%. However, the haemorrhage score was most useful in predicting which horses would mostly likely survive. For example, those horses predicted to survive based on the haemorrhage score would likely survive but those predicted to die may actually survive (PPV 54%; NPV 88%; sensitivity 64%; specificity 83%). Because of the low sensitivity based on this technique for the measurement of haemorrhage and to further determine the reliability and strength of the association of haemorrhage with death, we developed a more objective measure of this parameter using morphometric software. The strong association of poor short-term outcome with increasing

area of haemorrhage may be due to the architectural damage that results from extravasation of red blood cells into the lamina propria. The resulting increase in lamina propria area may contribute to the detachment of the epithelial lining which results in a breakdown of barrier function, although this was difficult to appreciate in the histologic sections (Fig 1). An additional mechanism of injury caused by the presence of increased red blood cells within the lamina propria may be release of free radicals and subsequent lipid peroxidation that would be expected to contribute to tissue damage [18, 19]. Others have indicated that a return of normal mucosal colour following surgical correction of large colon volvulus intraoperatively is an indicator of viability, as opposed to mucosa that remains black after correction of volvulus that indicates a poor prognosis for survival [20–22]. We speculate that this gross black appearance is directly associated with haemorrhage within the lamina propria, suggesting that accurate quantification of mucosal haemorrhage at surgery may improve veterinary surgeons' prognostic capabilities.

One limitation of the current study was the exclusion of cases that did not recover from general anaesthesia. An owner's decision to euthanise is based on many factors that may include economic concerns or the fact that a surgeon can rarely provide a definitive prognosis. Currently, the intraoperative decision to resect the large colon is based on surgeon preference according to the perceived level of colonic injury, and prior experience with the techniques. In cases of large colon volvulus, there is rarely a clear demarcation between viable and nonviable intestine, which makes the site and utility of large colon resection unclear [23]. Therefore, data on the survival of horses with large colon volvulus that undergo resection as compared to those that do not is critically needed to guide intraoperative decision making. The overall short-term survival of horses that recovered from surgery in our study where resection and anastomosis was performed was 77%, similar to that found by Mathis *et al.*, whose case inclusion criteria similarly only evaluated horses that recovered from anaesthesia [11]. These findings were substantially higher than the 47% reported by Driscoll *et al.*, however that study population included horses euthanised intraoperatively [1]. Despite an encouraging short-term outcome among the horses that recovered from general anaesthesia in our study, resection was not found to be statistically associated with an increased likelihood of short-term outcome. Furthermore, no parameters combined with resection in the multivariable model strengthened its association with short-term outcome. However, the population size was small ($n = 47$), reducing the statistical power necessary to properly interpret the negative finding of a lack of effect of resection or to build multivariable models. Additional studies using a larger sample size will be necessary to obtain more definitive evidence for or against large colon resection and anastomosis as a treatment for large colon volvulus. Additionally, this retrospective study could not control for the individual reasons surgeons selected cases for resection. Additional prospective studies are warranted to control for the many clinical decisions that are necessary when managing a horse with large colon volvulus. Future work on large colon volvulus will be directed towards further determining the impact of resection in these cases and to provide a surgery table-side test that accurately measures haemorrhage as a tool to more accurately guide surgical decisions.

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Fig 1.

Histomorphometric evaluation of colonic mucosal biopsies of horses with and without large colon volvulus. (A) The interstitial (I) crypt (C) ratio was defined as the ratio of the width of the inter-crypt lamina propria to the width of the crypts. The crypt length (CL) was also measured. (B) Haemorrhage score within the lamina propria of the mucosal biopsy was assigned a score from 0 to 4 (score 0, no haemorrhage; score 1, few individual red blood cells (RBCs) within the lamina propria; score 2, increased number of individual RBCs; score 3, appearance of clumps of RBCs; score 4, no clear demarcation between RBCs, obscuring the lamina propria). (C) Haemorrhage area was digitally quantified using ImageJ v.1.46[®].

Fig 2.

Box and whiskers plot of horses that were euthanised or survived based on haemorrhage area. Haemorrhage area measured from biopsies obtained from cases of large colon volvulus indicating that although most horses with a haemorrhage area less than 0.84 survived ($n = 27$) there was overlap in horses with a measurement greater than 0.84 ppi in that approximately equal numbers of horses were euthanised as compared to those that survived. Boxes represent interquartile range, single dividing line is the median, error bars represent standard deviation, and dots represent outliers.

Table 1

The univariate logistic regression variables tested for association with outcome
 Univariate logistic regression analysis of factors potentially associated with death in cases of large colon volvulus.

Variable	Category	No. (%) Horses	OR	95% CI	P
Crypt Length					
	392	17(36.2)			
	<392	30(63.8)	1.0	0.24–4.03	0.988
Age					
	9	23(48.9)	0.9	0.22–3.64	0.870
	<9	21(44.7)			
	Unknown	3(6.4)			
Breed *					
	TB	22(46.8)	0.2	0.03–0.94	0.042
	Non-TB	25(53.2)			
Gender					
	Male	12(25.5)			
	Female	35(74.5)	0.5	0.12–2.15	0.352
Luminal Epithelial Loss					
	50%	26(55.3)	-	-	-
	<50%	21(44.7)			
Glandular Epithelial Loss					
	50%	3(6.38)	1.1	0.10–11.8	0.937
	<50%	44(93.6)			
Interstitial: crypt *					
	>1	26(55.3)	13	1.44–108	0.022
	1	21(44.7)			
Mucosal Haemorrhage *					
	3	13(27.7)	8.8	1.94–39.6	0.005
	<3	34(72.3)			
Surgical Correction					
	Resection	22(46.8)	0.9	0.24–3.61	0.918

Variable	Category	No. (%) Horses	OR	95% CI	P
Hospital	Manual	25(53.2)			
	NCSU	17(36.2)	0.4	0.09–1.46	0.16
	Other	30(63.8)			

Data represents information for 47 horses with large colon volvulus. The OR represents the odds that a horse with large colon volvulus will not survive.

* Variable found to be statistically significant ($p<0.05$).
OR = Odds ratio. CI = Confidence Interval. P = P value.