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#### **Review Article: Celebrating 50 years of Equine Veterinary Journal**

### Fifty years of colic surgery

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#### **Summary**

Colic surgery is one of few treatments in which a veterinarian can use a skill to save an animal's life from a deadly disease within a short timeframe. Unfortunately, such success is not achieved without considerable risk for surgical failure, which is responsible for most complications in the immediate post-operative period. The last 50 years have witnessed considerable improvements in colic surgery, although a ranking of the most important ones might not meet with universal agreement. Teamwork plays a critical role in the final outcome, starting and finishing with the referring veterinarian and owner. These individuals are responsible for promptly transferring the horse to a surgical facility and then dealing with aftercare and delayed complications. The surgeon is responsible for the intervening steps, including the decision on the need for surgery, and works with the anaesthesiologist to help a metabolically challenged patient to tolerate surgery and anaesthesia. Although early referral and improved diagnostic procedures can have a positive influence on survival, perceived improvements in surgery and anaesthesia need to be reviewed with some circumspection. Although more rigorous definitions and statistical analyses used in recent studies can invalidate comparisons with older studies, complication rates appear to be on the rise, despite putative improvements in dealing with them. This trend tends to diminish the value of colic surgery through increasing costs, overreliance on post-operative pharmacological management, growing pessimism, high rates of intraoperative euthanasia, and possibly reduced long-term survival. Future efforts should address these concerns, mostly through emphasis on prompt referral, good surgical technique and reducing the cost of colic surgery to an affordable level that saves more lives.

Keywords: complications; colic; horse; surgery; survival

#### Introduction

Fifty years ago, as is still the case today, evaluation of the gastrointestinal tract by rectal palpation was recognised as a key clinical skill for examining the horse with colic [1]. Horses with gastrointestinal diseases, including colic, constitute the largest proportion of horses admitted as emergencies to referral hospitals [2,3], and colic has been ranked as the top medical problem treated by practitioners [4]. Colic episodes per 100 horse/equid years can range from 3.5 to 10.6 [5–9] or as a percentage of equids at risk from 2.8 to 2.9% [10,11] according to farm-based studies or owner reported data. In the general equine population, approximately 1.4–17.5% of horses with colic require or undergo surgery [5,6,12–16]. Improvements in surgical outcomes in horses with the most severe forms of colic have been attributed to early referral, advances in surgery, safer anaesthesia and improved aftercare [17,18]. Therefore, the purpose of this review is to critically assess these claims, with emphasis on those aspects of colic surgery that we can control.

#### Methods of data analysis

Statistical methods and inclusion criteria currently used to analyse survival data are more rigorous than those used in older studies, which complicates comparisons between studies over time. A common epidemiological approach to the study of colic and its causes uses the relative risk or risk ratio (RR) and the odds ratio (OR) [19]. The RR is determined in cohort studies as the ratio of the disease prevalence in exposed animals compared to its prevalence in nonexposed animals [19]. In cohort studies, a group exposed to the hypothetical causal agent or to a treatment is compared with a group not exposed to these factors [19], as in a recent study on the efficacy of lidocaine in horses after colic surgery

[20]. The OR is used in case–control studies as a measure of the odds of exposure to a factor in the cases to the odds of exposure in control subjects [19].

Most survival studies are retrospective in design and therefore can produce bias from flaws in definitions, data gathering and lack of randomisation [21]. Many studies examine short-term survival, which applies to either all horses undergoing surgery or only those that recovered from anaesthesia and are subsequently discharged from the clinic. Short-term studies to discharge provide useful information for the surgeon and owner about prognosis and about expected post-operative complications after different diseases and surgical procedures. By virtue of design, important information is disseminated in a timely manner by such studies. However, short-term data provide an incomplete picture, because discharged horses are still at risk of delayed complications and mortality related to the surgery, as from adhesions and recurrence of the original disease [22–24].

Long-term survival studies are preferred over short term and are usually longitudinal and prospective in design [25]. Long-term survival is generally modelled in terms of two related functions, survivor/survival function and hazard function [26]. The survival probability or survival function is the probability that an individual survives from the point of interest (recovery from general anaesthesia after surgery) to the specified future time period [26]. The hazard function is the probability that an individual under observation at a specific time has an event (e.g. death) at that time [26]. By comparison with survivor function, which focuses on an event (e.g. death) not happening, the hazard function takes the opposite approach [26].

The survivor function is usually estimated by the Kaplan–Meier analysis (Fig 1), which assesses the probability of survival using the number at risk at the time of each death [26–28]. The problem with survival analyses is that a proportion of the cases do not die by the end of the study period

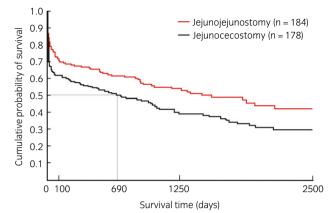


Fig 1: Kaplan–Meier survival curve after surgery to demonstrate the difference over time between two anastomoses, jejunojejunostomy vs. jejunocaecostomy. Note the rapid decline in both graphs during the early stages, which can be explained by post-operative deaths between anaesthetic recovery and hospital discharge [25]. The mortality rate then decreases over the first 100 days to assume a slower decline [25]. The fine line indicates the median survival time at 23 months for the jejunocecostomy group. Reproduced with permission from Equine Veterinary Journal Ltd. [175].

and their survival times will therefore be unknown [26]. This can also arise if a patient cannot be followed to its death by the time the study closes because it is lost to follow-up [26] for a number of reasons (e.g. sale, owner move or patient still alive at last recording interval). In such cases, the survival function extends beyond the end of the follow-up period for that individual, a situation referred to as right censoring [26]. A steep decline in survival early in the post-operative period for a disease or treatment [25] indicates a poor prognosis [26]. The 95% confidence limits of the survivor function can be determined, but these are usually wide at the end of the curve because of right censored cases [26]. The Logrank test is the most common and probably the most robust nonparametric test to compare two or more survival curves, such as those generated by two different surgical procedures or two different diseases [26,27,29].

The Kaplan–Meier analysis of survival data produces the median survival time (Fig 1), which is the time of recovery from surgery to when 50% of the subjects of interest have died [27]. The mean is not used because of the large skew that usually develops in data distribution [26]. Median survival times generated by long-term studies on colic survival differ considerably (Table 1), in contrast with survival rates for hospital discharge (see below). Median survival time is more likely to be meaningful when almost every patient has died, the number of patients is large, and the graph falls rapidly through the whole region between 70% and 30% alive [27]. These conditions are rarely met in colic survival studies. The starting point at recovery from anaesthesia is more commonly used [25,30-36] than starting at hospital discharge [37,38], because it includes cases with the highest mortality from early post-operative complications (Fig 1) [25] and therefore more accurately reflects the prognosis for the disease or its treatment [26]. An all-cause mortality is a more robust end point in survival analyses [26] than right censoring horses that die from a cause other than colic [37,38], because the latter approach relies too heavily on owner assessment of cause of death and falsely improves the survival curve [27].

The Cox Proportional Hazards Model is a survival analysis regression model that is commonly used to explore univariable and multivariable relationships in survival data in medical [29,39] and veterinary research [25]. The limitation of the univariable analysis is its focus on survival according to one factor of interest, and not accounting for the impact of confounding factors or covariates that could affect outcome [28,31]. The univariable analysis is used first to determine those variables that have a reasonable association with the disease and then these are examined further in multivariable comparisons [19,29].

In a final multivariable analysis, continuous and categorical variables with some evidence of association with survival in the univariable analysis are used to develop the final model [39,40]. If a large number of factors are to

be examined, with little information about the role of each one in prognosis, stepwise methods are used [39]. One approach is backward elimination, in which all covariables are included at the start and then eliminated, and another is forward selection, in which no covariables are included but some are added according to statistical significance at some predetermined level [41]. How well the model represents the data is determined by goodness-of-fit [42] or a likelihood ratio test [20]. Sample size is an important consideration in such studies because small data sets might not reveal the impact of some covariables [39]. Another approach to assess covariables in survival analysis is to use stratified analyses, when appropriate, such as comparing treatment groups adjusted by strata for age effects [29].

The paucity of cases and therefore low power for analysis of survival and risk factors in a single hospital is resolved by multicentre studies, such as the randomised controlled trial (RCT) [21]. Multicentre trials should be conducted in a prospective manner to reduce bias, and they require total compliance from enrolled hospitals, investigator blinding, funding to support research-related expenses, and owner and institutional approval when an interventional design could deny one group of horses a potentially effective treatment [19,43]. In multicentre survival analyses, homogeneity of management factors is assumed across hospitals so that diagnostic procedures and treatments are close to identical [26]. This is not always true, as evident in a study that examined a standardised group of surgical colic cases from two large referral hospitals [43]. The wide range of different drugs and strategies used complicated interpretations of drug effects, breed and hospital factors constituted major sources of variability, and differences in clinician decision-making between the two hospitals were important confounders [43].

#### Survival rates reported before 2000

In one of the earliest retrospective studies of a series of cases from a single hospital, Pearson et al. [44] reported that 10 of 16 horses (63%) recovered from anaesthesia were successfully treated by surgery. In other early studies on colic surgery, mortality was greater in horses with small intestinal lesions than with more distal lesions and with strangulating obstructions compared with nonstrangulating diseases [45]. However, subsequent studies reported some evidence of improvement over time with small intestinal surgery [46,47]. A report from a German hospital on 613 horses in which colic surgery was completed (recovered from anaesthesia) from 1979 to 1981 revealed 87.7% short-term survival (alive at discharge from the hospital) for a variety of small and large intestinal lesions, short-term survival was 82% [48].

Whereas previous studies had examined survival to discharge or shortterm survival, a study on 140 horses that had small intestinal resection and anastomosis between 1968 and 1986 included long-term survival data [30]. This study demonstrated improved survival rates in horses that had surgery towards the end of the study period, with a median survival time for surgery before 1 January 1980 of 8 days, compared with a median survival time after that date of 7.3 months (Table 1) [30]. Other signs of improvement over time in this era were reflected in clinical and laboratory findings at presentation in horses admitted after 1980 compared with previous admissions [30].

#### Survival rates reported from 2000 to 2017

Short-term survival rates in horses that had surgery of the small intestine and were allowed to recover from anaesthesia ranged from 68% to 100% in reports published between 2000 and 2017 [31,33–38,49–67]. Although these results would suggest a considerable improvement over studies from previous decades, many of the more recent studies failed to match the high survival rates reported from one hospital for small intestinal lesions before 1981 [48]. Also, the median survival times after small intestinal surgery reported after 2000 ranged widely from 18 days to 120 months (Table 1), and improvements in long-term survival between 1989 and 2017 were not evident in all studies (Table 1). This is consistent with the conclusion from another study that reported little if any change in survival after colic surgery in a 20-year period before 2003 [68]. Of some concern is evidence that cases in more recent reports probably were referred more promptly than in

TABLE 1: Median survival times in long	g-term studies on small intestinal surgery
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Authors [reference number]	Period covered	Type of surgery	Median survival time
, .	1968–1986	Resection and anastomosis	27 days
	Before January 1, 1980	Resection and anastomosis	8 days
	After January 1, 1980	Resection and anastomosis	7.3 months
Freeman et al. 2000 [31] 1994–1999	1994–1999	No resection	>24 months
		Jejunojejunostomy	>24 months
		Jejunocecostomy	>24 months
Proudman et al. 2002 [25] 1998–2000	1998–2000	Epiploic foramen entrapment	13.3 months
		Ileal impaction	>16.7 months
		Pedunculated lipoma	>16.7 months
		Jejunal strangulation	>16.7 months
Garcia-Seco et al. 2005 [32] 1987–2002	1987–2002	Lipoma only – all treatments	5 months
		Lipoma only – jejunocecostomy	3 months
		Lipoma only – jejunojejunostomy	>13.3 months
Proudman et al. 2005 [40] 1998–2004	1998–2004	All lesions – not epiploic foramen entrapment	63 months
		Epiploic foramen entrapment	25 months
		Repeat celiotomy	16.3 months
Proudman et al. 2007 [175] 1998–2006	1998–2006	Jejunojejunostomy	49 months
		Jejunocecostomy	23 months
Fogle et al. 2008 [33]	1994–2002	All lesions	18 days
	2003–2005	All lesions	>6 months
Freeman and Schaeffer 2010 [34] 1994-	1994–2005	Jejunocecostomy (HS)	97 months
		Jejunocecostomy (S)	96 months
Freeman and Schaeffer 2011 [35] 1993–2002	1993–2002	Jejunojejunostomy (strangulated IL)	120 months
		Jejunojejunostomy (strangulated CL)	72 months
		Jejunojejunostomy (nonstrangulated IL)	10 months
Freeman et al. 2014 [36]	1996–2011	No resection – strangulating lesions	120 months
Salem et al. 2016 [20] 2004–2014	2004–2014	Epiploic foramen entrapment	12.3 months
		Ileal impaction	>26.7 months
		Pedunculated lipoma	>26.7 months
	Idiopathic focal eosinophilic enteritis	>26.7 months	
Bauck et al. 2017 [184]	1998–2015	Repeat celiotomy after jejunal strangulation	90 months
	2011–2014	NS – Mortality in French horses	150 months <sup>a</sup>
		NS – Mortality in French horses	172 months <sup>b</sup>

Data are provided in chronological order with median survival times reported in some studies or determined from Kaplan–Meier graphs (Fig 1) and were converted to months when  $\geq$ 30 days. All data were from point of recovery from anaesthesia. IL, Interrupted Lembert; CL, Continuous Lembert; HS, Handsewn anastomosis; NS, No surgery; S, Stapled anastomosis; When median survival time is recorded as > the specified time period, follow-up ended at that time, so the true median survival time was not reached.

<sup>a</sup>In this citation, data are for saddle horses  $\geq$ 2 years old as determined from the survival curve with 0.5 as the median.

<sup>b</sup>This is from the same citation but given as the mean and median ages at death in supplementary data.

the past [30], which should have improved their survival rates (see below). However, some more recent data reveal median survival times after small intestinal surgery of 120 months [35,36], close to the median survival times determined in saddle horses in a large equine population (Table 1 [69]).

Recent studies reveal a high rate of return to resuming or starting in a sporting activity (76–86.1%) in horses that are discharged after colic surgery, and that 65–83.5% can achieve the same or a better performance level after surgery according to their owners [ $6_{2,70-73}$ ]. One study reported that Thoroughbred racehorses had similar performance variables after colic surgery as their untreated cohorts [74]. These findings are comparable to the rates of 93–94% return to intended activity for survivors between 1976 and 1991 [75,76], although comparisons between studies can be challenged by differences in populations and definitions.

#### Survival rates in last 50 years

When the preceding information is considered, reported survival rates during the last two to three decades might represent a slower gain compared with progress made in the previous decades. However, the starting point for early improvements approximately 50 years ago was from a pronounced nadir [30,44–46]. Also, many advances in colic surgery have emerged that should improve survival in the future. Evidence that old horses are equally as likely to survive colic surgery as

young horses [55,77,78], and foals can have discharge rates comparable to adults [73,79] should improve access to surgery in these groups. Modern absorbable suture materials and methods of application, as well as post-operative wound protection and support have reduced complications related to the abdominal incision [80-82]. The favourable response to nonsurgical treatment of common colonic diseases, such as right dorsal displacement of the colon (RDDC [83]) and nephrosplenic entrapment (NSE [84]) represent advances in management of colic. Recognition of the risk for colonic displacements to recur, such as RDDC [24] and NSE [85], has led to surgical prevention by colopexy [86] or colon resection [87]. Although laparoscopy is beyond the scope of this review, many laparoscopic methods have been developed to prevent recurrent colic, such as nephrosplenic space ablation [88], vaginal ring closure [89], and closure of the epiploic foramen by a mesh implant [90] or titanium helical coils [91]. Insertion of a specially constructed mesh at time of open correction of EFE represents a simple method of preventing recurrence of this disease [92]. Improvements in diagnosis will be addressed below.

#### Role of early referral in survival

The major benefit of early referral is reducing the severity of tissue injury and resulting endotoxaemia/systemic inflammatory response syndrome (SIRS) on admission [20,30]. Failure to refer promptly leads to deteriorating cardiovascular status, reflected through such negative prognostic indicators as elevated PCV [20,93–96], elevated heart rate [20,30,94,95,97,98], decreased total protein [40,52] and increased plasma lactate concentration [99,100].

The effect of early referral on survival is difficult to assess because measurable data are not readily obtained and the relationship between duration of colic and post-operative survival tends to follow a nonlinear pattern [56,76,93,101]. This pattern can be explained by the nature of diseases involved. For example, a horse with a severe and acute abdominal disease is usually referred without delay, but such diseases can have low survival rates [68], e.g. large colon volvulus (LCV). In contrast, when colic persists for several days, the underlying disease is generally less severe, such as a colon displacement or impaction, and is associated with less tissue damage and a more rapid recovery [68].

In one study, horses admitted after 1980 had lower reflux volume, PCV, and heart rate, and higher total leukocyte count at presentation compared with previous admissions [30]. These changes were associated with an improved survival over these timeframes [30], and probably marked the time point when the benefits of prompt referral became evident. An improvement in survival rates and a corresponding decrease in intraoperative euthanasia in horses with LCV over time [102] could also be attributed to a trend towards earlier referral in the recent cases. This is consistent with a study on horses with LCV that demonstrated an 86% survival rate associated with a decrease in colonic biopsy score by  $\sim 0.5$ per year, also attributed to earlier referral [103]. In a recent study on Thoroughbred mares with LCV, in which the overall survival to discharge was 88%, colic duration before admission was significantly related to survival [96]. Such survival rates for LCV are considerable improvements over the 34.7% reported in an earlier study, in which delays in referral were considered responsible for the poor outcome [104].

The favourable survival rates reported when strangulated small intestinal segments were judged to be viable and not require resection [32,36] clearly demonstrate the benefit of surgery before irreversible intestinal damage has developed. In one study, the mean duration of colic was significantly less for those horses that did not require a resection versus those that did [31]. Also early referral could reduce the risk of complications, such as post-operative reflux (POR) after strangulating lesions and diarrhoea after nonstrangulating lesions [105].

Some small intestinal strangulations might benefit from early referral through easier correction. For example, a 92% survival has been reported in horses treated by closed manual reduction of an inguinal hernia [106], compared with a short-term survival rate of 56-85.1% for those treated by surgery [51,56,68,107-111]. Presumably closed manual reduction is possible early in the disease course whereas surgery is required for hernias of sufficient duration to incur ischaemic damage [106]. In one multicentre study of this disease, 69% of affected horses survived if admitted before 10 h from onset of pain compared with 29% in those admitted later [107]. In 143 horses with entrapment in the epiploic foramen (EFE), surgery performed within 8 h from onset of colic had a survival rate of 75.6%, compared with 45.1% survival with surgery 12 h or more after onset [112]. Results of one study identified some referring veterinarians whose surgical colic cases had a higher risk of intra-operative death than others [98], possibly because of delays in referral. More encouraging was the finding in a recent study that 96% of horses that had surgery for colic had one visit by a veterinarian at the farm [16], which would suggest that referring veterinarians can accurately identify those cases that should undergo surgery and could refer them promptly.

#### **Role of diagnostic procedures**

In the last 3 decades, ultrasonography has emerged as a simple, accurate, noninvasive, and widely used method of diagnosing intestinal diseases in horses [113]. Examples of these are colonic displacements [114,115], colon entrapment over the nephrosplenic ligament [116], small intestinal strangulation [113], intestinal thickening [117], intussusceptions of small [118] and large intestine [119], ascarid burden [120], obstructive

cholelithiasis [121], intra-abdominal haemorrhage, peritonitis, visceral rupture [122] and many others. A major advantage of ultrasonography is safe assessment of an animal unsuitable for palpation per rectum because of size and temperament. It can also provide useful information on intestinal motility [123].

Although systemic lactate has long been recognised as a peritoneal [124] and systemic marker of poor tissue perfusion and anaerobic metabolism in horses [125–127], current analysers facilitate its rapid and accurate measurement in these fluids in horses with colic [128–130]. An elevated ratio of peritoneal fluid lactate to systemic lactate has improved diagnosis of ischaemic intestinal lesions [128] and assessment of prognosis for survival after surgery [130]. Systemic lactate can be used to guide volume expansion [131,132] and to assess recovery after colic surgery [74,99,100,132,133].

Epidemiological studies have improved our understanding of different types of colic and their causes [21], but also have yielded information of diagnostic value. For example, horses with compatible clinical and other findings can be identified by disease risk, such as recent coastal Bermuda grass hay consumption (ileal impaction [134]), old age (strangulating lipoma [135]), crib-biting (epiploic foramen entrapment [136–138]), American miniature horse and other small breeds (fecalith in small colon [139]), and origin from same premises as other cases with similar signs and confirmed diagnosis (grass sickness [140]).

#### Role of anaesthesia in survival

Despite improvements in facilities, monitoring equipment, ventilators, training and available drugs, anaesthesia-related fatalities for elective equine cases over the last 4 decades have remained at 0.9% or one death/ 111 anaesthetics [141–143], with ranges from 0.08% to 1.8%, [144–152], depending upon study design and definitions of mortality [143]. This rate is between 10- and 1000-fold greater than the mortality rate with anaesthesia for cats, dogs and human beings [143]. When emergency cases, such as colic surgery or Caesarean section, are included, mortality for horses ranges from 0.24% [152] to 19.5% [141,151]. The most common causes of death related to anaesthesia are cardiac arrest, fractures in the recovery stall [149] and postanaesthetic myopathy [152].

The use of isoflurane instead of halothane in recent years and the associated decrease in cardiovascular depression should improve survival. However, no significant difference in anaesthesia-related mortality could be shown between these inhalants in one study, except that isoflurane was possibly safer in young horses and reduced death from cardiac arrest, particularly in high risk cases [149]. Recent studies on isoflurane and sevoflurane for anaesthesia maintenance report fewer intraoperative cardiac arrests compared with reports from older studies on halothane [143]. In other studies on anaesthesia for colic, different anaesthetic induction agents and protocols, inhalation maintenance agents, administration of dobutamine or phenylephrine and intermittent positive pressure ventilation had no significant effect on outcome [98,153]. Nonetheless, these probably constitute important improvements in anaesthesia of horses with colic.

Over the timeframe of this review, one important advance in anaesthesia for horses with colic is the use of inhalant anaesthetics instead of chloral hydrate as in the preceding decades [45]. Also, the original version of balanced anaesthesia incorporated a muscle relaxant with halothane [154], possibly a less humane and less effective means of reducing cardiovascular depression from the inhalant than current protocols with continuous rate infusion with lidocaine and other agents [155,156]. Another improvement in equine anaesthesia is an apparent reduction in postanaesthetic myopathy, in both prevalence and severity [19].

If another Confidential Enquiry into Peri-anaesthetic Equine Fatalities (CEPEF-4) is conducted in the near future, this could include critical incident reporting (CIR), an approach that could help identify and correct problem areas in equine anaesthesia [142]. Safer anaesthetic techniques and reduction of human error through training and use of monitoring devices, guidelines, standards and checklists could also reduce anaesthesia-related mortality in horses [142,143]. Also, the future offers considerable promise in improving ventilatory support of the anaesthetised horse, based on a substantial growth in our understanding of pulmonary pathophysiology during anaesthesia [157].

#### Survival according to segment affected

To provide sufficient power for statistical analyses, many studies group all intestinal segments and diseases together, which ignores the wide variation in survival and complication rates between and within segments. For example, survival rates are higher after surgery for large versus small intestinal obstructions in adult horses [56,68,71,75,101,158] and foals [159,160] and the number of large intestinal lesions can be double that of small intestinal lesions in hospital-based studies [25,56,59,63,68,72,161-165]. Nonstrangulating obstructions account for a larger proportion of all diseases in the large intestine [56,76,78,161,165] than they do in the small intestine [31,37,52,56,71,77,166] and can have short-term survival rates ≥88% [24,59,63,88,167]. Both NSE and RDDC were not described in the English literature before 1977 [168,169], but their prominence in recent studies and favourable outcomes associated with them could explain improved overall survival from colic surgery over the last half century [24,63,68,76-78,81]. Therefore, such studies that group all intestinal segments together might not detect a lack of improvement in small intestinal surgery.

#### Role of intraoperative euthanasia

The role of intraoperative euthanasia in colic surgery deserves close scrutiny, because this process creates a selection bias that could spuriously improve survival rates compared with survival of all horses that undergo anaesthesia [63,81]. From 40 to 55% of surgical mortalities can be caused by death or euthanasia during surgery [68], with euthanasia usually for financial reasons and poor prognosis [63]. These deaths can account for 26-27% of all horses treated surgically [63,68], almost twice as many with small intestinal lesions compared with large intestinal lesions [71,160]. In one study, LCV and strangulating lipoma were the most common lesions in horses that were euthanatised intraoperatively after discussion with the owners about a poor prognosis [56]. Inappropriate decisions for intraoperative euthanasia could be based on misconceptions about effects of age on recovery [77,78], effects of surgery on athletic performance, or of disease on prognosis. Surgeon bias can be critical, such as an aversion to jejunocaecostomy [57] or a negative assessment of prognosis based on finding nonviable intestine [67,77,170]. Therefore, survival data should be provided for all horses that undergo surgery, not simply those that recover from anaesthesia.

Intraoperative euthanasia could represent a hidden source of failure and could deny a lifesaving surgery to many horses with a treatable lesion. Financial constraints are valid arguments against a difficult surgery with a fair prognosis (e.g. large colon resection) but are largely created by the profligate use of questionable but costly post-operative medications after small intestinal surgery [18]. More disconcerting still is the impression that intraoperative euthanasia has become more prevalent over time within hospitals [171] and between hospitals [47,67,68,113,170]. An approach that eschewed intraoperative euthanasia for small intestinal strangulation has produced favourable survival rates [34,35], suggesting that giving more horses a chance of completed surgery could be justified.

## Role of surgical procedures and anastomosis

Correction by reduction, enterotomy, decompression or manipulation as only treatments have a better prognosis than resection and anastomosis in most studies [31,32,36,50,56,59,67,172]. Studies on jejunojejunostomy in horses treated between 1989 and 2010 reported survival rates of 85.7-95% after this surgery [31,35,37,52,53,57,173]. However, the broad ranges reported for POR of 0 [31,35] to 63% with this anastomosis [37,53,57,62,173] would imply that an opportunity exists for improvement in technical aspects of this procedure. Jejunocecal and ileocecal anastomoses can constitute 32-68% of all small intestinal anastomoses [30,31,37,52,112] and can adversely affect outcome compared with other anastomoses [30,31,34,37,49,51,52,54,56,59,64,67,172,174,175]. However,

recent studies have documented short-term outcomes of 80 [38] to 91% [34], with good long-term survival rates (Table 1).

Although resection of all the strangulated colon is usually impossible with LCV, major benefits of this procedure are debulking devitalised tissue, thereby reducing the severity of post-operative endotoxaemia [87]. One of the most difficult aspects of this surgery is the lack of clinical and laboratory guidelines to assess colonic viability and hence the need for resection [87,176,177]. Despite survival rates of 68–77% after completed colon resection [176–178], resection was not found to be statistically associated with an increased likelihood of short-term survival in a recent study [179].

#### Post-operative complications and mortality

A triphasic pattern of survival has been identified after colic surgery (Fig 1), with most deaths in the first 10 days after surgery [25], when early postoperative complications could impact cost of treatment and survival [33,56,179]. However, little progress seems to have been made in reducing post-operative complication rates [180,181]. This is discouraging when the improved condition of horses at admission is considered, as well as the large array of post-operative medications at our disposal with putative ability to reduce complications (see below).

One of the most common complications of small intestinal surgery is POR, with a prevalence rate that varies widely from 10 to 73% [181], with evidence of unchanging or increasing prevalence over time (Fig 2 [20,33,52,163,164,171]). This last finding is difficult to reconcile with the trend towards early referral and presentation of horses in better overall condition over recent time periods (see above). Post-operative reflux probably spawns all other complications [52,181], is expensive to treat, prolongs hospitalisation, and has an adverse effect on the rate of post discharge colic [22] and survival [20,22,33,52,68,179]. Horses that develop POR can be 28.2-29.7 times less likely to survive than those without [52,166] and euthanasia for POR has been reported at 30% to 66% of affected horses [25,166,182]. Although intestinal inflammation induced by surgical manipulation is considered a possible cause of POR [183], the role of this process might be overestimated [181] relative to physical obstruction amenable to repeat celiotomy [184]. The possibility that POR is a multifactorial disease rather than simply a functional disorder should redirect management from medical treatment to surgical prevention [181].

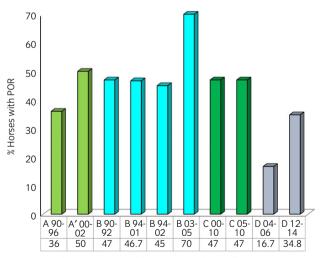


Fig 2: Bar graph of percentage of horses treated for small intestinal disease in four different hospitals (A–D) showing a lack of change or an increase in the percentage of horses that developed POR (actual percentages in bottom row of table) over 10- to 15-year time spans in each hospital. Each hospital used the same inclusion criteria for POR at each time period. Years covered in each report follow the letter designation and references are: 164, 165 (A,A'); 33, 52, 182 (B); 37, 162 (C); and 20 (D). A' indicates that data from hospital A were combined with data from another hospital that reported a lower prevalence of POR [165].

Post-operative colic (POC) has been reported in  $\leq$ 61% of horses following small intestinal resection and anastomosis [52,53,118] and in  $\leq$ 42% in horses with strangulating large colon lesions [178,185]. This complication can increase post-operative fatality after small intestinal surgery by 1.3 times compared with horses that do not develop this complication [33]. The number of colic episodes in the remainder of a horse's life after colic surgery can vary considerably from none to multiple, with almost half the discharged horses in one study being free of colic in the first year after small intestinal surgery [51]. In other studies, up to 32% of horses discharged had colic, either as single or multiple events [25,63,68]. Although adhesions or anastomotic problems could explain this complication in horses discharged after surgery, the comparable rate with cases treated medically in one hospital [68] would suggest that more complicated issues are involved.

#### Serosal adhesions – a success story?

Adhesions after colic surgery can go undetected, especially because horses with post-operative colic can be euthanised without necropsy [186] and adhesions are not the only cause of colic after discharge [23]. Nonetheless, the current rate of adhesion formation is regarded as approximately 6–13% after small intestinal surgery [31,76,187], compared with 22% in an early study [188]. The survival pattern, low rate of colic after hospital discharge in interrelated small intestinal studies would suggest that intra-abdominal adhesions in horses might be less common than once thought [31,34–36]. Despite evidence to the contrary in one study [23], adhesions are more common after small versus large intestinal surgery in horses [76,186].

Although omentectomy has been recommended to prevent adhesions, omental adhesions are a rare cause of colic [187,188]. Also, the concern that the potentially more dangerous bowel to bowel or bowel to mesentery adhesions might replace omental adhesions could be an argument against omentectomy [186]. Research has demonstrated that various solutions and antiadhesive barriers or membranes can prevent adhesions in end-to-end anastomoses in equine small intestine or in abraded small intestine [189-195] and might decrease morbidity and mortality from ischaemic intestinal diseases in horses [190]. In clinical studies on small intestinal surgery, intra-abdominal infusion of sodium carboxymethylcellulose (CMC) significantly improved survival rates [105] and a combined hyaluronate (HA) CMC membrane applied to an anastomosis reduced colic and mortality from colic [35]. However, these were retrospective studies and therefore subject to bias, lacked randomisation, had inconsistencies in surgical procedures between groups, and lacked information through necropsy or repeat celiotomy [35,105]. The (HA) CMC membrane is expensive, can only be applied to a small area, such as the primary lesion or anastomotic site, and can impair healing in human intestinal anastomoses [196]. Also, adhesions can form at distant sites, thereby suggesting a more pan-abdominal approach be taken to adhesion prevention rather than focus on the anastomosis [23].

Although application of a mesenteric flap around an anastomosis has been tested as an antiadhesive barrier in the research [197] and clinical settings [198], risks of mesenteric and anastomotic distortion with this procedure might outweigh the benefits [199]. PERIDAN™ is a purified fucoidan with antiadhesive, anticoagulant properties that can be applied safely to equine peritoneum, although its ability to prevent adhesions in horses is unknown [200]. Intraperitoneal heparin therapy seemed to reduce intra-abdominal adhesion formation in one study [22], but univariable analyses were used, so the role of confounders is unknown. Intravenous and subcutaneous injection of heparin decreased adhesions in an ischaemic jejunal model in a study on ponies [201] and intravenous dimethylsulphoxide alone and flunixin meglumine, potassium penicillin and gentamicin combined reduced adhesions in an ischaemia-reperfusion model in foals [202]. Post-operative repeated peritoneal lavage reduced adhesions induced experimentally by jejunal abrasion in mature horses [203]. However, the extent that many of these treatments are used clinically is unknown and clinical trials on their efficacy are lacking.

## Role of post-operative pharmacological management

Perceived improvements in survival rates with colic surgery have been attributed to improved pharmacological management of the horse postoperatively [18], especially with treatments designed to prevent adhesions [203], POR [166,204], endotoxaemia/SIRS [205] and reperfusion injury [206]. This assessment is flawed in many ways. Firstly, so many drugs are given routinely under current systems of post-operative care that the benefits of any of them cannot be deduced [166]. Secondly, there are few if any well-designed studies that show a benefit of any drug treatment. Thirdly, low complication and high survival rates after colic surgery achieved through a parsimonious approach to post-operative drug therapy [31,34–36] at least challenge the notion that aggressive post-operative drug therapy plays an important role in survival. The strongest argument in favour of a conservative approach to post-operative treatments is expense [207], which could drive the overall cost of colic surgery beyond what most owners can afford.

The most common post-operative complication of colic surgery is POR (see above). Widespread use of a continuous rate infusion of lidocaine "as a prokinetic" to prevent POR in horses [208,209] is predicated on reported efficacy [204] and improved short-term survival [166] with this treatment. However, none of these studies examined long-term survival and they were not all adequately randomised, used insufficient numbers to provide statistical power, included other drugs, involved high rates of lidocaine treatment under anaesthesia for control horses [166], and included diseases that might not represent the typical causes of POR [204]. The absence of a prokinetic effect in normal horses [210,211], questionable antiinflammatory benefits [212,213], and absence of a favourable costbenefit analysis raise some concerns about the use of lidocaine. A recent study demonstrated that lidocaine did not affect the prevalence of POR, total reflux volume, duration of reflux and post-operative survival after small intestinal surgery [20]. However, the enhanced visceral analgesic effect of lidocaine and flunixin meglumine combined [214] is a potential benefit in select cases. Although different prokinetic agents are available to treat or prevent POR [215], the overall results to date are disappointing [43,166].

Flunixin meglumine (FM) became available in the late 1970s as an NSAID that could reduce pain and with low risk of gastrointestinal and renal injury [216]. Subsequent studies demonstrated that FM provides analgesia [216] and blocks the effects of endotoxaemia in horses [217]. Because of the concern that FM, a nonspecific COX inhibitor, could paradoxically cause post-operative endotoxaemia by impairing recovery of the mucosal barrier [214], specific COX-2 inhibitors, such as firocoxib and meloxicam might be preferable [18,64,218]. However, when strangulated small intestine was left in situ, clinical evidence of post-operative endotoxaemia did not develop after twice daily full-dose FM [36], a finding that could challenge the concern about FM-induced failure of mucosal recovery. In another clinical study, FM did not appear to increase the risk of endotoxaemia or POR and had superior pain scores compared with meloxicam [64]. Also, FM does not appear to interfere with recovery of barrier integrity in the equine colonic mucosa after ischaemia [219]. A concern with COX-2 selective NSAIDs is growing evidence that they can interfere with healing of colonic anastomoses in human patients and laboratory animals [220].

Colic surgery is usually classified as clean or clean-contaminated, so that a single dose of preoperative antimicrobial drugs should be sufficient prophylaxis against surgical site infection (SSI [221]). However, current methods of antimicrobial usage in colic surgery might fail to follow best practices for dose and timing of administration [61]. Also the common practice of long-term post-operative usage might be unnecessary [222] and could increase the risks of antimicrobial resistance and post-operative salmonellosis [61].

Improved management of endotoxaemia or SIRS after colic surgery can be attributed to NSAIDs and i.v. fluids, and less commonly used agents include polymixin B, enteral adsorbents, and plasma [205,223]. Cryotherapy of the distal limbs [224] can attenuate lamellar damage [225] and should improve management of horses at risk or that develop laminitis from perioperative sepsis [25,31,51].

The potential for reperfusion injury to exacerbate inflammation in horses after colic surgery has led to studies on a large number of different treatments; however, consistent evidence of a beneficial response is lacking [226]. Carolina Rinse solution contains antioxidants and was designed to support organ viability for transplantation. It has shown some benefit in maintaining vascular permeability close to normal during reperfusion after a short period of low-flow ischaemia in the equine jejunum [206]. However, it is expensive and should be perfused through a mesenteric artery, which is technically challenging [206].

Although diagnosis, prevention and treatment of gastric ulcers represent advances in gastrointestinal diseases in horses [227], the impact of gastric ulcers on recovery from colic surgery is unclear [228]. In one study, gastric ulcers were more likely in horses with abdominal pain responsive to medical treatment than in those that required surgery [228]. Although American miniature horses, ponies, donkeys and others are at risk of hyperlipidaemia, hyperlipaemia and hepatic lipidosis when denied food before and after colic surgery, recognising these risks and using appropriate measures to prevent them represent an improvement in managing these cases [229]. Pre- and post-operative management of pain has improved over the period covered by this review, largely through an increased availability of effective analgesic drugs and a better understanding of the pathophysiology of pain itself [230].

#### **Fluid therapy**

Fluid therapy is a major advance in the treatment of colic [231], although the delivery volumes and rates selected in veterinary medicine tend to be arbitrary and most published guidelines lack scientific support [232]. There is some evidence that overhydration with sodium-rich crystalloids could be potentially harmful in human patients [233] and could reduce colloid osmotic pressure to levels associated with decreased survival in horses [234]. In horses that had surgery for small intestinal strangulation, a low intraoperative PCV predicted failure to recover from anaesthesia and a need for gastric decompression after surgery [67]. Overhydration was considered as a possible explanation for these PCV-related outcomes [67], especially because intestinal motility can be disrupted by crystalloidinduced intramural oedema [235]. However, the effects of overhydration and survival have not been established for horses. Fluid therapy has been improved in recent decades by inclusion of colloids and hypertonic saline (HSS [236]) to effectively expand the intravascular space in critical cases. Although beneficial in the surgical patient under general anaesthesia [237,238], effects on survival have not been established [52], and the high cost of colloids could limit use to horses with severe disease and poor prognosis.

Many horses with colic might benefit from early goal directed therapy (EGDT) for volume support, which is a strategy to improve the matching of oxygen delivery to oxygen consumption in septic patients early in the disease process [239]. Fluid responsiveness is an important concept in human medicine and distinguishes those patients who would benefit from fluid resuscitation from those who would not [240]. This finding underscores the need for measuring variables that appropriately guide EGDT, although such measurements could be difficult in the horse [241].

#### **Future directions**

Many improvements in colic surgery have evolved over the last 50 years, but the relative impact of any of them on survival is unclear. The future should focus on the following items that past experience has taught us could improve survival rates.

- Early referral will always be critical to improve survival and to reduce complications and costs. Efforts to educate owners and veterinarians on improving this process should be a priority, with emphasis on referring promptly when in doubt rather than seeking a high degree of diagnostic specificity on the farm [242].
- Reducing POR and other complications is a critical step to improve survival. In addition to adverse effects on performance and mortality, complications can create pessimism about prognosis and generate high costs, both of which could increase pre- and intraoperative euthanasia.
  POR has negative welfare implications, inflicted by the discomfort of

nasogastric intubation, dehydration, gastrointestinal distention and denial of food.

- The cost of colic surgery needs to be contained, largely through a more selective approach to drug usage and a greater emphasis on preventing complications [181]. The heavy focus on pharmacological management of POR [18] needs to be modified to include an approach that emphasises surgical prevention [31,34–36,181]. This could be modelled on the concept of "fast-track surgery," also called "enhanced recovery after surgery" (ERAS), applied to human gastrointestinal patients [243].
- Horses appear to tolerate early post-operative feeding (18–24 h) after small intestinal surgery [34–36], and, based on work in other species, this approach should be encouraged to improve intestinal motility [244] and anastomotic healing [245].
- More favourable outcomes in colic surgery associated with surgeon experience [31,32,38] and board certification in surgery [170] underscore the importance of training in colic surgery and the role of surgery itself in improving survival rates.
- Clinical governance and clinical audit should be used to improve the quality of patient care and the practice of surgery in veterinary hospitals involved in full service colic management [246].
- Intraoperative euthanasia, based on proposed indicators of prognosis [130,247], probably should be reevaluated, recognising that this approach reduces overall survival in an insidious manner, while possibly improving post-operative survival data through selection bias. Therefore, horses euthanised under anaesthesia should be included in assessments of colic survival. The strongest argument against intraoperative euthanasia is to prevent negative prognostic indicators generated in the past [130,247] from denying us the opportunity to improve survival in the future. Or, as once stated, those who look only to the past or present are certain to miss the future (John F. Kennedy).

#### Author's declaration of interests

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#### **Ethical animal research**

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