PAPER

Septic peritonitis from pyloric and non-pyloric gastrointestinal perforation: prognostic factors in 44 dogs and 11 cats

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Objectives: To identify potential prognostic factors affecting outcome in septic peritonitis caused by gastrointestinal perforation in dogs and cats.

Methods: A retrospective study. Animals operated on for septic peritonitis because of gastrointestinal perforation were evaluated. Risk factors assessed included age, duration of clinical signs, recent prior abdominal surgery, recent prior anti-inflammatory drug administration, placement of a closed-suction drain and location of perforation.

Results: Fifty-five animals (44 dogs and 11 cats) were included. The overall mortality was 63·6%. No association was found between age, duration of clinical signs or prior abdominal surgery and outcome. Animals with a history of prior anti-inflammatory drugs were significantly (P=0·0011) more likely to have perforation of the pylorus (73·3%). No significant difference in outcome was found between animals treated with closed-suction drains and those treated with primary closure or between pyloric perforation and perforation at other gastrointestinal sites.

Clinical Significance: Administration of anti-inflammatory drugs in dogs and cats is a significant risk factor for pyloric perforation. Pyloric perforation was not associated with a poorer outcome than perforation at other gastrointestinal sites. Placement of a closed suction drain did not improve outcome compared to primary closure.

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INTRODUCTION

Generalised peritonitis is a medical and surgical emergency, which often requires intensive and costly treatment. Both septic and non-septic causes of peritonitis are recognised, the former generally being characterised by inflammation of the peritoneum secondary to bacterial contamination and infection. The most frequent cause of septic peritonitis in small animals is gastrointestinal (GI) leakage causing intraperitoneal infection by commensal intestinal bacteria. Mortality in dogs and cats with septic peritonitis is reported with wide variation between 20 and 80% (Woolfson & Dulisch 1986, Hosgood & Salisbury 1988, Allen *et al.* 1992, King 1994, Swann & Hughes 2000, Lanz *et al.* 2001, Mueller *et al.* 2001, Staatz *et al.* 2002, Bonczynski *et al.* 2003, Levin *et al.* 2004, Shales *et al.* 2005). Rapid diagnosis, perioperative treatment to stabilise hypovolaemia, acid-base and electrolyte disturbances, as well as surgical correction of the source of peritoneal contamination are key to successful outcome.

Factors reported to influence outcome in a negative manner include preoperative activities of serum alanine aminotransferase (ALT) and γ-glutamyl transferase (GGT), hypotension that is not correctable with treatment by intravenous (iv) fluids, development of respiratory dysfunction, development of disseminated intravascular coagulation (King 1994, Winkler & Greenfield 2000, Grimes *et al.* 2011) and development of multiple organ

dysfunction syndrome (defined as dysfunction of at least two organ systems) (Kenney *et al.* 2010). The location of GI perforation has thus far not been found to influence prognosis. Indeed, previous studies investigating outcome following perforation of the colon compared to small bowel perforation found no difference in mortality despite a potentially greater degree of bacterial contamination in the former (Christou *et al.* 1993, Wylie & Hosgood 1994, Mueller *et al.* 2001). Perforation of the pylorus is technically more challenging to repair and may therefore carry a higher risk of complication, but to the authors' knowledge, no previous study has investigated whether pyloric perforation carries a worse prognosis than perforation at other GI sites. In addition, some reports suggest an association between the administration of non-steroidal anti-inflammatory drugs (NSAIDs) and pyloric perforation (Stanton & Bright 1989, Hinton *et al.* 2002), including studies based on pharmacovigilance data, toxicity studies and case series of dogs treated with NSAIDs or dogs presenting with gastric ulceration (Stanton & Bright 1989, Poortinga & Hungerford 1998, Lascelles *et al.* 2005, Case *et al.* 2010). However, the frequency with which NSAID or steroidal anti-inflammatory drug administration is associated with pyloric and other GI-site perforation is largely unknown. Finally, some studies have investigated outcome in dogs with open peritoneal drainage, closed suction drains or with primary abdominal closure following surgical correction of GI perforation and septic peritonitis (Lanz *et al.* 2001, Mueller *et al.* 2001, Staatz *et al.* 2002, Szabo *et al.* 2011), but few studies have compared outcome between treatment groups and, to the authors' knowledge, no study has directly compared outcome between primary closure and closed suction drains.

The main aim of this study was to identify the potential association between the site of GI perforation and outcome by retrospectively examining cases treated over a 9-year period. It was hypothesised that the location of GI perforation is a significant risk factor and that pyloric perforation carries a worse prognosis than perforation at other sites. The secondary aims of the study were to assess the association between a history of steroid or NSAID administration and pyloric perforation as well as the placement of closed-suction drains and outcome.

MATERIALS AND METHODS

The medical records of all cats and dogs that were treated surgically in Vetsuisse Faculty veterinary teaching hospital for septic peritonitis resulting from GI perforation between January 2002 and June 2011 were reviewed. Animals were admitted on an emergency basis both as primary care cases and by referral from private veterinarians during daytime and out-of-hours services.

Cases were included if a complete surgical record was available. The septic character of peritonitis was based on intraoperative findings and, in some cases, preoperative cytology of abdominal fluid. The surgical team was composed of a board-certified or third-year resident surgeon and an assistant (resident, intern or student). All cases of perforation of the pylorus were treated with primary closure of the perforation by pyloroplasty. All cases of small or large bowel perforation were treated with enterectomy and end-to-end anastomosis. All cases of gastric perforation, other than perforation of the pylorus, were treated with partial gastrectomy and primary closure. In general, postoperative treatments included iv fluids, broad-spectrum antibiotics and opiate-derived analgesics. The choice of anaesthetic protocol and perioperative medications and supportive care were at the discretion of the surgeon and anaesthesia team. The decision to place an intraoperative closed-suction drain was at the discretion of the surgeon.

Final outcome was considered good if the animal survived until hospital discharge and poor if the animal died or was euthanased before discharge. Euthanasia was only performed at the request of the owners, based on both financial and prognostic considerations, following recommendations and advice from the surgeon.

Data collected included the age, breed, gender and bodyweight of the animal, the duration of clinical signs before surgery, a history of recent abdominal surgery, recent prior administration of anti-inflammatory drugs (steroids or NSAIDs), intraoperative placement of a closed-suction intraperitoneal drain (Jackson-Pratt type), survival 24 hours after surgery and survival to hospital discharge (outcome). For statistical analyses, the location of GI perforation was categorised as pylorus (not including antrum and proximal duodenum) or other GI site.

Statistical analyses

Continuous variables (age at presentation, duration of clinical signs) were evaluated for far outliers using Grubbs' double-sided (alpha-level 0·05) and Tukey (1977) tests and summary statistics were performed. A single far outlier was excluded for duration of clinical signs. Evaluation of a difference between survivors and non-survivors for mean age and for mean duration of clinical signs was performed using independent samples *t* tests (duration of clinical signs was log transformed to achieve normality). Evaluation of an association between perforation site and survival, recent prior treatment with anti-inflammatory drugs and perforation site, recent prior treatment with anti-inflammatory drugs and survival, recent prior abdominal surgery and survival, and between placement of an intraperitoneal drain and survival was performed using Fisher's exact test. All statistical analyses were performed using commercial software (MedCalc version 12.4, Medcalc Software bvba). The level of significance was set at $P<0·05$.

RESULTS

A total of 72 animals underwent laparotomy for peritonitis during the study period. Of these, 55 of 72 (76%) had septic peritonitis resulting from GI perforation and were included in the study. The animals included 11 cats (8 domestic shorthair, 1 Persian, 1 Siamese and 1 Burmese) and 44 dogs (3 mixed-breed dogs and 41 dogs representing a total of 27 different pure breeds). Cats weighed a median of 4·3 (range: 2·1 to 6·5) kg and dogs weighed a median of 24·8 (range: 1·2 to 70) kg. The cats included five males (four neutered) and six females (five neutered). The dogs

included 29 males (13 neutered) and 15 females (eight neutered). The mean age of animals at presentation was 5·9 ±3·7 (median: 5·5, range: 0·5 to 16·6) years. The mean duration of hospitalisation was 4·2 (median: 3 days, range: 0·5 to 20) days. The overall mortality was 35 of 55 (63·6%).

There was no significant difference in mean age between animals that survived 24 hours postoperatively and those that did not or between animals that survived to hospital discharge and those that did not.

Gastrointestinal perforation was found in the pylorus in 21 of 55 (38%) cases, in other areas of the stomach in 6 of 55 (11%) cases, and in the intestine in 28 of 55 (51%) cases (24 in the small intestine and 4 in the colon). Only one case had two perforations (both in the small intestine). No statistical association was found between the location of pylorus and survival although more animals with perforation of the pylorus (15 of 21, 71·4%) died than did those with perforation at other sites (20 of 34, 58·8%) (Fig 1). Of the 15 animals that died following pyloric perforation, 5 were euthanased intraoperatively and 10 were euthanased postoperatively. Of the 20 animals that died following perforation at other GI sites, 6 were euthanased intraoperatively, 4 died postoperatively and 10 were euthanased postoperatively.

There was no significant association between duration of clinical signs before surgery and outcome or between the duration of clinical signs and survival at 24 hours postoperatively.

Nineteen animals had a recent prior abdominal surgery. There was no significant association between prior abdominal surgery and outcome or survival at 24 hours.

A total of 15 animals had a recent history of steroid or NSAID administration. In four cases, information regarding preoperative drug administration was unavailable. Although no significant association was found between prior drug history and outcome or survival at 24 hours (Fig 2), only 2 of 15 (13·3%) animals with a history of anti-inflammatory drugs survived compared to 14 of 36 (38·8%) animals not receiving anti-inflammatory drugs. Prior treatment with anti-inflammatory drugs was, however, significantly (P=0·0011) associated with perforation of the pylorus (11 of 19 (57·9%)) compared to perforation at other GI sites (4 of 32 (12·5%)) (Fig 3).

Of the 35 non-survivors, 21 of 35 (60%) died or were euthanased within 24 hours of surgery. Of the 34 animals that survived the first 24 hours after surgery, 24 of 34 (70·6%) had a closed-suction drain placed during surgery. The mortality was

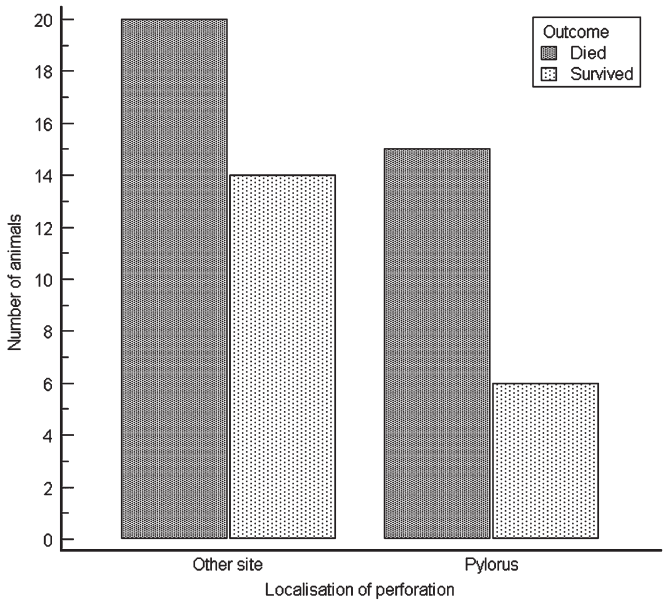

FIG 1. Frequency bar chart showing the location of gastrointestinal perforation and outcome in 55 dogs and cats

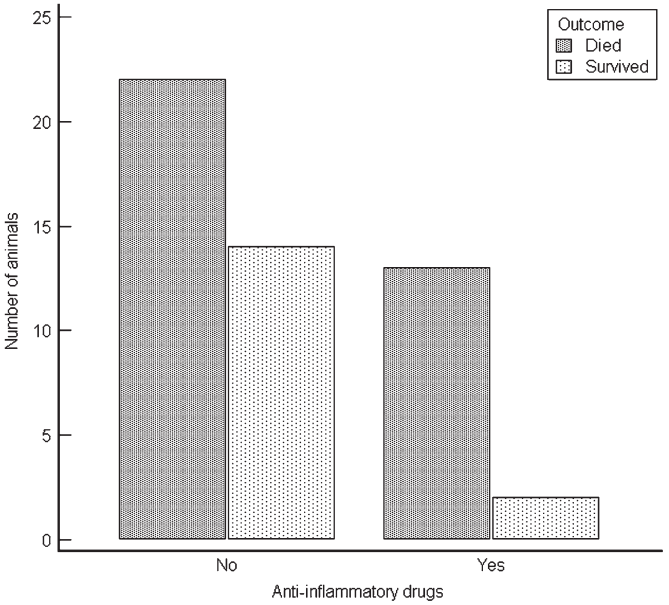

FIG 2. Frequency bar chart showing a prior history of anti-inflammatory drug administration and outcome in 55 dogs and cats

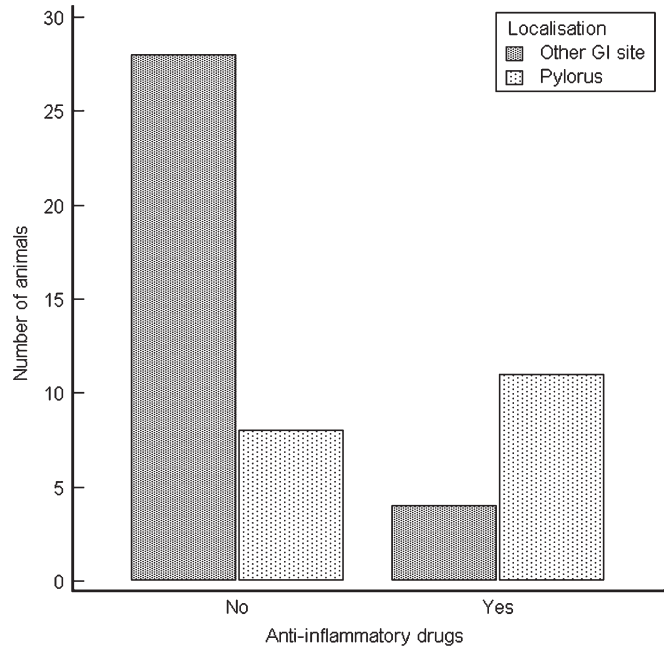

FIG 3. Frequency bar chart showing a prior history of anti-inflammatory drug administration and location of gastrointestinal perforation in 55 dogs and cats

41·7% (10 of 24) for the animals treated with a close suction drain and 40% (4 of 10) for animals treated with primary closure. There was no significant association between presence of a drain and survival to hospital discharge.

DISCUSSION

The wide range in mortality from 20 to 80% reported in previous publications on septic peritonitis resulting from GI perforation in small animals is likely due in part to the diversity of clinical cases and differences in intra- and perioperative procedures and care (Woolfson & Dulisch 1986, Hosgood & Salisbury 1988, Allen *et al.* 1992, King 1994, Swann & Hughes 2000, Lanz *et al.* 2001, Mueller *et al.* 2001, Staatz *et al.* 2002, Bonczynski *et al.* 2003, Levin *et al.* 2004, Shales *et al.* 2005). These differences also render direct comparison between results of this study and previous studies difficult. Moreover, due to the retrospective nature of this and many previous reports, a large number of confounding factors that may influence findings were undoubtedly present. These include differences in surgeon skill, pre- and postoperative supportive care and treatment, and concurrent illness affecting outcome, age and concurrent illness affecting prior treatment with anti-inflammatory medications, and surgeon identity, the animal's general clinical condition and intraoperative findings affecting the decision to place intraoperative drains. Results of this study must be interpreted with these limitations in mind and prospective studies are necessary to confirm the present findings.

Nevertheless, the mortality of 63·6% observed in this study lies within the range previously reported. However, this study included a relatively large number of cases with gastric and particularly pyloric perforation, which is rarely reported in previous studies except those investigating NSAID administration (Enberg *et al.* 2006). Similar to findings in other studies, the duration of clinical signs, prior surgery and age were not found to be associated with outcome in this study (Winkler & Greenfield 2000, Smeltoys *et al.* 2004, Eisele *et al.* 2010). However, only those animals treated surgically were included. It may therefore be argued that older animals or those subjected to recent previous surgeries are more likely to die or be euthanased before surgery.

Despite the high mortality in animals with pyloric perforation (71·4%) observed in this study, this was not found to be significantly different to mortality in animals with perforation at other GI sites, refuting the initial hypothesis that the technically more challenging surgery may impact on outcome. In a previous study of 16 dogs and cats with gastroduodenal perforation that were treated with a variety of techniques (open peritoneal drainage, primary ulcer closure, resection and anastomosis), mortality was found to be 56% (Hinton *et al.* 2002). However, direct comparison with this study is difficult as all cases included in this study were treated with pyloroplasty. Whether surgical technique may play a role in outcome cannot therefore be assessed. Moreover, analyses on larger numbers of cases may result in statistical significance where none was found in this study.

Changes in perioperative care, surgeon identity and surgical technique may have changed in the study period from 2002 and 2011, affecting outcome in animals in this study. However, a previous study reported no significant difference in survival among dogs treated surgically for septic peritonitis between 1988 and 1993 (21 of 33, 64%) and 1999 to 2003 (29 of 51, 57%) (Bentley *et al.* 2007). As differences due to progress in surgical and intensive care are likely greater in that study than during the current study period, it is unlikely that any such difference greatly affected survival in animals in this study.

Common predisposing factors reported for gastroduodenal ulcers include NSAID or corticosteroid administration, hepatic disease, major surgery, periods of high stress, shock, renal disease, other causes of decreased gastric circulation, gastric hyperacidity, GI neoplasia and idiopathic inflammatory bowel disease (Jerfens *et al.* 1992, Sullivan & Yool 1998, Simpson 2010). The concern regarding gastroduodenal ulceration and subsequent gastroduodenal perforation following NSAID or corticosteroid administration is based on pharmacovigilance data, toxicity studies or case series of dogs treated with NSAIDs or presenting with gastric ulceration (Stanton & Bright 1989, Poortinga & Hungerford 1998, Hinton *et al.* 2002, Liptak *et al.* 2002, Lascelles *et al.* 2005, Cariou *et al.* 2010, Case *et al.* 2010). Previous studies have shown that the pyloric region is most susceptible to ulceration due to NSAID administration (Stanton & Bright 1989, Boston *et al.* 2003). In this study, prior treatment with anti-inflammatory drugs was significantly associated with perforation of the pylorus compared to other GI sites, corroborating previous findings (Stanton & Bright 1989). As data from the medical records was often incomplete regarding the details of the duration and dose of prior medications, and some animals had a prior history of both steroid and NSAID administration, any possible effect of type of drug, dose or duration of administration on GI perforation could not be analysed in this study.

Only a few studies investigating the type of drainage used in small animals treated with septic peritonitis have been published and the advantage of drains remains controversial. Previous reports include studies in dogs treated with open peritoneal lavage (Orsher & Rosin 1984, Woolfson & Dulisch 1986, Greenfield & Walshaw 1987), with primary closure and no drainage (Lanz *et al.* 2001), with active suction drains (Mueller *et al.* 2001) and comparison of outcome in dogs treated with drains and open peritoneal lavage (Staatz *et al.* 2002). However, no previous study has directly compared outcome between animals treated with drains and those treated with primary closure at the same institution over the same time period. In this study, the mortality of 41·7% in animals treated with drains was similar to 30% observed in a previous study (Mueller *et al.* 2001) and no difference in mortality was found between animals treated with or without drains (41·6 *versus* 40%) in this study, suggesting that no advantage in treatment is attained through the use of drains compared to primary closure. However, the decision to place drains was at the discretion of the surgeon and was likely influenced by the surgeon's perception of prognosis, the severity of peritonitis, and the general condition of the animal. The extent to which drainage improves outcome following correction of the leakage site therefore remains unclear and prospective studies are needed to make conclusions in this regard.

In conclusion, the results of this study corroborate previous findings of an association between the administration of anti-inflammatory drugs and pyloric perforation in dogs and cats. Pyloric perforation was not associated with a worse outcome compared to perforation at other GI sites, but further studies are required to confirm this finding. No difference in survival was found between animals treated with closed suction drains and those treated with primary abdominal closure and prospective studies are warranted to establish the advantage, if any, of drains in animals with GI perforation after surgical correction of the leakage site.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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