Outcome following surgery to treat septic peritonitis in 95 cats in the United Kingdom

Abstract

Objective: To review the cause, management and outcome in a large group of cats with septic peritonitis (SP) within the United Kingdom (2008-2018) and to identify if previously identified prognostic factors were associated with survival.

Materials and Methods: Clinical records from ten UK referral hospitals were reviewed. Data collected included signalment, clinicopathological data, intra- and post-operative management. Serum albumin concentration, serum glucose concentration, serum lactate concentration, ionised calcium, presence of intraoperative hypotension, and correct empirical antibiosis were analysed via logistic regression for association with survival.

Results: Ninety-five cats were included. The overall survival rate was 66%. Lethargy (89%) and anorexia (75%) were the most common clinical signs of SP in the cat, with abdominal pain and vomiting in 44% and 27% of cases respectively. Gastro-intestinal leakage was the most common cause of contamination.

Intraoperative hypotension (p=0.033, OR 0.173, 95% CI 0.034-0.866) was associated with non-survival.

Clinical Significance: This study describes the largest group of cats with SP and an overall survival rate of 66%. Clinical signs and causes were similar to previous reports. Intraoperative hypotension was associated with non-survival.

Introduction

Septic peritonitis (SP) is characterised by inflammation of the peritoneum, secondary to bacterial, fungal or mycobacterial contamination of the peritoneal space. Successful treatment requires timely diagnosis, hemodynamic supportive treatment, surgical exploration of the abdomen with identification and control of the source of bacterial contamination, and intensive post-operative care (Parsons et al, 2009).

There is a limited number of studies evaluating SP in cats and the previously reported survival rates range from 20-70% (Mueller et al, 2001, Costello et al, 2004, Ruthrauff 2009, Parsons et al, 2009, Kellet-Gregory et al, 2010, Dayer et al, 2013, Kalafut et al, 2018, Scotti et al, 2019). Most studies have included only a small number of animals, but the largest study described 83 cases and investigated whether physical examination findings, admission clinicopathological data, time from presentation to surgical intervention, empirical antimicrobial use, or culture results were associated with outcome. It concluded that cats with elevated serum glucose concentration at presentation or receiving the incorrect empirical antibiosis were less likely to survive (Scotti et al, 2019). An earlier study assessing ionised calcium in 55 cats with SP did not show any association with survival to discharge, but failure for ionised calcium to normalize during hospitalisation was a negative prognostic indicator (Kellett-Gregory et al, 2010).

Electronic databases (Medline (Pubmed) and Science Direct) were searched with the keywords ‘septic peritonitis’ ‘cat’ ‘feline’ on June 2018, January 2020 and January 2021. Occasional single case reports of feline septic peritonitis were identified, **but no other case series or larger studies have been identified.**

The primary aim of this study was to report the survival and clinical findings for a large group of cats with SP in the United Kingdom. The secondary aim was to assess whether the serum albumin concentration, serum glucose concentration, serum lactate concentration, ionised calcium, presence of intraoperative hypotension, or correct empirical antibiosis were associated with survival. These factors have been investigated in previous studies in septic peritonitis and confirmed common findings of risk factors across multiple studies may guide further prospective research and aid clinical treatment.

Materials and Methods

Clinical records from January 2008 to January 2018 were reviewed from ten UK small animal referral hospitals (5 private and 5 university multidisciplinary institutions). A data table and guidelines for completion were submitted to each institution. Inclusion criteria was any cat having surgery for bacterial SP diagnosed either by the presence of degenerate neutrophils and intracellular bacteria on abdominocentesis sample cytology, and /or a peritoneal fluid-to-blood glucose value greater than 1.12mmol/L difference (Bonczynski at al, 2003), and / or a positive peritoneal fluid culture. Cats were excluded if they did not have any clinicopathological data available (minimum of venous blood gas analysis required), the data set was excessively incomplete in multiple areas, or the primary surgeon in charge of the case was not a specialist in small animal surgery

(Diplomate of the European College of Veterinary Surgeons / Diplomate of the American College of Veterinary Surgeons / RCVS Diplomate in Small Animal Soft Tissue Surgery) or resident working under direct specialist supervision. Surgical case log records were searched using the keywords 'septic peritonitis', data was filtered to include only the study period (January 2008 - January 2018) and to only include feline patients. The search was performed during July/August 2018 by six operators working independently but using the same search criteria. Information obtained from clinical records included signalment, clinical signs/examination findings and presence of concurrent disease, duration of clinical signs prior to surgery, clinical pathology data (haematology, serum biochemistry, electrolytes, venous blood gas analysis) from the immediate pre-operative period (within 12 hours of the start of surgery), method of diagnosis, whether any relevant previous surgery had been performed, American Society of Anesthesiologists (ASA) physical status classification system status (as determined by a board-certified anaesthetist or European College of Veterinary Anaesthesia and Analgesia / European College of Veterinary Surgeons / American College of Veterinary Surgeons or a resident under their supervision), source of bacterial contamination, method of abdominal closure, use of closed negative pressure abdominal drains, incidence of intra-operative hypotension (defined as systolic blood pressure <90mmHg, or mean blood pressure <60mmHg for at least 10 minutes), incidence of intra-operative death, perioperative/postoperative antibiosis, bacteria type and sensitivity profile, enteral feeding tube placement (including type), and histopathology. Survival to hospital discharge was recorded as a binary outcome. Of those which failed to survive, cause of death was recorded (intra-operative vs post-operative, death vs euthanasia). For those

cases that survived, duration of hospitalisation to discharge was recorded. Bacterial sensitivity profiles were assessed to determine whether appropriate empirical antibiotics were chosen.

Statistics

Descriptive statistics were used to report results for all variables. Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed data were reported as mean ± standard deviation and non-normally distributed data as median (range). In order to investigate for prognostic factors (albumin concentration, neutrophil count, serum glucose concentration, ionised calcium, presence of intraoperative hypotension, correct empirical antibiosis) univariable binary logistic regression was used to calculate odds ratio's (OR) and 95% confidence intervals (95%CI). Factors with a p value < 0.1 were analysed in a multivariable logistic regression model. Goodness-of-fit is reported via a Hosmer-Lemeshow test. Significance was set at $p < 0.05$.

Results

One hundred and twenty-three cats were identified by the surgical case log searches and assessed for eligibility, of which 28 records were excluded for excessively incomplete data sets. 95 cats were included. Breeds included domestic shorthair (n=55), domestic longhair (n=10) and exotic (n=30). There were 65 male cats (61 neutered, 4 entire) and 30 female cats (28 neutered, 2 entire). Median patient weight 4.1kg (1.4-9.5kg) and age was 63 months (4-249 months). The most common clinical signs and clinical

examination findings at presentation are shown in Table 1. Median time from onset of clinical signs until surgery was 3.5 days (0-42 days).

Sixty-three cats survived to discharge (66%). Of the 32 cats that did not survive, four did not survive the anaesthetic event, 12 died in the post-operative period, and 16 were euthanized in the post-operative period.

The source of peritoneal bacterial contamination is shown in Table 2. Twenty cats (21%; 12 survivors and 8 non-survivors) had undergone a previous procedure implicated as a cause of the peritonitis, including enterotomy/enterectomy which had fully or partially dehisced (n=15), laparotomy ovariohysterectomy (n=1), negative exploratory coeliotomy with subsequent necrotising pancreatitis (n=1), cystocentesis which resulted in septic uroabdomen (n=1), septic biliary peritonitis following ultrasound guided cholecystocentesis (n=1) and biopsy of an abscessed mesenteric lymph node (n=1). Of those 15 cats with a dehisced enterotomy/enterectomy, 13 (87%) survived.

Haematology and serum biochemistry results are shown in Tables 3 and 4 respectively.

Diagnosis of SP was made cytologically in 82 cases (86%) and on culture of peritoneal fluid in 13 cases (14%). Peritoneal-to-blood glucose was not used as the primary diagnostic method by any center for the included cases.

ASA grade is shown in table 5. Intra-operative hypotension occurred in 10 (16%) survivors and 18 (56%) non-survivors. Intra-operative cardiopulmonary arrest resulting in

patient death occurred in three cases, and in one case the patient was euthanised intra-operatively due to diffuse mass lesions affecting the ileocaecal-colic junction, mesentery and diaphragm. The abdomen was closed primarily in all cases and open peritoneal drainage was not reported in this cohort. An abdominal drain was placed at the discretion of the surgeon in 41 cases (27 survivors,14 non-survivors). Surviving patients were hospitalised for a median of 6 days (1-38 days). A feeding tube was placed at the time of surgery in 50 cats (36 survivors, 14 non-survivors), comprising 37 oesophagostomy tubes, four gastrostomy tubes, four jejunostomy tubes, and five naso-oesophageal tubes.

Histology was available for 58/91 (60%) of the surviving cats; neoplasia was identified in 12 of these samples (7 survivors, 5 non-survivors). Positive post-operative aerobic cultures were available for 64 cases; of the remaining cases 4 cultures were not available as they were not submitted / cancelled following intra-operative death and were negative in 27 cases (all had received systemic antibiotics pre-sampling). The most commonly cultured organism was *Escherichia coli* (n=30). Other organisms cultured were *Pasteurella* spp. (n=6), *Enterococcus faecalis* (n=6), *Bacteroides* spp. (n=3), *Streptococcus* spp. (n=4), *Clostridia* spp. (n=3), *Proteus* spp. (n=3), *Actinomyces* spp. (n=3), *Staphylococcus* spp. (n=2), mixed anaerobes (n=2), *Yersinia* spp. (n=1), *Pseudomonas* spp. (n=1), and *Nocardia* spp. (n=1). Intra-operative and post-operative antibiotics were administered by intravenous injection in all cases and continued enterally with restoration of enteral nutritional intake. Antibiotic choices used are shown in Table 6.

Antimicrobial susceptibility testing was available for 54 cultures (for 10 cases type of bacteria was available but it was not possible to retrieve sensitivity data). Initial empirical antibiotic choice was deemed to be effective in 41/54 cases, with 28 (52%) cases that survived and 13 (48%) that did not. Where initial empirical antibiotic choice was deemed unsuitable, 8 (62%) cases survived and 5 (38%) did not.

Univariate analysis of potential prognostic factors identified from previous studies was as follows: albumin concentration (p=0.008, OR 1.112 95%CI 1.028-1.204), correct empirical antibiosis (p=0.653, OR 1.346, 95%CI 0.368-4.923), serum lactate concentration (p=0.051, OR 0.746, 95%CI .556-1.002), serum glucose concentration (p=0.360, OR 1.062, 95%CI 0.933-1.209), ionised calcium (p=0.392, OR 2.593, 95%CI 0.292-23.134), presence of intraoperative hypotension (p=0.000, OR 0.147, 95%CI 0.056-0.388). The factors albumin concentration, lactate concentration and hypotension were used to build the multivariable model, which is shown in table 7. Only intraoperative hypotension showed significance in the multivariable model (p=0.033, OR 0.173 95%CI 0.034-0.866). Hosmer-Lemeshow goodness-of-fit for the model was p=0.431.

Discussion

The overall survival rate in this study was 66%, and the aetiopathogenesis, clinical signs and outcome are similar to what has previously been reported for SP in cats treated surgically. In agreement with previous studies we found lethargy (89%) and anorexia (75%) to be the most common clinical signs of SP in the cat, with abdominal pain and

vomiting in only 44% and 27% of cases respectively. Gastro-intestinal leakage was the most common cause of contamination. This is the largest group of cats reported with SP, and this information provides more evidence regarding prognosis and clinical signs for decision making.

Intraoperative hypotension (defined as systolic blood pressure <90mmHg, or mean blood pressure <60mmHg for at least 10 minutes) was associated with an approximately 82% decrease in the odds of survival (p=0.033, OR 0.173 95%CI 0.034-0.866) . Hypotension associated with sepsis is multifactorial, often secondary to reduced intravascular volume, loss of systemic vascular resistance, and decreased cardiac contractility. Septic shock is defined as persistent hypotension despite adequate fluid resuscitation and carries a worse prognosis than sepsis alone in humans (Schoenberg et al, 1998). Anaesthetic agents decrease blood pressure via decreasing cardiac contractility and systemic vascular resistance in a dose-dependent fashion, however sustained hypotension during anaesthesia of a systemically healthy animal is unlikely in the referral setting. Therefore, sustained intraoperative hypotension during surgery for SP in cats likely indicates those cats with more severe sepsis or septic shock. Unfortunately, the presence of pre-operative septic shock was incompletely recorded and temporal associations between hypotension and possible causes could not be fully investigated. The increased odds of mortality in hypotensive patients may therefore be as a direct result of sustained intraoperative hypotension and decreased oxygen delivery to vital organs, or secondary to more severe pre-existing pathology.

Reduced serum albumin concentration was statistically associated with death on univariable analysis but not multivariable analysis (p=0.241, OR 1.064, 95%CI 0.959-1.180). Hypoalbuminemia in sepsis is caused by decreased synthesis, increased leakage into the interstitial / third space compartment, and persistent catabolism, and is associated with a worse prognosis in humans with surgical sepsis (Sun et al, 2015). Reports in cats have been contradictory, with some studies finding that hypoalbuminaemia had no effect or resulted in increased mortality.

Dehiscence following full thickness gastrointestinal biopsy in cats has been reported previously in a study of 172 cats (two cases (1.2%) confirmed and four (2.3%) cases presumed). However, there is a lack of information on the management of the subsequent SP (Swinbourne et al, 2017). Based on a literature search, the management of SP subsequent to enterotomy/enterectomy dehiscence is only reported in 5 cases (Parsons et al, 2009), of which 4 cases survived (80%) and 1 was euthanised (20%), which is a similar proportion to the larger number we report of 15 cases (87% survival). Dogs with SP have a higher prevalence of gastrointestinal origin SP than cats in our study (51%), with 75% of 64 dogs with SP in one study having a gastrointestinal source (Dickinson et al, 2015). Of these 42 (62.6%) had undergone a previous abdominal surgery. In one study of 20 dogs with SP of gastrointestinal origin only, 80% of animals had breakdown of an enterotomy/enterectomy (Adams et al, 2014). Therefore, in a population of animals with SP, intestinal dehiscence appears to be a less prevalent cause in cats compared to dogs.

Initial antibiotic choice for cases of SP in cats is empirically based on clinicians' determination of the most likely bacterial contaminants, and the antibiotics most likely to be effective against these contaminants and application of rational antimicrobial usage consensus guidelines to ensure appropriate stewardship and minimise the development of resistance. Previous literature has documented that the majority of bacterial contaminants are gram-negative (Parsons et al, 2009; Costello et al, 2004) but has not reported sensitivity testing. Scotti et al, 2019 showed a survival benefit associated with appropriate initial empirical antibiotic selection, however no such benefit was noted in our study (p=0.653, OR 1.346, 95%CI 0.368-4.923). Scotti et al, 2019 also reported that serum glucose concentration was significantly greater in cats with SP that did not survive. In our study there was no association between glucose concentration and survival (p=0.360, OR 1.062, 95%CI 0.933-1.209).

In previous studies, ionised hypocalcaemia (<1.2mmol/L) has been found to be prevalent in cats with SP, and its failure to normalise associated with poorer prognosis (Kellet-Gregory, 2010). Our study only looked at ionised calcium at a single time-point (pre-operative) and so could not draw direct comparison, however pre-operative ionised calcium concentration was not associated with survival.

Parson et al, 2009 reported that serum lactate may be a useful prognostic indicator in cats with SP, with lactate levels in survivors being significantly lower than non-survivors. We did not find that lactate was statistically significantly associated with survival in the univariate (p=0.051, OR 0.746, 95%CI .556-1.002) or multivariable models. Serum

lactate concentration was only available for 44 of the 95 cats in this study and therefore lack of significance may demonstrate a genuine lack of association or be a Type II error associated with limited sample size. Low overall sample size and certain variables only having data input for a limited number of cases are limitations of this study, which may result in Type II statistical error. A further limitation is that it is a retrospective study with data collected by multiple authors, which may enable reporting inaccuracies and selection bias. This is a multi-center study only based in the United Kingdom, therefore cats may have been treated differently based on which center they were managed at, and differences may exist between cats in the UK and cats in other geographical locations. An additional limitation was only including cats where surgery was attempted. This was designed to prevent a skew towards non-survival due to euthanasia for financial reasons. However, this may result in a bias towards overall survival of SP, as cats that were considered too unwell for anaesthesia and surgery were not included.

In conclusion, this is the largest retrospective report of septic peritonitis in cats. The overall survival rate was 66%, which is important information for veterinarians and owners. Intraoperative hypotension was associated with failure to survive to discharge.

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