PAPER

Impact of intra-operative hypotension on mortality rates and post-operative complications in dogs undergoing cholecystectomy

R. Hattersley[1,*], F. Downing[‡], S. Gibson[‡], J. Demetriou[*], K. Elmenhorst[†], N. Kulendra[¶], B. Mielke[§] and S. Woods[‖]

[*]Dick White Referrals, Cambridgeshire, UK
[†]Anderson Moores Veterinary Specialists, Hampshire, UK
[‡]Davies Veterinary Specialists, Hertfordshire, UK
[§]Royal Veterinary College, Hertfordshire, UK
[¶]North Downs Specialist Referrals, Surrey, UK
[‖]Veterinary Specialists Scotland, Livingston, UK

[1]Corresponding author email: rachel.hattersley@dwr.co.uk

Objectives: To report the mortality rate within a cohort of dogs undergoing cholecystectomy and investigate the impact of intra-operative hypotension on mortality.

Materials and Methods: Clinical records at five UK referral centres were reviewed for dogs undergoing cholecystectomy. Data collected included presenting signs, pre-operative blood test results, intra-operative data including frequency and duration of hypotension and the incidence and type of post-operative complications.

Results: Data from 119 dogs were included. Sixteen dogs (13%) died before discharge and by 28 days after surgery the total mortality was 19 dogs (17%). Hypotension lasting over 10 minutes during general anaesthesia occurred in 65 dogs (54.6%), with a mean ± sd duration of 36.1 ± 30.0 minutes. Intra-operative hypotension or the number of hypotensive episodes did not appear to be associated with in-hospital or 28-day mortality. American Society of Anaesthesiologists grade (of fitness for surgery) was significantly associated with both in-hospital and 28-day mortality on univariable analysis, as were post-operative hypoproteinaemia, ileus and pancreatitis. However on multivariable analysis, only ileus and pancreatitis were found to significantly impact mortality.

Clinical Significance: Dogs presenting with a higher American Society of Anaesthesiologists grade appear to have a higher risk of mortality, although intra-operative hypotension did not appear to be part of this risk.

Journal of Small Animal Practice (2020)
DOI: 10.1111/jsap.13199

Accepted: 2 June 2020

INTRODUCTION

Gall bladder mucoceles (GBMs), resulting from excessive mucin secretion and subsequent production of hyperviscous bile (Kesimer *et al.* 2015), are the most common indication for cholecystectomy in dogs (Allerton *et al.* 2018). Associations are documented between GBM formation and endocrinopathies (Mesich *et al.* 2009, Gookin *et al.* 2015), hyperlipidaemia (Kutsunai *et al.* 2014), breed (Kutsunai *et al.* 2014, Allerton *et al.* 2018) and reduced gall bladder motility (Tsukagoshi *et al.* 2012).

The mortality rate in dogs undergoing cholecystectomy ranges from 21.7 to 40% (Pike *et al.* 2004, Worley *et al.* 2004, Malek *et al.* 2013, Jaffey *et al.* 2018, Youn *et al.* 2018). This figure is higher than the 1.33% mortality rate previously reported for sick

JSAP JOURNAL OF SMALL ANIMAL PRACTICE

dogs (American Society of Anaesthesiologists (ASAs) classification score 3-5) undergoing general anaesthesia (Brodbelt 2009). Dogs undergoing non-elective cholecystectomy have been reported to have a higher mortality rate (20%) than those undergoing elective surgery (2%) (Youn *et al*. 2018).

In addition to the increased mortality rate associated with cholecystectomy in symptomatic dogs, we have also observed that dogs undergoing cholecystectomy are at risk of developing important post-operative complications, including systemic inflammatory response syndrome (SIRS), sepsis, pancreatitis and ileus. Previous studies have identified immediate post-operative hypotension, elevated serum lactate, elevated creatinine levels, gall bladder rupture and septic peritonitis as negative prognostic indicators for survival in dogs undergoing surgery (Malek *et al*. 2013, Jaffey *et al*. 2018). Jaffey *et al*. (2019) reported a number of variables which appear to affect prognosis in dogs with GBMs including total serum/plasma bilirubin concentration, age, clinical signs, concurrent hyperadrenocorticism and the Pomeranian breed (Jaffey *et al*. 2019).

Hypotension during anaesthesia has been reported to occur in 74% of dogs undergoing cholecystectomy (Burns *et al*. 2014) and can have detrimental effects on perfusion and oxygen delivery to vital organs. In humans, intra-operative hypotension lasting more than 10 minutes has been associated with organ injury, with the risk increasing as blood pressure decreases (Wesselink *et al*. 2018). Due to the high incidence of gastrointestinal dysfunction after cholecystectomy, we hypothesised that there may be an association between intra-operative hypotension and post-operative complications including death.

The aim of this study was to describe mortality and complication rates in dogs undergoing cholecystectomy and investigates the association between intra-operative hypotension and mortality prior to discharge and within the first 28-day post-operatively. Secondary outcomes included the influence of peri-operative biliary peritonitis, surgical technique, surgeon experience and post-operative hypoproteinaemia, pancreatitis, regurgitation and ileus on mortality.

MATERIALS AND METHODS

Clinical records of dogs undergoing cholecystectomy between 2006 and 2017 at five referral hospitals in the UK were reviewed. Dogs were included in the study if there was a minimum follow-up period of at least 28-day post-surgery or if death was documented during this time. Pre-operative information collected included signalment (age, breed, gender, weight), relevant medical history (presenting complaint, duration of clinical signs and concurrent medical conditions), blood test results (including albumin and total protein) and ASA scores. The surgery was recorded as routine or emergent based on the opinion of the primary surgeon. The aetiology of the underlying disease process was determined from the ultrasound report and histology findings.

Peri-operative data collected included details of anaesthetic management: duration of anaesthesia, anaesthesia drug protocol, the incidence of hypotension (defined as a mean invasive arterial blood pressure (MAP) of <60 mmHg or a Doppler pressure of <90 mmHg) and the peri-operative analgesia and antibiosis given. The surgical report was reviewed to obtain the total duration of all surgical procedures (minutes) and the method of common bile duct flushing if performed (anterograde via the cystic duct *versus* retrograde flushing via a duodenotomy or a combination of both). A diagnosis of bile peritonitis was made if the surgeon had detected bile in the abdomen during surgery. Additional surgical procedures performed at the same time, such as feeding tube placement or liver biopsy were also recorded. The experience of the primary surgeon was documented; experience was defined as, 1 – European College of Veterinary Surgeons (ECVS) resident; 2 – board-eligible surgeon; 3 - ECVS diplomate of less than 5 years' experience; 4 - ECVS diplomate with greater than 5 years' experience.

Details of post-surgical complications were recorded. Pancreatitis was diagnosed based on abdominal ultrasound, elevated CPLi or other biochemistry changes or on histopathology. Ileus was diagnosed based on detection of amotile distension of the intestines or stomach by ultrasonography. Vomiting/regurgitation was recorded if this was witnessed by clinical staff in the post-operative period and recorded in the clinical notes. Survival to discharge, 28-day survival rates and the reason for euthanasia (if performed) were also documented.

Ethical approval for the study was obtained before data collection from the ethical committee of the Association of Veterinary Anaesthetists (AVA). Data were collected using Excel (Microsoft ® Excel ® 2016 MSO.). Statistical analysis to assess association between peri-operative hypotension and death was performed using Fisher's exact test. Secondary outcomes were also assessed using a Fisher's exact test and logistic regression to calculate odds ratio (OR) and 95% confidence intervals (CI), using StataIC 13 (StataCorp Texas, USA). P values <0.05 were considered significant. Factors significantly associated with death were analysed in a multivariable logistic regression model, removing subsequent non-significant factors. Descriptive data are reported as mean +/– sd or median + range.

RESULTS

Data from 119 dogs undergoing cholecystectomy at five UK centres were included. The most commonly presented breeds were: Border terrier (n = 35), cross breed (n = 13), miniature schnauzer (n = 9), Shetland sheepdog (n = 8) and bichon frise (n = 7). Age at presentation was 108 ± 32.7 (mean ± sd) months, bodyweight was 14.3 ± 9.7 kg, with 64 females (61 neutered, three entire) and 55 males (37 neutered, 18 entire).

The most common clinical signs at presentation were vomiting in 83 dogs (70%), lethargy in 50 (42%), anorexia/inappetence in 52 (43.6%), abdominal pain in 25 (21%) and icterus in 21 dogs (17.6%). The median duration of clinical signs was 27 days (range 1-365 days). Eight dogs were reported to be asymptomatic. Fifty-five dogs were reported to have concurrent medical conditions: six dogs with hyperadrenocorticism, six dogs with diabetes mellitus and two dogs with hypothyroidism. Pre-operative blood values are presented in Table 1.

Underlying aetiology, based on ultrasound findings, histology of the gall bladder or a combination of both (where available) was identified for 115 dogs. Ninety-one dogs had a GBM, 18 dogs had cholecystitis, four dogs had cholelithiasis and two dogs had a neoplastic lesion.

ASA scores, recorded in 118 cases, ranged from 2 to 5 (Table 2) and were significantly associated with in-hospital mortality (P = 0.004), and 28-day mortality (P = 0.032). Dogs with a higher ASA score were more likely to die. No in-hospital deaths occurred in dogs with an ASA score of 2. Surgery was emergent in 39 dogs, and the proportion of emergency surgeries compared to elective increased with increasing ASA score: 8% of ASA 2, 34.6% of ASA 3, 70% of ASA 4 and 100% of ASA 5 (Table 2). However, when analysed in a multivariable model, ASA score was not associated with in-hospital or 28-day mortality.

All dogs were premedicated and included acepromazine/methadone (n = 20), dexmedetomidine/methadone (n = 23), fentanyl (n = 1) and methadone alone (n = 75). Anaesthesia was induced using alfaxalone in 44 dogs, propofol in 74 and a combination of fentanyl and midazolam in one dog. Anaesthesia was maintained using an inhalant agent in 94 dogs using isoflurane and in 22 dogs using sevoflurane. This information was not available for three dogs. Fentanyl or alfentanil was administered peri-operatively in 113 of the 119 dogs. Epidural anaesthesia was administered in 25 dogs. Inotropes were administered peri-operatively in 13 dogs and vasopressors in six. Blood products were administered in seven dogs. One hundred and ten dogs received peri-operative antibiotics; cefuroxime (n = 71), amoxicillin clavulanate (n = 29), amoxicillin (n = 5), metronidazole (n = 2), clindamycin (n = 1), marbofloxacin (n = 1) and enrofloxacin (n = 1).

Mean duration of anaesthesia was 174 (sd ± 63.5) minutes and mean duration of surgery (for all dogs, including those undergoing an additional procedure or feeding tube placement) was 99 (sd ± 43.4) minutes. Hypotension lasting over 10 minutes during general anaesthesia occurred in 65 dogs (54.6%), with a mean ± sd duration of 36.1 ± 30.0 minutes. There was no significant association between hypotension and the in-hospital (OR: 1.45; 95% CI: 0.49-4.30) or 28-day mortality rates (OR: 1.18; 95% CI: 0.43-3.20) (Table 4).

There was no association between the surgical experience of the primary surgeon and in-hospital and 28-day mortality rates. However, EVCS diplomates with less than five years' experience had the highest rates of in-hospital and 28-day mortality rates (Table 3). The common bile duct was flushed at surgery in 82 (70.1%) dogs. Of these dogs, 41 were flushed in an anterograde direction, 36 in a retrograde direction and five in both directions. Oesophagostomy feeding tubes were placed in 30 dogs and one dog had a gastrostomy tube placed. Fifty-four additional procedures were performed during surgery on 24 dogs; liver biopsy (n = 19), enterotomy/intestinal biopsy (n = 8), pancreatic biopsy (n = 6), liver lobectomy (n = 6), cystotomy (n = 4), choledochal stent placement (n = 3), splenectomy (n = 2), castration (n = 2), ovariohysterectomy (n = 2), removal of a mammary mass (n = 1) and gastropexy (n = 1).

Biliary peritonitis at surgery was documented by the surgeon in 20 dogs; of these, three (15%) died in hospital, compared with 11 of 97 dogs (11%) in which biliary peritonitis was not diagnosed. Biliary peritonitis at surgery was not significantly associated with in-hospital (P = 0.7) or 28-day mortality rates (P = 0.5). There was no bacterial growth on culture of gall bladder tissue or bile in 71 of 105 tested dogs. Growth was reported in 34 dogs: isolates reported included *Escherichia coli* (n = 14), *Enterococcus spp* (n = 12), *Staphylococcus spp* (n = 3), *Streptococcus spp* (n = 2), *Klebsiella pneumoniae* (n = 2) and *Moraxella spp* (n = 1).

Median post-operative hospitalisation was five days (range 1-14 days). Post-operative complications occurred in 64 (53.8%)

Table 1. Pre-operative blood parameters

Blood parameters	Mean	Standard reference range	Range in case cohort
Bilirubin	70.4	0–16 umol/L	0.1–768.5
Albumin	28.4	25–40 g/L	14–42
Urea	5.71	2.5–7.4 mmol/L	1.6–33
Creatinine	78.61	40–145umol/L	30–322
Alanine transferase	857.3	13–88 IU/L	17–5308
Alkaline phosphatase	2618.4	14–105 IU/L	31–12,547
Packed cell volume	43.6	37–55%	29–66.4
Leucocyte count	18.9	6.0–15.0 ×10^9/L	5.6–70

Table 2. Mortality rate in dogs undergoing cholecystectomy based on American Society of Anaesthesiologists (ASA) score

ASA score	Total number of dogs	Number of emergency procedures (% of dogs in ASA group)	Number of in-hospital deaths (% deaths in ASA group)	Number of deaths by 28 days (% deaths in ASA group)
2	25	2 (8)	0 (0)	2 (8)
3	81	28 (34.6)	11 (13.6)	12 (14.8)
4	10	7 (70)	4 (40)	4 (40)
5	2	2 (100)	1 (50)	1 (50)

Table 3. Case distribution and mortality rates according to surgeon experience

Surgeon experience	Number cases (% of total)	In-hospital mortality rate (% of experience band)	28 day mortality rate
Resident	10 (8.4%)	1/10 (10%)	1/8 (12.5%)
Board eligible	14 (11.8%)	1/14 (7.1%)	2/14 (14.3%)
ECVS diplomat (< 5 years)	41 (34.5%)	8/41 (19.5%)	9/38 (23.7%)
ECVS diplomat (> 5 years)	54 (45.4%)	6/54 (11.1%)	7/66 (10.6%)

Resident = person undergoing an approved ECVS/ACVS residency training program; Board eligible = a person who has completed and ECVS/ACVS residency but not yet passed the relevant certifying examination

Table 4. The effect of post-operative hypoproteinaemia, ileus and pancreatitis on the risk of death prior to discharge and by 28 days after surgery

Complication	Risk of death prior to discharge			Risk of death by 28 days after surgery		
	OR	95% CI	P value	OR	95% CI	P value
Hypotension	1.45	0.49–4.30	0.49	1.18	0.43–3.20	0.75
Hypoproteinaemia	13.4	3.23–55.52	<0.001*	10.5	2.88–38.57	<0.001*
	15.54	*2.97–81.35*	*0.001**	*12.48*	*2.34–66.47*	*0.003**
Ileus	19.8	3.22–121.92	0.001*	27.08	2.80–261.40	0.004*
	26.15	*2.63–260.33*	*0.005**	*38.54*	*2.39–621.67*	*0.01**
Pancreatitis	4.08	1.25–13.34	0.02*	3.55	1.16–10.80	0.026*

Results are reported as odds ratio (OR) and 95% confidence interval. All of these complications are associated with and increased likelihood of death in dogs undergoing cholecystectomy (*significant findings (P <0.05)). Italics denote significant factors from multivariable analysis

dogs, including vomiting/regurgitation (n = 39), pancreatitis (n = 22), hypoproteinaemia (n = 24) and ileus (n = 6). Post-operative complication was associated with increased mortality in-hospital (OR: 4.42; 95% CI: 1.19-16.43; P = 0.014) but not at 28-days. Post-operative hypoproteinaemia, ileus or pancreatitis post-surgery was associated with death before discharge and at 28-days post-operatively (Table 4). When analysed in a multivariable model, only hypoproteinaemia and ileus were associated with increased death in-hospital and at 28 days. The development of post-operative vomiting or regurgitation was not associated with death before discharge (OR: 2.09; 95% CI: 0.68-6.48) or by 28-days post-operatively (OR: 1.5; 95% CI: 0.51-4.44). Other complications were documented in 17 dogs: septic peritonitis (n = 3), nausea without regurgitation (n = 3), infection at the oesophagostomy tube site (n = 3), inappetence (n = 3), hypokalaemia (n = 1), ascites – transudate (n = 1), urinary incontinence (n = 1), peripheral oedema (n = 1), seizures (n = 1), urethral prolapse (n = 1) and subcutaneous haemorrhage (n = 1).

Sixteen out of 119 dogs (13.4%) did not survive to discharge from hospital. Thirteen dogs were euthanased; two dogs intra-operatively due to poor prognosis associated with surgical findings and one dog was euthanased post-operatively due to prognosis based on the histology results (high-grade lymphoma). Cardiorespiratory arrest occurred in three dogs at six hours, one day and seven days post-surgery, respectively. In those dogs that were euthanased due to a post-operative complication, reasons for euthanasia included persistent regurgitation (n = 3), septic peritonitis (n = 1), biliary peritonitis (n = 1), paraparesis (n = 1), ascites (n = 1), acute kidney injury and severe pancreatitis (n = 1), uncontrollable seizures (n = 1) and SIRS (n = 1). Median post-operative day for euthanasia was 2.5 (range 1-6). Data for 28-day survival were recorded in 110 dogs, of these 19 (17.3%) did not survive, the additional three deaths after discharge occurred in ASA 2 and 3 dogs.

DISCUSSION

The overall mortality rates prior to discharge and by 28 days after surgery in this group of dogs were comparable to recent studies (Allerton *et al.* 2018, Jaffey *et al.* 2018, 2019, Youn *et al.* 2018). As in some previous studies, dogs which survived to discharge were likely to still be alive at 28 days after surgery. (Malek *et al.* 2013). The signalment and presenting signs were consistent with previous studies (Allerton *et al.* 2018, Youn *et al.* 2018, Jaffey *et al.* 2019)

A higher ASA grade was associated with a higher risk of mortality prior to discharge in this cohort on univariable analysis. Seventeen percent of dogs (16/93) with an ASA grade of 3-5 died before discharge – much higher than a previously published mortality rate of 1.33% in ASA grade 3-5 dogs (undergoing any type of surgery) in the UK (Brodbelt 2009). However, several other studies also report that higher ASA grades are associated with an increased risk of mortality (Bille *et al.* 2012, Gil & Redondo 2013, Portier & Ida 2018). This suggests that dogs with a higher ASA grade requiring cholecystectomy may be at an increased risk of death. However, as ASA grading takes in to account multiple factors, some of which may be more easily addressed than others, decisions regarding pre-operative stabilisation should be made on a case by case basis.

The need for emergency cholecystectomy was also associated with a higher risk of mortality prior to discharge although the definition of what constituted an emergency was based on the opinion of the surgeon. Youn *et al.* (2018) reported that dogs with clinical signs (*e.g.* vomiting and lethargy) and, more specifically, icterus (as an indicator of more advanced hepatobiliary disease) had a lower rate of survival to discharge (Youn *et al.* 2018). In contrast, Jaffey *et al.* (2019) reported that vomiting decreased the odds of death in multivariable analysis, but also reported that the clinical utility of total bilirubin as a biomarker to predict death was poor even in a much larger case cohort than that presented here. Thus far no specific individual prognostic factor has been consistently identified as important.

The incidence of peri-operative hypotension in dogs undergoing cholecystectomy in this study population was 53.4%. Whilst this is higher than the rate of 7–10.3% reported in general small animal anaesthesia (Gaynor *et al.* 1999, Mcmillan & Darcy 2016), it is much lower than previously reported rates of hypotension in dogs undergoing cholecystectomy, which reached 74% in one study (Burns *et al.* 2014). The reasons a patient may develop hypotension during anaesthesia are often complex and multifactorial. Patient-related factors that may contribute to the development of hypotension include pre-existing cardiac disease, hypovolaemia and sepsis. Anaesthetic-related factors include positive pressure ventilation, drug-induced, dose-dependent

vasodilation (*e.g.* propofol and isoflurane) and reductions in cardiac output (Bilotta *et al.* 2001). It is also reasonable to assume that the increased incidence of hypotension during anaesthesia in patients undergoing cholecystectomy may be explained by the biliary disease itself and associated co-morbidities, which is reflected in their higher ASA status. Furthermore, the method of blood pressure assessment (*e.g.* direct *versus* oscillometric) was not standardised in this case cohort, as it is retrospective, which could have introduced further variation.

Interestingly, there was no difference in mortality rates between dogs experiencing one or more hypotensive episode of at least 10 minutes duration during general anaesthesia and those that did not. Whilst this is consistent with a previous study in dogs (Youn *et al.* 2018), it is in conflict with human studies that have linked intra-operative hypotension with an increased risk of death and the development of complications such as myocardial infarction (MI) (Monk *et al.* 2005, Walsh *et al.* 2013, Sun *et al.* 2015, Wesselink *et al.* 2018). It is generally accepted that during periods of hypotension autoregulation of organ blood flow is lost, meaning that perfusion is directly dependent on arterial pressure (Thooft *et al.* 2011). However, it is also important to note that increasing arterial blood pressure does not guarantee improved tissue perfusion; for example, whilst increases in systemic vascular resistance elevate blood pressure, cardiac output and tissue perfusion may be reduced. Therefore, despite apparent arterial hypotension, it may be that organ perfusion was sufficient to prevent injury. In addition, it may be due to species differences between humans and dogs or that the comparatively small sample size in this study was not sufficient to allow the identification of differences in mortality rates between these groups. Assessment of organ perfusion and of microcirculatory status, *e.g.* by side-stream dark field imaging, may be a more accurate way of predicting survival but unfortunately this technology is not widely available for clinical veterinary use (Goedhart *et al.* 2007).

It is also interesting that surgeon experience did not impact on patient outcome because, intuitively, we may expect a more experienced surgeon to be less likely to make surgical errors than a surgical resident (Campbell *et al.* 2018, Korovin *et al.* 2020). However there is evidence from human medicine that it is the experience of the supervising surgeon rather than the resident which impacts upon the rate of intra-operative adverse events (Wojcik *et al.* 2018). As a system of resident supervision exists in all institutions contributing to this case cohort, this may explain the lack of difference between the different experience groups. Furthermore, experience with a specific surgical procedure may differ between surgeons independently of overall surgical experience. However, it may also be that patient-related systemic factors may have more of an impact on mortality than surgeon experience in this cohort of cases.

Post-operative complication was associated with increased mortality in-hospital. Previous studies have identified immediate post-operative hypotension, elevated serum lactate, elevated creatinine levels, gall bladder rupture and biliary peritonitis as negative prognostic indicators for survival in dogs (Malek *et al.* 2013, Jaffey *et al.* 2018). However, to our knowledge, the impact of post-operative complications on mortality rates in dogs undergoing cholecystectomy has not previously been investigated. Based on our statistical analysis, hypoproteinaemia and ileus are associated with significant morbidity after cholecystectomy in this case cohort and so taking measures to reduce such complications (*e.g.* placement of epidural catheters to improve post-operative analgesia without systemic opioid adverse effects) may improve patient survival. It is, however, important not to over interpret this finding given the apparently low incidence of these complications, the wide 95% CI and the retrospective nature of the study where it is possible post-operative ileus and hypoproteinaemia may not have been documented in the clinical records. As borne out in previous reports, risk factors for death vary hugely and thus prognostic factors (and the statistical analysis performed on data sets without large numbers of adverse events) must be interpreted with caution.

Biliary peritonitis at the time of surgery was not associated with a worse outcome, which differs from the findings of Jaffey *et al.* (2018), who reported that dogs presenting with a ruptured gall bladder at surgery were 2.7 times more likely to die than those without bile peritonitis. The aetiology of death in these cases appears to be complex and multi-factorial and so a definitive conclusion on the effect of pre-existing biliary peritonitis on 28-day mortality rates cannot be drawn from this dataset.

The main limitations of this study are defined by its retrospective nature. While this case cohort represents one of the larger case series published on this topic and dogs were only included that had complete case records, the case population is inevitably somewhat heterogeneous in terms of the presenting clinical signs, clinicopathological abnormalities and surgical findings. Furthermore, a larger case cohort would have limited the likelihood of type II statistical errors.

In conclusion, the rate of survival to discharge and 28-day survival rates are comparable to previous studies. Peri-operative hypotension and surgeon experience did not impact prognosis. Negative prognostic factors suggested by this case cohort include the need for emergency surgery, development of post-operative hypoproteinaemia, ileus and pancreatitis. However, on multivariable analysis, only post-operative hypoproteinaemia and ileus were associated with death.

Declaration of conflict of interest

None of the authors has a conflict of interest relevant to this manuscript.

References

Allerton, F., Swinbourne, F., Barker, L., *et al*. (2018) Gall bladder mucoceles in border terriers. *Journal of Veterinary Internal Medicine* **32**, 1618-1628

Bille, C., Auvigne, V., Libermann, S., *et al*. (2012) Risk of anaesthetic mortality in dogs and cats: an observational cohort study of 3546 cases. *Veterinary Anaesthesia and Analgesia* **39**, 59-68

Bilotta, F., Fiorani, L., La Rosa, I., *et al*. (2001) Cardiovascular effects of intravenous propofol administered at two infusion rates: a transthoracic echocardiographic study. *Anaesthesia* **56**, 266-271

Brodbelt, D. (2009) Perioperative mortality in small animal anaesthesia. *Veterinary Journal* **182**, 152-161

Burns, B. R., Hofmeister, E. H. & Brainard, B. M. (2014) Anesthetic complications in dogs undergoing hepatic surgery: cholecystectomy versus non-cholecystectomy. *Veterinary Anaesthesia and Analgesia* **41**, 186-190

Campbell, B. M., Lambrianides, A. L. & Dulhunty, J. M. (2018) Open cholecystectomy: exposure and confidence of surgical trainees and new fellows. *International Journal of Surgery* **51**, 218-222

Gaynor, J. S., Dunlop, C. I., Wagner, A. E., *et al*. (1999) Complications and mortality associated with anesthesia in dogs and cats. *Journal of the American Animal Hospital Association* **35**, 13-17

Gil, L. & Redondo, J. I. (2013) Canine anaesthetic death in Spain: a multicentre prospective cohort study of 2012 cases. *Veterinary Anaesthesia and Analgesia* **40**, e57-e67

Goedhart, P. T., Khalilzada, M., Bezemer, R., *et al*. (2007) Sidestream dark field (sdf) imaging: a novel stroboscopic led ring-based imaging modality for clinical assessment of the microcirculation. *Optics Express* **15**, 15101-15114

Gookin, J. L., Correa, M. T., Peters, A., *et al*. (2015) Association of gallbladder mucocele histologic diagnosis with selected drug use in dogs: a matched case-control study. *Journal of Veterinary Internal Medicine* **29**, 1464-1472

Jaffey, J. A., Graham, A., Vaneerde, E., *et al*. (2018) Gallbladder mucocele: variables associated with outcome and the utility of ultrasonography to identify gallbladder rupture in 219 dogs (2007-2016). *Journal of Veterinary Internal Medicine* **32**, 195-200

Jaffey, J. A., Pavlick, M., Webster, C. R., *et al*. (2019) Effect of clinical signs, endocrinopathies, timing of surgery, hyperlipidemia, and hyperbilirubinemia on outcome in dogs with gallbladder mucocele. *Veterinary Journal* **251**, 105350

Kesimer, M., Cullen, J., Cao, R., *et al*. (2015) Excess secretion of gel-forming mucins and associated innate defense proteins with defective mucin unpackaging underpin gallbladder mucocele formation in dogs. *PLoS One* **10**, e0138988

Korovin, L. N., Farrell, T. M., Hsu, C. H., *et al*. (2020) Surgeons' expertise during critical event in laparoscopic cholecystectomy: an expert-novice comparison using protocol analysis. *American Journal of Surgery* **219(2)**, 340-345

Kutsunai, M., Kanemoto, H., Fukushima, K., *et al*. (2014) The association between gall bladder mucoceles and hyperlipidaemia in dogs: a retrospective case control study. *Veterinary Journal* **199**, 76-79

Malek, S., Sinclair, E., Hosgood, G., *et al*. (2013) Clinical findings and prognostic factors for dogs undergoing cholecystectomy for gall bladder mucocele. *Veterinary Surgery* **42**, 418-426

Mcmillan, M. & Darcy, H. (2016) Adverse event surveillance in small animal anaesthesia: an intervention-based, voluntary reporting audit. *Veterinary Anaesthesia and Analgesia* **43**, 128-135

Mesich, M. L., Mayhew, P. D., Paek, M., *et al*. (2009) Gall bladder mucoceles and their association with endocrinopathies in dogs: a retrospective case-control study. *The Journal of Small Animal Practice* **50**, 630-635

Monk, T. G., Saini, V., Weldon, B. C., *et al*. (2005) Anesthetic management and one-year mortality after noncardiac surgery. *Anesthesia and Analgesia* **100**, 4-10

Pike, F. S., Berg, J., King, N. W., *et al*. (2004) Gallbladder mucocele in dogs: 30 cases (2000-2002). *Journal of the American Veterinary Medical Association* **224**, 1615-1622

Portier, K. & Ida, K. K. (2018) The ASA physical status classification: what is the evidence for recommending its use in veterinary anesthesia? a systematic review. *Frontiers in Veterinary Science* **5(31)**, 204

Sun, L. Y., Wijeysundera, D. N., Tait, G. A., *et al*. (2015) Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. *Anesthesiology: The Journal of the American Society of Anesthesiologists* **123**, 515-523

Thooft, A., Favory, R., Salgado, D. R., *et al*. (2011) Effects of changes in arterial pressure on organ perfusion during septic shock. *Critical Care* **15**, R222

Tsukagoshi, T., Ohno, K., Tsukamoto, A., *et al*. (2012) Decreased gallbladder emptying in dogs with biliary sludge or gallbladder mucocele. *Veterinary Radiology & Ultrasound* **53**, 84-91

Walsh, M., Devereaux, P. J., Garg, A. X., *et al*. (2013) Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology: The Journal of the American Society of Anesthesiologists* **119**, 507-515

Wesselink, E. M., Kappen, T. H., Torn, H. M., *et al*. (2018) Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. *British Journal of Anaesthesia* **121**, 706-721

Wojcik, B. M., Lee, J. M., Peponis, T., *et al*. (2018) Do not blame the resident: the impact of surgeon and surgical trainee experience on the occurrence of intraoperative adverse events (iaes) in abdominal surgery. *Journal of Surgical Education* **75**, e156-e167

Worley, D. R., Hottinger, H. A. & Lawrence, H. J. (2004) Surgical management of gallbladder mucoceles in dogs: 22 cases (1999-2003). *Journal of the American Veterinary Medical Association* **225**, 1418-1422

Youn, G., Waschak, M. J., Kunkel, K. a. R., *et al*. (2018) Outcome of elective cholecystectomy for the treatment of gallbladder disease in dogs. *Journal of the American Veterinary Medical Association* **252**, 970-975