RESEARCH PAPER

Retrospective study of intra-anesthetic predictors of prolonged hospitalization, increased cost of care and mortality for canine patients at a veterinary teaching hospital

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Abstract

Objective To determine the impact of intraoperative anesthetic variables on the length of hospitalization, cost of care and mortality in dogs.

Study design Retrospective, observational study.

Animals A total of 235 dogs undergoing general anesthesia.

Methods Medical records of dogs undergoing general anesthesia between 2007 and 2014 at the University of Georgia Veterinary Teaching Hospital were reviewed. Data collected included demographic data, American Society of Anesthesiologists (ASA) physical status, type and duration of anesthesia, hemodynamic variables, temperature, ventilation, fluid therapy and adjunctive drugs administered. Outcome variables were length of hospitalization in the intensive care unit (ICU), hospital charges and survival to discharge.

Results The only factor significantly associated with duration of ICU care was higher ASA status ($p < 0.0001$). Factors associated with increased cost of hospitalization were ICU duration ($p < 0.0001$), anesthesia duration ($p < 0.0001$), hemorrhage amount ($p < 0.0001$), colloid use ($p = 0.0081$), increased age ($p = 0.0253$), increased weight ($p = 0.0293$) and presence of hypertension ($p = 0.0179$). Overall mortality rate was 5.1%. The only factors negatively associated with survival were the administration of colloids ($p < 0.0008$) and ASA status ($p = 0.0314$).

Conclusions and clinical relevance Several intrinsic patient factors and intraoperative hemodynamic variables were significantly associated with postoperative morbidity and mortality in dogs. These factors might have prognostic value in conjunction with preoperative risk assessment, and patient outcome may be improved by stricter intraoperative control of these variables.

Keywords cost, dog, hospitalization, monitoring, survival.

Introduction

Most of the veterinary literature focuses on preoperative risk factors for adverse anesthetic events (Garcia de Carellan Mateo et al. 2015). Increasing emphasis has been placed on the conjecture that intraoperative anesthetic management has an important impact on both short- and long-term patient morbidity and mortality (Proudman et al. 2006; Brodbelt et al. 2007, 2008). It is widely accepted that adverse events that occur under general anesthesia can affect not only immediate recovery, but also long-term outcome. However, while studies in the human literature have evaluated associations between adverse anesthetic events and subsequent morbidity and mortality (Reich et al. 2002; Monk et al. 2005; Kheterpal et al. 2009; Tassoudis et al. 2011; Kertai et al. 2014), no such large-scale population studies comparing stability under anesthesia and case outcome exist in veterinary medicine.

Evidence from both human and veterinary literature suggests a substantial contribution of preoperative risk factors to adverse outcomes, and numerous classification schemes have been used to characterize these risks (Leung & Dzankic 2001; Lupei et al. 2014). Perhaps the most widely used is the American Society of Anesthesiologists (ASA) physical status classification system, which uses a patient's physical status to help predict the anesthetic risk. Studies in human (Lupei et al. 2014), equine (Dugdale et al. 2016) and small companion animal anesthesia (Brodbelt et al. 2008) have shown an increased risk of death associated with higher ASA status.

One study (Lupei et al. 2014) further demonstrated an association between ASA status and postoperative intensive care unit (ICU) outcome in humans. The length of hospitalization in the ICU, use of mechanical ventilation (MV), number of acquired organ dysfunctions, vasopressor treatment and readmission to the ICU increased with patient ASA status $\geq$3. Unsurprisingly, in addition to the poorer patient outcome, increased time of hospitalization in the ICU was also associated with substantial increases in healthcare cost.

Despite the growing literature describing preoperative risk factors in both human and veterinary medicine, the effect of intraoperative variables, such as abnormal hemodynamic parameters, are not well characterized. One group (Kheterpal et al. 2009) evaluated both pre- and intraoperative risk factors for perioperative cardiac adverse events (CAEs) in humans within 30 days of noncardiac surgery. Of 7740 operations, 1.1% of patients experienced a CAE. Independent predictors of risk included advanced age, high body mass index, emergency surgery, duration of the procedure, intraoperative administration of packed red blood cells, intraoperative hypotension, defined as mean arterial pressure (MAP) <50 mmHg or heart rate (HR) >100 beats minute^{-1} and preexisting cardiovascular disease.

Such data are less abundant in the veterinary literature. Despite the presumption that abnormalities such as hypotension or tachycardia under anesthesia are likely to be associated with poorer recovery, specific literature addressing the impact of intraoperative anesthetic hemodynamic management on perioperative outcomes is more limited than in human medicine. One study (Grimes et al. 2011) demonstrated an association between intraoperative hypotension and the development of septic peritonitis following gastrointestinal surgery in dogs. Another study (Duke et al. 2006) showed a decreased incidence of postanesthetic myopathy in horses when MAP was maintained above 70 mmHg compared with only 60 mmHg during general anesthesia. Similar studies addressing a broad range of outcomes are lacking. The purpose of the present preliminary study was to determine the impact of numerous intraoperative anesthetic variables on morbidity surrogates: cost of care, length of hospitalization and survival to discharge. The hypothesis was that intraanesthetic events had a significant effect on duration of ICU stay, cost of hospitalization and survival to discharge.

Materials and methods

Animals

Medical records of dogs undergoing general anesthesia between 2007 and 2014 at the University of Georgia Veterinary Teaching Hospital were reviewed. General anesthesia is defined here as a drug-induced unconsciousness characterized by a controlled and reversible depression of the central nervous system and analgesia sufficient to allow endotracheal intubation. Records were randomly selected across the years of interest. Cases that had an anesthesia charge code on the invoice were considered for inclusion. Cases that did not have a complete anesthesia record were excluded. There were no other exclusion criteria. From this sample, more than 200 cases were enrolled in a sequential fashion. The sample size was estimated to require 10 dogs per variable of interest for a multivariable model (Guglielminotti et al. 2015).

Data collection

Data collected from the medical record included demographic data such as species, breed, age, body weight, reproductive status and ASA status. The anesthetic agent (inhalant anesthetics and injectable agents), duration of anesthesia and intraoperative complications were recorded. When a gas analyzer was used, end-tidal inhalant (FE'Inhalant) peak and nadir were recorded, and the area under the curve (AUC) of FE'Inhalant concentration for the duration of the procedure was calculated. Cardiovascular parameters recorded included HR, blood pressure and the type of arrhythmia if applicable. Hypotension was defined as a MAP below 60 mmHg or a systolic arterial pressure (SAP) below 90 mmHg (Haskins 2015). Hypertension was defined as a SAP above 145 mmHg

(Brown et al. 2007). The peak and nadir of blood pressure, duration of hypo- or hypertension, and AUC were recorded. Bradycardia was defined as an HR below 60 beats minute^{-1}, while tachycardia was an HR above 160 beats minute^{-1} (Haskins 2015). The rate pressure product (RPP = HR × SAP), a measure of myocardial workload and oxygen demand, was calculated. For tachycardic patients, HR peak and AUC were determined. Whether or not tachycardia occurred concurrently with hypotension or bradycardia concurrently with hypertension was also recorded.

Ventilation of the patient was characterized as spontaneous or controlled with MV, and hypercapnia and hypocapnia were defined as an end-tidal carbon dioxide ($P_E'CO_2$) above 6.1 kPa (45 mmHg) and below 4.7 kPa (35 mmHg), respectively.

Intravenous (IV) administration of crystalloid fluids was recorded in mL kg^{-1} hour^{-1}, while colloids were recorded as total volume per kg body weight, since they were typically administered as boluses. In addition, drugs acting on the cardiovascular system, such as atropine, glycopyrrolate, dopamine, dobutamine, ephedrine, epinephrine, norepinephrine, phenylephrine and vasopressin were recorded. Any patients administered adjunctive therapies, such as neuromuscular blocking agents (NMBAs) and local anesthetic blocks, were also identified. Several other parameters were reported. The peak and nadir of body temperature were recorded. Hypothermia was defined as a body temperature below 35.0 °C and hyperthermia >39.2 °C (Haskins 2015). The temperature AUC was calculated. If blood loss occurred, estimates of hemorrhage and administration of any blood transfusions were recorded. Recovery time, defined as the time between the end of anesthesia and endotracheal extubation, was calculated, and postoperative oxygen therapy was reported when needed.

All data were evaluated for an association with three key outcomes: the duration of hospitalization in the ICU when applicable, total cost of hospitalization, and whether the patient survived to discharge, died or was euthanized. Both dogs that died and those that were euthanized were included in the nonsurvivor category. All monetary data were reported in United States dollars (USD).

Statistical analysis

All analyses were performed using SAS V 9.4 (SAS, NC, USA). For hospital bill and days in ICU outcomes, all variables with $p < 0.15$ in a linear model (linear regression for numerical variables, *t* test for binary and ANOVA for categorical variables) were entered into a stepwise multiple linear regression. The final variables selected by the stepwise procedure were then entered into a second stepwise multiple linear regression. The final models from the second stepwise procedure included the same variables as the first stepwise procedure for both hospital bill and days in ICU, but had more accurate parameter estimates because of less missing data.

For survival to discharge, all variables with $p < 0.15$ in a logistic model (likelihood ratio *p* value) were entered into a stepwise multiple logistic regression. The final variables selected by a stepwise procedure were then entered into a second stepwise multiple logistic regression. The final model from the second stepwise procedure included the same variables as the first stepwise procedure with the exception of hypothermia (yes/no), which was removed, but had more accurate parameter estimates because of less missing data. For all stepwise selection procedures, the significance level for staying or leaving the model was set to $p < 0.15$.

Collinearity diagnostics were used to evaluate parameters for collinearity. Hypotension AUC was removed from the discharge analysis because of collinearity with hypotension duration. Parametric data were reported as mean ± standard deviation. Nonparametric data were reported as median (interquartile range). Significance was set at alpha < 0.05.

Results

Study population

A total of 235 dogs with complete medical records were included in the study. The most represented breed was the Labrador Retriever (Appendix A). There were 101 spayed females, 25 intact females, 80 castrated males and 29 intact males. Age and body weight were 6.9 ± 4.1 years and 20.2 ± 13.9 kg, respectively. Each ASA status (I–V) was represented, with ASA II (48.5%) and ASA III (31.1%) being the most common. ASA I (6.4%), ASA IV (3.4%) and ASA V (0.4%) were less common.

Type and duration of anesthesia

General anesthesia was maintained with inhaled agents in most dogs; isoflurane was used in 207 animals (88.1%), sevoflurane in 23 animals (9.8%) and desflurane in four animals (1.7%). Only one animal was administered total IV anesthesia (propofol

constant rate infusion, CRI), and one animal administered a propofol CRI in conjunction with sevoflurane. Commonly used adjunctive injectable anesthetics included ketamine, lidocaine and fentanyl CRIs. There was no association between type of anesthesia (e.g., different inhalants) or F_E'Inhalant peak or nadir with any outcome measure. Locoregional anesthetic techniques were applied in 80 animals (34.0%), and four animals (1.7%) were administered NMBAs. Anesthesia and recovery time were 177.2 ± 95.6 and 20.9 ± 17.6 minutes, respectively.

Cardiovascular variables, $P_E'CO_2$ and body temperature

Most dogs had altered hemodynamic variables under general anesthesia. Hypotension was present in 142 dogs (60.4%), with a duration of 20 (4–49) minutes. Hypertension occurred in 76 animals (32.3%), with a duration of 10 (5–45) minutes. A total of 35 animals (14.9%) experienced both hypo- and hypertension during their anesthetic event.

Heart rate abnormalities were common: 41 dogs (17.4%) were bradycardic and 14 of these (34.1% of bradycardic animals) experienced concurrent hypertension. Tachycardia was slightly more frequent, affecting 48 dogs (20.4%). The majority of tachycardic dogs (32 animals; 66.7%) experienced concurrent hypotension. Other arrhythmias were relatively uncommon and reported only in eight dogs. Of these dogs, five experienced second-degree atrioventricular (AV) block, and one had both second-degree AV block and a lone ventricular premature complex during pericardiectomy. Arrhythmias of the remaining three dogs were not classified in the medical record, but two of these were associated with patent ductus arteriosus ligation.

The vast majority of dogs (230 animals, 97.8%) were administered IV fluids (crystalloids and/or colloids) and drugs acting on the cardiovascular system (antimuscarinics, inotropes and/or vasopressors). In case of fluid therapy, most dogs (158 dogs, 67.5%) were administered crystalloids at a rate between 5 and 15 mL kg^{-1} $hour^{-1}$. Only 29 animals (12.3%) were administered colloids, with most of them (20 animals, 68.9%) being administered under 10 mL kg^{-1} total volume. Hemorrhage was reported in 82 dogs (34.9%), with six animals requiring a transfusion. Antimuscarinic agents were the most commonly administered cardiovascular drugs (137 dogs, 58.3%), followed by dopamine and dobutamine (60 dogs, 28.1%; Appendix B).

Hypocapnia was present in 150 animals (63.8%), while hypercapnia was present in 170 animals (72.3%). Both hypocapnia and hypercapnia occurred in 100 animals (42.6%) during their anesthetic event and MV was employed in 157 cases (66.8%).

Hypothermia and hyperthermia were recorded in 56 (23.8%) and six dogs (2.6%), respectively.

Case outcomes

Duration of hospitalization

Numerous variables were associated with the duration of hospitalization in the ICU, total cost of hospitalization and whether the patient survived to discharge. With regard to duration of hospitalization, the univariable analysis suggested that ASA status ($p < 0.0001$), anesthesia duration ($p = 0.0123$), tachycardia ($p = 0.0426$), increased RPP peak ($p = 0.0164$) and temperature AUC ($p = 0.0351$) contributed to longer hospitalization. Likewise, despite no effect of intraoperative hypotension ($p = 0.438$), administration of colloids ($p = 0.0003$), colloid volume per kg body weight ($p = 0.0127$) and dobutamine ($p = 0.0396$) were positively associated with longer hospitalization (Table 4). However, once all these variables were evaluated in the multivariable analysis, only higher ASA status ($p < 0.0001$) was significantly associated with longer duration of hospitalization in the ICU (Table 1). Increased anesthesia duration approached significance but was not a robust predictor of prolonged hospitalization ($p < 0.0571$; Table 1).

Cost of hospitalization

With regard to factors affecting the final hospital charges, univariable analysis indicated increases in costs associated with ASA status ($p < 0.0001$), age ($p = 0.0035$), anesthesia duration ($p < 0.0001$), duration of stay in the ICU ($p < 0.0001$), intraoperative hypertension ($p = 0.0178$), hypertension AUC ($p = 0.031$), SAP peak ($p = 0.0024$), tachycardia ($p = 0.049$), RPP peak ($p = 0.0004$), hemorrhage amount ($p = 0.001$), temperature nadir ($p = 0.0015$), temperature AUC ($p < 0.0001$), hypothermia duration ($p = 0.0244$) and recovery time ($p = 0.0053$). Although intraoperative hypotension was not significantly associated with increased cost ($p = 0.8852$), the administration of colloids ($p < 0.0001$), colloid volume per kg body weight ($p < 0.0001$) and dopamine ($p = 0.0012$) were associated with increased hospital charges in the

Table 1 Multivariable analysis of predictors of length of hospitalization (days) in the intensive care unit (ICU)

Variable	Partial R^2	Model R^2	C(p)[a]	Parameter estimate	Standard error	*p*
ASA status	0.1033	0.1033	7.9096	1.0689	0.2328	<0.0001
Anesthesia duration	0.0205	0.1238	5.4609	0.0033	0.0017	0.0571
RPP peak	0.0159	0.1397	4	6E−5	3E−3	0.0644

A total of three variables were included in the model: American Society of Anesthesiologists (ASA) status, rate pressure product (RPP) peak and anesthesia duration.
[a]Mallow's Cp [C(p)] is a goodness-of-fit measure where a smaller value indicates a better fit.

univariable analysis. Importantly, once variables were evaluated in the multivariable model, only ICU duration ($p < 0.0001$), anesthesia duration ($p < 0.0001$), older age ($p = 0.0253$), higher weight ($p = 0.0293$), hemorrhage amount ($p < 0.0001$), hypertension ($p = 0.0179$) and administration of colloids ($p = 0.0081$) and dopamine ($p = 0.0437$) significantly contributed to increased cost of hospitalization (Table 2).

Survival to discharge

Of the 235 dogs, 12 died or were euthanized, yielding a perianesthetic mortality rate of 5.1% for this study population. Patients that were alive at discharge had significantly lower hospital charges [1680 (1176−2359) USD] than those that died or were euthanized [2629 (2067−4375) USD; $p = 0.0137$; Table 3].

Factors associated with survival to discharge in the univariable analysis included ASA status, presence of hypothermia, temperature nadir, administration of colloids, colloid volume per kg body weight, administration of dopamine, hemorrhage amount and hypertension AUC (Tables 3 and 5). ASA status was strongly linked with survival ($p < 0.0001$), with higher ASA status yielding poorer outcome. Dogs that died were more likely to be hypothermic ($p = 0.0301$), and the temperature nadir for patients that did not survive to discharge [94.6 (92.3−97.4) °F] was lower than that of surviving patients [96.3 (95.0−97.7) °F; $p = 0.0036$]. The use of dopamine was also different in living patients *versus* nonsurvivors ($p = 0.0019$). Only 17 of 223 living patients (7.6%) were administered dopamine, whereas 41.7% of nonsurvivors (five of 12 animals) were treated with this inotropic agent. Similarly, colloids were more commonly administered to those who did not survive ($p < 0.0001$; Table 5). Nonsurvivors were administered a higher dose of colloids of 5.3 (0.0−16.6) compared with 0.0 (0.0−0.0) mL kg^{-1} ($p < 0.0001$; Table 3). Additionally, only 22 of 222 discharged animals (9.9%) were administered colloids, whereas seven of 12 nonsurvivors (58.3%) were administered colloids. Hemorrhage amount ($p = 0.0009$) and hypertension AUC ($p = 0.0285$) were also greater for nonsurvivors. Importantly, once all these variables were evaluated in the multivariable model, only increasing ASA status ($p = 0.0314$) and the administration of a larger volume of colloids per kg body weight ($p = 0.0008$) were significantly associated with whether a patient survived to discharge, died or was euthanized (Table 6).

Table 2 Multivariable analysis of predictors of increased hospital charges

Variable	Partial R^2	Model R^2	C(p)	Parameter estimate	Standard error	*p*
ICU duration	0.5114	0.5114	108.38	328.23	22.65	<0.0001
Anesthesia duration	0.0785	0.5899	59.886	2.83	0.57	<0.0001
Age	0.0135	0.664	18.173	2.37	1.05	0.0253
Weight	0.0072	0.6795	12.252	8.44	3.85	0.0293
Sex	0.004	0.6892	10.004	−260.11	161.37	0.1086
Colloids	0.0148	0.6506	24.853	436.88	163.36	0.0081
Dopamine	0.0057	0.6851	10.603	369.42	182.02	0.0437
Hypertension	0.0083	0.6723	14.859	257.25	107.75	0.0179
Hemorrhage	0.0459	0.6358	32.368	2.12	0.52	<0.0001

A total of nine variables were included: intensive care unit (ICU) duration, anesthesia duration, age, weight, sex, colloid administration, dopamine administration, presence of hypertension and hemorrhage amount.

Table 3 Univariable analysis of continuous variables for alive *versus* dead patients

Variables	Alive	Dead	*p*
Hospital charges (USD)	1680 (1176–2,359) [1768–2092]	2629 (2067–4375) [1973–4030]	0.0137
ICU Stay (days)	0.7 (0–2.2) [1.3–1.9]	0.5 (0–4.7) [0.1–4.5]	0.347
Hemorrhage amount (mL)	0.0 (0.0–0.0) [9.6–25.2]	0.0 (0.0–177.5) [–66.56–486.6]	0.0009
Inhalant AUC/duration	0.2 (0.1–0.2) [0.1–0.3]	0.1 (0.1–0.3) [0.1–0.2]	0.7893
Anesthesia duration (minutes)	165.0 (105.0–231.0) [164.7–190]	153 (94.0–255.3) [111.6–239]	0.9434
Temperature/duration	5.2 (4.1–6.0) [4.8–5.9]	5.4 (3.6–6.2) [3.5–7.8]	0.8155
Hypothermia duration	0.0 (0.0–0.0) [10.2–19.7]	0.0 (0.0–75.0) [–2.8–81.9]	0.0764
Temperature nadir (°F)	96.3 (95.0–97.7) [96.1–96.7]	94.6 (92.3–97.4) [93.3–96.8]	0.0036
Colloid volume (mL kg^{-1})	0.0 (0.0–0.0) [0.3–1.0]	5.3 (0.0–16.6) [2.2–14.9]	<0.0001
Crystalloid volume (mL kg^{-1} $hour^{-1}$)	9.2 (6.7–13.2) [9.5–12.2]	14.1 (7.5–18.5) [8.2–21.5]	0.3182
ASA status	2.0 (2.0–3.0) [2.1–2.4]	3.0 (2.5–3.5) [2.4–3.8]	<0.0001
HR Peak (beats $minute^{-1}$)	135.0 (115.0–157.0) [–291.5–1446.0]	142.5 (123.5–173.8) [127.7–176.1]	0.765
Tachycardia duration (minutes)	0.0 (0.0–0.0) [3.2–7.6]	0.0 (0.0–8.8) [–12.3–44.0]	0.1413
Tachycardia AUC	0.0 (0.0–0.0) [52.8–167.9]	0.0 (0.0–0.0) [–395.8–1164]	0.2829
RPP/duration	1918.0 (1542.0–2380.0) [1893.0–242,344]	1981.0 (1522.0–2531.0) [1614.0–2363.0]	0.7631
SAP peak (mmHg)	136.0 (120.0–150.8) [134.7–141.6]	138.5 (120–144) [124.4–142.9]	0.5402
Hypotension duration (minutes)	5.0 (0.0–30.0) [15.7–24.9]	15.0 (0.0–48.75) [1.2–86.3]	0.0755
Hypotension AUC	0.0 (0.0–222.5) [137.3–247.1]	107.3 (0.0–239.3) [–111.2–1001]	0.1194
SAP nadir (mmHg)	84.0 (72.0–96.0) [82.4–87.2]	80.5 (69.8–96.0) [63.9–91.5]	0.1666
Age (months)	85.0 (36.5–120.0) [75.4–88.4]	109.0 (82.5–133.8) [76.3–135.4]	0.0963
Weight (kg)	19.7 (7.8–30.4) [18.4–22.1]	18.7 (6.1–31.5) [11.5–29.6]	0.9405

ASA, American Society of Anesthesiologists; AUC, area under the curve; CI = confidence interval; HR, heart rate; ICU, intensive care unit; IQR, interquartile range; RPP = rate pressure product; SAP, systolic arterial pressure; USD, United States dollars. Data are presented as median (IQR; 95% CI).

Discussion

Until about the past decade, relatively little was known about how intraoperative anesthetic factors affected surgical outcome in humans, and even less is still known in veterinary medicine. The retrospective study presented here provides new insight regarding how hemodynamics, body temperature, $P_E'CO_2$ and type (e.g., different inhalants) and duration of anesthesia might affect morbidity and mortality in dogs.

The present study examined the influence of numerous pre- and intra-anesthetic variables on three key patient outcomes: duration of hospitalization in the ICU, cost of hospitalization and survival to discharge. While many factors appeared to contribute to these outcomes, once subjected to multivariable analysis for confounding effects, only a limited number of variables demonstrated significant effects. The only variables that influenced duration of hospitalization were ASA status and anesthesia duration. The total hospital charges were affected by several factors, including age, weight, ICU duration, anesthesia duration, hemorrhage amount, administration of colloids and presence of intraoperative hypertension. The only variables that were significant poor prognostic indicators for survival to discharge were ASA status and administration of colloids.

Despite the fact that blood pressure and HR are monitored closely in anesthetized patients, little is known about how abnormal values might affect morbidity and mortality. In dogs, intraoperative hypotension has been identified as a risk factor for the development of septic peritonitis after gastrointestinal surgery (Grimes et al. 2011), as well as surgical site infection following a range of other surgical procedures (Turk et al. 2015).

The data presented here affirm that hypotension under general anesthesia is common, affecting 60.4% of the study population. Notably, the majority of tachycardic animals had experienced concurrent hypotension and was perhaps mounting a compensatory response. However, tachycardia as a response

Table 4 Comparison of hospital charges, in United States dollars (USD), and intensive care unit (ICU) duration (in days) in univariable analysis

Variable	Hospital charges (USD)	*p*	ICU duration (days)	*p*
Sex		0.0808		0.6384
F/S	1854 (1097–2553) [1779–2336]		0.7 (0–2.6) [1.4–2.4]	
F/I	1391 (712.5–1885) [1063–1791]		0.7 (0.0–2.2) [0.6–2.4]	
M/C	1897 (1445–2498) [1861–2398]		0.7 (0.1–1.6) [1.0–2.1]	
M/I	1476 (1148–2212) [1401–2243]		0.7 (0.0–2.2) [0.7–2.1]	
Hypotension		0.8852		0.438
Yes	1706 (1231–2468) [1797–2190]		0.7 (0.3–2.5) [1.4–2.1]	
No	1670 (1059–2335) [1672–2265]		0.7 (0.0–1.7) [1.0–2.0]	
Hypertension		0.0178		0.1129
Yes	1592 (1059–2344) [1929–2614]		0.7 (0.3–2.7) [1.4–2.7]	
No	1977 (1296–2637) [1667–2028]		0.7 (0.0–1.7) [1.2–1.8]	
Tachycardic		0.049		0.0426
Yes	2056 (1455–2898) [1928–2682]		1.0 (0.0–3.0) [1.4–3.2]	
No	1643 (1104–2390) [1721–2083]		0.7 (0.0–2.0) [1.2–1.8]	
Colloids		<0.0001		0.0003
Yes	2550 (1838–3436) [2376–3688]		2.7 (0.7–5.3) [2.0–4.2]	
No	1643 (1086–2220) [1684–1992]		0.7 (0.0–1.7) [1.1–1.7]	
Dopamine		0.0012		0.0579
Yes	2750 (1638–3559) [2096–3563]		0.8 (0.3–5.0) [1.2–4.0]	
No	1676 (1164–2285) [1739–2063]		0.7 (0.0–1.9) [1.3–1.9]	
Dobutamine		0.1608		0.0396
Yes	2007 (1474–2995) [1878–2619]		1.7 (0.7–3.6) [1.6–3.1]	
No	1651 (1117–2354) [1752–2115]		0.7 (0–1.7) [1.2–1.8]	
Hypothermic		0.1289		0.5022
Yes	1904 (1426–2484) [1846–2513]		1.0 (0.7–2.3) [1.2–2.4]	
No	1619 (1054–2349) [1694–2073]		0.7 (0.0–1.7) [1.2–1.9]	

CI = confidence interval; F/I, female intact; F/S, female spayed; IQR, interquartile range; M/C, male castrated; M/I, male intact; USD, United States dollars. Data are presented as median (IQR; 95% CI).

to hypercarbia, increased sympathetic tone or hypovolemia cannot be ruled out. Despite the commonality of hypotension in this patient population, no direct effect of hypotension on the duration of hospitalization in the ICU, cost of hospitalization or survival to discharge was identified. However, administration of colloids was associated with both a higher cost of care and a poorer patient outcome (increased mortality). Furthermore, in our institution, treatment of hypotension is generally initiated if a negative trend is observed, before the blood pressure reaches the cut-off values defined here. Thus, any influence of colloid support on survival in the absence of a direct effect of hypotension could be because of aggressive management of declining blood pressure before critical levels are reached in high-risk (i.e., high ASA status) patients.

Although far less common than hypotension, 32.3% of animals became hypertensive during their anesthetic event. Hypertension could be a physiological response to nociception, drugs, hypercarbia, electrolyte or fluid imbalance, inadequate anesthetic depth or the result of cardiovascular pathology (Haskins 2015). Interestingly, 35 of 76 (46.1%) hypertensive animals also experienced hypotension at some point during their anesthetic event, perhaps indicating increased cardiovascular instability and/or difficulty in the anesthetic management of these patients.

In a recent report of adverse event surveillance, intra-anesthetic hypertension that was not pain related was reported in 1.7% of canine and feline patients at the Queen's Veterinary School Hospital in the United Kingdom (McMillan & Darcy 2016). However, the goal of the study was to evaluate an adverse event surveillance tool, and not to assess the impact of these adverse events on patient outcome. In the present study, intraoperative hypertension was much more frequent, affecting 32.3% of dogs, and it was significantly associated with increased cost of

Table 5 Comparison of categorical variables for alive *versus* dead patients in univariable analysis

Variables	Alive (*n*)	Dead (*n*)	*p*
Sex			0.8639
F/S	24	1	
F/I	75	5	
M/C	27	2	
M/I	97	4	
Hypotension			0.6875
Yes	134	8	
No	86	4	
Hypertension			0.197
Yes	74	2	
No	146	10	
Bradycardia			0.3529
Yes	40	1	
No	183	11	
Tachycardia			0.2829
Yes	44	4	
No	179	8	
Tachycardia with Hypotension			0.2874
Yes	29	3	
No	191	9	
Hypocarbia			0.1697
Yes	140	10	
No	75	2	
Hypercarbia			0.126
Yes	159	11	
No	56	1	
Dopamine			0.0019
Yes	17	5	
No	206	7	
Dobutamine			0.9619
Yes	36	2	
No	187	10	
Colloids			0.0001
Yes	22	7	
No	200	5	
Hypothermia			0.0301
Yes	50	6	
No	165	6	

F/I, female intact; F/S, female spayed; M/C, male castrated; M/I, male intact. The number of cases in each category and the *p* value comparing discharged and not discharged patients is indicated.

Table 6 Multivariable logistic regression analysis for alive *versus* dead patients

Variable	Parameter estimate	Standard error	Chi-square	*p*
ASA status	−1.4776	0.6866	4.6308	0.0314
Colloid volume kg^{-1}	−0.2216	0.0659	11.296	0.0008

Two variables were included in the analysis: American Society of Anesthesiologists (ASA) physical status and colloid volume administered per kg body weight.

care. Although hypertension did not affect the duration of hospitalization or ultimately survival, its presence nonetheless may suggest increased complexity in the management of certain cases. For example, one dog anesthetized for pacemaker placement was hypertensive for nearly 3 hours and was later euthanized with myocarditis identified at necropsy. Another dog that was hypertensive for over an hour required treatment for seizure that occurred upon emergence from anesthesia.

Interestingly, only 41 animals were bradycardic, but 137 were administered an antimuscarinic agent (atropine or glycopyrrolate). This incongruence is due, in part, to the fact that many animals were administered antimuscarinics with their premedication, representing prophylactic use rather than therapeutic intervention. Notably, bradycardia was not associated with any outcome measure. Conversely, while there was no impact of intraoperative tachycardia on ICU duration or survival, it increased the total hospital charges.

The only factor that had a significant impact on the duration of hospitalization was ASA status. The fact that higher ASA status was associated with longer hospitalization was not surprising, given that animals that were more critically ill and undergoing more complex and time-consuming procedures would require more intensive care. The requirement for ancillary hemodynamic support in the form of colloids and positive inotropes during anesthesia suggests that these animals were less stable under anesthesia, thus necessitating more intensive care and postoperative monitoring. Notably, longer anesthesia and recovery times were not associated with longer overall hospitalization, although the former approached significance.

Although only one factor was found to contribute significantly to longer hospital stays, numerous factors contributed to increased cost of that stay. Longer anesthetic events and longer stays in the ICU predictably increased costs, as did administration of colloids and dopamine. This increased cost is most likely a function of both the prolonged hospital stay and the added expense of numerous interventions. Patients with higher hospital charges were administered more costly interventions, such as transfusions, which reflects increased complexity of the management of these patients. Other contributing factors

included older age and increased weight of the patient undergoing anesthesia, presence of intraoperative hypertension and increased hemorrhage. Increased age and weight have previously been associated with increased risk of mortality in cats (Brodbelt 2010), while hypertension (Reich et al. 2002) and administration of packed red blood cell transfusions (Kheterpal et al. 2009) have been associated with poor outcomes in humans.

The only factors significantly affecting survival to discharge were the ASA status and administration of colloids, with higher ASA status and a larger volume per kilogram of colloids being positively associated with death. Given the role of colloids in treating hypovolemia and hypotension, this may suggest that greater hemodynamic instability is an important poor prognostic indicator in the sickest patients undergoing general anesthesia. However, it may also indicate that the use of colloids is harmful to these patients. Whether the former or the latter is the case is difficult to determine with a retrospective study design.

A previous study in the United Kingdom demonstrated that increased age, independent of ASA status, was a risk factor for perianesthetic mortality (Brodbelt et al. 2008), and similar associations were identified in our patient population. Increasing ASA status was associated with both longer hospitalization and death. Notably, animals in the present study that were less likely to be discharged had significantly higher hospital charges, which may suggest that despite more aggressive management of these high-risk patients during a protracted hospital stay, these animals were relatively refractory to interventions.

Several limitations of this study must be acknowledged. First, the retrospective nature of the study imposed some constraints on the data that were available for comparison and analysis. As an example, blood pressure measurement could not be standardized in advance, which may have introduced variability in the assessment of hypotension depending on whether a patient was monitored via invasive, oscillometric or Doppler blood pressure modalities. Similarly, capnographs and anesthetic gas analyzers were not used on all patients, limiting the ability to determine an effect of MV or inhalant levels. Additionally, cases were managed by several different anesthesiologists, who may have each taken different approaches to the management of similar cases. For example, one anesthesiologist might tend to give antimuscarinics with the premedication, while another may wait until clinically significant bradycardia develops before administering these agents. Additionally, the impact of evaluating anesthetic outcomes at a single institution, as opposed to a multicenter study, inherently limits the number of anesthesiologists contributing to the data pool, which may introduce unintended bias. However, the random sampling of anesthetic records prevented one anesthesiologist at the institution from contributing more to the data pool than the others.

Another limitation is that the assignment of ASA status is relatively subjective. One study evaluating interobserver variability demonstrated that major discrepancies in status assignment could occur even when observers are given identical information (McMillan & Brearley 2013). Additionally, preoperative assignment of ASA status may inherently influence intraoperative anesthetic management, contributing to differences in charges accrued and tenure in the ICU. Thus, these variables may be inextricably linked, confounding attempts to identify specific intraoperative variables that affect patient outcome independent of preoperative risk assessment. Nonetheless, the positive association of ASA status with multiple outcome measures in the present study indicates that ASA assignment remains a valuable tool.

In conclusion, this preliminary study demonstrates that certain intrinsic patient factors and intraoperative hemodynamic variables can have a significant impact on postoperative morbidity and ultimately mortality in dogs. Hence, these factors may have a prognostic value when taken together with a thorough preoperative risk assessment. Additional prospective studies will help determine the generalizability of these results, and whether patient outcomes can be improved and cost to owners can be reduced by stricter control of these intraoperative factors.

Acknowledgements

The authors would like to thank Ms. Danielle Minardi for her invaluable assistance with compiling and digitizing all the medical records, and Dr. Deborah Keys for her statistical expertise.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

MDS: data collection and interpretation, statistical analysis and preparation of manuscript. CY: data collection and analysis. MB: data interpretation and preparation of the manuscript. EHH: design, data management, statistical analysis and preparation of manuscript.

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Received 5 August 2016; accepted 24 April 2017.

Available online 7 June 2017

Appendix A. Number of dogs in each breed category.

Dog breed	Number of individuals
Labrador Retriever	28
Mixed Breed	26
Golden Retriever	14
Dachshund	11
Shih Tzu	10
Pug	9
Yorkshire Terrier	9
English Bulldog	8
Jack Russell Terrier	7
Australian Shepherd	6
Beagle	5
Border Collie	5
Chihuahua	5
Cocker Spaniel	4
Doberman Pinscher	4
German Shepherd	4
Staffordshire Pitbull Terrier	4
Boxer	3
Dachshund (Miniature)	3
Great Dane	3
Rat Terrier	3
Rottweiler	3
Springer Spaniel	3
Others	58
Total Dogs	235

Appendix B. Number and relative percentage of dogs administered specific agents for cardiovascular support.

Drug	Number of dogs	% of dogs
Atropine	15	6.4
Dobutamine	38	16.2
Dopamine	22	9.4
Ephedrine	4	1.7
Epinephrine	2	0.9
Glycopyrrolate	122	52.0
Norepinephrine	1	0.4
Phenylephrine	5	2.1
Vasopressin	1	0.4

