Association between body mass and hypotension in dogs under general anaesthesia

Citation for published version:
Miller, L, Duncan, J, Handel, I, Shaw, D, McKenzie, HE & Greenhalgh, S 2023, 'Association between body mass and hypotension in dogs under general anaesthesia', *Journal of Small Animal Practice*, pp. 1-9.
https://doi.org/10.1111/jsap.13671

Digital Object Identifier (DOI):
10.1111/jsap.13671

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Journal of Small Animal Practice

Congress is... coming!

The UK's largest small animal congress is set to return to Manchester Central, taking centre stage on 21-23 March 2024.

CONNECTING you with thought leaders and innovators in small animal practice. BSAVA Congress 2024 promises to deliver an **ENRICHING** and inspiring learning experience with 3 days of lectures, panel discussions and interactive sessions. Explore the exhibition for insights into the latest industry innovations and share experiences with your peers all within an exciting and engaging environment.

Be part of BSAVA's commitment to **EDUCATING** the small animal veterinary profession.

Get ready to book your tickets when registration opens on 12 October!

bsavacongress.com

CONNECTING | EDUCATING | ENRICHING

ORIGINAL ARTICLE

Association between body mass and hypotension in dogs under general anaesthesia

L. Miller *,[1], J. C. Duncan*, I. G. Handel*, D. J. Shaw*, H. E. McKenzie† and S. N. Greenhalgh *

*The Royal (Dick) School of Veterinary Studies & The Roslin Institute, The University of Edinburgh, Easter Bush, Midlothian, EH25 9RG, UK
†PDSA, Whitechapel Way, Priorslee, Telford, Shropshire, TF2 9PQ, UK

[1]Corresponding author email: lmille10@ed.ac.uk

Objectives: To investigate the association between body mass and hypotension during general anaesthesia in dogs undergoing surgical and diagnostic procedures within a referral hospital.

Materials and Methods: Retrospective evaluation of the anaesthetic records of 1789 dogs was performed. Data on signalment, anaesthetic protocol and physiological variables, including mean arterial pressure, were collected. A multivariable generalised linear model was used to identify associations between explanatory variables, including body mass, and hypotension.

Results: In the population studied, increasing body mass (per 10 kg) was significantly associated with decreasing odds of hypotension (odds ratio 0.68; 95% confidence interval: 0.60 to 0.77). Additional variables associated with a decreased odds of hypotension were pre-anaesthetic medication with alpha-2 agonists (odds ratio 0.63; 95% confidence interval 0.48 to 0.82) and increased body temperature (per 1°C) during general anaesthesia (odds ratio 0.77; 95% confidence interval 0.67 to 0.88). Brachycephaly (odds ratio 1.72; 95% confidence interval 1.25 to 2.38), ASA physical status classification >3 (odds ratio 2.03; 95% confidence interval 1.16 to 3.56), undergoing a surgical procedure (*versus* diagnostic) (odds ratio 1.57; 95% confidence interval 1.10 to 2.23) and bradycardia (odds ratio 1.37; 95% confidence interval 1.05 to 1.80) were independently associated with increased odds of hypotension.

Clinical significance: Dogs of lower body mass and brachycephalic breeds may be at higher risk of hypotension during general anaesthesia or alternatively represent subpopulations in which accurate blood pressure measurement presents a greater challenge. Monitoring blood pressure accurately in these groups requires particular attention and provisions for treating hypotension should be readily accessible.

Journal of Small Animal Practice (2023); 1–9
DOI: 10.1111/jsap.13671

Accepted: 8 August 2023

INTRODUCTION

Hypotension is the most commonly reported complication of general anaesthesia (GA) in dogs (Gaynor *et al.* 1999, Redondo *et al.* 2007, Carter *et al.* 2017), with a reported incidence ranging from 7% to 38% (Gaynor *et al.* 1999, Mazzaferro & Wagner 2001, Redondo *et al.* 2007). During GA, hypotension is typically defined within the veterinary literature as a mean arterial pressure (MAP) lower than 60 mmHg (Gaynor *et al.* 1999, Waddell 2000), below which perfusion of, and oxygen delivery to, vital organs may be compromised (Mazzaferro & Wagner 2001). Although some studies have not detected any association between intraoperative hypotension and adverse outcomes in specific surgical populations (Dixon & Fauber 2017, Hattersley *et al.* 2020), intraoperative hypotension in dogs has been associated with morbidities including

An abstract of this work was presented at the Association of Veterinary Anaesthetists Spring Meeting 2022.

neurological deficits, intestinal dehiscence, septic peritonitis and increased postoperative pain (Broadstone 1999, Grimes *et al.* 2011, Rossmeisl *et al.* 2013, Snowdon *et al.* 2016, Latimer *et al.* 2019).

In humans, as well as morbidities including myocardial injury and acute kidney injury, intraoperative hypotension has been associated with increased postoperative mortality (Monk *et al.* 2005, Walsh *et al.* 2013, Sun *et al.* 2015, Wesselink *et al.* 2018). Research within the human field has sought to identify predictors of intraoperative hypotension. Age, American Society of Anesthesiologists (ASA) physical status classification and the use of specific pharmaceutical agents are all considered to be risk factors (Reich *et al.* 2005).

Limited data on risk factors for hypotension during GA have been identified within the veterinary literature. A strong negative association (R^2=0.99) between body mass and probability of hypotension under GA was reported as an incidental finding in a study examining whether drug choice for pre-anaesthetic medication might be associated with incidence of hypotension in female dogs being neutered (Martin-Flores *et al.* 2019). A similar finding was reported in dogs undergoing thoracolumbar hemilaminectomy (Bruniges & Rioja 2019). Conversely, other studies have not identified any association between body mass and hypotension (Lizuka *et al.* 2013, Costa *et al.* 2015). Proposed explanations for the previously identified associations between low body mass and hypotension include an increased likelihood of hypothermia, bradycardia and relative anaesthetic overdose, in addition to greater relative haemorrhage in smaller patients (Brodbelt *et al.* 2008, Martin-Flores *et al.* 2019).

Given the high incidence of hypotension reported during GA in dogs, identifying underlying risk factors is important because this could ultimately lead to patient benefit through adoption of strategies that reduce the overall risk to the individual. Most simply, variables that are under control of the anaesthetist could be avoided or countered. Even identification of risk factors intrinsic to the patient and/or outside of the direct control of the anaesthetist could result in patient benefit through appropriate pre-anaesthetic preparation, adoption of additional preventative strategies, more diligent peri-anaesthetic monitoring and earlier intervention.

The aim of this study was to determine whether the previously reported association between body mass and hypotension persists within a larger and more diverse canine population undergoing GA. A secondary aim of this study was to identify whether other patient, anaesthetic or procedural factors might be associated with risk of hypotension.

MATERIALS AND METHODS

The study was approved by the Royal (Dick) School of Veterinary Studies Veterinary Ethical Review Committee (Reference 49.20). Informed, written consent for the use of patient data was provided by owners at time of patient admittance to the Hospital for Small Animals, University of Edinburgh, as part of the standard hospital consent form. The study is reported in accordance with the STROBE-Vet Statement guidelines (Sargeant *et al.* 2016).

The Hospital for Small Animals, University of Edinburgh, is a large teaching and referral hospital accepting secondary and tertiary referrals (elective and emergency), primarily from across Scotland and North England. It has European and/or American Diplomates in the following specialities: anaesthesia, behaviour, cardiology, dermatology, diagnostic imaging, emergency and critical care, internal medicine, neurology and neurosurgery, oncology, ophthalmology, orthopaedic surgery and soft tissue surgery. The hospital employs over 50 clinicians and over 100 nursing staff, providing veterinary care to approximately 10,000 patients annually. All GAs are overseen by a board-certified or board-eligible anaesthetist, with anaesthetics carried out by specialists, residents, interns and registered veterinary nurses.

All dogs presenting to the hospital and undergoing GA between the period of December 2018 and June 2020 were identified following a search of the veterinary practice management software (Provet Cloud©). The medical records of each identified case were subsequently searched to retrieve the record for retrospective evaluation. All GAs were eligible for inclusion, whether scheduled, elective or emergency. Where any dog received more than one GA during the stated time period, only the most recent record was evaluated. In incidences where the anaesthetic record was missing, these cases were excluded from the study. Additional exclusion criteria included a GA duration of less than 30 minutes and records in which body mass or MAP were not recorded. For all eligible cases, the following patient and procedural data were collected from evaluation of the corresponding anaesthetic record: age, breed (as reported by the owner and/or in the clinical history provided by the referring veterinarian), brachycephaly [Yes or No (Y/N)], sex and neuter status, body mass, body condition score (1 to 9), ASA grade (1 to 5), overall procedure type (diagnostic or surgical). Surgical and diagnostic procedures were further subdivided as follows: surgical procedures were categorised as neurologic, orthopaedic, soft tissue or other surgery; diagnostic procedures were categorised as endoscopy, magnetic resonance imaging (MRI), radiography/CT, other imaging or other diagnostic (Table S1). Brachycephaly was defined by breed, as previously reported (O'Neill *et al.* 2020).

As per hospital procedure, the anaesthetic record is updated every 5 minutes. The following anaesthetic data were taken from each record: anaesthetic drug protocol (Table S2), GA duration, lowest heart rate (HR) recorded, occurrence of bradycardia (defined as a HR of <60 beats per minute) (Y/N), lowest MAP recorded, lowest body temperature recorded, use of mechanical ventilation at any time point (Y/N), method of blood pressure measurement (non-invasive/invasive). Choice of non-invasive or invasive blood pressure monitoring was at the discretion of the attending anaesthetist. Non-invasive blood pressure measurements were obtained using oscillometric technologies (either Datex-Ohmeda S/5™ Compact Anesthesia Monitor or Cardell® Insight Veterinary Monitor). In cases where blood pressure measurements were obtained invasively, this was achieved using the

Datex-Ohmeda S/5™ Compact Anesthesia Monitor and a standardised technique, as previously described (Waddell 2000). For each case, it was documented whether or not hypotension occurred at any time point during GA (Y/N). Hypotension was defined as two or more consecutive blood pressure readings at an interval of ≥5 minutes where MAP was <60 mmHg. When any case was identified as having an episode of hypotension during GA, the following additional data in relation to the specific episode of hypotension were collected: HR, temperature, use of mechanical ventilation (Y/N), time from induction of anaesthesia.

All anaesthetic records were evaluated in random order by the first author, with collected data used to populate a custom database (Excel; Microsoft). Data were checked and imported into the R statistical package (version 3.6.1, R Core Team 2021) via RStudio (version 1.2.1335, R Studio Team 2016). Descriptive statistics for continuous variables are displayed as median and range.

Multivariable generalised linear models (mvGLM; Calcagno 2019) were used to assess associations between possible explanatory variables and hypotension (Y/N). To facilitate analysis, body mass was categorised into 10 kg intervals and GA time per 30 minutes. ASA physical status classification was categorised as follows: ASA I and II (well), ASA III (unwell), ASA IV and ASA V (severely compromised).

In order to assess which possible explanatory variables (patient characteristics, perioperative drugs and perioperative factors) were associated with hypotension, mvGLM with binomial errors were used. The set of possible explanatory variables was in excess of 20, and the potential for interactions between these was considerable, thereby making standard multivariable model selection and simplification both laborious and subjective. Therefore, a weighted model averaging technique was adopted (Burnham *et al.* 2011). Possible explanatory variables for inclusion in the initial model were chosen based on clinical experience and previous published data (Table 1).

To identify the possible explanatory variables suitable for inclusion within the final mvGLM, the *glmulti* package (version 1.0.7, Calcagno 2019) was used with a genetic algorithm to identify a set of candidate multivariable models containing different combinations of potential explanatory variables. The averaged effect sizes of variables within the best-fit models were calculated and visualised on model-averaged importance plots. Where the model-averaged importance of terms was >0.8 for any given variable, this was subsequently included within the final mvGLM. The best-fit model from the selection of candidate multivariable models was determined through calculation of the bias-corrected Akaike Information Criteria (AICc) using the *AICcmodavg* package (version 2.3-1, Mazerolle 2020) and subsequent identification of the lowest AICc (Burnham *et al.* 2011).

Coefficients and standard errors of each explanatory variable included within the final mvGLM were extracted and odds ratios (ORs) and 95% confidence intervals (CIs) calculated. An odds ratio plot was created. Odds ratios with 95% CIs not crossing one were considered significant.

Table 1. List of potential explanatory variables for hypotension in 1789 dogs under general anaesthesia that were used to determine the best-fit model

	Initial explanatory variables	Responses
Patient characteristics	Age	Months
	Sex	Male entire
		Male neutered
		Female entire
		Female neutered
	Brachycephalic breed	Yes
		No
	Weight	kg/10
	Body condition score	1 to 3 (underweight)
		4 and 5 (normal weight)
		6 to 9 (overweight)
	ASA physical status classification	1 and 2 (well)
		3 (unwell)
		4 and 5 (severely compromised)
Procedural Data	General anaesthetic duration (minutes)	minutes/30 (i.e. per 30 minutes)
Procedure type		Surgical
		Diagnostic
Premedication	Acepromazine	Yes
		No
	Alpha-2 agonist	Yes
		No
	Full mu agonist	Yes
		No
Induction	Propofol	Yes
		No
	Alfaxalone	Yes
		No
Maintenance	Isoflurane	Yes
		No
	Sevoflurane	Yes
		No
Administered during general anaesthesia	Full mu agonist	Yes
		No
	Ketamine	Yes
		No
	Lidocaine	Yes
		No
	Dexmedetomidine	Yes
		No
Features of general anaesthesia	Bradycardia	Yes
		No
	Lowest temperature	°C
	Mechanical ventilation	Yes
		No

Brachycephaly was defined by breed, as previously reported (O'Neill *et al.* 2020).
Bradycardia was defined as a heart rate of <60 beats per minute

RESULTS

A total of 1932 cases were returned by the database search for the period from December 2018 to June 2020. Following application of the exclusion criteria, 1789 GA episodes were included within the study (Fig 1).

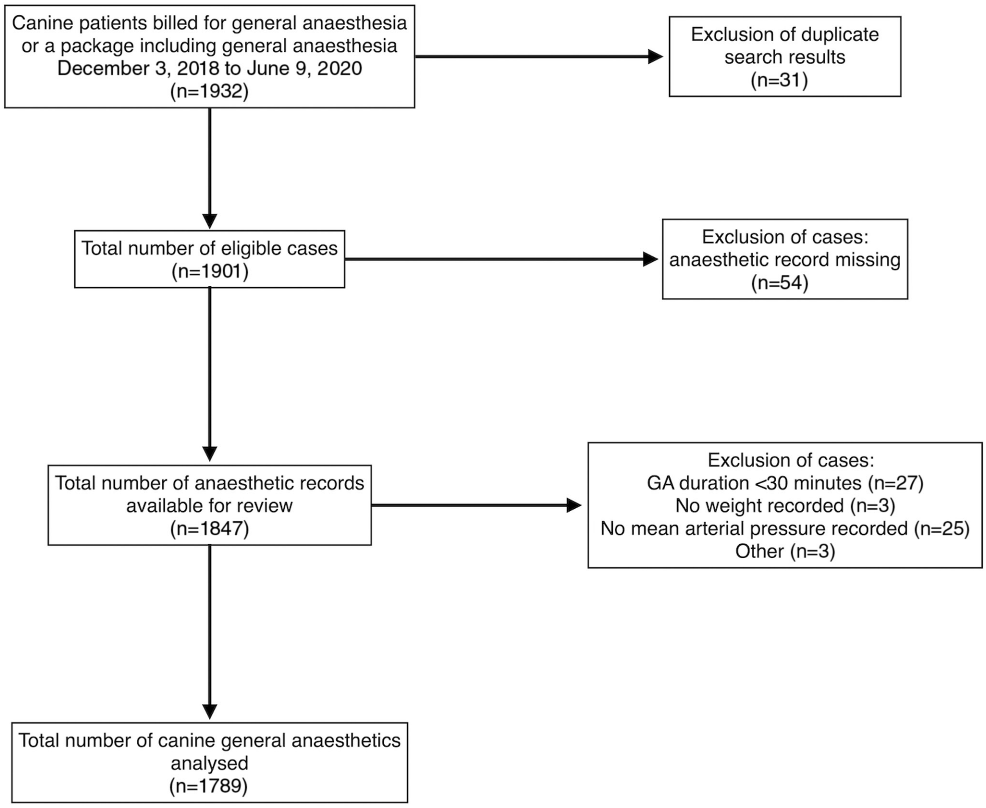

FIG 1. Flow diagram to summarise the application of inclusion and exclusion criteria to canine patients anaesthetised between December 2018 and June 2020, identifying 1789 anaesthetic records eligible for analysis

Population characteristics and procedural data are presented in Table 2 and Tables S1 to S3. The median (range) age and mass of dogs within the study was 74 (0 to 202) months and 17.2 (1.1 to 90) kg, respectively. Labrador retrievers, mixed breeds, cocker spaniels and French bulldogs were the predominant breeds represented; further detail is provided in Table S3. Median (range) duration of GA for all dogs was 141 (30 to 745) minutes, with 57% of cases undergoing surgical procedures and 43% anaesthetised for diagnostic procedures. Additional details regarding the types of surgical and diagnostic procedures undertaken are presented in Table S1. Anaesthetic and analgesic agents used are presented in Table S2.

Out of 1789 cases included, 581 (32%) were documented as having experienced at least one episode of hypotension during GA, with a median (range) time to first hypotensive episode of 31 (0 to 265) minutes post anaesthetic induction. For cases identified as hypotensive, summary data relating to HR and temperature at the first documented episode are provided in Table 3, along with the number being mechanically ventilated.

Table 4 summarises population and procedural data for dogs that experienced hypotension during GA and those that did not. Overall, 91% (1634) of dogs had blood pressure measured by non-invasive modalities; blood pressure was monitored by non-invasive methods in 521 of 581 (90%) dogs experiencing hypotension and 1113 of 1208 (92%) dogs that did not.

Within the initial model, 22 possible explanatory variables were included (Table 1). A total of 11 explanatory variables were included within the final mvGLM (Table 5). Seven explanatory variables of note were identified from the mvGLM as being significantly associated with altered odds of hypotension (Fig 2). Increasing body mass (per 10 kg) was independently associated with decreased odds of hypotension (OR 0.68; 95% CI, 0.60 to 0.77). In addition, administration of an alpha-2 agonist as part of the pre-anaesthetic medication was significantly associated with reduced odds of developing hypotension (OR 0.63; 95% CI, 0.48 to 0.82), as was increasing temperature (per 1°C) (OR 0.77; 95% CI, 0.67 to 0.88).

Variables independently associated with increased odds of hypotension were brachycephaly (OR 1.72; 95% CI, 1.25 to 2.38), ASA physical status classification >3 (OR 2.03; 95% CI, 1.16 to 3.56), undergoing a surgical procedure (*versus* diagnostic) (OR 1.57; 95% CI, 1.10 to 2.23) and bradycardia (OR 1.37; 95% CI, 1.05 to 1.80).

DISCUSSION

This single-centre, retrospective, cross-sectional study of 1789 canine GAs identified an independent association between body mass and hypotension, with increasing body mass associated with decreasing odds of hypotension. While this association has been reported in smaller studies analysing relatively homogeneous populations (Bruniges & Rioja 2019, Martin-Flores *et al.* 2019), the results of the current study indicate that the association persists in a larger, more diverse canine population undergoing a greater range of procedures. Previously suggested

Table 2. Population characteristics of included cases

Age (months)† [n=1787 (99.9%)]	74 (0 to 202)
Body mass (kg)†	17.2 (1.1 to 90)
Sex	
Female, neutered	576 (32)
Male, neutered	568 (32)
Male, entire	406 (23)
Female, entire	239 (13)
Breed	
Labrador retriever	221 (12)
Crossbreed	217 (12)
Cocker spaniel	131 (7)
French bulldog	100 (6)
Other	1120 (63)
Brachycephalic	308 (17)
Body condition score [n=1069 (60%)]	
1	2 (0.2)
2	14 (1.3)
3	49 (4.6)
4	279 (26)
5	328 (31)
6	196 (18)
7	124 (12)
8	58 (5.4)
9	19 (1.8)
ASA status [n=1333 (75%)]	
1	309 (23)
2	644 (48)
3	299 (22)
4	79 (5.9)
5	2 (0.2)

ASA American Society of Anesthesiologists
Data are presented as n (%) unless otherwise stated. n=1789 unless otherwise stated. Brachycephaly was defined by breed, as previously reported (O'Neill *et al.* 2020)
†Data are presented as median (range)

Table 3. Number of, and additional details relating to, cases identified as experiencing at least one hypotensive episode during general anaesthesia

		n
Hypotensive cases†	581 (32)	1789
Onset of hypotension (minutes post induction)	31 (0 to 265)	581
Lowest MAP (mmHg)	50 (20 to 59)	581
Heart rate at onset of hypotension (bpm)	85 (35 to 230)	575
Mechanical ventilation at onset of hypotension†	110 (19)	581
Temperature at onset of hypotension (°C)	37 (33.5 to 39.4)	216

MAP Mean arterial pressure, bpm Beats per minute
Data are presented as median (range) unless otherwise stated. Hypotension was defined as two or more consecutive blood pressure readings at an interval of ≥5 minutes where MAP was <60 mmHg
†Data are presented as n (%)

hypotheses for the association between body mass and hypotension were a predisposition of lighter patients to hypothermia and increased relative haemorrhage. The current findings suggest that the association between body mass and hypotension exists independently of body temperature, HR and procedure type (surgical *versus* diagnostic). Alternatively, it should be considered that the association identified may not have a physiological explanation but rather reflect difficulties in accurate blood pressure measurement in dogs of lower body mass.

The incidence of hypotension in this study is within the range of that previously reported (Gaynor *et al.* 1999, Mazzaferro & Wagner 2001); at least one episode of hypotension was reported in almost one third of cases. Notably, hypotension is not just a problem of lengthy anaesthetics. Time from induction to hypotension was ≤30 minutes in approximately half of the hypotensive cohort. Odds of hypotension did not increase significantly with duration of anaesthesia.

While peri-anaesthetic hypotension has previously been associated with multiple morbidities in dogs (Broadstone 1999, Grimes *et al.* 2011, Rossmeisl *et al.* 2013, Snowdon *et al.* 2016,

Table 4. Population characteristics and procedural data for hypotensive and non-hypotensive sub-populations

	Hypotensive	Non-hypotensive
Number of cases	581	1208
Age (months)†	69 (0 to 202)	77 (0 to 192)
Body mass (kg)†	11.9 (1.1 to 77.5)	20.2 (2.3 to 90)
Sex		
Female, neutered	175 (30)	401 (33)
Male, neutered	162 (28)	406 (34)
Male, entire	149 (26)	257 (21)
Female, entire	95 (16)	144 (12)
Breed		
Labrador retriever	55 (10)	166 (14)
Crossbreed	58 (10)	159 (13)
Cocker spaniel	37 (6)	94 (8)
French bulldog	58 (10)	42 (4)
Other	373 (64)	747 (62)
Brachycephalic	147 (25)	161 (13)
Body condition score, n	352	717
1	1 (0.3)	1 (0.1)
2	8 (2.3)	6 (0.8)
3	24 (6.8)	25 (3.5)
4	102 (29)	177 (25)
5	105 (30)	223 (31)
6	59 (17)	137 (19)
7	31 (8.8)	93 (13)
8	16 (4.5)	42 (5.9)
9	6 (1.7)	13 (1.8)
ASA status, n	438	895
1	89 (20)	220 (25)
2	195 (45)	449 (50)
3	114 (26)	185 (21)
4	40 (9)	39 (4.4)
5	0 (0)	2 (0.2)
GA duration (minutes)†	160 (35 to 745)	132 (30 to 685)
Procedure type		
Surgical	373 (64)	639 (53)
Diagnostic	208 (36)	569 (47)
Procedure subdivision		
Soft tissue	228 (39)	380 (32)
MRI	114 (20)	191 (16)
Endoscopy	55 (9.5)	199 (17)
Orthopaedic	73 (13)	151 (13)
Radiography/CT	32 (5.5)	157 (13)
Neurology	50 (8.6)	68 (5.6)
Other surgery	22 (3.8)	40 (3.3)
Other diagnostic	5 (0.9)	22 (1.8)
Other imaging	2 (0.3)	0 (0)
Lowest heart rate (bpm)†	65 (29 to 161)	62 (25 to 164)
Mechanical ventilation	221 (38)	390 (32)
Lowest temperature (°C)†	36.2 (32.3 to 39.5), *n* = 460	36.8 (33 to 39.9), *n* = 902

ASA American Society of Anesthesiologists, GA General anaesthesia, bpm Beats per minute
Data are presented as n (%) unless otherwise stated. Hypotension was defined as two or more consecutive blood pressure readings at an interval of ≥5 minutes where mean arterial pressure was <60 mmHg. Brachycephaly was defined by breed, as previously reported (O'Neill *et al.* 2020)
†Data are presented as median (range)

Table 5. Odds ratios (OR), 95% confidence intervals (CI) and P values for the explanatory variables for hypotension in 1789 dogs under general anaesthesia (GA) that were included within the final multivariable generalised linear model

	Final explanatory variables	Responses	OR (95% CI)	P value
Patient characteristics	Sex	Female entire	Reference	
		Female neutered	0.69 (0.47 to 1.00)	0.05
		Male entire	0.87 (0.58 to 1.31)	0.47
		Male neutered	0.66 (0.45 to 0.97)	0.03
	Non-brachycephalic breed		Reference	
	Brachycephalic breed		1.72 (1.25 to 2.38)	<0.01
	Body mass	kg/10	0.68 (0.60 to 0.77)	<0.01
	ASA status	1 and 2 (well)	Reference	
		3 (unwell)	1.33 (0.94 to 1.87)	0.08
		4 and 5 (severely compromised)	2.03 (1.16 to 3.56)	0.01
Procedural data	General anaesthetic duration (per 30 minutes)	minutes/30 (i.e. per 30 minutes)	1.04 (0.99 to 1.09)	0.09
Procedure type	Diagnostic		Reference	
	Surgical		1.57 (1.10 to 2.23)	0.01
Premedication	Alpha-2 agonist		0.63 (0.48 to 0.82)	<0.01
	Full mu agonist		0.75 (0.53 to 1.07)	0.10
Administered during GA	Dexmedetomidine		0.63 (0.48 to 1.01)	0.04
Features of GA	Bradycardia		1.37 (1.05 to 1.80)	0.02
	Lowest body temperature	Per 1°C	0.77 (0.67 to 0.88)	<0.01

ASA American Society of Anesthesiologists
Hypotension was defined as two or more consecutive blood pressure readings at an interval of ≥5 minutes where mean arterial pressure was <60 mmHg. Brachycephaly was defined by breed, as previously reported (O'Neill *et al.* 2020). Bradycardia was defined as a heart rate of <60 beats per minute

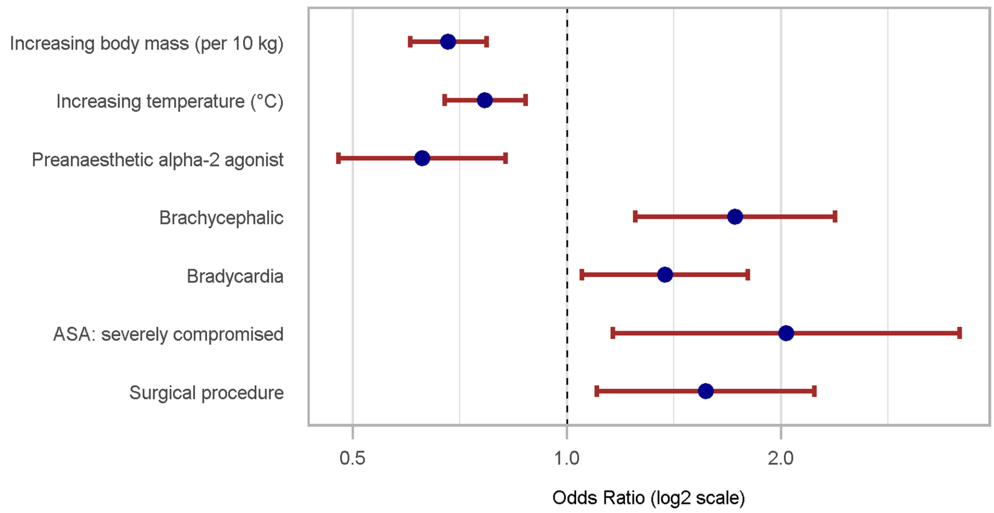

FIG 2. Odds ratios (dots) and 95% confidence intervals (error bars) for the seven explanatory variables identified by the multivariable generalised linear model as being significantly associated with hypotension during general anaesthesia in 1789 dogs. Odds ratio values greater than one indicate increased odds of hypotension. Hypotension was defined as two or more consecutive blood pressure readings at an interval of ≥5 minutes where mean arterial pressure was <60 mmHg. 'Temperature' is lowest recorded body temperature. Bradycardia was defined as a heart rate of <60 beats per minute. ASA, American Society of Anesthesiologists physical status classification; 'severely comprised' comprises ASA 4 and 5. See Table 5 for reference variables

Latimer *et al.* 2019), an association between hypotension and post-anaesthetic mortality has only been reported within the human literature (Monk *et al.* 2005). The effects of hypotension on mortality in dogs undergoing GA remain unknown, although the Confidential Enquiry into Perioperative Small Animal Fatalities identified lighter patients (<5 kg) to be at increased risk of anaesthetic mortality (Brodbelt *et al.* 2008). Further work is required to clarify the relationship between hypotension during anaesthesia and long-term mortality rates in dogs of lower body mass.

Brachycephalic breeds were identified as having significantly greater odds of developing hypotension in comparison to non-brachycephalic breeds. Although brachycephaly has been associated with a generally increased risk of peri-anaesthetic complications (Gruenheid *et al.* 2018), a specific association with hypotension has not previously been reported and was somewhat unexpected. Brachycephalic breeds have previously been reported to have higher conscious arterial blood pressures in comparison to mesocephalic and dolichocephalic breeds (Hoareau *et al.* 2012, De Melo Dias *et al.* 2016). One possible explanation for the increased odds of hypotension during GA in brachycephalic breeds is their previously reported increased vagal tone (Doxey & Boswood 2004, Doyle *et al*. 2020). This could result in a predisposition to bradycardia and consequently reduced cardiac output during GA. However, the results of the current study suggest an association between brachycephaly and hypotension independent of the presence of bradycardia. Systematic under-reading of blood pressure due to the limb conformation of brachycephalic breeds cannot be ruled out since blood pressure was predominantly measured using non-invasive oscillometric techniques.

Inclusion of an alpha-2 agonist within the pre-anaesthetic medication protocol almost halved the odds of hypotension. This finding is consistent with those reported by Martin-Flores *et al*. (2019), whereby dogs administered acepromazine had nearly three times greater odds of developing hypotension than those administered dexmedetomidine. In addition, a prospective randomised crossover study of six dogs undergoing isoflurane anaesthesia identified that hypotension was prevented by pre-anaesthetic medication with dexmedetomidine when compared to acepromazine (Grasso *et al*. 2015). Other studies have not identified differences in the incidence of hypotension under GA when comparing the use of alpha-2 agonists and acepromazine for pre-anaesthetic medication (Grint *et al*. 2010, Petruccione *et al*. 2021). Alpha-2-adrenoreceptor agonist-induced vasoconstriction may offer some protection against hypotension during GA. The greater degree of sedation reported in comparison to acepromazine (Petruccione *et al*. 2021) may permit greater reductions in inhalant anaesthetic agent requirements and the dose-dependent cardiovascular depression associated with their use.

Increasing body temperature was also identified to be independently associated with decreased odds of hypotension. This finding is similar to that of Bruniges & Rioja (2019), who reported a reduced risk of hypotension with increased temperature. Hypothermia during GA can cause reductions in blood pressure via a number of mechanisms including reductions in vascular tone and impairments of myocardial and baroreceptor function (Clark-Price 2015). Additionally, hypothermia results in a reduction in minimum alveolar concentration. This must be accounted for by a reduction in the concentration of inhalant agent administered to avoid exacerbating the negative inotropic and vasodilatory effects of the volatile agents (Clark-Price 2015).

An ASA physical status classification >3 was associated with increased odds of hypotension, a finding consistent with that in the human literature, where higher ASA classification has been identified as a risk factor for intraoperative hypotension (Reich *et al*. 2005, Südfeld *et al*. 2017). This result is likely to reflect the fact that patients with severe systemic disease will have impairments in cardiovascular system function. In this study, the contemporaneously assigned ASA physical status classification was considered to be the single, most useful variable to reflect the pre-anaesthetic state of the patient population. The consistency of ASA physical status classification as a prognostic indicator of anaesthetic mortality risk within 24 hours of GA in dogs has been recognised (Portier & Ida 2018). Dogs undergoing surgical procedures, as opposed to diagnostic procedures, also had increased odds of hypotension during GA. This finding in such a heterogenous population, particularly with respect to procedure type, may reflect a number of elements that differentiate dogs undergoing surgical rather than diagnostic procedures: higher insensible water losses, greater haemorrhage, increased requirement for anaesthetic and analgesic drugs.

Several limitations to the present study must be highlighted. Data were collated and analysed retrospectively. Normotension was not confirmed in all cases before the induction of anaesthesia so it is possible that some dogs were already hypotensive at the time of induction of anaesthesia. The predominant modality used for blood pressure measurements was non-invasive oscillometry, providing less accurate results in comparison to direct invasive monitoring, particularly in cases of severe hypotension (Sedgwick *et al*. 2021). In addition, blood pressure measurement site was not standardised or recorded. Patient size, equipment availability and technical skill are all factors that may limit the ability to monitor blood pressure invasively. Non-invasive modalities for blood pressure measurement have been validated in the dog (Skelding & Valverde 2020, Felisberto *et al*. 2022), but not for all sizes, conformations and conditions. Ultimately, the methodology of blood pressure measurement in this study reflects current clinical practice and the data it provides is that by which case management decisions are made.

The frequency, duration or severity of hypotensive episodes were not evaluated. Studies in humans have specifically investigated the degree to which patients can tolerate a given severity and duration of hypotension without consequence (Walsh *et al*. 2013, Wesselink *et al*. 2018). Similar analyses in the veterinary literature remain to be undertaken. Certain aspects of anaesthetic management that may influence blood pressure were not analysed, including inhalant anaesthetic agent percentage or the volume of intravenous fluid administered during GA. Although use of locoregional techniques was recorded in a binary fashion (Y/N), additional detail specifically relating to type, technique and efficacy, was not recorded. In consideration of the potential for different locoregional techniques to have contrasting effects on blood pressure, locoregional anaesthesia was not included as a potential explanatory variable as any findings from its incorporation within the analysis would be challenging to interpret. Assessment of the effects of locoregional techniques on risk of hypotension is likely best assessed in controlled studies evaluating specific techniques. Furthermore, the quantification of intraoperative haemorrhage during surgical procedures was not reliably recorded and it was therefore not possible to ascertain the effect of degree of haemorrhage on risk of hypotension in this study. Neither response to treatment of hypotension nor longer-term outcome of the dogs included was investigated, as this was not the aim of the study. The full consequences of hypotension during GA on morbidity in, and mortality of, dogs like those comprising the studied population remain to be determined.

Hypotension remains a common complication of anaesthesia in dogs, with those of lower body mass and brachycephalic breeds potentially at higher risk. Monitoring of blood pressure in dogs of low body mass or with abnormal conformation may present a challenge to the clinician. The results of the current study highlight the need for both accurate monitoring and adequate preparation for effective intervention in these patients. The inclusion of an alpha-2 agonist within the pre-anaesthetic medication may be a protective factor against hypotension during GA, although selection of anaesthetic protocol must remain tailored to the individual patient. While it should be emphasised that association does not equate to causation, the results of this retrospective study provide insight into possible risk factors for hypotension in dogs during GA. This facilitates targeted research into key risk factors and possible prevention or treatment strategies. In addition, improved awareness of factors associated with hypotension should promote appropriate pre-anaesthetic preparation for at-risk cases which, combined with assiduous monitoring and early intervention, could reduce both incidence and duration of hypotension under GA. The benefits of this to the individual patient are currently unquantifiable but should not be underestimated.

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.

Author contributions

Lucy Miller: Conceptualization (equal); investigation (lead); methodology (equal); visualization (equal); writing – original draft (lead); writing – review and editing (equal). **Juliet C. Duncan:** Conceptualization (equal); formal analysis (lead); methodology (equal); software (equal); supervision (supporting); visualization (equal); writing – review and editing (equal). **Ian G. Handel:** Formal analysis (equal); software (equal); writing – review and editing (equal). **Darren J. Shaw:** Formal analysis (equal); software (equal); writing – review and editing (equal). **Hayley E. McKenzie:** Investigation (supporting); writing – review and editing (equal). **Stephen N. Greenhalgh:** Conceptualization (lead); formal analysis (equal); investigation (supporting); methodology (equal); supervision (lead); visualization (equal); writing – original draft (supporting); writing – review and editing (equal).

References

Broadstone, R. V. (1999) Prolonged anesthetic recovery. *Clinical Techniques in Small Animal Practice* **14**, 56-64

Brodbelt, D. C., Pfeiffer, D. U., Young, L. E., *et al*. (2008) Results of the confidential enquiry into perioperative small animal fatalities regarding risk factors for anesthetic-related death in dogs. *Journal of the American Veterinary Medical Association* **233**, 1096-1104

Bruniges, N. & Rioja, E. (2019) Intraoperative anaesthetic complications in dogs undergoing general anaesthesia for thoracolumbar hemilaminectomy: a retrospective analysis. *Veterinary Anaesthesia and Analgesia* **46**, 720-728

Burnham, K. P., Anderson, D. R. & Huyvaert, K. P. (2011) AIC model selection and multimodel inference in behavioral ecology: some background, observations, and comparisons. *Behavioural Ecology and Sociobiology* **65**, 23-35

Calcagno, V. (2019) glmulti: model selection and multimodal inference made easy. R package version 1.0.7.1. https://cran.r-project.org/web/packages/glmulti/index.html. Accessed October 10, 2020

Carter, J. E., Motsinger-Reif, A. A., Krug, W. V., *et al*. (2017) The effect of heart disease on anesthetic complications during routine dental procedures in dogs. *Journal of the American Animal Hospital Association* **53**, 206-213

Clark-Price, S. (2015) Inadvertent perianaesthetic hypothermia in small animal patients. *Veterinary Clinics of North America: Small Animal Practice* **45**, 983-994

Costa, R. S., Raisis, A. L., Hosgood, G., *et al*. (2015) Preoperative factors associated with hypotension in young anaesthetised dogs undergoing elective desexing. *Australian Veterinary Journal* **93**, 99-104

De Melo Dias, M. L., Morris, C. F. M., Moreti, B. M., *et al*. (2016) Anatomical, cardiovascular and blood gas parameters in dogs with brachycephalic syndrome. *Acta Scientiae Veterinariae* **44**, 1356

Dixon, A. & Fauber, A. E. (2017) Effect of anesthesia-associated hypotension on neurologic outcome in dogs undergoing hemilaminectomy because of acute, severe thoracolumbar intervertebral disk herniation: 56 cases (2007-2013). *Journal of the American Veterinary Medical Association* **250**, 417-423

Doxey, S. & Boswood, A. (2004) Differences between breeds in a measure of heart rate variability. *Veterinary Record* **154**, 713-717

Doyle, C. R., Aarnes, T. K., Ballash, G. A., *et al*. (2020) Anesthetic risk during subsequent anesthetic events in brachycephalic dogs that have undergone corrective airway surgery: 45 cases (2007-2019). *Journal of the American Veterinary Medical Association* **257**, 744-749

Felisberto, R., Gonzalez, A. G., Flaherty, D., *et al*. (2022) Validation of oscillometric blood pressure measurement using a Datex S/5 compact multiparameter monitor in anaesthetized adult dogs. *Veterinary Anaesthesia and Analgesia* **49**, 156-164

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

Grasso, S. C., Ko, J. C., Weil, A. B., *et al*. (2015) Hemodynamic influence of acepromazine or dexmedetomidine premedication in isoflurane-anesthetized dogs. *Journal of the American Veterinary Medical Association* **246**, 754-764

Grimes, J. A., Schmiedt, C. W., Cornell, K. K., *et al*. (2011) Identification of risk factors for septic peritonitis and failure to survive following gastrointestinal surgery in dogs. *Journal of the American Veterinary Medical Association* **238**, 486-494

Grint, N. J., Alderson, B. & Dugdale, A. H. A. (2010) A comparison of acepromazine-buprenorphine and medetomidine-buprenorphine for preanesthetic medication of dogs. *Journal of the American Veterinary Medical Association* **237**, 1431-1437

Gruenheid, M., Aarnes, T. K., McLoughlin, M. A., *et al*. (2018) Risk of anesthesia-related complications in brachycephalic dogs. *Journal of the American Veterinary Medical Association* **253**, 301-306

Hattersley, R., Downing, F., Gibson, S., *et al*. (2020) Impact of intra-operative hypotension on mortality rates and post-operative complications in dogs undergoing cholecystectomy. *Journal of Small Animal Practice* **61**, 624-629

Hoareau, G. L., Jourdan, G., Mellema, M., *et al*. (2012) Evaluation of arterial blood gases and arterial blood pressures in brachycephalic dogs. *Journal of Veterinary Internal Medicine* **26**, 897-904

Latimer, C. R., Lux, C. N., Grimes, J. A., *et al*. (2019) Evaluation of short-term outcomes and potential risk factors for death and intestinal dehiscence following full-thickness large intestinal incisions in dogs. *Journal of the American Veterinary Medical Association* **255**, 915-925

Lizuka, T., Kamata, M., Yanagawa, M., *et al*. (2013) Incidence of intraoperative hypotension during isoflurane-fentanyl and propofol-fentanyl anaesthesia in dogs. *The Veterinary Journal* **198**, 289-291

Martin-Flores, M., Mostowy, M. M., Pittman, E., *et al*. (2019) Investigation of associations between preoperative acepromazine or dexmedetomidine administration and development of arterial hypotension or bradycardia in dogs undergoing ovariohysterectomy. *Journal of the American Veterinary Medical Association* **255**, 193-199

Mazerolle, M. J. (2020) AICcmodavg: model selection and multimodel inference based on (Q)AIC(c). R package version 2.3.1. https://cran.r-project.org/package=AICcmodavg. Accessed October 10, 2020

Mazzaferro, E. & Wagner, A. E. (2001) Hypotension during anesthesia in dogs and cats: recognition, causes and treatment. *Compendium on Continuing Education for the Practicing Veterinarian* **23**, 728-737

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

O'Neill, D. G., Pegram, C., Crocker, P., *et al*. (2020) Unravelling the health status of brachycephalic dogs in the UK using multivariable analysis. *Scientific Reports* **10**, 17251

Petruccione, I., Murison, P. J., Flaherty, D., *et al*. (2021) Comparison between dexmedetomidine and acepromazine in combination with methadone for premedication in brachycephalic dogs undergoing surgery for brachycephalic obstructive airway syndrome. *Veterinary Anaesthesia and Analgesia* **48**, 305-313

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

R Core Team (2021) R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. www.r-project.org. Accessed August 20, 2023

R Studio Team (2016) RStudio: integrated development for R [Online], version 1.2.1335, Boston, MA. www.rstudio.com/. Accessed August 20, 2023

Redondo, J. I., Rubio, M., Soler, G., *et al*. (2007) Normal values and incidence of cardiorespiratory complications in dogs during general anaesthesia. A review of 1281 cases. *Journal of Veterinary Medicine Series A* **54**, 470-477

Reich, D. L., Hossain, S., Krol, M., *et al*. (2005) Predictors of hypotension after induction of general anaesthesia. *Anesthesia and Analgesia* **101**, 622-628

Rossmeisl, J. H., White, C., Pancotto, T. E., *et al*. (2013) Acute adverse events associated with ventral slot decompression in 546 dogs with cervical intervertebral disc disease. *Veterinary Surgery* **42**, 795-806
Sargeant, J. M., O'Connor, A. M., Dohoo, I. R., *et al*. (2016) Methods and processes of developing the strengthening the reporting of observational studies in epidemiology – veterinary (STROBE-Vet) statement. *Journal of Veterinary Internal Medicine* **30**, 1887-1895
Sedgwick, S., Lorenzutti, A. M., Araos, J. B., *et al*. (2021) Evaluation of an oscillometric blood pressure monitor in anesthetized dogs: agreement with direct measurements and ability to detect hypotension. *Research in Veterinary Science* **135**, 162-166
Skelding, A. & Valverde, A. (2020) Review of non-invasive blood pressure measurement in animals: part 2 – evaluation of the performance of non-invasive devices. *Canadian Veterinary Journal* **61**, 481-498
Snowdon, K. A., Smeak, D. D. & Chiang, S. (2016) Risk factors for dehiscence of stapled functional end-to-end intestinal anastomoses in dogs: 53 cases (2001-2012). *Veterinary Surgery* **45**, 91-99
Südfeld, S., Brechnitz, S., Wagner, J. Y., *et al*. (2017) Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. *British Journal of Anaesthesia* **119**, 57-64
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* **123**, 515-523
Waddell, L. S. (2000) Direct blood pressure monitoring. *Clinical Techniques in Small Animal Practice* **15**, 111-118
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* **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

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. General anaesthesia (GA) duration, procedure type and subdivision for 1789 included cases

Table S2. Anaesthetic and analgesic medications administered to 1789 included cases

Table S3. Recorded breed of 1789 included cases