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ORIGINAL RESEARCH

Anaesthetic mortality in dogs: A worldwide analysis and risk assessment

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Abstract

Background: Ensuring patient safety during small animal anaesthesia is crucial. This study aimed to assess anaesthetic-related deaths in dogs globally, identify risks and protective factors and inform clinical practice.

Methods: This prospective cohort multicentric study involved 55,022 dogs from 405 veterinary centres across various countries. Data on anaesthesia-related deaths from premedication to 48 hours post-extubation were collected. Logistic regression was used to analyse patient demographics, American Society of Anesthesiologists (ASA) classification, procedure type and anaesthetic drugs used.

Results: Anaesthetic-related mortality was 0.69%. Most deaths occurred post-operatively (81%). Age, obesity and a higher ASA classification score were associated with increased mortality. Urgent procedures, non-urgent but unscheduled anaesthesias and short procedures also had higher mortality. Some sedatives, systemic analgesics, hypnotics and the use of locoregional anaesthesia were linked to a decrease in mortality.

Limitations: The limitations of the study include the non-randomised sample, potential selection bias, lack of response rate quantification, variable data quality control, subjectivity in classifying causes of death and limited analysis of variables.

Conclusion: Careful patient evaluation, drug selection and monitoring can be associated with reduced mortality. These findings can be used to develop guidelines and strategies to improve patient safety and outcomes. Further research is needed to refine protocols, enhance data quality systems and explore additional risk mitigation measures.

INTRODUCTION

Anaesthesia is an essential tool in veterinary clinical practice. It allows surgical and diagnostic procedures that would otherwise be impossible. However, as a controlled nervous system intoxication, anaesthesia can lead to complications and sometimes cause death. Despite vast improvements in monitoring, anaesthetic techniques and patient care in recent decades, the risk of anaesthesia-related death in small animals emphasises the ongoing necessity for research to enhance safety during anaesthesia and recovery.

In 1951, Albrecht and Blakely led the first investigation into anaesthetic-related mortality in small animals at the Angell Memorial Animal Hospital in Boston, USA. Their study reported an intraoperative mortality of 0.26% in dogs.[1] Years later, in 1990, Clarke and Hall undertook the first major multicentric study, which documented 41,881 anaesthetics in the UK and observed a perioperative mortality of 0.23%.[2] Another crucial study, the Confidential Enquiry into Perioperative Small Animal Fatalities, was also carried out in the UK between 2002 and 2004, involving 98,036 canine anaesthetics and sedations from 117 participating centres. This research played a vital role in comprehending anaesthetic mortality in small animals, establishing an overall rate of 0.18% for anaesthetic-related deaths in dogs.[3] However, almost 15 years have passed since this publication. The speciality has evolved, and recent studies conducted in different countries, such as those by Gil and Redondo in Spain,[4] Itami et al. in Japan,[5] Matthews et al. in

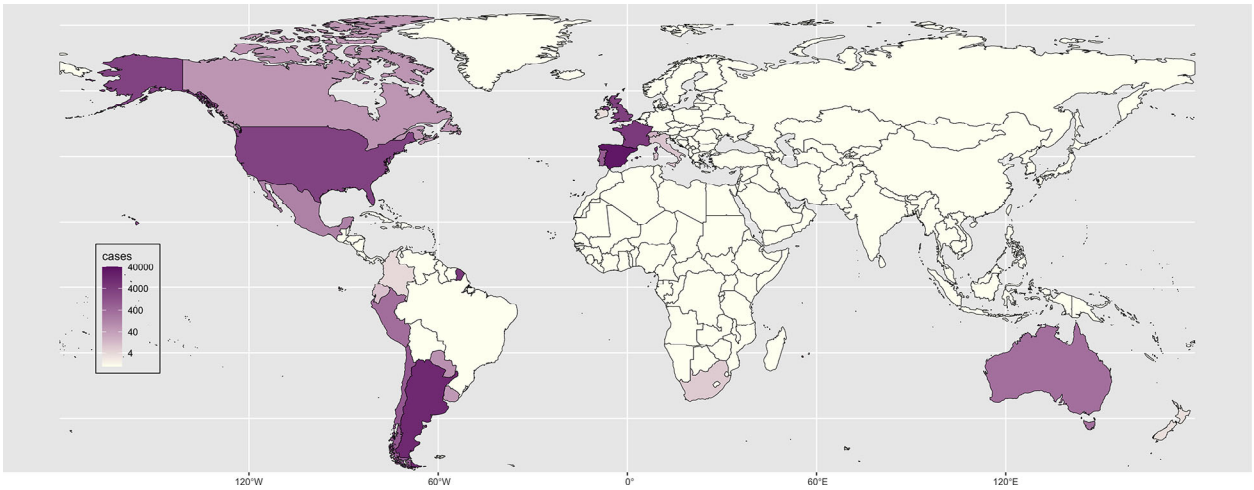

FIGURE 1 Heatmap of the number of cases submitted by country

the USA[6] and Shoop-Worrall et al. in the UK,[7] have provided further insights into the current landscape of anaesthetic mortality in this species.

Several studies have identified risk and protective factors that may be associated with increased or decreased mortality during anaesthesia. For example, factors such as advanced age,[7,8] decreased bodyweight,[8] higher American Society of Anesthesiologists (ASA) health status scores,[4,5,7,8] urgent procedures,[7,8] anaesthesia for major rather than minor procedures,[8] the use of halothane for maintenance of anaesthesia instead of isoflurane following injectable agent induction[8] and induction and maintenance with volatile agents[8] have been associated with higher odds of death. In contrast, using opioids and NSAIDs during the same anaesthetic has decreased the risk of perioperative death.[4] It is crucial to comprehend these risk factors to create effective strategies to help prevent anaesthesia-related deaths.

The objective of this research was twofold: (1) to establish the present anaesthetic-related mortality in dogs across a wide range of countries, and (2) to identify significant factors that can increase or decrease the risk of death during anaesthesia in this species. We aimed to provide valuable information to develop strategies to improve patient safety during anaesthesia.

MATERIALS AND METHODS

This observational, prospective, multicentric cohort study received ethical approval from the Ethics Committee of the Universidad Cardenal Herrera-CEU (CEEA 22/07). The study took place from February 2016 to December 2022 and involved 405 veterinary centres across various countries, including Spain, Argentina, France, the UK, the USA, Chile, Portugal and Australia (Figure 1).

The enrolled veterinary centres comprised primary care clinics, referral-only facilities and university hospitals. Their recruitment was accomplished through dissemination via various anaesthesia-related scientific societies, including the Sociedad Española de Anestesia y Analgesia Veterinaria in Spain, the Asociación de Anestesia y Analgesia de la República Argentina in Argentina, the Sociedad de Anestesiología Veterinaria de Chile in Chile and the Association of Veterinary Anaesthesiologists in Europe. Emails were also sent to diplomates and residents of the American College of Veterinary Anesthesia and Analgesia and the European College of Veterinary Anaesthesia and Analgesia. Additionally, the project was promoted through social media platforms such as Facebook, Twitter and LinkedIn. Finally, partial results of the study were also presented at various national and international congresses to encourage participation from attendees.

A PDF form was created and distributed to the participants for use in every instance of canine anaesthesia, regardless of the purpose or specific anaesthesia protocol employed (Supporting Information S1). This form was designed to be accessible and fillable using various devices, such as smartphones (Android or iPhone), tablets, laptops or computers. Once completed, the forms were automatically emailed to a designated email account. The data from the records were then extracted and exported into a spreadsheet. Each returned form captured a total of 146 variables. The data were partially anonymised to comply with the privacy regulations outlined in the General Data Protection Regulation of the European Union 2016/679.

The enrolled centres received a PDF form and instructions translated into the users' language (English, Spanish and French) to ensure proper comprehension and standardisation of data collection criteria (Supporting Information S2). Non-native Spanish, English or French speakers chose the form translated into their second language. A concise summary of the recorded variables, along with their definitions and grouping, is presented in Table 1. Participants were encouraged to include all dogs that underwent anaesthesia in the study. For this study, anaesthesia was defined as a hypnotic state, in which hypnotic drugs or combinations were used, that could facilitate endotracheal intubation, regardless of

TABLE 1 Recorded variables, definitions and grouping

Hospital: Name of the veterinary clinic or hospital where the anaesthetic was performed.

Vet or nurse/tech: Qualification of the person who performed the anaesthetic.

Date: The date on which the anaesthetic took place.

Case: Case identification (cases were sequentially numbered to preserve privacy and anonymity).

Species: Dog or cat.

Sex: Male (M) or female (F). If the patient was neutered, this was also recorded.

Breed:

Age: In years. Patients were classified into different age groups: paediatric (<3 months), young (3–12 months), adult (>1–5 years), senior (>5–12 years) and geriatric (>12 years).

Weight: In kg.

Body condition score: Classified into five classes—1: cachectic; 2: thin; 3: average, 4: semi-obese and 5: obese.

ASA: Physical status using the classification of the American Society of Anesthesiologists:
- ASA I: Normal healthy animal, no underlying disease.
- ASA II: Minor disease present. Animals with slight to mild systemic disturbance, animal able to compensate.
- ASA III: Evident disease present. Animal with moderate systemic disease or disturbances, mild clinical signs. That is, anaemia, moderate dehydration, fever, low-grade heart murmur or cardiac disease.
- ASA IV: Significantly compromised by disease. Animals with pre-existing systemic disease or disturbances of a severe nature. That is, severe dehydration, shock, uraemia, toxaemia, high fever, uncompensated heart disease, uncompensated diabetes, pulmonary disease or emaciation.
- ASA V: Moribund. Surgery is often performed in desperation on animals with life-threatening systemic diseases. Advanced heart, kidney, liver or endocrine disease cases, profound shock, severe trauma, pulmonary embolus or terminal malignancy.

Scheduling: If the anaesthetic was scheduled, not scheduled but not urgent, or urgent.

Reason for anaesthesia: Described shortly. For example: 'ovariohysterectomy', 'digestive endoscopy', 'hip luxation', 'radius and ulna fracture', 'pyometra', etc.

Surgery: Classification of the reason for anaesthesia:
- Minor: Anaesthesia for minor procedures in which cavities are not open. For example, wound suture, orchiectomy, mastectomy, ophthalmic surgery, scrotal or perineal hernia, etc.
- Abdominal: Procedures that imply a laparotomy. For example, enterectomy, pyometra, cystotomy, gastrotomy, splenectomy, etc.
- Ortho: Anaesthesia for orthopaedic surgery or neurosurgery—fractures, luxations, hemilaminectomies, etc.
- Diagnostic: If the anaesthetic was performed for diagnostic purposes—digestive endoscopy, CT, MRI, radiography, blood collection, etc.
- Thoracic: Surgeries opening the thoracic cavity (thoracotomies)—diaphragmatic hernia, cardiac or pulmonary surgery, pneumothorax, etc.

Protocol
- TIVA: Total intravenous anaesthesia. If maintenance was carried out using parenteral drugs.
- Inhalational: Maintenance was done with volatile anaesthetics; induction could be done using parenteral drugs.
- PIVA: Partial intravenous anaesthesia. Maintenance using volatile anaesthetics, but constant rate infusions were used (ketamine, fentanyl, lidocaine, etc.).

Monitoring: Level of monitoring:
- Basic: Monitoring was performed using a stethoscope/pulse palpation, respiratory rate and temperature only.
- Average: Clinical monitoring plus non-invasive instrumental monitoring (pulse oximetry, capnography, ECG, non-invasive arterial pressure).
- Advanced: Invasive instrumental monitoring (cardiac output, invasive arterial pressure, blood gases).

Anaesthetic protocol: The drugs used and in which phases they were used were recorded (premedication, induction, maintenance, postoperative).

Locoregional: If locoregional techniques were employed. Epidural or block: Description of the technique (epidural sacrococcygeal, quadratus lumborum block, Transversus abdominis plane block, sciatic and femoral block, etc.).

Fluid therapy: Fluids employed—saline, Ringer's lactate, glucosaline, colloid (gelatine or dextran) or other (if not on the list).

O_2/Air: If oxygen or medical air were administered.

Intubation: If the tracheal intubation was performed or not.

Circuit: The circuit employed. Circle Ayre's T piece or other (write the name of this circuit in this case).

Mechanical ventilation: If ventilation was used or not. Indicate the ventilatory mode: volume-controlled ventilation, pressure-controlled ventilation, synchronised intermittent mandatory ventilation.

Neuromuscular blocking agents: If they were employed (or not) and, if so, what ones were used.

Other drugs: If some emergency drugs were employed—atropine, dobutamine, dopamine, adrenaline, phenylephrine, noradrenaline, neostigmine, pimobendane, etc.

Duration of anaesthesia: Short—less than 15 minutes; medium—between 15 and 60 minutes; long—longer than 60 minutes.

Timetable: If anaesthesia was performed during the standard working hours or out of hours.

Hospitalisation: If the patient was hospitalised (only during the day or overnight) or not.

Death: Yes or no. If the patient died, the moment when this occurred was classified as premedication, induction, maintenance, operating room (death in theatre after the end of maintenance drugs), <3 hours (first 3 hours in the recovery room), 3–6 hours, 6–24 hours, 24–48 hours. It was also noted if the dog was euthanased for medical or surgical reasons.

Comments: Suspected cause of death, pre-existing diseases, previous medical treatments, emergency treatment, etc.

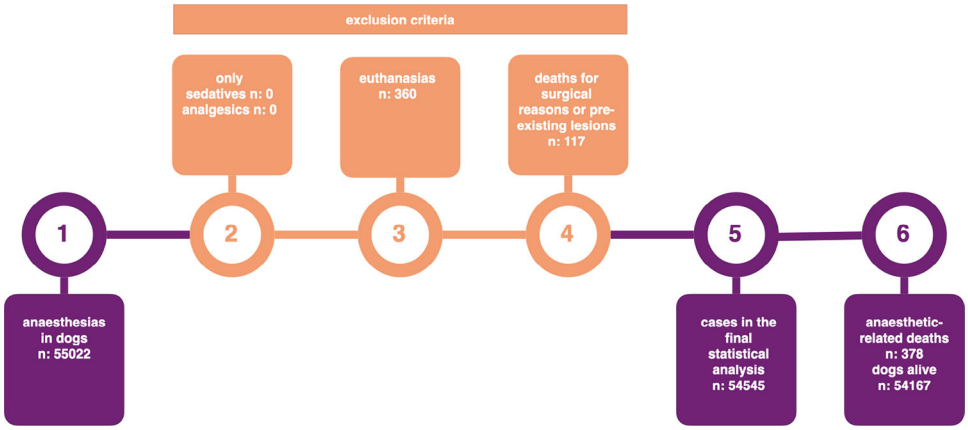

FIGURE 2 Flow diagram of the recruitment, exclusion and follow-up of the anaesthetic cases

whether intubation was performed. Therefore, dogs that received only sedatives or analgesics without proceeding to anaesthesia were excluded from the study.

Data were collected from the time of administering the pre-anaesthetic medication to 48 hours after extubation. If a dog died within this timeframe, additional information was requested by email, including details about the circumstances of death, any anaesthesia or surgical complications, further treatment or drugs administered, and the results of any postmortem examination performed, if applicable.

The principal investigator (J.I.R.) classified the deaths into three categories: (1) anaesthesia-related death (if the death or euthanasia could be directly or partially attributed to anaesthesia), (2) euthanasia (if the animal was euthanased due to the severity of pre-existing injuries), and (3) medical/surgical-related death (if the death resulted from surgical complications or disease progression during the study period). The statistical analysis excluded deaths related to euthanasia and medicine/surgery, focusing only on deaths directly associated with anaesthesia (Figure 2). In addition, the phase of anaesthesia during which the death occurred was classified as intraoperative (if it occurred during pre-anaesthetic medication, induction or maintenance periods) or postoperative (if it occurred after extubation in the operating room or within the first 48 hours after extubation).

Statistical analysis

Certain variables were grouped or categorised to increase the study's statistical power. Age was divided into distinct groups, and a new ordinal variable named AGE_CATEGORIES was created, which included paediatric (<3 months), young (3–12 months), adult (>1–5 years), senior (>5–12 years) and geriatric (>12 years). The body condition score (BCS) was classified into five classes (scored out of 5)—1: cachectic, 2: thin, 3: average, 4: semi-obese and 5: obese. Physical status was categorised according to the ASA classification. The SURGERY variable classified the reason for anaesthesia as MINOR (minor procedures without open cavities), ABDOMINAL (procedures involving laparotomy), ORTHO (orthopaedic or neurosurgical procedures), DIAGNOSTIC (for diagnostic purposes) and THORACIC (surgeries opening the thoracic cavity). The level of monitoring (MONITORING) was categorised as BASIC (basic monitoring with stethoscope/pulse palpation, respiratory rate and temperature), AVERAGE (clinical monitoring plus non-invasive instrumental monitoring) and ADVANCED (invasive instrumental monitoring techniques). Sedatives administered during premedication (PREMED_DRUG) were grouped into several categories: NONE, ACEPROMAZINE, ACEPROMAZINE PLUS BENZODIAZEPINES, ALPHA2 AGONISTS and ALPHA2 AGONISTS PLUS BENZODIAZEPINES. Analgesic medications were categorised into two variables according to their purpose and the stage at which they were administered: ANALGESIA_PREM_DRUG and ANALGESIA_MAIN_DRUG. These variables included several categories: NONE, NSAIDS, OPIOID PURE, OPIOID PURE PLUS NSAIDS, OPIOID PARTIAL AGONIST/ANTAGONIST and OPIOID PARTIAL AGONIST/ANTAGONIST PLUS NSAIDS. Induction drugs (INDUCTION_DRUG) were classified as INHALATORY if halogenated inhalational drugs were used, while maintenance drugs (MAINTENANCE_DRUG) were categorised as ISOFLURANE, SEVOFLURANE, PROPOFOL and OTHER. LOCOREGIONAL and VENTILATION variables were dichotomous variables (yes/no).

Initially, a descriptive study was performed. The 'prop.test' function of the stats package in the R programming language was used to estimate the risk of anaesthesia-related death and calculate confidence intervals (CI). Afterwards, a multivariable logistic regression model was employed to investigate the association between anaesthesia-related death and various demographic and clinical factors using the 'finalfit' package for the R programming language. Binary logistic regression analysis used a subset of selected variables regarding signalment, ASA, the reason for anaesthesia and

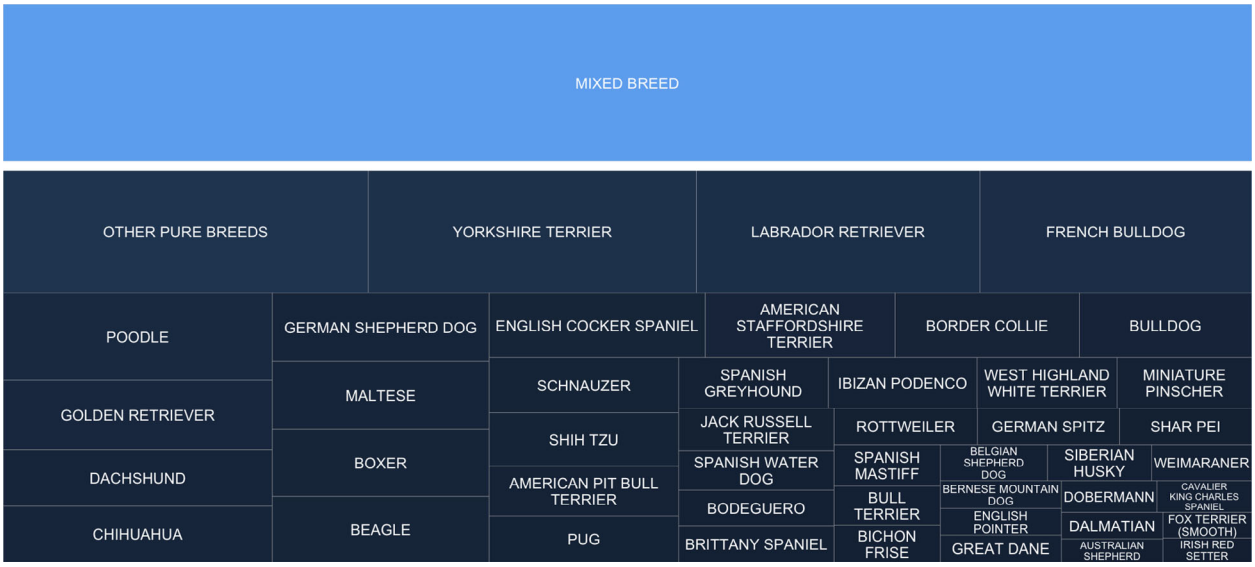

FIGURE 3 Treemap displaying the breeds of the dogs included in this study. Each breed's area is proportional to the number of dogs

details of the anaesthetic protocol using the following grouped variables: SEX, AGE_CATEGORIES, BCS, ASA, SCHEDULED, SURGERY, MONITORING, DURATION, PREMED_DRUG, ANALGESIA_PREM_DRUG, INDUCTION_DRUG, MAINTENANCE_DRUG, ANALGESIA_MAIN_DRUG, LOCOREGIONAL and VENTILATION. For this analysis, categories with an insufficient number of cases were excluded. The analysis was conducted after removing cases with missing values. Variables with a *p*-value of less than 0.05 were considered statistically significant. The model's goodness of fit was assessed using the Hosmer–Lemeshow (H&L) test, the Akaike information criterion (AIC) and concordance statistics (*C*-statistics).

The results were reported as the number of cases (*n*; %), median (range), odds ratio (OR), 95% CI and *p*-value (*p*), as appropriate.

RESULTS

Records for a total of 55,022 canine anaesthesias were received. The median (range) age and weight of the dogs were 6.0 (0.1–22.0) years and 14.0 (0.1–99.5) kg, respectively. Regarding the breed, mixed breeds were the most frequent (n = 16,252; 29.3%), and the rest were pure breeds (n = 38,770; 70.7%), representing 268 different breeds. The most frequently anaesthetised pure breeds were Yorkshire terriers (n = 3184; 5.7%), Labrador retrievers (n = 2757; 5.0%), French bulldogs (n = 2641; 4.8%) and poodles (n = 1849; 3.3%) (Figure 3). Detailed demographic data, reasons for anaesthesia, details of the procedures and descriptions of the anaesthetic techniques employed are presented in Table 2.

The duration of data collection was 2526 days (6 years, 11 months). The median (range) of cases received per day was 23 (1–194). The median number of cases per centre was 268 (51–4032). Spain (n = 29,517; 53.6%), Argentina (n = 11,555; 21.0%), France (n = 4560; 8.3%), the UK (n = 3139; 5.7%) and the USA (n = 2898; 5.3%) were the countries that sent the most cases (Figure 1).

The frequency of drug usage is displayed in Table 3. Overall, alpha$_2$-agonists were the most frequently used sedatives in pre-anaesthetic medication (n = 35,385; 64.7%), followed by benzodiazepines (n = 6689; 12.3%) and acepromazine (n = 4974; 9.1%). Propofol was the predominant hypnotic agent for induction (n = 45,748; 83.8%), while isoflurane was the most widely used agent for the maintenance of anaesthesia (n = 40,505; 74.3%). Methadone was the most commonly used opioid in pre-anaesthetic medication (n = 31,326; 57.4%), and meloxicam was the most common NSAID (n = 4913; 8.9%). Fentanyl was the most widely used opioid during maintenance (n = 10,287; 18.9%). In the early postoperative period, the most frequently used analgesics were buprenorphine (n = 5829; 10.6%), tramadol (n = 8173; 14.4%) and methadone (n = 5424; 9.9%), meloxicam (n = 16,131; 29.4%) and carprofen (n = 3451; 6.3%).

Out of the 855 dogs that died, 378 deaths were considered related to anaesthesia. Therefore, the anaesthesia-related mortality in this study was 0.69% (95% CI: 0.62%–0.76%). A total of 117 dogs died due to pre-existing injuries or surgical or medical reasons (0.21%), and 360 dogs were euthanased (0.65%). None of the dogs was euthanased due to anaesthetic-related causes.

Anaesthetic-related mortality by ASA (95% CI) was as follows: ASA I—0.08% (0.04%–0.16%), ASA II—0.24% (0.19%–0.30%), ASA III—1.00% (0.84%–1.20%), ASA IV—6.47% (5.46%–7.65%) and ASA V—15.73% (11.69%–20.78%).

Seventy-one dogs died in the intraoperative period and 307 dogs died in the postoperative period. In detail, the distribution of deaths related to anaesthesia occurred during different phases: 21 during induction (5.6%), 50 during maintenance (13.2%), 43 during recovery in the operating theatre after extubation

TABLE 2 Demographic data of the dogs, details of the procedure and description of the anaesthetic techniques employed

Variable	Category	Dogs	% Dogs	Dead dogs	% Dead dogs
SEX	Female	28,250	51.3	217	0.77
	Male	26,772	48.7	161	0.60
AGE	Paediatric	202	0.4	6	2.97
	Young	8187	14.9	37	0.45
	Adult	15,657	28.5	75	0.48
	Senior	26,867	48.8	185	0.69
	Geriatric	4109	7.5	74	1.80
BODY CONDITION SCORE	Normal	39,463	71.7	215	0.54
	Cachectic	313	0.6	13	4.15
	Thin	6230	11.3	68	1.09
	Semi-obese	7716	14.0	61	0.79
	Obese	1300	2.4	21	1.62
ASA	I	10,392	18.9	8	0.08
	II	29,927	54.4	72	0.24
	III	12,397	22.5	124	1.00
	IV	2039	3.7	132	6.47
	V	267	0.5	42	15.7
REASON	Minor	19,073	34.7	61	0.32
	Abdominal	14,525	26.4	198	1.36
	Orthopaedics	9724	17.7	46	0.47
	Diagnostic	10,928	19.9	33	0.30
	Thoracic	772	1.4	40	5.18
SCHEDULED	Scheduled	48,719	88.5	203	0.42
	Non-scheduled	3344	6.1	61	1.82
	Emergency	2959	5.4	114	3.85
DURATION	Long	23,180	42.1	181	0.78
	Medium	29,213	53.1	160	0.55
	Short	2629	4.8	37	1.41
TIMETABLE	Normal	53,019	96.4	320	0.60
	Out-of-hours	2003	3.6	58	2.90
MONITORING	Advanced	6596	12.0	69	1.05
	Basic	5787	10.5	17	0.29
	Medium	42,639	77.5	292	0.68
TYPE	Inhalatory	40,202	73.1	194	0.48
	Parenteral	4097	7.4	36	0.88
	PIVA	10,723	19.5	148	1.38
LOCOREGIONAL	No	35,014	63.6	278	0.79
	Yes	20,008	36.4	100	0.50
VENTILATION	No	31,988	58.1	214	0.67
	Yes	23,034	41.9	164	0.71

Note: Dogs: number of dogs included in each category. % Dogs: proportion of dogs included in the category in relation to the total number of dogs studied. Dead dogs: number of dogs that died for anaesthetic-related reasons within each category. % Dead dogs: proportion of dogs included in the category that died for anaesthetic-related reasons, in relation to the number of dogs included in that category.
Abbreviations: ASA, American Society of Anesthesiologists; PIVA, partial intravenous anaesthesia.

(11.4%), 48 within the first 3 hours of hospitalisation (12.7%), 50 between 3 and 6 hours (13.2%), 94 between 6 and 24 hours (24.9%) and 72 between 24 and 48 hours (19.0%) (Figure 4).

Concerning the logistic regression model, the initial number of cases was 54,545. However, 9390 of these cases had missing values, resulting in a final number of 45,155 being used in the model. The multicollinearity analysis revealed that none of the variables had a variance inflation factor above 2.4, suggesting that no collinearity was present. The multivariable logistic regression model demonstrated a strong fit with an AIC of 2633.6, a *C*-statistic of 0.882 and an H&L of $\chi^2(8)$ 8.62 ($p = 0.375$).

TABLE 3 The number (*N*) and percentage of cases (%) in which the drugs were used by phase of the anaesthetic protocol.

	Premedication		Induction		Maintenance		Postoperative	
Drugs	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**
Acepromazine	5000	9.1	0	0.0	430	0.8	938	1.7
Medetomidine	9545	17.3	0	0.0	307	0.6	241	0.4
Dexmedetomidine	26,039	47.3	0	0.0	2051	3.7	3357	6.1
Midazolam	6127	11.1	7490	13.6	546	1.0	76	0.1
Diazepam	639	1.2	3777	6.9	174	0.3	30	0.1
Morphine	1408	2.6	0	0.0	786	1.4	1768	3.2
Methadone	31,598	57.4	0	0.0	1017	1.8	5467	9.9
Pethidine	323	0.6	0	0.0	25	0.0	74	0.1
Fentanyl	2128	3.9	4301	7.8	10,425	18.9	1239	2.3
Buprenorphine	481	0.9	0	0.0	30	0.1	5844	10.6
Butorphanol	5739	10.4	0	0.0	40	0.1	522	0.9
Tramadol	4178	7.6	0	0.0	176	0.3	8200	14.9
Remifentanil	738	1.3	1202	2.2	4048	7.4	8	0.0
Carprofen	686	1.2	0	0.0	0	0.0	3460	6.3
Meloxicam	4924	8.9	0	0.0	0	0.0	16,172	29.4
Coxib	1452	2.6	0	0.0	0	0.0	3023	5.5
Propofol	0	0.0	46,132	83.8	2697	4.9	0	0.0
Alfaxalone	1194	2.2	6359	11.6	110	0.2	0	0.0
Ketamine	4695	8.5	10,806	19.6	6813	12.4	1627	3.0
Thiopental	0	0.0	272	0.5	0	0.0	0	0.0
Etomidate	0	0.0	252	0.5	0	0.0	0	0.0
Isoflurane	0	0.0	822	1.5	40,876	74.3	0	0.0
Sevoflurane	0	0.0	40	0.1	10,004	18.2	0	0.0
Desflurane	0	0.0	0	0.0	48	0.1	0	0.0

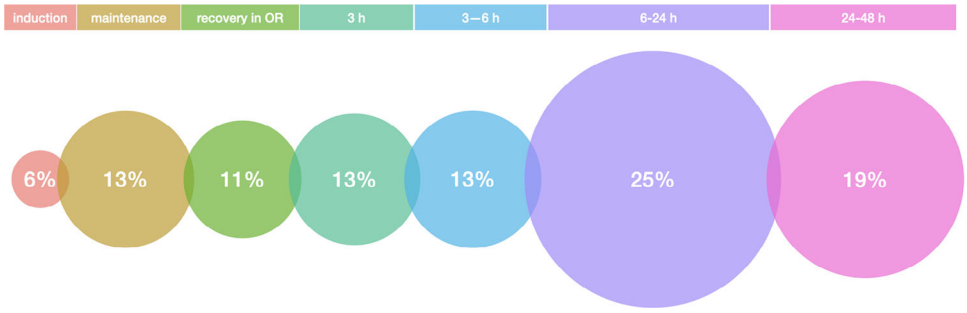

FIGURE 4 Plot of the timing of death of the dogs that died from anaesthetic-related causes. OR, operating room

The analysis revealed several demographic and clinical associations with anaesthesia-related death. Increased mortality risk was observed in paediatric and geriatric dogs compared to adult dogs and in obese dogs compared to dogs with an average BCS. Dogs classified as ASA II–V had a higher mortality risk than those classified as ASA I. Unscheduled or emergency procedures, abdominal, orthopaedic/neurosurgical and thoracic surgeries, and a longer duration of anaesthesia were also associated with an increased risk of death. In contrast, the use of acepromazine, alpha$_2$-agonists, pure opioids alone or in combination with NSAIDs, partial agonists or agonist–antagonists plus NSAIDs as analgesics in pre-anaesthetic medication, the use of sevoflurane instead of isoflurane for maintenance of anaesthesia, and the use of locoregional techniques were associated with a reduced likelihood of death. A detailed report of the data, including OR, 95% CI and *p*-value (*p*), is presented in Figure 5.

DISCUSSION

The present study, conducted across 405 veterinary centres worldwide and involving 55,022 cases, revealed an anaesthetic-related mortality of 0.69%. In other words, one dog out of 145 died between the

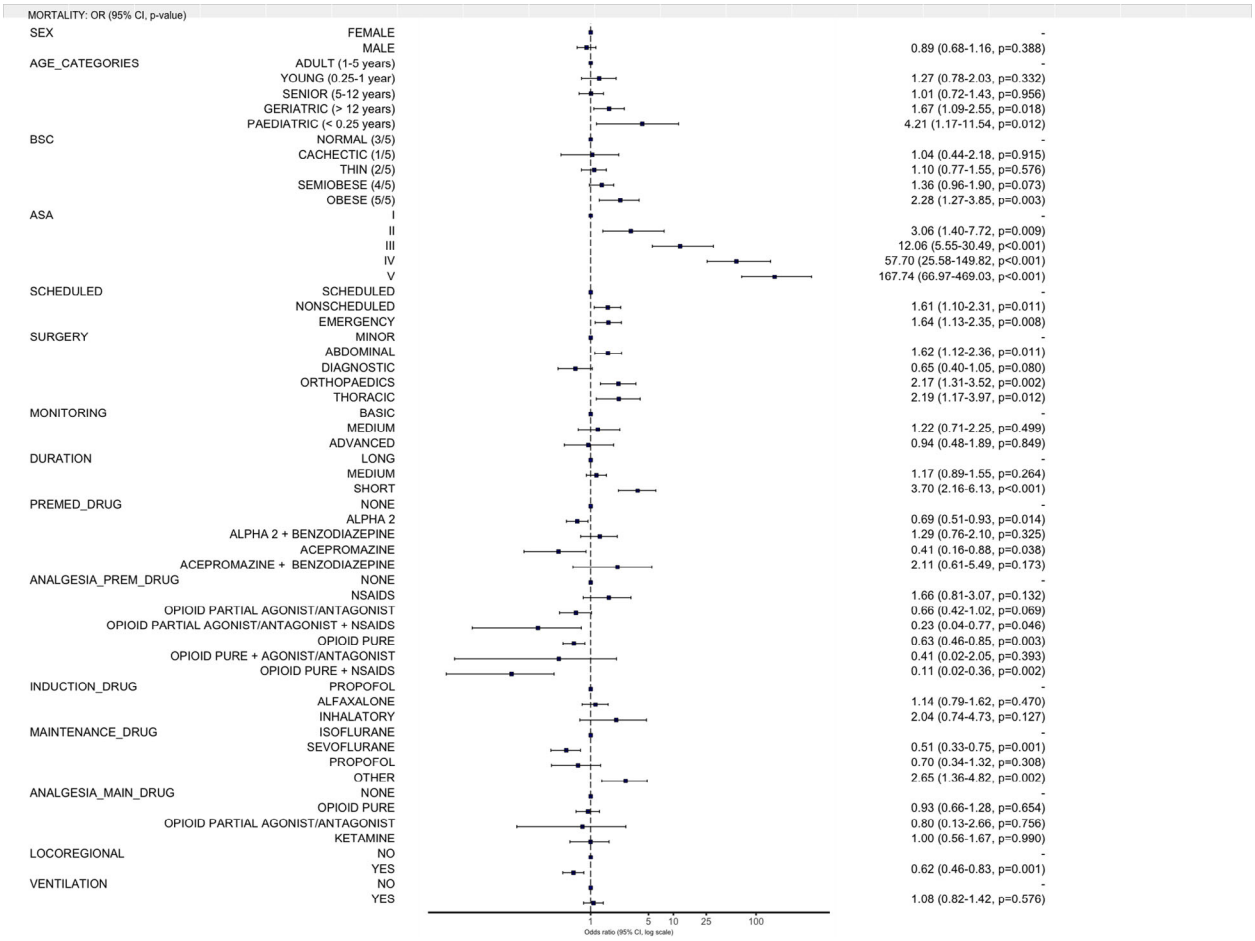

FIGURE 5 Forest plot of the logistic regression model for the risk of anaesthetic-related death in dogs. The dotted vertical line represents an odds ratio (OR) of 1.0. When a predictor variable falls on the dotted line, it means there is no significant difference in the outcome variable's odds between the reference level of the predictor and other levels ($p > 0.05$). ORs to the right of the dotted line indicate an increased risk of death, while those to the left suggest a protective effect. The farther away the OR is from the dotted line, the stronger the association between the predictor and outcome variables. 95% CI, 95% confidence interval.

administration of pre-anaesthetic medication and the first 48 hours after extubation due to anaesthesia-related causes. This mortality is significantly higher than that reported in human medicine, where 1–2 deaths per 100,000 anaesthetics are generally reported in developed countries.[9–11] It is worth noting that anaesthetic-related deaths in veterinary anaesthesia, regardless of the species involved, are considerably higher than in humans,[3,12] with rates up to 100 times higher than those observed in human anaesthesia.[13]

The mortality observed in this study is consistent with the results reported by Itami et al.[5] However, it is lower than the findings reported by Gil and Redondo,[4] but higher than those reported in other multicentric studies.[6–8] It is important to note that comparing anaesthesia-related mortality between studies can be challenging due to variations in study design, the specific population studied, differences in anaesthetic management, variations in the definition of death and variations in the length of follow-up periods. Hence, when making comparisons, it is crucial to consider the differences in study designs. The present study is a purely prospective cohort study. In contrast, other studies performed a nested case–control study.[6] A prospective cohort study involves selecting a group and collecting real-time data, while a case–control study involves retrospectively gathering data by selecting cases and controls from an existing cohort (or population), which may introduce bias.[14]

The differences between studies can also be explained by the population being studied. A higher proportion of sick patients (ASA III, IV and V) leads to higher overall mortality. In our study, 26.7% of patients were considered high risk; in other studies, this proportion ranged from 4% to 7%.[2,3,15] Our study's greater proportion of high-risk patients could explain the differences observed. Some studies that included a high proportion of ASA III–IV patients showed a higher risk of anaesthetic-related mortality than that reported in this paper.[4,16,17]

Another factor that can confound the comparison of investigations is the variation in the definition of such deaths. The present study followed a similar description to that used in other studies.[7,8] However, other studies may have more precise or broader definitions, leading to the inclusion of various phenomena.[2] Additionally, variations in the follow-up period also contribute to the difficulty in comparing results. This study followed dogs for up to 48 hours after extubation. However, other studies have chosen different

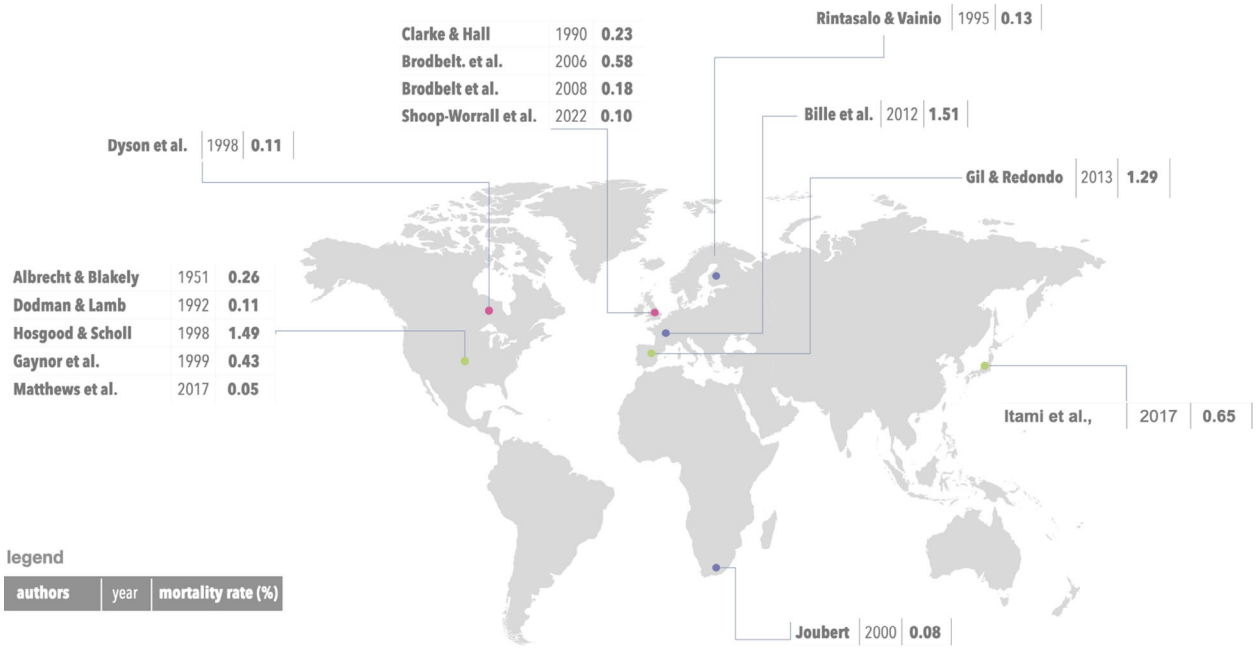

FIGURE 6 Comparative analysis of anaesthetic mortality rates in dogs across various studies.

durations. For example, some studies focused only on intraoperative mortality,[1] while others examined the first 24 hours[4] or up to 15 days after anaesthesia.[7] The length of the follow-up period theoretically affects the probability of detecting deaths. In human studies, patients are commonly followed for a month after anaesthesia[9,18–20] or even longer[21,22] because certain anaesthetic complications may only become apparent weeks or months after the procedure. Further studies with extended follow-up periods in veterinary medicine are warranted to accurately assess long-term mortality.

This study is the first examination of anaesthesia-related deaths across multiple countries simultaneously. Previous multicentric studies have been limited to a single country or region, such as the UK,[2,7,8] the USA,[6,23] Finland,[24] South Africa,[25] Japan,[5] Canada[15] or Spain.[4] It is important to note that the situation in each country may not be directly extrapolated to another, as differences in practices and resources can affect anaesthetic-related mortality. Similar variations in mortality between countries have been observed in human anaesthesiology studies, particularly between developed and developing regions.[10] Moreover, some published studies focused on individual hospitals, providing valuable data specific to those institutions.[1,17,26–28] However, the present study showed a worldwide picture with data from various clinics, from primary care to referral centres. For the reader's convenience, the mortalities reported in the previously cited studies are presented in Figure 6, providing a visual representation of the variability in anaesthetic-related mortality across different countries.

In this study, most deaths (81%) occurred in the postoperative period, aligning with the findings of other studies.[4,5,8] These results highlight the importance of focusing on patient care during this critical phase. Based on these findings, it is essential to emphasise the significance of postoperative monitoring and interventions in the veterinary anaesthesia community. Better attention and care during the postoperative period may reduce anaesthetic-related mortality in dogs. However, further studies are warranted to test this hypothesis.

The results of this study indicated that paediatric and geriatric dogs had an increased mortality risk during anaesthesia, which differs from previous studies that primarily focused on senior dogs.[6,8] Elderly dogs are known to be more susceptible to various disease processes and have reduced physiological reserves. Similarly, neonatal and paediatric dogs may have immature physiological systems, making them less capable of responding adequately to hypotension, hypothermia and other physiological challenges.[6,8,29]

This study also identified obesity as a risk factor for mortality during canine anaesthesia, which has not been recognised in previous research. While the impact of obesity on human anaesthesia is well established,[30] its influence on canine anaesthesia remains unclear. Obesity can affect multiple physiological systems, including the endocrine, respiratory and cardiovascular systems, and it may also alter the pharmacokinetics of anaesthetic drugs due to changes in body composition.[31] Adjusting drug dosages based on ideal body mass is crucial to avoid overdosing, particularly with rapidly acting induction agents such as propofol.[32] Moreover, obesity can impact respiratory parameters such as elastance, resistance and functional residual capacity, potentially leading to hypoventilation in obese dogs.[33] Studies have also shown that obese dogs may exhibit increased systolic blood pressure and left ventricular free wall

thickness.[34] Considering these findings, it would be advisable to contemplate implementing weight loss programmes for obese dogs before undergoing routine procedures involving anaesthesia.[35]

The ASA classification has consistently been recognised as a significant prognostic factor for anaesthesia-related mortality in the literature,[4,7,8] and this study further supports this assertion. Therefore, it is necessary to prioritise patient stabilisation and enhance their physical condition, as these measures could significantly reduce the probability of death. The ASA physical status scoring system, a simple and practical tool, is valuable in identifying an elevated risk of anaesthesia-related mortality within the first 24–72 hours following the procedure.[36] However, the ASA score can be subjective, and clinicians have inconsistent ASA physical status assignments. Several studies have found only fair to moderate inter-rater agreement among human anaesthesiologists when assigning ASA scores.[37] Although subjective, the ASA classification is a dependable and unbiased predictor of complications and mortality after anaesthesia. As a result, even though the ASA score may involve personal judgement, it is still crucial for foreseeing perioperative risks and enhancing patient outcomes.

Previous studies have demonstrated that urgent procedures are associated with higher mortality.[7,8] Interestingly, this study found that non-urgent but unscheduled anaesthesia also had higher mortality than scheduled procedures, and short procedures resulted in higher mortality than more prolonged procedures. These events may be attributed to overconfidence among anaesthetists during short and non-scheduled procedures, leading to potential neglect of safety measures employed during more prolonged operations, such as proper pre-anaesthetic examination and adequate patient monitoring, intravenous line placement and intubation, or the use of non-optimised premedication. Furthermore, neglecting pre-anaesthetic assessment has been associated with increased odds of death during anaesthesia.[5,6] Additional investigations should clarify this point.

Abdominal, orthopaedic and neurosurgical interventions, and especially thoracic interventions, carry a higher mortality risk than minor surgeries. There is limited information on the effect of the reason for anaesthesia on mortality in small animals. Previous studies suggest higher mortality rates for major procedures than for minor ones.[8] In a similar procedure classification study, orthopaedic and thoracic surgeries were associated with higher mortality in the univariate analysis, although not in the multivariable analysis, probably due to a small sample size.[4] Abdominal surgeries included gastrointestinal surgery, reproductive surgery in female dogs, haemoabdomen and urinary system surgery. While elective ovariohysterectomy has been linked to low mortality,[6,38] including septic patients and other complex cases within the abdominal surgery category could explain the higher mortality reported.[39–41] In addition, abdominal surgery often increases heat loss, contributing to a higher likelihood of death.[42] Orthopaedic procedures are typically performed on dogs with fractures or luxation resulting from trauma, and these patients may have additional undetected injuries that necessitate thorough examination before anaesthesia.[43] Hemilaminectomies, included in this class, have also been associated with high mortality.[44] Thoracic surgeries are recognised for their complexity and have the highest mortality risk. For example, diaphragmatic hernia repair in dogs and thoracoscopic-assisted lung lobectomy have been associated with notably elevated mortality.[45,46] Further research categorising procedures thoroughly and examining their impact on mortality, as proposed in human surgery,[47] could identify areas for improvement and facilitate the development of strategies to enhance patient safety and outcomes in veterinary anaesthesia.

These findings highlight the importance of considering age, obesity, ASA classification, procedure emergency and reason for anaesthesia as potential risk factors in canine anaesthesia and emphasise the need for individualised care and tailored anaesthetic management based on patient characteristics. By considering these factors, veterinary professionals may reduce the risk of anaesthesia-related complications and enhance patient safety during procedures.

The choice of anaesthetic drugs also appeared to influence the risk of death, with lower mortality observed when using sedatives such as acepromazine or alpha$_2$-agonists. Controversially, combinations of alpha$_2$-agonists or acepromazine with benzodiazepines did not show the same protective effect, despite their increasing popularity in clinical practice.[48,49] Alpha$_2$-agonists and phenothiazines can reduce hypnotic doses and pre-surgical stress, and the analgesic properties of alpha$_2$-agonists may contribute to more effective pain management.[49–51] Therefore, using these sedatives as part of the pre-anaesthetic medication is advisable unless contraindicated. Similarly, patients treated with systemic analgesics, such as pure opioids or combinations of opioids with NSAIDs, partial opioids or agonist–antagonists plus NSAIDs, exhibited lower mortality, consistent with previous reports.[4]

Using sevoflurane for maintaining anaesthesia, rather than isoflurane, has been linked to lower mortality. However, despite the acknowledged pharmacokinetic variances between these two agents, studies have yet to conclusively establish the superiority of one over the other until now.[52,53] Although the clinical disparities between the drugs seem minor, specific comparative investigations indicate that sevoflurane causes less respiratory depression,[54] maintains higher blood pressure levels and facilitates faster recovery times than isoflurane.[55] Historically, isoflurane has been proven safer than halothane in dogs.[8] Further studies should investigate why sevoflurane appears safer than isoflurane in maintaining anaesthesia in dogs.

Locoregional anaesthesia also reduced anaesthetic-related mortality, in line with human anaesthesia

findings.[56–58] This is the first report of such an association in veterinary anaesthesia. The techniques described in this study range from simple intratesticular blocks or epidural anaesthesia to more advanced ultrasound-guided peripheral blocks. These approaches have been linked to reduced hypnotic doses, improved cardiovascular and respiratory stability during the procedure and decreased perioperative stress.[59–61] In human anaesthesia, combining locoregional and general anaesthesia has shown better intraoperative haemodynamics than general anaesthesia alone.[62,63] Our research emphasises the importance of systemic analgesics and locoregional techniques in significantly reducing mortality. Pain should not be ignored, as it can lead to fatal outcomes.[64] Prioritising pain prevention, diagnosis, and treatment is crucial for enhancing animal welfare and minimising the risk of death during anaesthesia and recovery.

There are some limitations to this study that need to be acknowledged. It is important to note that clinics and hospitals were not randomly chosen for this study. The clinicians who participated were explicitly invited, possibly leading to a selection bias. This means that the participants were likely mostly anaesthesia specialists or those with a particular interest in the field, which could limit the applicability of the findings and negatively impact the accuracy of risk factor identification and incidence risk estimates. Future research with a more diverse sample must validate and generalise these findings. Second, it was difficult to determine the participating centres' response rate, as many reported cases irregularly. Although they were instructed to record all anaesthetics, the absence of a systematic monitoring or control mechanism may have affected the data quality. For instance, cases may have been less likely to be included during busy periods, out-of-hours or emergency situations. Future studies should establish robust data quality systems to ensure the accuracy and reliability of the data. Third, another limitation of our study is the subjectivity in classifying a death as anaesthetic or non-anaesthetic related. Determining the cause of death should not be based on subjective opinions, and there is a need for objective methods to establish the cause of death in future studies.[65] Finally, we have analysed a limited number of variables in this article due to the vast amount of data collected. Regrettably, we could not study several other crucial variables, as they were not included in the study design. For example, we could not examine how the type of centre (first opinion, referral centre or university hospital) impacts mortality. It is plausible that university hospitals and referral centres have higher mortality than first-opinion centres due to the complexity of the cases they handle.[3,26] However, as this was self-reported, we could not gather standardised information on clinic types. Furthermore, it is vital to consider how veterinary anaesthesia is developing in different countries. What may be considered a referral hospital in one country may be a large clinic in another. Therefore, further research is necessary to investigate the role of these other secondary variables in the likelihood of anaesthetic-related death and clarify some aspects that were not thoroughly examined in this paper. Despite these limitations, our study provides valuable insights into anaesthetic-related deaths in dogs and highlights the areas that require further attention and investigation. By addressing these limitations and conducting more comprehensive studies in the future, we can continue to enhance our understanding of anaesthesia-related mortality in dogs and work towards improving patient safety and outcomes in veterinary anaesthesia.

CONCLUSION

In conclusion, this study revealed an overall anaesthetic-related mortality of 0.69% in dogs, with a high percentage of deaths occurring during the postoperative period. In addition, the study identified various risk and protective factors that can inform clinical decision making and enhance patient safety. These findings provide valuable insights that can guide improvements in anaesthetic practices and contribute to developing strategies to reduce the incidence of anaesthetic-related deaths in dogs. By implementing these measures, we can strive to enhance animals' overall wellbeing during anaesthesia and improve their outcomes.

AUTHOR CONTRIBUTIONS

Conceptualisation: José I. Redondo. *Methodology*: José I. Redondo and Luis Domenech. *Formal analysis*: José I. Redondo, Pablo E. Otero, Fernando Martínez-Taboada, Luis Doménech, Eva Zoe Hernández-Magaña and Jaime Viscasillas. *Investigation*: José I. Redondo, Pablo E. Otero, Fernando Martínez-Taboada, Luis Doménech, Eva Zoe Hernández-Magaña and Jaime Viscasillas. *Writing*: José I. Redondo, Pablo E. Otero, Fernando Martínez-Taboada and Jaime Viscasillas. *Supervision*: José I. Redondo. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

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The authors received no specific funding for this work.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT
This study received ethical approval from the Ethics Committee of the Universidad Cardenal Herrera-CEU (CEEA 22/07).

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SUPPORTING INFORMATION

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

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