

ORIGINAL RESEARCH

Anaesthetic mortality in cats: A worldwide analysis and risk assessment

José I. Redondo¹  | Fernando Martínez-Taboada^{2,3}  | Jaime Viscasillas⁴  |
Luis Doménech⁵  | Reyes Marti-Scharfhausen⁶ | Eva Z. Hernández-Magaña¹  |
Pablo E. Otero⁷ 

¹Departamento de Medicina y Cirugía Animal, Facultad de Veterinaria, Universidad Cardenal Herrera-CEU, Valencia, Spain

²Sydney School of Veterinary Science, University of Sydney, Sydney, New South Wales, Australia

³3A Animal Anaesthesia and Analgesia, Victoria, Australia

⁴Anicura Valencia Sur Hospital Veterinario, Valencia, Spain

⁵Departamento de Matemáticas, Física y Ciencias Tecnológicas, Escuela Superior de Enseñanzas Técnicas, Universidad Cardenal Herrera-CEU, Valencia, Spain

⁶Anicura Indautxu Hospital Veterinario, Bilbao, Spain

⁷Department of Anaesthesiology and Pain Management, Facultad de Ciencias Veterinarias, Universidad de Buenos Aires, Buenos Aires, Argentina

Correspondence

José Ignacio Redondo García, Departamento de Medicina y Cirugía Animal, Facultad de Veterinaria, Universidad Cardenal Herrera-CEU, C/Tirant lo Blanch, 7. 46115, Alfara del Patriarca, Valencia, Spain.
Email: nacho@uchceu.es

Abstract

Background: Patient safety is essential in small animal anaesthesia. This study aimed to assess anaesthesia-related deaths in cats worldwide, identify risk and protective factors and provide insights for clinical practice.

Methods: A prospective multicentre cohort study of 14,962 cats from 198 veterinary centres across different countries was conducted. Data on anaesthesia-related deaths, from premedication up to 48 hours postextubation, were collected. Logistic regression was used to analyse patient demographics, American Society of Anesthesiologists (ASA) classification, procedure type and anaesthetic drugs.

Results: The anaesthesia-related mortality was 0.63%, with 74.5% of deaths occurring postoperatively. Cats with cachexia, a higher ASA status or who underwent abdominal, orthopaedic/neurosurgical or thoracic procedures exhibited elevated mortality. Mechanical ventilation use was associated with increased mortality. Mortality odds were reduced by the use of alpha₂-agonist sedatives, pure opioids in premedication and locoregional techniques.

Limitations: Limitations include non-randomised sampling, potential biases, unquantified response rates, subjective death cause classification and limited variable analysis.

Conclusions: Anaesthetic mortality in cats is significant, predominantly postoperative. Risk factors include cachexia, higher ASA status, specific procedures and mechanical ventilation. Protective factors include alpha₂-agonist sedatives, pure opioids and locoregional techniques. These findings can help improve anaesthesia safety and outcomes. However, further research is required to improve protocols, enhance data quality and minimise risks.

INTRODUCTION

Anaesthesia is essential in veterinary clinical practice. It enables surgical and diagnostic procedures that would otherwise be impossible. Despite improvements in monitoring, anaesthetic techniques and patient care, the risk of anaesthesia-related mortality, especially in cats, is still a concern. Therefore, further research is necessary to enhance safety during anaesthesia.

Albrecht and Blakely published the first study of anaesthetic mortality in small animals in 1951, reporting cases seen at the Angell Memorial Animal Hospital

in Boston. The authors reported an intraoperative mortality of 0.36% in cats.¹ The first survey specifically on feline anaesthesia was carried out by Dodman in Scotland in 1977, and this reported a mortality of 0.3%.² Clarke and Hall's research in the UK in 1990 was the first major multicentre study in veterinary anaesthesia. Fifty-three practices were recruited, 41,881 anaesthetics were recorded and an anaesthetic risk of perioperative death of 0.29% in cats was reported.³ The Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF) was also undertaken in the UK between 2002 and 2004, and 79,178 anaesthetics and sedations were recorded in cats in 117 participating

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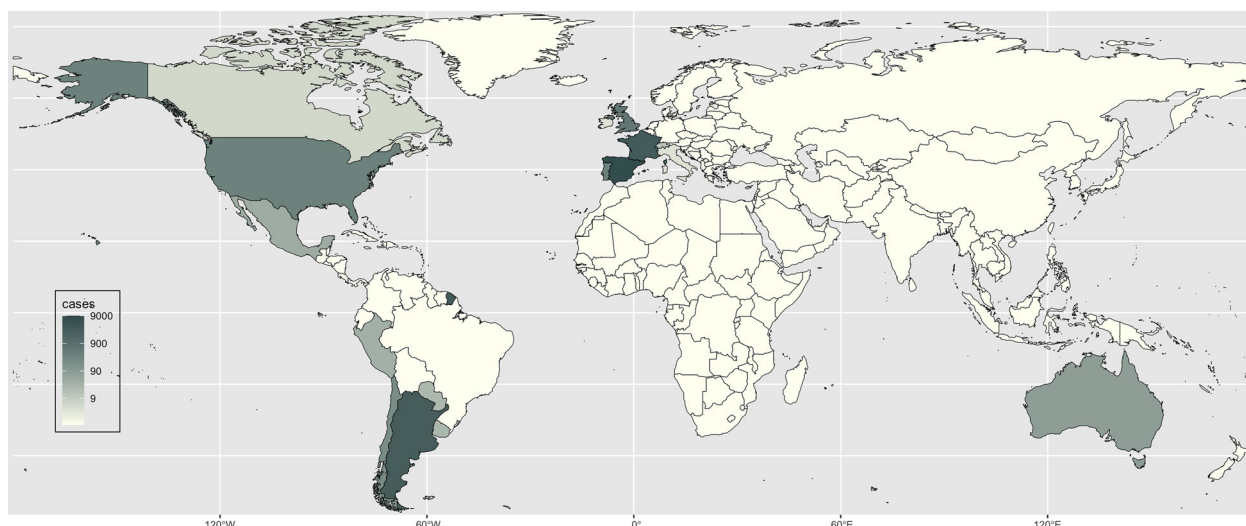


FIGURE 1 Heatmap of the number of cases submitted by country

centres. The CEPsAF represented a significant contribution to the field of feline anaesthesia. This study revealed that the overall incidence of anaesthesia-related deaths in cats was 0.26%.⁴ A more recent study reported a mortality of 0.11% in the United States.⁵

Understanding the risk factors associated with anaesthetic-related mortality is essential for developing strategies to reduce its incidence. Some studies have underlined the risk and protective factors that would minimise anaesthetic mortality in cats. Poor health status,⁴ age,^{4,5} underweight⁴ or overweight,⁵ female cats,⁶ procedural urgency^{4,5} and complexity,⁴ endotracheal intubation⁴ and fluid therapy⁴ have been identified as risk factors. Conversely, pulse monitoring⁴ and pulse oximetry^{4,5} have been associated with reduced odds of death.

This research had two main goals: first, to determine the current anaesthesia-related mortality in cats across multiple countries, and second, to identify significant factors that could either increase or decrease the risk of death for this species during anaesthesia. This information could help to develop future strategies to improve patient safety during anaesthetic procedures.

MATERIALS AND METHODS

This observational, prospective, multicentre cohort study took place from February 2016 to December 2022 and involved 198 veterinary centres across various countries, including Spain, Argentina, France, the UK, the United States, Chile, Portugal and Australia (Figure 1).

The project was disseminated through various anaesthesia associations to veterinary centres, including primary care clinics, referral-only facilities and university hospitals. These associations included 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. Additionally, emails were sent to diplomates and residents of the American College of Veterinary Anaesthesia and Analgesia and the European College of Veterinary Anaesthesia and Analgesia. To maximise the visibility of the project, posts were published on Twitter, LinkedIn and Facebook explaining the details of the study and actively inviting veterinarians to participate. These posts outlined the project's purpose, participation criteria and how veterinary professionals and centres could contribute. The study's preliminary results were also presented at national and international conferences to invite attendees to participate. During the study period, multiple centres were recruited to participate. While some centres participated for the entire study duration, others only participated for shorter periods. However, all centres were encouraged to send all the cases they anaesthetised during their respective participation periods. Challenges were encountered in conducting an audit due to the diverse nature of participating centres and the variability in their data recording practices. Despite these difficulties, efforts were made to implement procedures to verify the data quality.

The participants were asked to complete a PDF form for each anaesthesia (Supporting Information S1). The form was designed for easy access and to be filled on various devices, including smartphones, tablets, laptops and computers. Once submitted, the forms were automatically sent to a designated email account. The data extracted from the forms included 146 variables per submission, and these were compiled into a spreadsheet. Some information, such as the clinic's name and case number, was anonymised to comply with the privacy regulations outlined in the General Data Protection Regulation of the European Union 2016/679.

To ensure comprehensibility and standardisation of the data collection criteria, the PDF form and instructions were translated into the users' languages,

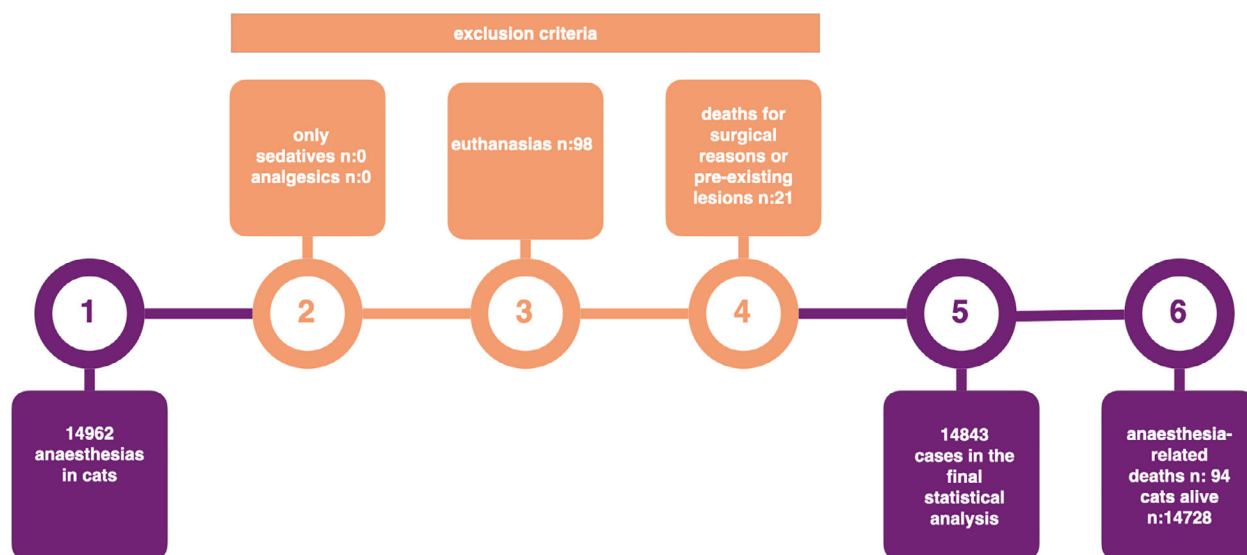


FIGURE 2 Flow diagram of the recruitment, exclusion and follow-up of the anaesthetic cases

namely, English, Spanish and French (Supporting Information S2). Participants who were not native speakers of any of these languages selected the form in whichever language they considered their second language. Table 1 presents a comprehensive overview of the recorded variables and their definitions and grouping. Participants were encouraged to include all cats that underwent anaesthesia during the study. For this research, anaesthesia was described as the state of hypnosis induced using hypnotic drugs or a combination of drugs that allowed endotracheal intubation of the animal, regardless of whether the intubation was carried out. Therefore, cats that received only sedatives or analgesics without proceeding to anaesthesia were excluded from the study.

The data were collected during the period between administration of the preanaesthetic medication and 48 hours after extubation. In the event of a cat's death within this timeframe, additional information was solicited via email. This request included details concerning the circumstances of death, any anaesthesia or surgical complications, subsequent treatment or drug administration and the outcomes of any postmortem examination.

The principal investigator (J.I.R.) categorised the reasons for deaths into three groups: (1) anaesthesia-related death (when the death—or euthanasia—was directly or partially attributed to anaesthesia), (2) euthanasia (when the animal was euthanased due to the severity of pre-existing injuries), and (3) medical/surgery-related death (when the death resulted from surgical complications or disease progression during the study period). The statistical analysis focused solely on deaths directly associated with anaesthesia, excluding those related to euthanasia due to pre-existing lesions and deaths due to medical/surgery reasons (Figure 2). Additionally, the phase of anaesthesia during which 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, from transfer to hospitalisation within the first 48 hours after extubation).

ance periods) or postoperative (if it occurred after extubation in the operating room, from transfer to hospitalisation 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, creating a new ordinal variable named AGE CATEGORIES. This variable included paediatric (<3 months), young (3–12 months), adult (>1 to 5 years), senior (>5 to 12 years) and geriatric (>12 years) age groups. Body condition score (BCS) was classified into five classes: 1, cachectic; 2, thin; 3, average; 4, semi-obese; and 5, obese. Physical status was categorised based on the American Society of Anesthesiologists (ASA) classification. The SURGERY variable classified the reason for anaesthesia as MINOR (minor procedures without open cavities), ABDOMINAL (procedures involving laparotomy), ORTHOPAEDIC (orthopaedic or neurosurgical procedures), DIAGNOSTIC (for diagnostic purposes) and THORACIC (surgeries opening the thoracic cavity). The level of monitoring (MONITORING) was categorised as BASIC (monitoring only with stethoscope/pulse palpation, respiratory rate and temperature), MEDIUM (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 based on their purpose and the stage at which they were administered: ANALGESIA PREM DRUG and ANALGESIA MAIN DRUG. These variables

TABLE 1 Recorded variables and definitions.

- HOSPITAL: Name of the veterinary clinic or hospital where the anaesthesia was performed.
- VET or NURSE/TECH: Qualification of the person who performed the anaesthesia.
- DATE: The date on which the procedure 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, it was also recorded.
- BREED
- AGE: In years. Cases were classified into paediatric patients (<3 months), young patients (3–12 months), adults (1–5 years), seniors (5–12 years) and geriatric patients (>12 years).
- WEIGHT: In kg.
- BODY CONDITION SCORE: Classified into five classes: cachectic, thin, average, semi-obese and 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 can 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 condition or disturbances of a severe nature. That is, severe dehydration, shock, uraemia, toxemia, high fever, uncompensated heart disease, uncompensated diabetes, pulmonary disease and 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 and terminal malignancy.
- SCHEDULING: If anaesthesia 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 opened. For example, wound suture, orchiectomy, mastectomy, ophthalmic surgery, scrotal or perineal hernia, etc.
- ABDOMINAL: Procedures which 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 anaesthesia 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
- Total intravenous anaesthesia: if maintenance was carried out using parenteral drugs.
- Inhalational: maintenance was done with inhalant drugs; induction could be done using parenteral drugs.
- Partial intravenous anaesthesia: maintenance using inhalant drugs, 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, TAP block, sciatic and femoral block, etc.).
- FLUID THERAPY: Fluids employed: saline, Ringer's lactate, glucosaline, colloid (gelatine or dextran) or other.
- O ₂ /AIR: If oxygen or medical air were administered.
- INTUBATION: If the tracheal intubation was done or not.
- CIRCUIT: The circuit employed. Circle Ayre's T piece or other (write the name of the 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.
- NMBA: If neuromuscular blocking agents were employed (or not) and what drugs were used.
- OTHER DRUGS: If emergency drugs were employed: atropine, dobutamine, dopamine, adrenaline, phenylephrine, noradrenaline, neostigmine and pimobendan.
- DURATION OF ANAESTHESIA: Brief, 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: Whether the patient was hospitalised (only during the day or overnight).
- DEATH: Yes or no. If the patient died, the moment it 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, 6–26 hours, 24–48 hours. If the cat was euthanased for medical or surgical reasons, it was also noted.
- COMMENTS: Suspected cause of death, pre-existing diseases, previous medical treatments, emergency treatment, other comments.

Abbreviation: ASA, American Society of Anesthesiologists.

included several categories: NONE, NSAIDS, OPIOID PURE, PURE OPIOID PLUS NSAIDS, OPIOID PARTIAL AGONIST/ANTAGONIST and OPIOID PARTIAL AGONIST/ANTAGONIST PLUS NSAIDS. Induction drugs (INDUCTION DRUGS) were classified as INHALATORY if halogenated inhalational drugs were used, PROPOFOL if propofol was employed as an induction agent, and were categorised as OTHER otherwise. The hypnotic used in maintenance (MAINTENANCE DRUG) was split into four categories: ISOFLURANE, SEVOFLURANE, PROPOFOL and OTHER. Finally, the LOCOREGIONAL and VENTILATION variables were dichotomous (yes/no).

The statistical analysis used R 4.3.0, a language and environment for statistical computing and graphics. Initially, a descriptive analysis was conducted to estimate the risk of anaesthetic death and calculate confidence intervals (CIs) using the 'prop.test' function from the stats package in the R programming language. Subsequently, a multivariable logistic regression model, employing the 'finalfit' package for R, was used to explore the association between anaesthesia-related death and various demographic and clinical factors. Binary logistic regression analysis utilised a subset of selected variables, including SEX, AGE CATEGORIES, BSC, ASA, SCHEDULED, SURGERY, MONITORING, DURATION, SEDATIVES, ANALGESIA PREM DRUG, INDUCTION DRUG, MAINTENANCE DRUG, ANALGESIA MAIN DRUG, LOCOREGIONAL and VENTILATION. In instances where categories with consistently low case counts ($n < 40$) could not be combined or aggregated, they were excluded from the analysis. Also, the analysis excluded cases with missing values. Statistical significance was defined as a p -value of less than 0.05, and variables meeting this criterion were considered significant. The goodness of fit for the model was assessed using the Hosmer–Lemeshow test (H&L), the Akaike information criterion (AIC) and the concordance statistics (C-statistics). The results are reported as the number of cases (n , %), median (range), odds ratio (OR), 95% CI and p -value, as appropriate.

RESULTS

This study analysed a dataset comprising 14,962 anaesthetic records in cats. The median age was 2 years (range 0.1–22), and the median weight was 3.7 kg (range 0.3–15.0). Most cats were European shorthair ($n = 10,000$; 66.8%), while mixed breed ($n = 2129$; 14.2%), British shorthair ($n = 968$; 6.5%), Persian ($n = 478$; 3.2%), Siamese ($n = 372$; 2.5%) and Maine coon ($n = 211$; 1.4%) cats were also well represented. The distribution of these breeds can be observed in Figure 3. For detailed demographic information, reasons for anaesthesia, scheduling, timetables, anaesthetic techniques employed, and the number and percentage of deaths for each category, refer to Table 2.

The duration of data collection was 2526 days (6 years, 11 months). The median number of cases

received per day was 5 (range 0–40). The median number of cases per centre was 48 (range 6–1520). Spain ($n = 7483$; 50.5%), France ($n = 3072$; 20.7%), Argentina ($n = 2660$; 17.9%), the UK ($n = 557$; 3.8%) and the United States ($n = 325$; 2.2%) were the countries that reported the most cases (Figure 1).

Table 3 provides an overview of the pharmacological approach used in anaesthetic protocols. In summary, α_2 -agonists were the most commonly used sedatives during premedication (76.0%). Propofol was the primary hypnotic agent used for the induction of anaesthesia (58.3%), followed by alfaxalone (24.8%) and inhalatory agents (5.2%). Isoflurane was the preferred anaesthetic agent used during maintenance (65.5%), with sevoflurane being less frequently used (16.2%). Methadone was the most commonly used opioid during premedication (56.6%), followed by butorphanol (12.6%). Meloxicam (10.0%) was the predominant non-steroidal anti-inflammatory drug (NSAID) used in premedication. During the maintenance phase, fentanyl was the most frequently administered opioid (13.7%). Buprenorphine (19.0%) and meloxicam (38.6%) were commonly used as analgesics during the early postoperative period.

Of the 14,962 cats anaesthetised, a total of 213 died. Of those, 94 deaths were directly associated with anaesthesia, 21 occurred due to surgery, medical reasons or pre-existing injuries, and 98 cats were euthanased due to poor prognosis. None of the cats was euthanased due to anaesthesia-related causes. Consequently, the overall mortality was 0.63% (95% CI: 0.51%–0.77%), signifying one fatality for every 159 anaesthetised cats.

Anaesthetic mortality by ASA (95% CI) were—ASA I: 0.07% (0.03%–0.17%), ASA II: 0.25% (0.14%–0.42%), ASA III: 0.93% (0.64%–1.34%), ASA IV: 7.01% (5.03%–9.68%) and ASA V: 33.33% (21.97%–47.03%).

Twenty-four cats died in the intraoperative period and 70 cats died in the postoperative period, representing 25.5% (95% CI: 18.1%–35.1%) and 74.5% (95% CI: 67.0%–84.0%) of cat deaths, respectively. In detail, the distribution of deaths related to anaesthesia per anaesthetic phase was as follows: six during induction, 18 during the maintenance phase, 13 during recovery in the operating theatre, 41 within the first 24 hours postprocedure and 16 between 24 and 48 hours postprocedure. A visual representation of the timing of cat deaths is provided in Figure 4.

Concerning the logistic regression model, the initial number of cases was 14,832. However, 58 of these cases had missing values, resulting in a final number of 14,774 being used in the model. The multicollinearity analysis revealed that none of the variables had a variance inflation factor above 2.9, suggesting no collinearity. The multivariable logistic regression model demonstrated a strong fit with an AIC of 864.5, a C-statistic of 0.912 and an H&L of $\chi^2(8)$ 4.01 ($p = 0.856$).

Multivariable logistic regression analysis revealed several demographic and clinical factors associated with anaesthesia-related mortality. Cachectic



FIGURE 3 Treemap displaying the breeds analysed in this study. The area for each breed is proportional to the number of cats

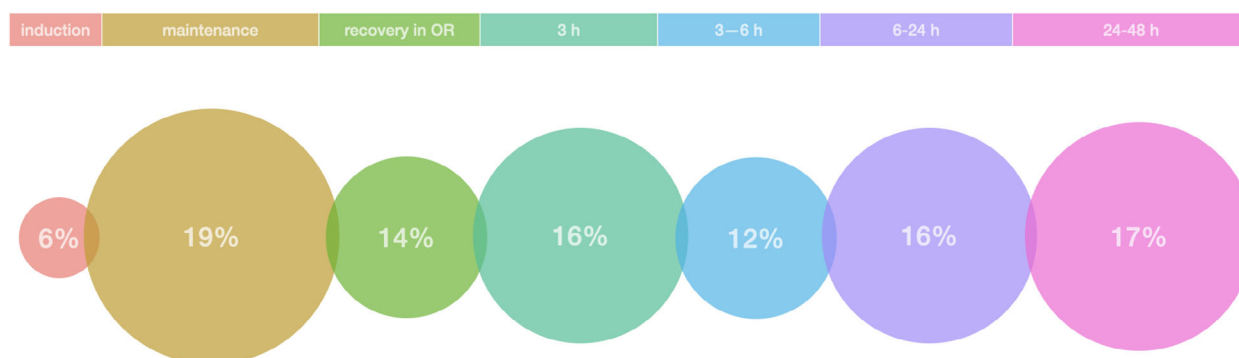


FIGURE 4 Plot of the timing of the death of the cats. OR, operating room

individuals, those with a higher ASA status, ventilated patients and those undergoing abdominal, orthopaedic/neurosurgical or thoracic surgeries exhibited increased mortality. In contrast, the odds of death decreased when α_2 -agonists were used as sedatives or when pure opioids were administered alone as analgesics during premedication. Using locoregional techniques was also related to a decrease in mortality. For a detailed report of the data, including ORs, 95% CIs and *p*-values, refer to Figure 5.

DISCUSSION

The present study, involving 14,962 cases and conducted across 198 veterinary centres worldwide, revealed an overall incidence of anaesthesia-related deaths in cats of 0.63%. In summary, one in 159 cats died under anaesthesia. In the past, mortality in feline patients has been reported to be higher than that in dogs.^{3,7} Cats have unique anatomical, physiological and pharmacological characteristics, which make feline anaesthesia challenging.⁸ In recent decades, there has been tremendous progress in understanding feline anaesthesia and pain management, and clinicians have improved anaesthetic management in cats.^{9–11} However, the mortality in this species is still far from that observed in human medicine, which is

estimated to be between one death in 150,000 and one death in 500,000 anaesthetics.^{12,13}

The mortality reported in this study is higher than that reported in other multicentric studies of feline anaesthesia.^{5,14,15} Comparing mortality and the risks of death from anaesthesia between studies can be challenging due to differences in study design, population, management, death definition and follow-up periods. Hence, when making comparisons, it is crucial to consider the differences in study design. The present study is a purely prospective cohort study. In contrast, other studies performed a case-control analysis.⁵ A prospective cohort study involves selecting a group and collecting real-time data. In contrast, a case-control study involves retrospectively gathering data by selecting cases and controls from an existing cohort (or population), which may introduce bias.¹⁶ The differences between studies can also be explained by the population being studied. The risk of death is higher in sick patients (ASA III, IV and V). In our study, 18.2% of patients were considered high risk; in other studies, this proportion ranged from 3.8% to 7.6%.^{3,7,17} Our study's more significant proportion of high-risk patients might explain the differences observed. However, other studies including a high proportion of ASA III–IV patients showed a higher risk of anaesthetic-related death than found in our study.^{18–21} The random inclusion of centres

TABLE 2 Demographic data of the cats, number and percentage of cats who died, details of the procedure and description of the anaesthetic techniques employed

Variable	Category	Cats (<i>n</i>)	Dead cats (<i>n</i>)	Percentage of cats dead
SEX	Female	7733	41	0.53
	Male	7229	53	0.73
AGE	Paediatric	117	3	2.56
	Young	6016	14	0.23
	Adult	4098	25	0.61
	Senior	3658	37	1.01
	Geriatric	1015	15	1.48
BCS	Normal	10,463	46	0.44
	Cachectic	172	11	6.40
	Thin	2654	25	0.94
	Semi-obese	1360	6	0.44
	Obese	313	6	1.92
ASA	I	6107	4	0.07
	II	5312	13	0.24
	III	2966	27	0.91
	IV	513	33	6.43
	V	64	17	26.56
REASON	Minor	5465	14	0.26
	Abdominal	5297	35	0.66
	Orthopaedics	1549	13	0.84
	Diagnostic	2420	14	0.58
	Thoracic	231	18	7.79
SCHEDULED	Scheduled	13,338	61	0.46
	Non-scheduled	995	8	0.80
	Emergency	629	25	3.97
DURATION	Long	4994	46	0.92
	Medium	8218	35	0.43
	Brief	1750	13	0.74
TIMETABLE	Normal	14,562	84	0.58
	Out-of-hours	400	10	2.50
MONITORING	Advanced	1185	18	1.52
	Basic	2302	9	0.39
	Medium	11,475	67	0.58
PROTOCOL	Inhalatory	11,094	70	0.63
	Parenteral	2742	13	0.47
	Partial intravenous anaesthesia	1126	11	0.98
LOCOREGIONAL	No	10,139	74	0.73
	Yes	4823	20	0.41
VENTILATION	No	11,982	56	0.47
	Yes	2980	38	1.28

Abbreviations: ASA, American Society of Anesthesiologists; BCS, body condition score.

throughout the project and the extended duration of case solicitation may potentially influence the population characteristics and, consequently, the death rate.

Another factor that can confound the comparison of investigations is the variation in the definition of death. In this study, anaesthetic death was defined as

any death occurring between premedication and 48 hours after extubation from causes that were either wholly or partly related to anaesthesia. A similar definition was used in other studies.^{14,15} However, other articles may have more precise or broader definitions, including various phenomena, for example,

TABLE 3 The number and percentage of cases in which various drugs were used, categorised by phase of the anaesthetic protocol

Drugs	Premedication	%	Induction	%	Maintenance	%	Postoperative	%
Acepromazine	389	2.60	0	0.00	110	0.74	215	1.44
Medetomidine	4166	27.84	0	0.00	80	0.53	28	0.19
Dexmedetomidine	7205	48.16	0	0.00	404	2.70	271	1.81
Midazolam	3027	20.23	1282	8.57	140	0.94	13	0.09
Diazepam	111	0.74	307	2.05	20	0.13	9	0.06
Morphine	582	3.89	0	0.00	661	4.42	810	5.41
Methadone	8448	56.46	0	0.00	251	1.68	934	6.24
Pethidine	157	1.05	0	0.00	6	0.04	13	0.09
Fentanyl	310	2.07	651	4.35	2047	13.68	251	1.68
Buprenorphine	907	6.06	0	0.00	31	0.21	2841	18.99
Butorphanol	1884	12.59	0	0.00	20	0.13	208	1.39
Tramadol	845	5.65	0	0.00	23	0.15	1310	8.76
Remifentanyl	66	0.44	121	0.81	452	3.02	0	0.00
Carprofen	26	0.17	0	0.00	0	0.00	77	0.51
Meloxicam	1496	10.00	0	0.00	0	0.00	5771	38.57
Coxibs	439	2.93	0	0.00	0	0.00	830	5.55
Propofol	0	0.00	8724	58.31	1036	6.92	0	0.00
Alfaxalone	2272	15.19	3705	24.76	161	1.08	0	0.00
Ketamine	2486	16.62	3085	20.62	1349	9.02	415	2.77
Thiopental	0	0.00	23	0.15	3	0.02	0	0.00
Etomidate	0	0.00	13	0.09	0	0.00	0	0.00
Isoflurane	0	0.00	692	4.63	9800	65.50	0	0.00
Sevoflurane	0	0.00	92	0.61	2421	16.18	0	0.00
Desflurane	0	0.00	0	0.00	2	0.01	0	0.00

Note: Some of the drugs were employed simultaneously.

non-anaesthesia-related deaths.³ Additionally, variations in the follow-up period also contribute to the difficulty in comparing results. For example, some studies focused only on intraoperative mortality,¹ while others examined the first 24 hours^{19,20} or 15 days after anaesthesia.¹⁴ The length of the follow-up period theoretically affects the probability of detecting deaths. In human studies, patients are commonly followed up for a month after anaesthesia^{13,22–24} or even longer^{25,26} 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 investigation of anaesthesia-related feline deaths across multiple countries simultaneously. Previous multicentric studies have been limited to a single country or region, such as the United Kingdom,^{2–4} the United States,^{5,27,28} Finland,²⁹ South Africa,³⁰ Canada¹⁷ or Spain.^{19,20} The differences in practices and resources can significantly affect anaesthetic mortality, rendering direct comparisons between countries challenging. This observation has been particularly noted in human anaesthesia studies, specifically when comparing developed and developing regions.³¹ Some studies have focused on specific hospitals, providing meaningful information that may only be relevant to those centres.^{1,18,28,32,33} In contrast,

the current research provides a global perspective by collecting data from multiple clinics, including primary care and referral centres. Figure 6 visually represents the differences in anaesthesia-related mortality across various countries and institutions, as reported in previous studies.

The cases documented in this study reveal a notable occurrence of fatalities in cats following surgery, which is consistent with findings in other studies.^{5,19,20,34} This observation reinforces the understanding that the postoperative phase is indeed critical. Cats have a high incidence of anaesthetic complications such as hypothermia,³⁵ hypotension,²⁸ hypoventilation, hypoxia³⁶ and pain.⁹ Additional efforts should therefore be made to improve postoperative care to reduce feline anaesthesia-related deaths.

Cats with cachexia were more likely to die than cats with an average BCS. Weight loss is often a clinical sign of disease in cats.^{37,38} Cats often hide their clinical signs, and clinicians sometimes need to perform diagnostic tests that require anaesthetising the cat when the condition is already established or progressing. For instance, sometimes the reason for anaesthetising cachectic cats is the placement of a feeding tube, and this procedure is known to contribute to high mortality.³⁹ Anaesthesia in cachectic cats should be considered high-risk anaesthesia. Other studies found that cats that were obese⁴ or just

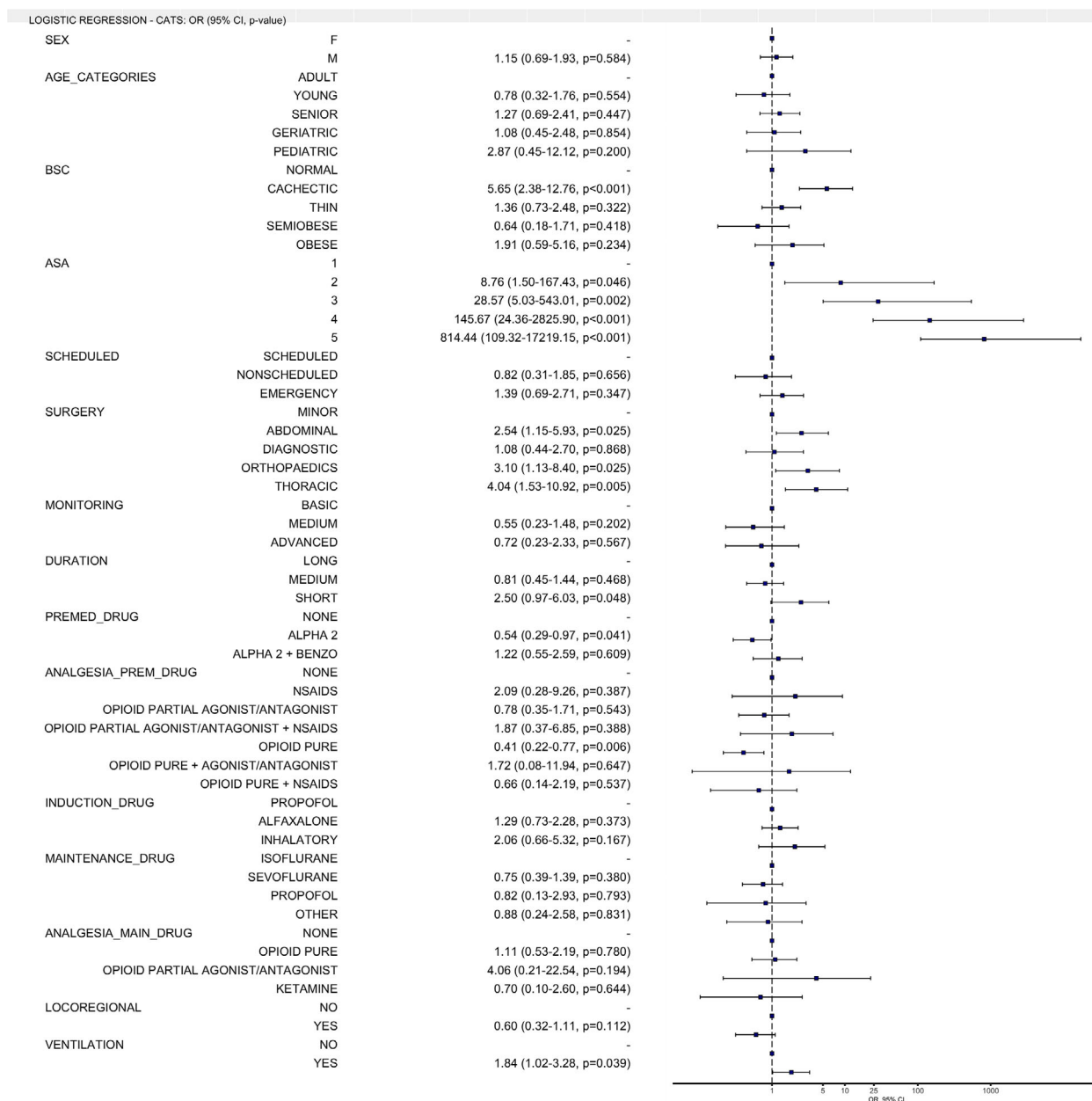


FIGURE 5 Forest plot of the logistic regression model for the risk of anaesthesia-related death in cats. The dotted vertical line represents an odds ratio (OR) of 1.0. When a predictor variable falls on the dotted line, there is no significant difference in the outcome variable's odds between the reference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

overweight⁵ have an increased risk. However, in this study, an increased risk in obese patients was not observed. Controversially, categorising patients into specific groups based on these parameters may have introduced variability in our results. For instance, variations in the body condition or age interpretation within each category could influence the observed associations. The age classifications used in this study differ from internationally recognised definitions, such as the 2021 AAHA-AAFP Feline Life Stage Guidelines.⁴⁰ However, they were used prior to these guidelines, based on our previous work. Their limitations and potential for misclassification bias are acknowledged.

The ASA classification is widely recognised as a significant predictor of anaesthesia-related mortality. This current study further reinforces this affirmation, as supported by previous research.^{4,14} Hence, it is crucial to prioritise patient stabilisation and improve their physical condition, as these measures have the potential to decrease the likelihood of death significantly. The ASA physical status scoring system, a straightforward and practical tool, is invaluable for identifying an increased risk of anaesthesia-related mortality within 24–72 hours postprocedure.⁴¹ Nonetheless, the subjectivity of the ASA score can lead to inconsistent assignments by clinicians, as evidenced by various studies showing only fair to moderate inter-rater agreement among human anesthesiologists.⁴²

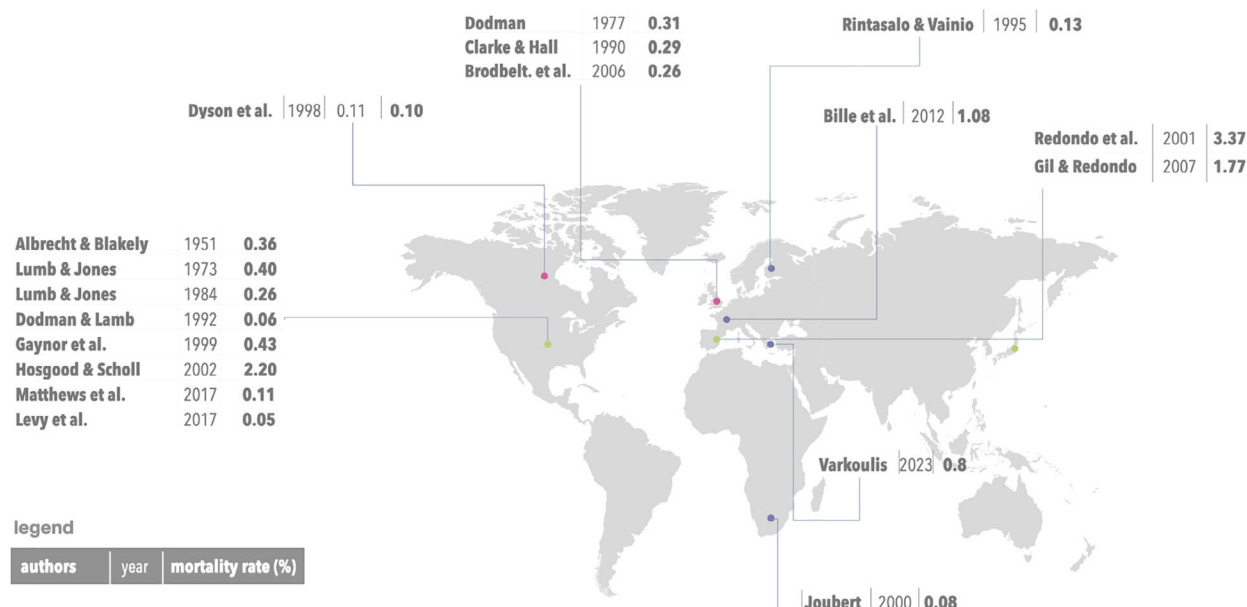


FIGURE 6 Comparative analysis of anaesthetic mortality in cats across various studies

Although subjective, the ASA classification reliably predicts complications and mortality after anaesthesia. Therefore, despite personal judgement, the ASA score is still significant in anticipating perioperative risks and improving patient outcomes. Consequently, it is strongly recommended to implement this classification in the preanaesthetic evaluation of cats.

Reports have shown that major procedures are associated with higher mortality than minor ones.⁴ Abdominal surgeries include various procedures, such as gastrointestinal surgery, urinary system surgery, haemoabdomen surgery and reproductive surgery in female cats. Elective ovariohysterectomy, for example, has a low mortality.^{5,6} However, the category of abdominal surgery includes complex cases and septic patients, which could contribute to a higher mortality overall. This finding is consistent with findings from other studies.^{43–45} Furthermore, abdominal surgery increases heat loss, raising mortality risk.³⁵ Orthopaedic procedures typically involve cats with fractures or luxations resulting from trauma,⁴⁶ and these patients may have additional undetected injuries that necessitate a thorough examination before anaesthesia.⁴⁷ This assessment is crucial for the patient's safety and helps identify any risk factors or physiological changes that could affect the anaesthesia plan.⁴⁸ Thoracic surgeries exhibited the highest odds ratio for death. Examples of thoracic surgery included diaphragmatic hernia repair, which has notably elevated mortality in cats.⁴⁹ Mortality after thoracotomy is higher in cats than in dogs.⁵⁰ Performing thoracic surgeries on cats is complex due to limited space and the size difference between the patient's body and the surgeon's hands. Further research that thoroughly categorises procedures and investigates their impact on mortality, as proposed in human surgery,⁵¹ could identify areas for improvement and facilitate the development of strategies to enhance

patient safety and improve outcomes in veterinary anaesthesia.

The study found that mechanical ventilation during anaesthesia increases the mortality risk in cats, regardless of cause or other factors. Ventilation is an essential tool to manage respiratory depression, which is frequently associated with general anaesthesia. Proper ventilation plays a significant role in maintaining the cat's oxygenation and normocapnia. However, this approach can be challenging for smaller patients. Current small animal anaesthesia ventilators are not designed to deliver small tidal volumes; therefore, it is easy to induce volume or barotrauma in cats. Moreover, there is a risk that the ventilated cats may have had a higher risk or significant comorbidities. Inadequate ventilation can result in various complications, such as low oxygen saturation or hypoxemia, high levels of carbon dioxide or hypercapnia, patient-ventilator desynchrony, air leakage, air resistance, barotrauma, volutrauma and haemodynamic instability.⁵² Ventilation can also cause direct damage to the lungs.⁵³ When adjusting ventilation settings, it is also crucial to account for species differences in the respiratory system. For instance, cats possess a more compliant respiratory system than dogs.⁵⁴ Using the same ventilation settings for both species could result in overinflation of a cat's lungs.⁵⁵ Investing in adequate equipment and understanding the impact of mechanical ventilation on feline patients could reduce feline anaesthesia-related mortality.

The choice of anaesthetic drugs is a significant factor influencing mortality. The use of α_2 -agonists as sedatives in premedication is associated with lower mortality. These agents reduce the need for hypnotics, alleviate presurgical stress and provide analgesic properties.⁵⁶ Therefore, their inclusion in preanaesthetic medication is advised unless contraindicated. However, the combination of α_2 -agonists and

benzodiazepines does not confer the same protective effect. This lack of effect may be attributed to the increased release of catecholamines caused by benzodiazepines in cats.^{57,58} The reduction in catecholamines, which is observed when α_2 -agonists are used alone,⁵⁸ indicates a decreased neurohumoral stress response and may be more beneficial.⁵⁷ Similarly, patients treated with pure opioids demonstrated lower mortality, consistent with previous reports in dogs.⁵⁹ Opioids offer potent pain relief throughout the perioperative period, enhancing patient comfort.⁹ These drugs have sedative properties, effectively mitigating anxiety and stress. They also have sedative properties, effectively mitigating anxiety and stress, thereby reducing the required dosage of hypnotic agents and assisting in mitigating cardiorespiratory depression induced by these agents.^{8,9,60}

Local and regional anaesthesia were also associated with decreased anaesthesia-related mortality, consistent with findings in human anaesthesia studies.^{61–63} Notably, this is the first instance of such a correlation being reported within veterinary anaesthesia. The techniques outlined in this study encompass a spectrum of procedures, ranging from uncomplicated intratesticular blocks,⁶⁴ dental blocks,⁶⁵ epidural anaesthesia⁶⁶ and intraperitoneal blocks⁶⁷ to more advanced ultrasound-guided peripheral blocks.^{68,69} These various approaches have been associated with a decrease in the required hypnotic doses, enhancement of cardiovascular and respiratory stability during the procedure and a reduction in perioperative stress levels.^{64,66,68,69} Combining locoregional and general anaesthesia in human anaesthesia has shown better intraoperative haemodynamics than in general anaesthesia alone.^{70,71} Our research has revealed that combining systemic analgesia with locoregional techniques can significantly reduce mortality. The effective management of pain must not be underestimated, as its neglect can culminate in fatal consequences.⁷² Thus, pain prevention, diagnosis and treatment are pivotal for elevating animal welfare standards^{9,73} and mitigating mortality risk during anaesthesia and the subsequent recovery phase.

Although it could be argued that the administration of drugs or the use of specific techniques during anaesthesia (e.g., ventilation or locoregional techniques) has little impact on postoperative death, research suggests otherwise. The potential effects of anaesthetic drugs, both positive and negative, extend beyond the intraoperative phase and may also affect the likelihood of death in the postoperative period. However, it is difficult to conduct a comprehensive analysis due to limited data on variables studied during the recovery or postoperative phase. This complexity underscores the challenge of assessing the specific effects of preanaesthetic medication and other drugs. Therefore, cautious interpretation is necessary, and further research is imperative to better understand the postoperative impact of these drugs.

This study has several limitations. Clinics and hospitals were not randomly selected. Instead, participation relied on explicit clinician invitations, potentially introducing selection bias. This might skew the sample towards anaesthesia specialists or those interested in the field, impacting risk assessment accuracy. Future research should validate the findings across more diverse participants to address this concern. Assessing response rates for participating centres was challenging, potentially affecting data quality despite instructions to record all cases. Robust data quality protocols should be established in future studies for enhanced accuracy and reliability. Another limitation is the subjectivity in classifying deaths as anaesthesia-related, which underscores the need for objective methods for identifying such deaths.⁷⁴ Despite the collection of vast amounts of data, this article analyses only a limited number of variables, excluding some crucial factors, such as the impact of different medical centre types (first opinion, referral or university hospitals) on mortality. Mortality may be higher in university hospitals and referral centres than in first-opinion centres, due to the more severe cases seen at these centres.^{7,75} The study's focus on signalment and intraoperative factors resulted in limited data on the postoperative variables studied, which may have led to misinterpretations. The lack of detailed postoperative data collection hindered a comprehensive analysis of postoperative death contributors. Acknowledging these limitations calls for future research tailored to the intricacies of the postoperative phase, with targeted studies focusing on recommended variables such as monitoring and recovery protocols.

Despite its limitations, this study lays the groundwork for future research to enhance protocols and ensure patient safety in feline anaesthesia. Further investigation is needed to address gaps in knowledge and improve the understanding of anaesthesia-related mortality in cats, leading to better patient safety and evidence-based veterinary practices.

CONCLUSION

In conclusion, the overall anaesthetic mortality for cats in this study was 0.63%. Most deaths occurred during the postoperative period. There are risk and protective factors that could help in clinical decision making. Cats with cachexia, higher ASA status or undergoing abdominal, orthopaedic/neurosurgical or thoracic procedures exhibited elevated mortality. Mechanical ventilation use was also associated with increased mortality. In contrast, mortality odds were reduced by the use of α_2 -agonist sedatives, pure opioids in premedication and locoregional techniques. The findings of this study may help guide the development of strategies to reduce the incidence of anaesthesia-related deaths in cats.

AUTHOR CONTRIBUTIONS

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

ACKNOWLEDGEMENTS

We want to thank the veterinarians and nurses at the participating centres for their hard work in gathering information. With their efforts, this project was possible. Special thanks to Nicola J. Martinez and Ana Doñate for their invaluable assistance and expertise in reviewing and documenting the research.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

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 CEU Cardenal Herrera (CEEA 22/07).

ORCID


José I. Redondo  <https://orcid.org/0000-0001-5377-9650>

Fernando Martínez-Taboada  <https://orcid.org/0000-0002-0083-4764>

Jaime Viscasillas  <https://orcid.org/0000-0003-0162-941X>

Luis Doménech  <https://orcid.org/0000-0002-8443-2972>

Eva Z. Hernández-Magaña  <https://orcid.org/0000-0002-8850-040X>

Pablo E. Otero  <https://orcid.org/0000-0002-0901-7269>

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SUPPORTING INFORMATION

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

How to cite this article: Redondo JI, Martínez-Taboada F, Viscasillas J, Doménech L, Marti-Scharfhausen R, Hernández-Magaña EZ, et al. Anaesthetic mortality in cats: A worldwide analysis and risk assessment. *Vet Rec*. 2024;e4147. <https://doi.org/10.1002/vetr.4147>