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# Characterization of dynamic compliance of the respiratory system in healthy anesthetized dogs

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**Introduction:** In clinical practice, evaluating dynamic compliance of the respiratory system ( $C_{dyn}$ ) could provide valuable insights into respiratory mechanics. Reference values of  $C_{dyn}$  based on body weight have been reported, but various factors may affect them and the evidence is scanty. This study aimed to establish a reference interval for  $C_{dyn}$  and identify associated variables.

**Methods:** Data were collected from 515 client-owned dogs requiring anesthesia, excluding those with lower airway disease. The dogs were anesthetized, the tracheas intubated, and lungs ventilated at clinicians' discretion across 11 centers in six countries, with no restrictions on anesthesia protocols or ventilation settings, except avoiding inspiratory pauses. Three  $C_{dyn}$  measurements from three consecutive breaths per dog were recorded using a standardized form, which also documented factors affecting  $C_{dyn}$  identified through literature and an online survey. Various spirometry technologies were used. The substantial variance in  $C_{dyn}$  measurements led to a comprehensive analysis using a multiple linear regression model. Multicollinearity (variables highly correlated with each other) was addressed by investigating, transforming, or excluding factors. Initial simple linear regression assessed each variable's individual effect on  $C_{dyn}$ , followed by a multiple linear regression model constructed via stepwise forward selection and backward elimination.

**Results:** The best-fitting model identified a linear relationship between  $C_{dyn}$  and body mass when the following conditions were met: high BCS (Body Condition Score), orotracheal tubes <7% smaller than predicted, the use of a D-lite flow sensor, and the absence of a high FIO<sub>2</sub> (>80%) exposure for more than 10 minutes before  $C_{dyn}$  measurement. In cases where these conditions were not met, additional factors needed to be incorporated into the model. Low (1/9, 2/9, 3/9) and medium (4/9, 5/9) BCS, an orotracheal tube of the

predicted size or larger and longer inspiratory times were associated with increased  $C_{dyn}$ . The use of alternative spirometry sensors, including Ped-lite, or prolonged exposure to high  $FIO_2$  levels resulted in decreased  $C_{dyn}$ .

**Conclusion and clinical relevance:** Establishing a reference interval for  $C_{dyn}$  proved challenging. A single reference interval may be misleading or unhelpful in clinical practice. Nevertheless, this study offers valuable insights into the factors affecting  $C_{dyn}$  in healthy anesthetized dogs, which should be considered in clinical assessments.

#### KEYWORDS

anesthesia, compliance, dogs, dynamic compliance, monitoring, respiratory mechanics, spirometry, ventilation

## 1 Introduction

Spirometry is a common monitoring modality used in clinical practice in anesthetized dogs (1). The pressure-volume relationship of the respiratory system (P-V) is fundamental for assessing its mechanics during mechanical ventilation (2). Compliance is defined as the change in lung volume per unit change in pressure gradient; it may be measured for lung, thoracic cage, or both [i.e., respiratory system; (3)]. Compliance plays a pivotal role in understanding respiratory physiology in veterinary anesthesia, particularly when dogs are mechanically ventilated. It is commonly displayed by modern monitors, and generally calculated dividing the expired gas volume by the change in the airway pressure (plateau pressure—positive end expiratory pressure). Various types of compliance, including dynamic compliance ( $C_{dyn}$ ), static compliance ( $C_{stat}$ ), and quasi-static compliance, have been utilized to evaluate respiratory system function in response to interventions and different influencing factors (4–7). Both  $C_{stat}$  and quasi-static compliance require an inspiratory pause. Quasi-static compliance, obtained with inspiratory pauses of variable durations below 3 s, did not provide accurate  $C_{stat}$  values in healthy dogs (8).  $C_{dyn}$  offers a real-time assessment of respiratory performance during mechanical ventilation, enabling the early detection of changes in airway resistance—such as bronchospasm, secretions, and tube kinking—as well as alterations in the elastic component (9).

Despite decades of research on P-V curves, our comprehensive understanding of the P-V relationship remains incomplete (2).  $C_{dyn}$  can be assessed as a loop or as a numerical value. A flatter loop suggests lower compliance, potentially indicating stiffening of lung tissue or the chest wall, whereas a steeper loop indicates higher compliance (10). Veterinary anesthetists typically use the shape and steepness of the P-V loop independently of numerical values for  $C_{dyn}$  to guide their clinical decisions (1). The shape and steepness of P-V loops are greatly influenced by the scale of the P-V graph displayed. The axes scales can be altered either manually or automatically by devices. Therefore, interpreting  $C_{dyn}$  based on the steepness of a P-V curve through subjective visual observation may lead to incorrect conclusions, particularly given the existing gap in the literature concerning  $C_{dyn}$  usual values. Creating a quantitative reference range for  $C_{dyn}$  may assist clinical interpretation of changes in lung mechanics.

However, developing a reference range is likely to be challenging due to the different variables influencing compliance

that have been identified in dogs. Body mass is a logical variable due to its impact on tidal volume ( $V_T$ ), as described by Stahl (11), and indicated in equations reported by Asorey et al. (12) and Bradbrook et al. (13). Additionally, the influence of body position on  $C_{dyn}$  (13) and inspiratory time (14) have been demonstrated. These variables underscore the multifaceted nature of compliance measurements and highlight the need for establishing reference intervals specific to the canine population.

The goals of this prospective, exploratory study were to establish a reference interval for  $C_{dyn}$  in anesthetized dogs and to identify the variables impacting  $C_{dyn}$ .

## 2 Materials and methods

### 2.1 Centers included

This study was carried out in 11 centers located in five countries: Australia, France, Switzerland, The United Kingdom, and The United States of America. An overall ethical approval was granted by the Ethical Review Group of the Association of Veterinary Anesthetists (2019-007). This approval was sufficient for the following centers: Southern Counties Veterinary Specialists, Davies Veterinary Specialists, Manchester Veterinary Specialists, Small Animal Hospital of the University of Glasgow, University of California and VetAgro Sup. The project was further approved by the relevant local ethical committees at Murdoch University (R3186/19), the University of Bristol (VIN/18/032), the University of Sydney (2019/1617), and Vetsuisse Faculty Bern & Zürich (BE78/18).

### 2.2 Case selection by centers

Cases were collected between July 2019 and November 2023. If the hospital's admission or anesthesia consent forms lacked authorization to record clinical data, an informed owner consent form was provided by study organizers.

Based on a full physical examination, client-owned dogs with an ASA classification of I and II (American Society of Anesthesiologists) undergoing anesthesia according to their clinical condition were recruited at the discretion of the responsible anesthetists in each center. The exclusion criterion included:

history of lung disease, known lower respiratory tract disease and any intra-anesthetic complication (e.g., hypotension, hypoxaemia) at the time of the measurement. The tracheas of the dogs had to be intubated (orotracheal intubation) and the lungs mechanically ventilated for them to be included in the study.

## 2.3 Anesthetic management and ventilation monitoring

A variety of spirometry technologies and monitors is commonly used in veterinary anesthesia (1) and different models were available in the centers involved in the study. Therefore, the equipment type was not restricted.

The original plan was to conduct calibration checks on the monitors just before beginning data collection at each center. However, due to significant delays caused by the COVID-19 pandemic, data was collected without considering the calibration status of the monitors.

Cases were managed according to normal clinical practice in the hospitals, without any special adaptation for the study. Dogs were anesthetized, monitored, and ventilated as appropriate, with no restrictions on anesthesia protocol or ventilation settings, except a request not to use any inspiratory pause.

Cases were performed by any anesthetist at any of the centers, under the supervision of a main local coordinator. Whenever possible, the measurements of  $C_{dyn}$  were to be recorded within the first hour of establishing controlled mechanical ventilation. Immediately prior to recording  $C_{dyn}$ , the anesthetists ensured leaks were absent and that there was no dog-ventilator asynchrony. Measurements were postponed if a leak was detected based on evaluating closure of the P-V loop, the difference between inspiratory and expiratory volumes, inadequate airway pressure and flow, and capnography waveforms in relation to chest wall movements. For each subject, measurements of  $C_{dyn}$  from three consecutive breaths were recorded.

## 2.4 Data collection form

Factors likely to impact on  $C_{dyn}$ , identified from previous literature and through an online survey, were recorded. These factors included:

- Body mass (in kg),
- Internal diameter (in mm) and length (in cm) of the orotracheal tubes,
- Age (in months),
- Breed,
- Body Condition Score (BCS) scored out of 9 (<https://wsava.org/wp-content/uploads/2020/01/Body-Condition-Score-Dog.pdf>),
- Morphology (brachymorphic, dolichomorphic, mesomorphic; subjective evaluation),
- Positioning (dorsal, lateral, or sternal recumbency) with or without Trendelenburg (No, Trendelenburg or reverse Trendelenburg),
- Breathing system (circle or Mapleson),
- Spirometry sensor/monitor used (classified for analysis as: D-Lite, Pedi-Lite, other),
- The use of Heat and Moisture Exchangers (HMEs, present or absent between the spirometry sensor or the breathing system and the orotracheal tube),
- The inspired fraction of oxygen ( $FIO_2$ , %),
- Whether or not a  $FIO_2$  above 80% was maintained for 10 minutes or more before  $C_{dyn}$  determination (yes or no),
- The time elapsed between the induction of anesthesia and the measurements (in minutes),
- The ventilation mode (volume-controlled or pressure-controlled ventilation),
- The positive end-expiratory pressure set at the time of the measurements (PEEP, in  $cmH_2O$ ),
- The inspiratory time (in seconds, calculated from the respiratory rate and the inspiratory to expiratory ratio setting),
- The drugs administered before the measurements (yes or no, for alpha-2 adrenergic receptor agonists, acepromazine, alfaxalone, anti-muscarinic, benzodiazepines, butorphanol, intravenous lidocaine, isoflurane, ketamine, mu-agonist opioids, neuromuscular blocking agents, propofol, and sevoflurane),
- The administration of a locoregional block, an epidural or a spinal injection (yes or no).

Some variables were recorded only to confirm that the individual cases were not subject to any obvious anesthetic complications at the time of measurement (e.g., hemoglobin saturation <94%, end tidal  $CO_2$  > 60 mmHg, Mean Arterial Pressure <60 mmHg), but were not included in the statistical analysis.

A standard data collection form was used in each case. The data collection form was trialed by three clinical anesthetists before the start of the study to ensure it was comprehensive and easily filled. The form is presented in Figure 1. The data obtained from the various centers was compiled in an Excel file.

## 2.5 Data curation

Data was excluded from cases with more than 15% variation in  $C_{dyn}$  across the three measurements. A 15% threshold was arbitrarily chosen by the authors as it accounted for potential variability in the precision of the instruments.

Cases containing missing or obviously incorrect values within selected variables were flagged. Data from those cases was excluded when variables were analyzed independently. If a factor was included in the final multiple linear regression model, data from the cases with missing or incorrect values were excluded. For each test, the total number of cases included in the analysis is reported.

In addition, categories (i.e., factors likely to impact  $C_{dyn}$ ) that appeared in fewer than 25 cases (an arbitrary number) were not considered in the analysis.

| Compliance & resistance reference intervals study                                                                                                                                                                                                                         |  | Maintenance:                                                                                                                                              |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Case Number: .....                                                                                                                                                                                                                                                        |  | Drug: <input type="checkbox"/> Isoflurane <input type="checkbox"/> Sevoflurane <input type="checkbox"/> Desflurane <input type="checkbox"/> Propofol TIVA |  |
| Breed: .....                                                                                                                                                                                                                                                              |  | <input type="checkbox"/> Alfaxalone TIVA <input type="checkbox"/> Ketamine/tiletamine-zol. <input type="checkbox"/> Other                                 |  |
| Age: .....years .....months old                                                                                                                                                                                                                                           |  | Breathing system:                                                                                                                                         |  |
| Weight: .....kg                                                                                                                                                                                                                                                           |  | <input type="checkbox"/> Circle <input type="checkbox"/> Mapleson A <input type="checkbox"/> Mapleson D <input type="checkbox"/> Other                    |  |
| BCS: <input type="checkbox"/> 1/9 <input type="checkbox"/> 2/9 <input type="checkbox"/> 3/9 <input type="checkbox"/> 4/9 <input type="checkbox"/> 5/9 <input type="checkbox"/> 6/9 <input type="checkbox"/> 7/9 <input type="checkbox"/> 8/9 <input type="checkbox"/> 9/9 |  | FiO <sub>2</sub> : .....% for .....min / then .....% for .....min                                                                                         |  |
| Morphology: <input type="checkbox"/> Dolichomorphic. <input type="checkbox"/> Mesomorphic <input type="checkbox"/> Brachymorphic                                                                                                                                          |  | HME: <input type="checkbox"/> YES <input type="checkbox"/> NO                                                                                             |  |
| Procedure:                                                                                                                                                                                                                                                                |  | Analgesia:                                                                                                                                                |  |
| <input type="checkbox"/> Dentistry                                                                                                                                                                                                                                        |  | Infusion: <input type="checkbox"/> Opioid <input type="checkbox"/> Alpha-2 agonist                                                                        |  |
| Diagnostics / internal medicine:                                                                                                                                                                                                                                          |  | <input type="checkbox"/> Ketamine <input type="checkbox"/> Lidocaine <input type="checkbox"/> Other                                                       |  |
| <input type="checkbox"/> Imaging (CT/MRI/X-rays) <input type="checkbox"/> Dermatology <input type="checkbox"/> Gastroscopy                                                                                                                                                |  | Loco-regional:                                                                                                                                            |  |
| <input type="checkbox"/> Other diagnostics                                                                                                                                                                                                                                |  | <input type="checkbox"/> Epidural/spinal WITH local anaesthetic                                                                                           |  |
| Neurosurgery:                                                                                                                                                                                                                                                             |  | <input type="checkbox"/> Other block                                                                                                                      |  |
| <input type="checkbox"/> Brain <input type="checkbox"/> Neck <input type="checkbox"/> Thoracolumbar spine                                                                                                                                                                 |  | NMB: <input type="checkbox"/> None <input type="checkbox"/> Non-depolarizing <input type="checkbox"/> Suxamethonium                                       |  |
| Ophthalmology:                                                                                                                                                                                                                                                            |  | Other drugs: <input type="checkbox"/> Anticholinergics <input type="checkbox"/> Benzodiazepine <input type="checkbox"/> Other                             |  |
| <input type="checkbox"/> Eye surgery <input type="checkbox"/> Eyelids/annexes surgery <input type="checkbox"/> Ophta. diagnostics                                                                                                                                         |  | VENTILATION:                                                                                                                                              |  |
| Orthopaedic:                                                                                                                                                                                                                                                              |  | Time start ventilation: .....h .....min - Time measurement: .....h .....min                                                                               |  |
| <input type="checkbox"/> Forelimb <input type="checkbox"/> Hind limb <input type="checkbox"/> Other orthopaedic surgery                                                                                                                                                   |  | Ventilation mode: <input type="checkbox"/> Pressure controlled ventilation                                                                                |  |
| Soft tissue:                                                                                                                                                                                                                                                              |  | <input type="checkbox"/> Volume controlled ventilation                                                                                                    |  |
| <input type="checkbox"/> Laparoscopy <input type="checkbox"/> Laparotomy <input type="checkbox"/> Skin/mammary                                                                                                                                                            |  | Spirometer used: .....                                                                                                                                    |  |
| <input type="checkbox"/> BOAS <input type="checkbox"/> Urogenital <input type="checkbox"/> Other soft tissue                                                                                                                                                              |  | VT: (set).....mL - (delivered).....mL                                                                                                                     |  |
| <input type="checkbox"/> Other                                                                                                                                                                                                                                            |  | Ppeak: .....cmH <sub>2</sub> O - PEEP: .....cmH <sub>2</sub> O                                                                                            |  |
| Position: <input type="checkbox"/> Sternal <input type="checkbox"/> Dorsal <input type="checkbox"/> Lateral } <input type="checkbox"/> Trendelenburg <input type="checkbox"/> Inverted Trendelenburg                                                                      |  | Respiratory rate: ..... - I:E: .....                                                                                                                      |  |
| Premedication: (time) .....h .....min                                                                                                                                                                                                                                     |  | SpO <sub>2</sub> : .....% - ETCO <sub>2</sub> : .....mmHg - MAP: .....mmHg                                                                                |  |
| <input type="checkbox"/> Acepromazine <input type="checkbox"/> Alfaxalone <input type="checkbox"/> α2-agonist <input type="checkbox"/> Anticholinergic                                                                                                                    |  | <input type="checkbox"/> NO DOG-VENTILATOR ASYNCHRONY (checked)                                                                                           |  |
| <input type="checkbox"/> Benzodiazepine <input type="checkbox"/> Butorphanol <input type="checkbox"/> Ketamine. <input type="checkbox"/> μ-agonist (Mu)                                                                                                                   |  | <input type="checkbox"/> NO LEAK (tested)                                                                                                                 |  |
| <input type="checkbox"/> Tiletamine-zolazepam <input type="checkbox"/> Other                                                                                                                                                                                              |  | Compliance 1: .....                                                                                                                                       |  |
| Induction: (time) .....h .....min                                                                                                                                                                                                                                         |  | Resistance 1: .....                                                                                                                                       |  |
| <input type="checkbox"/> Alfaxalone <input type="checkbox"/> Benzodiazepine <input type="checkbox"/> Etomidate <input type="checkbox"/> Ketamine <input type="checkbox"/> Opioid                                                                                          |  | Compliance 2: .....                                                                                                                                       |  |
| <input type="checkbox"/> Propofol <input type="checkbox"/> Thiopentone <input type="checkbox"/> Tiletamine-zolazepam <input type="checkbox"/> Other                                                                                                                       |  | Resistance 2: .....                                                                                                                                       |  |
| Endotracheal tube:                                                                                                                                                                                                                                                        |  | Compliance 3: .....                                                                                                                                       |  |
| Internal diameter: .....mm                                                                                                                                                                                                                                                |  | Resistance 3: .....                                                                                                                                       |  |
| Length: .....cm                                                                                                                                                                                                                                                           |  |                                                                                                                                                           |  |

FIGURE 1  
Data collection form for dynamic compliance ( $C_{dyn}$ ) of the respiratory system in dogs. Standardized data collection form used across 11 centers in six countries to assess  $C_{dyn}$  in a cohort of 515 dogs. The form includes fields for recording variables that were identified as potentially influencing  $C_{dyn}$ . Each center adhered to the same protocol for data collection to ensure consistency and reliability of the data across different locations.

## 2.6 Number of animals

The sample size was determined to ensure adequate statistical power for evaluating the reference interval of  $C_{dyn}$  in dogs under anesthesia and determining the possible influence of 20 variables and 21 drugs and loco regional techniques. We integrated previously published data on compliance variability to estimate a standard deviation ( $\sigma$ ) of 6.6 mL/cmH<sub>2</sub>O (13). Using this information, along with a desired precision ( $\delta$ ) of  $\pm 5$  mL/cmH<sub>2</sub>O, a significance level ( $\alpha$ ) of 0.05, and a desired power ( $1-\beta$ ) of 0.80, the required sample size was calculated. Considering the multicentre nature of the study, an arbitrary design effect of 1.5 was applied to adjust the sample size calculation, accounting for potential variability between centers. The resulting required sample size, considering both multicentre adjustment and compliance standard deviation, was determined to be  $\sim 303$  dogs. Since the study was non-invasive, data collection was limited in time rather than once the predetermined number of cases was reached. This approach aimed to maximize the chances of obtaining sufficient representation for each evaluated variable.

## 2.7 Statistical analysis

Statistical analysis was performed using R version 4.3.2 (15). The “pwr” package was used to perform the sample size calculation. The package “readxl” was used to import the data in R (16). The package “ggplot2” was used for graphical representations, unless stated otherwise (17).

The average of the three consecutive  $C_{dyn}$  measurements from each case was calculated and used for analysis. Descriptive statistics were also performed to summarize the data. The distribution of  $C_{dyn}$  was visually evaluated and tested for normality using both the Shapiro-Wilk and the Anderson-Darling normality tests.

In response to the substantial variance observed, and to comprehensively analyse the impact of the various factors on  $C_{dyn}$ , a multiple linear regression model was developed.

First, a simple linear model was created using the “lm” function from the “lme4” package to analyse the relationship between  $C_{dyn}$  (dependent variable) and body mass (predictor variable). The relationship between  $C_{dyn}$  and body mass was graphically represented with the linear regression line and 95% confidence interval. For comparison,

previously published linear regressions lines were also reported (12, 13).

Further analysis was conducted on variables considered likely to affect  $C_{dyn}$  in the order of anticipated importance, as determined by the authors. Initially, a correlation matrix was created to identify potential multicollinearities between the factors (e.g., BCS and morphology). Multicollinearities occur when two or more variables are highly correlated with each other. Specifically, if the absolute correlation coefficient between any two variables was  $>0.4$ , their relationship was investigated further and possible transformations or exclusions were considered.

Of the many factors assessed, a collinearity was expected between body mass and internal diameter of oro-tracheal tubes (18). Nevertheless, a marked effect of the internal diameter of the orotracheal tubes on  $C_{dyn}$  was suspected, therefore, it was considered relevant to keep this parameter after transformation. Because of multicollinearities, the deviation from the mean diameter of the investigated population rather than the absolute value of the diameter was evaluated. A graph plotting the internal diameter of the orotracheal tubes and the body mass was generated and three types of models were considered to model their relationship: root models, logarithmic models, and excitatory Emax models. Both difference and ratio of the internal diameter of the tube to its “predicted value” (i.e., the internal diameter expected from the various models for a given body mass) were investigated for each subject. The various approaches were compared using linear regression model metrics (AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; adjusted  $R^2$ , Adjusted Coefficient of Determination) and ANOVA (Analysis of Variance) in R. A direct linear regression of the continuous variable or the use of cut-off values on the difference or ratio to create categories of internal diameters of orotracheal tubes (Low, Medium, and High) were tested and the best-fit was selected.

Multicollinearity was also expected between the length of the orotracheal tubes and their internal diameter, as well as with body mass. As, according to the Hagen-Poiseuille equation, the length of the orotracheal tubes should physically demonstrate less potential to influence  $C_{dyn}$  than their internal diameters, it was decided to test the length of the orotracheal tubes only if their internal diameter had no significant effect on the  $C_{dyn}$  adjusted to body mass model and to ignore it otherwise.

After addressing multicollinearities, the remaining individual variables were characterized through descriptive statistics and graphical representations (frequency histograms to describe the representativity of the eventual various subcategories within each variable). Direct relationship to  $C_{dyn}$  was evaluated using median boxplot, Wilcoxon rank-sum (if there were only two categories within the factors considered) or Kruskal-Wallis test followed by *post-hoc* Dunn's test if necessary for pairwise comparisons (for factors with more than two categories) and/or linear regression. Transformation of the data to create simplified categories was tested where appropriate and the final variable selected based on best model metrics (see below). The significance of each variable's addition to the linear regression of  $C_{dyn}$  adjusted to body mass was tested to identify potential candidates for inclusion in the multiple linear regression model. During this first selection of

the variables, violation of conditions for linear regression were not tested.

Finally, a multiple linear regression model was built using a stepwise forward selection and backward elimination technique. Cases containing missing or obviously incorrect information in one of the categories were excluded from the analysis for that category only, and if the variable was included in the final model. Decision on candidates' selection was made based on the overall picture. The predictors were removed and added one by one according to anticipated relevance based on their variable-specific  $p$ -values. At each step, the AIC, BIC, adjusted  $R^2$ , and  $p$ -values (ANOVA model comparison) were evaluated. For AIC and BIC, lower values were preferred for better model fit. For adjusted  $R^2$ , higher values indicated a better fit. Linearity, homoscedasticity, independence of residuals, normality of residuals and multicollinearity were assessed using residuals plots, the Durbin-Watson statistic, the Shapiro-Wilk test, and variance inflation factors, respectively.

Statistical significance was considered when  $p < 0.05$ .

### 3 Results

A total of 515 cases were recruited. Data from 12 cases in which  $C_{dyn}$  varied by more than 15% across the three measurements were excluded from the analysis. Cases with missing or obviously incorrect data in selected variables were excluded when analyzing variables independently, and from the total dataset only after their inclusion in the final model was confirmed. This approach resulted in varying case numbers across analyses, as detailed in relevant sections of the [Supplementary data](#). A total of 462 cases were included in the final model.

A variety of breeds was represented. [Table 1](#) lists the breeds and the number of dogs of each breed included in the study. Due to insufficient numbers of each breed, the effect of breed on  $C_{dyn}$  was not investigated.

Based on insufficient data, the following categories were not included in the analysis: Trendelenburg (only four animals were positioned in Trendelenburg and eight in inverted Trendelenburg); breathing system type (circle breathing systems were used in most dogs; the use of a Mapleson A and D were reported in only one and seven cases, respectively); the administration of etomidate, desflurane and intravenous lidocaine (reported in only eight, one and 19 cases, respectively).

Descriptive statistics and the frequency histogram of  $C_{dyn}$  are reported in [Table 2](#) and as [Supplementary material](#) ([Section 1](#) and [Supplementary Figure 1](#)). Normal distribution was rejected.

Body mass was selected as the first predictor variable for  $C_{dyn}$  based on prior research indicating a significant relationship between these variables. The line of best fit of  $C_{dyn}$  against body mass crossing the origin and the model from Asorey et al. (12) for comparison are presented in [Figure 2A](#). The line of best fit of  $C_{dyn}$  against body mass with free intercept and the model published by Bradbrook et al. (13) for comparison are presented in [Figure 2B](#). Both linear models and their comparison are reported as [Supplementary material](#) ([Section 2](#) and

TABLE 1 Breeds and number of individuals.

| Breed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Number  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Mixed breed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 95      |
| French Bulldog                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 37      |
| Labrador Retriever                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 36      |
| English Springer Spaniel                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 18      |
| Cocker Spaniel                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 16      |
| Golden Retriever                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 14      |
| Dachshund                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 13      |
| German Shepherd, Pug                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 12 each |
| Beagle, Border Collie, Boxer, Staffordshire Bull Terrier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 10 each |
| Chihuahua                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 9       |
| Jack Russell Terrier, Shih Tzu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 8 each  |
| Dalmatian, English Bulldog, Whippet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7 each  |
| Boston Terrier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 6       |
| American Staffordshire Terrier, Bernese Mountain Dog, Lurcher, Maltese, Yorkshire Terrier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 5 each  |
| Border Terrier, Rhodesian Ridgeback                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 4 each  |
| Australian Shepherd, Bichon Frisé, Bolonka Zwetna, Cavalier King Charles Spaniel, Cockerpoo, Doberman Pinscher, Greyhound, Labradoodle, Lhasa Apso, Miniature Dachshund, Newfoundland, Rottweiler, Siberian Husky, West Highland White Terrier                                                                                                                                                                                                                                                                                                                                                                                    | 3 each  |
| American Bulldog, Beauceron, Cairn Terrier, Cane Corso, Cavapoo, Chow-Chow, Collie, Dogue de Bordeaux, Flat Coated Retriever, Gascon Saintongeais, Great Dane, Lagotto Romagnolo, Miniature Schnauzer, Norfolk Terrier, Pembroke Welsh Corgi, Pomeranian, Saint Bernard, Schnauzer, White Swiss Shepherd                                                                                                                                                                                                                                                                                                                          | 2 each  |
| Akita Inu, Anatolian Shepherd dog, Australian Cobberdog, Basset Hound, Bearded Collie, Belgian Shepherd, Bergamasco Shepherd, Biewer Terrier, Dutch Shepherd, German Short Haired Pointer, German Spaniel, Gordon Setter, Greater Swiss Mountain Dog, Griffon, Hovawart, Irish Soft Coated Wheaten Terrier, Irish Terrier, Krömförländer, Leonberger, Malinois, Miniature Bull Terrier, Miniature Poodle, N/A, Old English Sheepdog, Old English Bulldog, Pitt bull terrier, Plummer Terrier, Pointer, Royal Puddle, Shetland Sheepdog, Shiba Inu, Standard Poodle, Tibetan Terrier, Toy Poodle, Weimaraner, Welsh Corgi Cardigan | 1 each  |

Distribution of breeds and number of individuals for each breed in a total of 462 dogs that were retained in the final statistical analysis. The data was collected from 11 centers across six countries in a study aiming to establish the reference interval of dynamic compliance ( $C_{dyn}$ ) and identify variables that have the potential to influence  $C_{dyn}$ .

Supplementary Tables 1A, B). The model with intercept was kept for further development according to better performance metrics (Supplementary Table 1C).

The internal diameter of the orotracheal tubes was the second factor in the order of anticipated importance determined by the authors. As the correlation coefficient between body mass and internal diameter of the orotracheal tubes was 0.4, further investigation was warranted before the relationship between internal diameter of the orotracheal tubes and  $C_{dyn}$  was analyzed. Detailed results for the relationship between internal diameter of the orotracheal tubes and body mass are presented as Supplementary material (Section 3, Supplementary Table 2 and Supplementary Figure 2). The best fitting prediction of orotracheal tube against body mass was a sigmoid Emax model

TABLE 2 Descriptive statistics of  $C_{dyn}$  (in mL/cmH<sub>2</sub>O) in a cohort of 515 dogs anesthetized in 11 centers across six countries.

| Dynamic compliance of the respiratory system in anesthetized dogs |                    |          |                |
|-------------------------------------------------------------------|--------------------|----------|----------------|
| $n = 515$                                                         |                    |          |                |
| Mean                                                              | Standard deviation |          |                |
| 29.83                                                             | 19.9               |          |                |
| Median                                                            | Minimum            | Maximum  |                |
| 24.67                                                             | 2.33               | 106.33   |                |
| Range                                                             | Skew               | Kurtosis | Standard error |
| 104                                                               | 1                  | 0.68     | 0.8            |

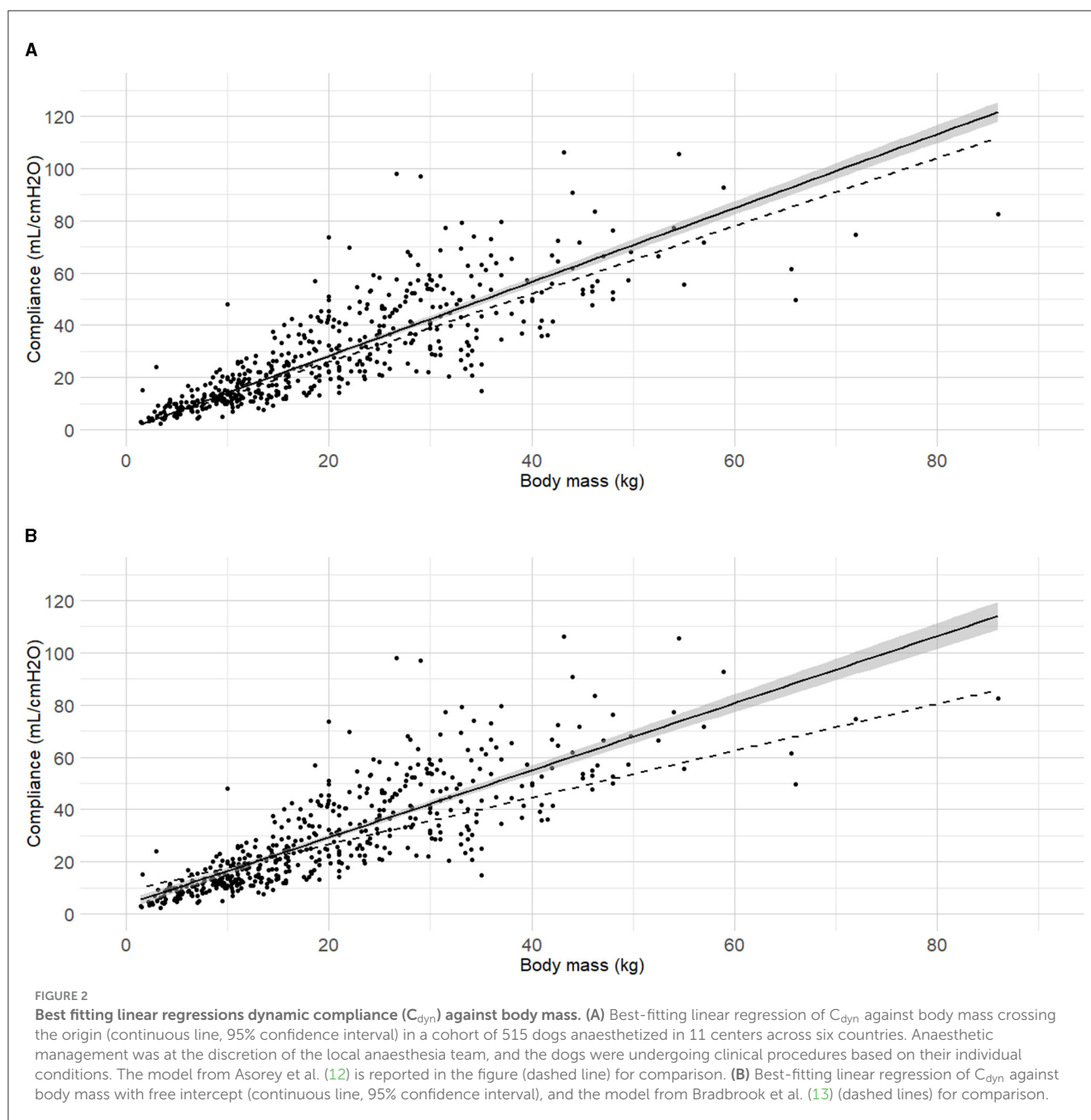
Anesthetic management was at the discretion of the local anesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

(Supplementary Section 4 and Supplementary Figure 3). Based on best models' performance metrics, internal diameter was categorized as "Small" if more than 7% smaller than its predicted value, or "Medium/large" if above. The Figure 3 represents the  $C_{dyn}$  against the body mass with the linear regressions. The effect of the internal diameter of the orotracheal tube on the  $C_{dyn} \sim$  body mass model is reported in Table 3.

The correlation coefficients between the length of the orotracheal tubes and their diameters and the length of the orotracheal tubes and body mass were 0.46 and 0.74, respectively. As the internal diameter of the orotracheal tubes impacted the  $C_{dyn} \sim$  body mass model, the influence of the length of the orotracheal tube was not investigated. No other multicollinearity was identified (i.e., the absolute correlation coefficient between all the other variables were  $< 0.4$ ).

Body condition score was also identified as factor influencing  $C_{dyn}$ . According to model comparisons, the BCS were best divided into the following three categories: "low BCS" (1/9, 2/9 and 3/9), "medium BCS" (4/9 and 5/9), and "high BCS" (6/9, 7/9, 8/9 and 9/9). The frequency histogram of BCS, boxplots of  $C_{dyn}$  for each BCS are presented in Supplementary material (Section 6, Supplementary Figures 5A–C). Linear regressions of  $C_{dyn}$  against body mass for the subgroup of "low BCS," "medium BCS," and "high BCS" were calculated (Table 3) and graphically represented (Figure 4).

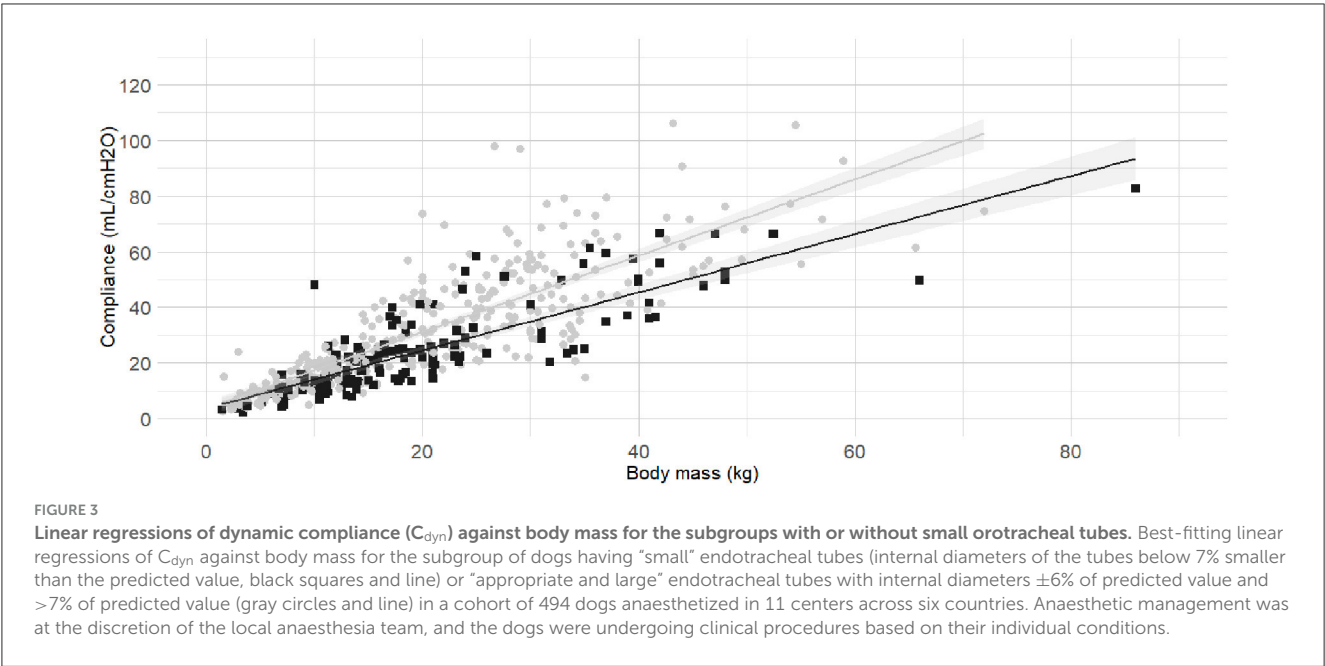
The following variables had a significant impact on  $C_{dyn}$  and improved the  $C_{dyn} \sim$  body mass model when considered individually (i.e., reduction in both AIC and BIC, and  $p < 0.05$ ): morphology, lateral recumbency, spirometry sensor used, the administration of  $FIO_2 > 80\%$  for at least 10 minutes before the measurements, time elapsed between anesthesia induction and the measurements, inspiratory time set on the ventilator, and ventilation mode. Their effect on the  $C_{dyn} \sim$  body mass model and associated figures is reported in Table 3. Additional information on the individual variables can be found in the Supplementary material (Section 7 and Supplementary Figures 6A, B; Section 8 and Supplementary Figures 7A, B; Section 9 and Supplementary Figures 8A, B; Section 12 and Supplementary Figures 11A, B; Section 13 and Supplementary Figure 12; Section 14 and Supplementary Figure 13; Section 15 and Supplementary Figures 14A, B).



The development of the multiple linear regression model involved using stepwise forward selection and backward elimination techniques. The procedures and criteria for model selection are detailed in [Supplementary material \(Section 17 and associated Supplementary Tables\)](#). Variables were added or removed iteratively, with the goal of achieving a model that balanced fit and simplicity. The final model is presented in [Table 4](#). The variables included were selected based on their contribution to the model's performance, as reflected in the evaluation criteria described. The best-fitting model identified a linear relationship between  $C_{dyn}$  and body mass when the following conditions were met: a "high BCS," "small" orotracheal tubes (<7% smaller than predicted), the use of a D-lite flow sensor, and the absence of

a high  $FIO_2$  (>80%) exposure for more than 10 minutes prior to  $C_{dyn}$  measurement. In cases where these conditions were not met, additional factors needed to be incorporated into the model. Factors such as a "Low (1/9, 2/9, 3/9) and Medium (4/9, 5/9) BCS," an orotracheal tube with an internal diameter not <7% smaller than the predicted value (i.e., an orotracheal tube of the predicted size or larger) and longer inspiratory times were associated with increased  $C_{dyn}$ . Conversely, the use of alternative spirometry sensors, including Ped-lite, or prolonged exposure to high  $FIO_2$  levels resulted in decreased  $C_{dyn}$ .

Linearity was confirmed (Residuals Plot, [Figure 12](#)). Homoscedasticity was not confirmed ( $p < 0.001$ ). Independence was confirmed (Durbin-Watson test,  $p = 0.486$ ). Normality of



**TABLE 3** Linear regression models for dynamic compliance ( $C_{dyn}$ ) in anesthetized dogs.

| Best fitting linear regression                               | Adjusted $R^2$ | AIC      | BIC      | $p$ -value | Graphical representation |
|--------------------------------------------------------------|----------------|----------|----------|------------|--------------------------|
| $C_{dyn} \sim \text{Mass}$                                   | 0.659          | 3,898.02 | 3,910.68 |            | Figure 2B                |
| $C_{dyn} \sim \text{Mass, ETT}$                              | 0.679          | 3,797.00 | 3,813.00 | <0.001     | Figure 3                 |
| $C_{dyn} \sim \text{Mass, BCS}^*$                            | 0.679          | 3,774.07 | 3,795.05 | <0.001     | Figure 4                 |
| $C_{dyn} \sim \text{Mass, Morphology}$                       | 0.669          | 3,812.39 | 3,833.41 | <0.001     | Figure 5                 |
| $C_{dyn} \sim \text{Mass, Position}^{**}$                    | 0.658          | 3,813.35 | 3,830.14 | 0.036      | Figure 6                 |
| $C_{dyn} \sim \text{Mass, Sensor}$                           | 0.666          | 3,795.49 | 3,816.47 | 0.001      | Figure 7                 |
| $C_{dyn} \sim \text{Mass, FIO}_2 >80\%_{10 \text{ minutes}}$ | 0.661          | 3,807.74 | 3,824.54 | 0.005      | Figure 8                 |
| $C_{dyn} \sim \text{Mass, Time post induction}$              | 0.664          | 3,740.64 | 3,757.37 | <0.001     | Figure 9                 |
| $C_{dyn} \sim \text{Mass, Inspiratory time}$                 | 0.676          | 3,606.53 | 3,623.14 | <0.001     | Figure 10                |
| $C_{dyn} \sim \text{Mass, Ventilation mode}$                 | 0.659          | 3,790.22 | 3,806.99 | 0.011      | Figure 11                |

Best-fitting linear regression models for  $C_{dyn} \sim \text{Body mass}$  and subsequent models incorporating additional factors to improve fit (orotracheal tube smaller than 7% of the predicted internal diameter for that body mass, body condition score, morphology, the lateral position, the sensor used to determine  $C_{dyn}$ , the administration of  $>80\%$  oxygen for at least 10 minutes before the measurements, the inspiratory time and the respiratory mode. Metrics reported include Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), adjusted  $R^2$ , and  $p$ -values, along with the figure number. Data from a cohort of 515 dogs under general anesthesia, collected from 11 centers across six countries, were analyzed to establish the reference interval of dynamic compliance ( $C_{dyn}$ ) and identify potential influencing variables.

\*Three categories: low, medium, and high BCS.  
\*\*Two categories: lateral or not.

Residuals (QQ Plot, Figure 13) was not confirmed (Shapiro-Wilk test,  $p < 0.001$ ). Multicollinearity was confirmed (Variance inflation factors  $< 1.3$ ). To account for heteroscedasticity, robust standard errors were calculated using the more conservative Davidson and Mackinnon heteroscedasticity-consistent estimators (via the *Sandwich* package in R). The results, including recalculated  $p$ -values, are presented in Table 4. Additionally, to address the non-normality of the residuals, estimates were re-evaluated through bootstrapping ( $n = 10,000$ ; *Boot* package in R) to obtain bias-corrected estimates and 95% confidence intervals (Table 4).  
Age, the presence or absence of HMEs, the  $F_{I}O_2$  and the PEEP levels did not have any significant effect when integrated to the multiple regression linear model. Additional information on the

individual variables can be found in the Supplementary material (Section 5 and Supplementary Figures 4A, B; Section 10 and Supplemental Figures 9A–C; Section 11 and Supplemental Figures 10A, B; Section 16 and Supplemental Figures 15A, B). The administration of alfaxalone, alpha-2 adrenergic receptor agonists, anti-muscarinic, isoflurane, propofol, and sevoflurane had a significant effect on  $C_{dyn}$  (Yes/No for each drug; Wilcoxon rank-sum test  $p$ -value = 0.012, 0.012, 0.002, 0.007, 0.013, and 0.036, respectively). However, their individual effect was minimal to negligible on the  $C_{dyn} \sim \text{body mass}$  model and they were not included in the final model. The ventilation mode (Supplementary Section 15 and Supplementary Figures 14A, B), the administration of acepromazine, benzodiazepines, butorphanol, ketamine,

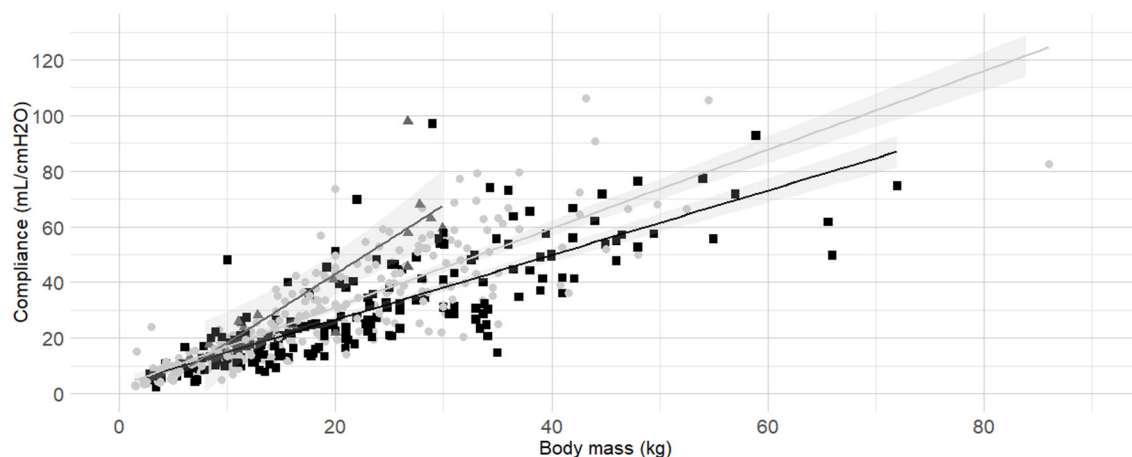


FIGURE 4

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass for the subgroups low, medium and high Body Condition Score (BCS).**

Best-fitting linear regressions of  $C_{dyn}$  against body mass for the for the subgroup of low (dark gray triangles and line, BCS 1–3), medium (light gray circles and line, BCS 4–5), and high BCS (black squares and line, BCS 6–9) in a cohort of 491 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

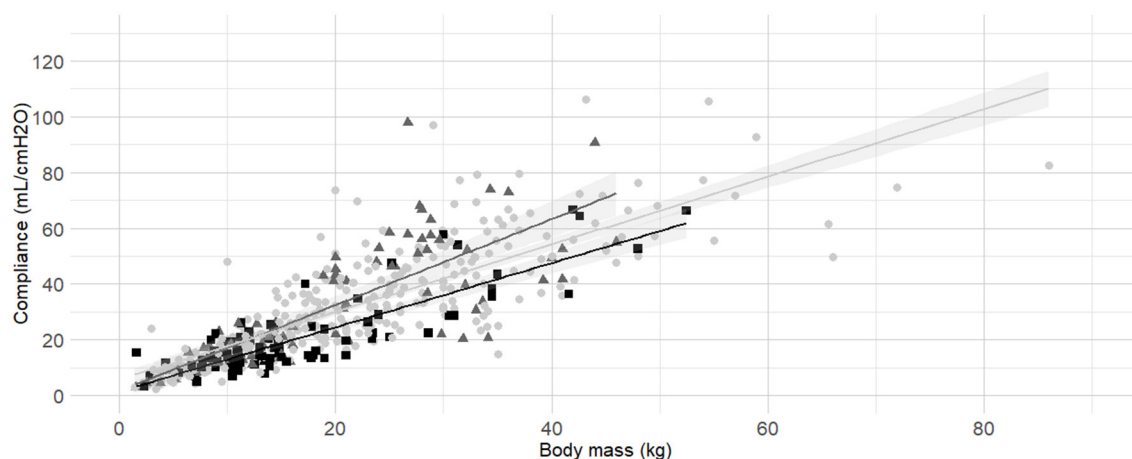


FIGURE 5

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass for the subgroups brachymorphic, dolichomorphic and mesomorphic.**

Best-fitting linear regressions of  $C_{dyn}$  against body mass for the for the subgroup of morphology including dolichomorphic (dark gray triangles and line), mesomorphic (light gray circles and line), and brachymorphic (black squares and line) in a cohort of 494 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

mu-agonist opioids and neuromuscular blocking agents and the use of loco-regional blocks or epidural anesthesia did not significantly influence  $C_{dyn}$  (Yes/No for each drug or technique; Wilcoxon rank-sum test  $p$ -value = 0.711, 0.841, 0.222, 0.368, 0.811, 0.442, 0.235, 0.861, and 0.735, respectively).

## 4 Discussion

The main aim of this study was to establish a reference interval for  $C_{dyn}$  in anesthetized dogs. The large variance detected in  $C_{dyn}$  indicated that it was too inaccurate to

develop a reference range and that modeling was required to estimate  $C_{dyn}$ . Our findings demonstrated that  $C_{dyn}$  could be quantified relative to body mass. However, it was also notably affected by the internal diameter of orotracheal tubes, BCS, inspiratory time settings, the type of sensor used for  $C_{dyn}$  determination, and exposure to  $\text{FIO}_2 > 80\%$  for at least 10 minutes prior to measurement. These findings illustrate that a single reference interval would be misleading or unhelpful in clinical practice due to the varying combinations of factors that can alter the measurement in different ways. Despite this, our study provides valuable insights into the factors affecting  $C_{dyn}$  in anesthetized dogs and emphasizes the need

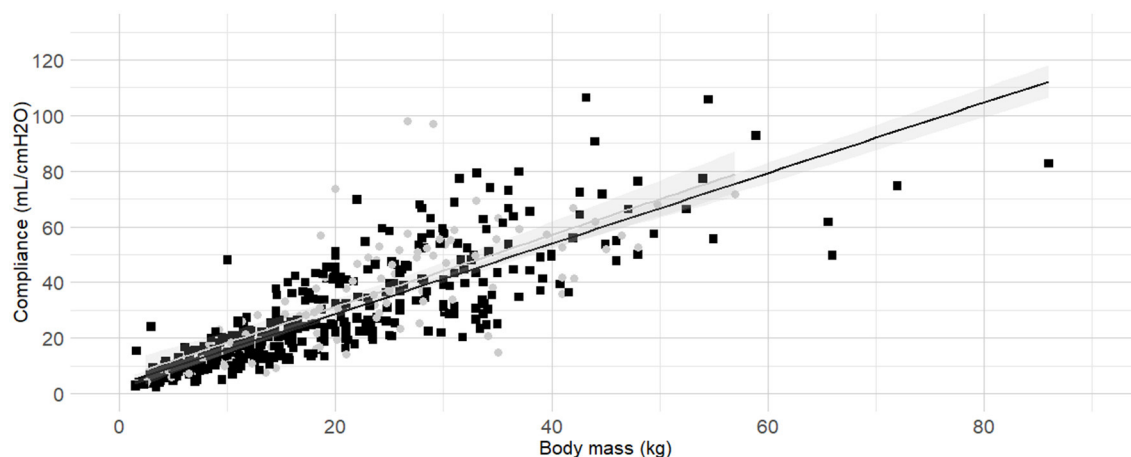


FIGURE 6

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass in lateral recumbency or not.** Best-fitting linear regressions of  $C_{dyn}$  against body mass in lateral recumbency (gray circles and line) or in another position (black squares and line) in a cohort of 492 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

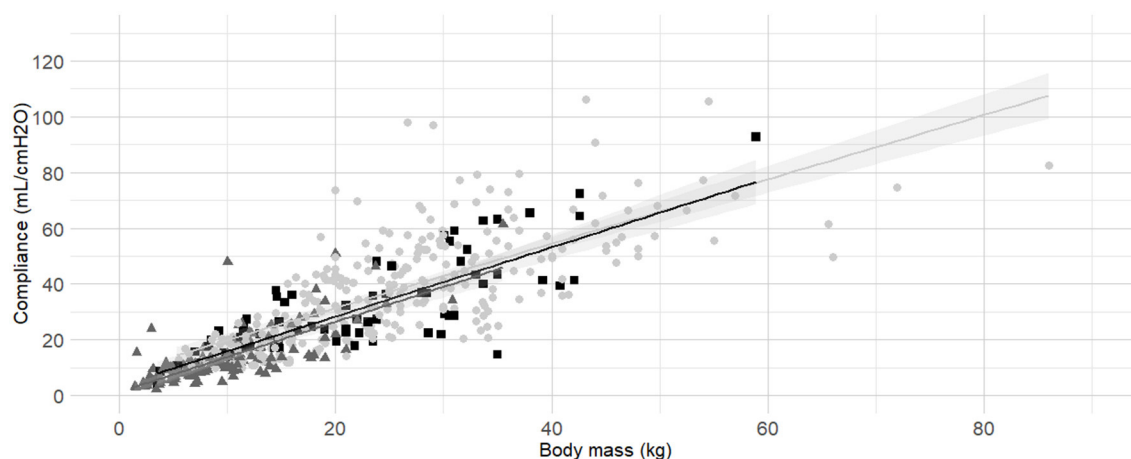


FIGURE 7

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass according to the sensor used to establish  $C_{dyn}$  (Pedi-lite, D-lite or any other spirometry sensor).** Best-fitting linear regressions of  $C_{dyn}$  against body mass according to sensors used to measure: D-Lite (light gray circles and line), Pedi-Lite (dark gray triangles and line), or others (black squares and line) in a cohort of 491 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

for careful consideration of these variables in both clinical and research settings.

Our results demonstrated a linear relationship between  $C_{dyn}$  and body mass in dogs, corroborating previously documented findings (11–13). This relationship was incorporated into all subsequent modeling. However, our study offered significant insights not captured in previous investigations and highlighted that body mass alone was insufficient to reliably predict  $C_{dyn}$ . Our unique approach, derived from consultations with the veterinary anesthesia community (1), enabled us to further investigate prospectively the influence of numerous factors.

In our study, the impact of the inspiratory time on  $C_{dyn}$  was evaluated. We observed that varying inspiratory times significantly influenced the readings obtained. The characteristics of the inspiration have been shown to influence compliance values. Both  $C_{stat}$  and quasi-static compliance require an inspiratory pause. Varying inspiratory pauses of  $<3$  s gave different values of quasi-static compliance and did not provide accurate  $C_{stat}$  values in healthy dogs (8). Here, the significant impact of the inspiratory time on  $C_{dyn}$  was demonstrated, confirming earlier findings (14). The first publication about D-lite flow sensors states that “some systematic error in compliance measurement is introduced if a ventilation mode without a pause and well-defined

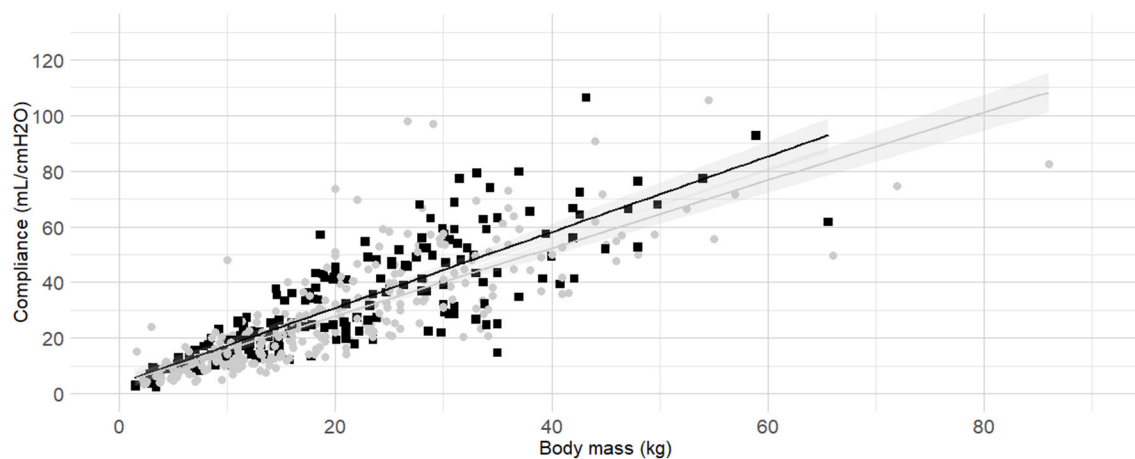


FIGURE 8

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass according to the administration or not of an inspired fraction of oxygen ( $FIO_2$ ) above 80% for a minimum of 10 minutes before the measurements.** Best-fitting linear regressions of  $C_{dyn}$  against body mass according to the administration (grey circles and line) or not (black squares and line) of a  $FIO_2 > 80\%$  for at least 10 minutes before the measurement in a cohort of 492 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

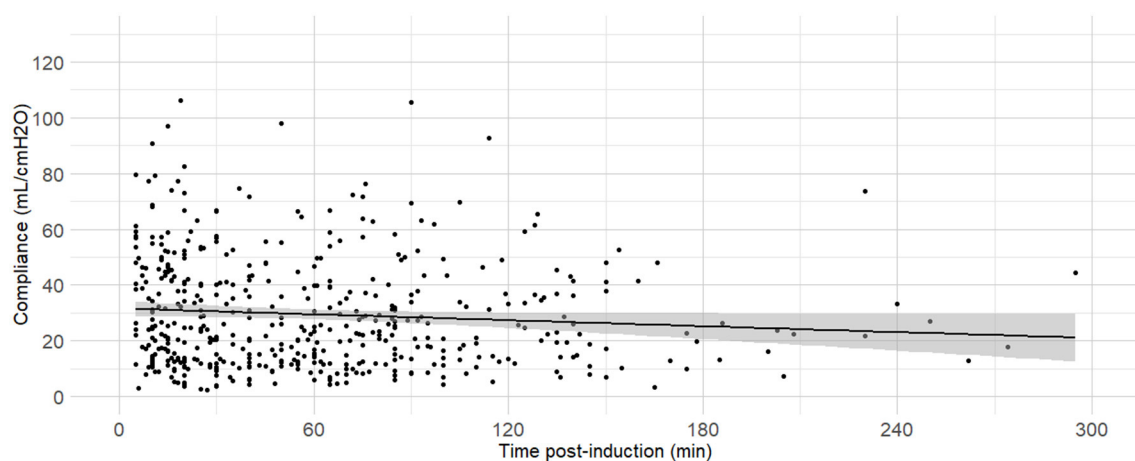


FIGURE 9

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against the time between anaesthesia induction and the measurements.** Best-fitting linear regressions of  $C_{dyn}$  against time (in minutes) between induction of general anaesthesia and the  $C_{dyn}$  determination in 484 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

plateau pressure is used. However, even then, trends will be quite informative.” (19). In clinical anesthesia and in many studies, the inspiratory-to-expiratory ratio is set, and the respiratory rate is adjusted to maintain a target partial pressure of expired carbon dioxide. Clinicians wishing to monitor changes in  $C_{dyn}$  or quasi-static compliance over time should consider the importance of inspiratory time and keep it consistent in their assessments. The characteristics of the inspiratory settings (inspiratory time or the inspiratory-to-expiratory ratio and the respiratory rate set, and inspiratory pause) should also be systematically reported in research.

Our results also showed an influence of the internal diameter of orotracheal tubes on  $C_{dyn}$ , as documented previously (13).

However, Bradbrook et al. stated that “since ETT (Endotracheal Tube) diameter was probably dependent upon body size and therefore body weight, only body weight was investigated further by general additive modeling” (13). By including more dogs in our study, we were able to further investigate and model this relationship. This allowed us to identify a diameter cut-off value of 7% below the predicted value, below which  $C_{dyn}$  is negatively impacted. It is worth noting that monitors using multiple linear regression of the whole respiratory cycle to calculate or estimate  $C_{dyn}$  might be less affected by airway resistance (20). Further investigation is necessary to validate these findings across a wider range of monitoring technologies and techniques.

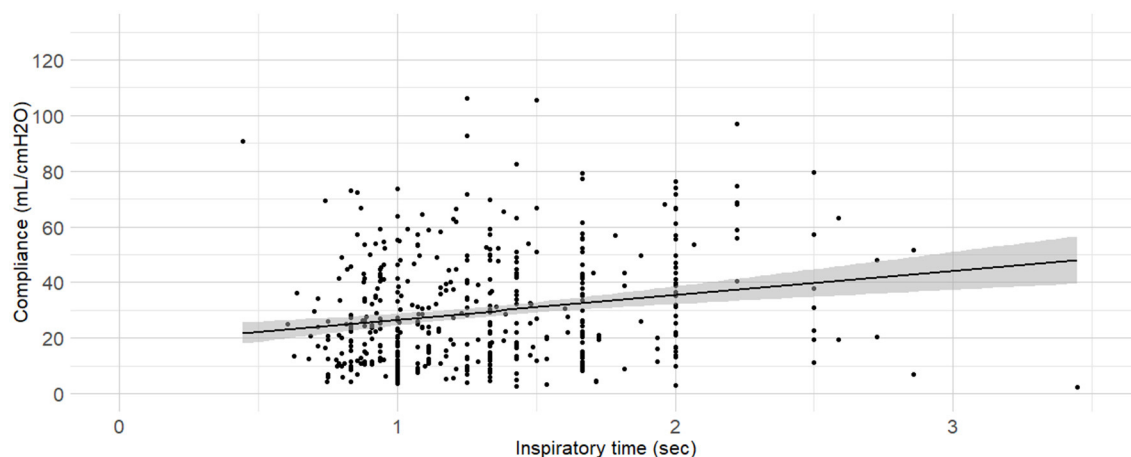


FIGURE 10

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against the inspiratory time set.** Best-fitting linear regressions of  $C_{dyn}$  against inspiratory time set on the ventilator (in minutes) at the time of  $C_{dyn}$  determination in 470 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

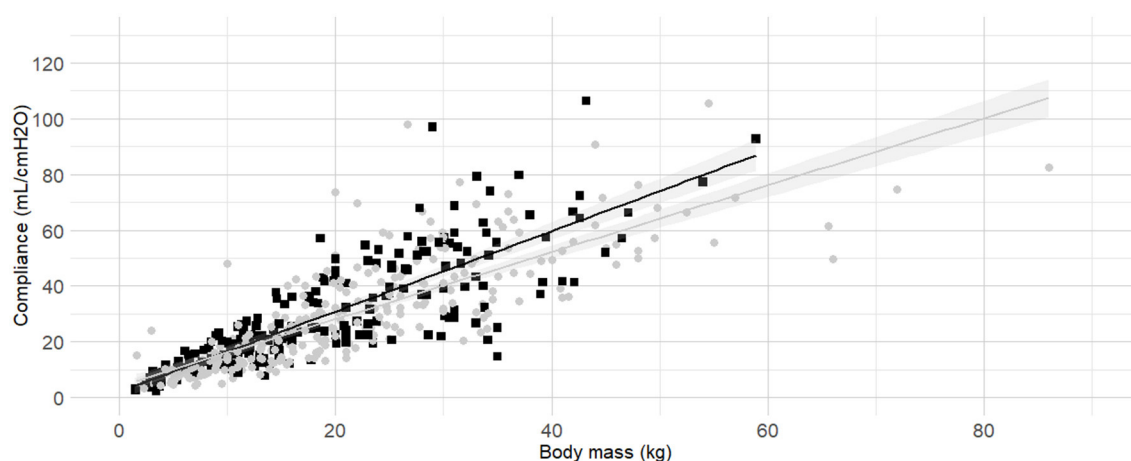


FIGURE 11

**Linear regressions of dynamic compliance ( $C_{dyn}$ ) against body mass according to the administration or not of an inspired fraction of oxygen ( $FIO_2$ ) above 80% for a minimum of 10 minutes before the measurements.** Best-fitting linear regressions of  $C_{dyn}$  against body mass according to the modes of ventilation set, volume-controlled ventilation (gray circles and line), pressure-controlled ventilation (black squares and line) in a cohort of 489 dogs anaesthetized in 11 centers across six countries. Anaesthetic management was at the discretion of the local anaesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions.

Interestingly, in our study an  $FIO_2$  above 80% for at least 10 minutes resulted in lower calculated values of  $C_{dyn}$ . Previous research showed that administering a low  $FIO_2$  (40%) to ventilated dogs was associated with less atelectasis formation compared to administering a high  $FIO_2$  (21). Mathematical modeling of absorption atelectasis kinetics indicated that the process developed fairly rapidly, based on human data (22). The 10-minutes cut-off was chosen because a complete collapse would mathematically develop in <10 minutes if a 3-minutes pre-oxygenation was followed by 100% oxygen administration (22). The time spent at a high  $FIO_2$  was previously shown not to influence compliance (12). However, in that study, the dogs received a high  $FIO_2$  for  $34 \pm 18$  minutes, with the duration of high  $FIO_2$  administration being the focus of the analysis. Our findings might reflect

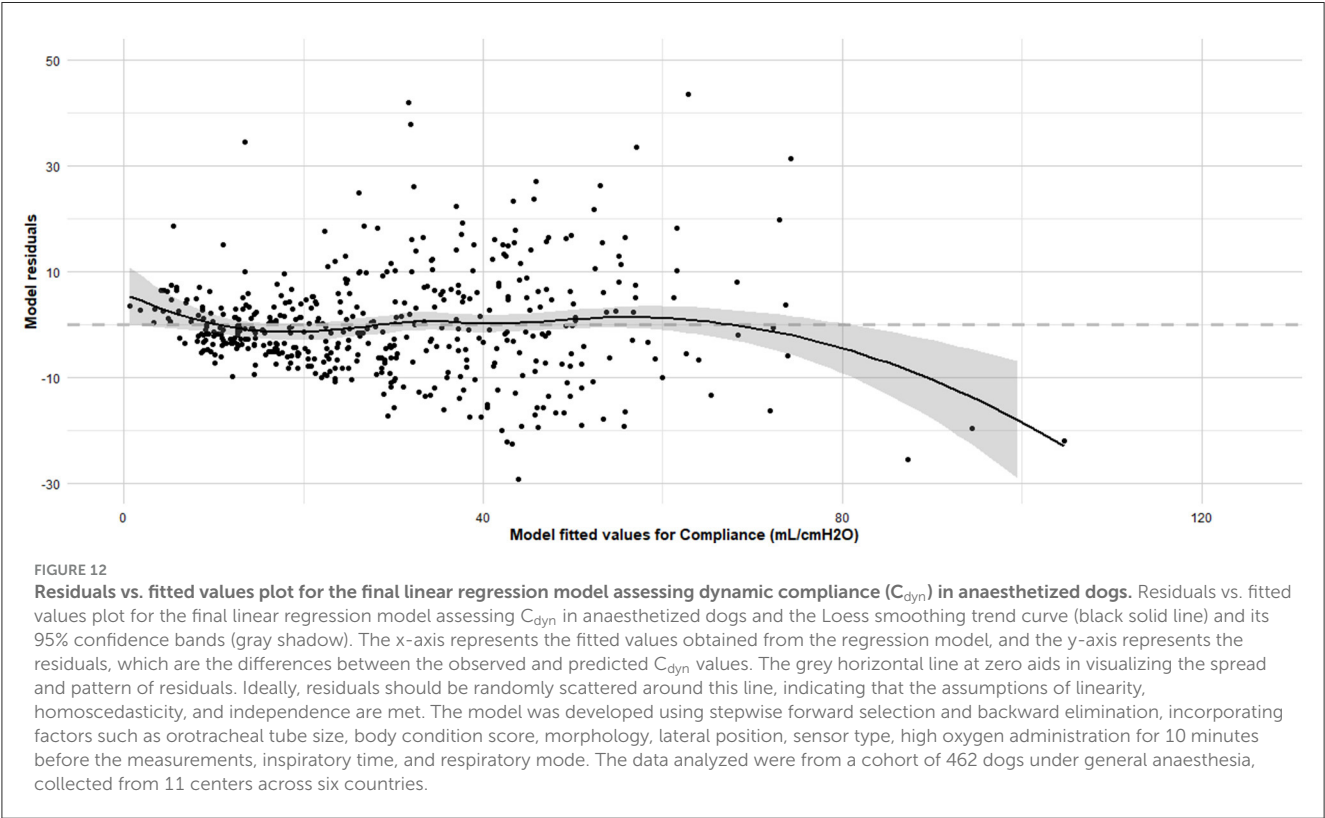
a clinical manifestation of absorption atelectasis, suggesting its rapid development in dogs *in vivo*, as supported by the mathematical model.

In our model, the ventilation mode did not influence  $C_{dyn}$ . However, previous research described higher compliance values when pressure-controlled ventilation was used compared to volume-controlled ventilation (23). Lower peak airway pressures tend to develop with pressure-controlled ventilation compared to volume-controlled ventilation (24), presumably because decelerating flow patterns enhance ventilation distribution in lungs with varying mechanical properties (25). In their study, Fantoni et al. used  $C_{stat}$  with a 4-s inspiratory hold, reflecting improved lung compliance without the resistive component of the airway and orotracheal tube. They targeted similar tidal

TABLE 4 Linear regression models for dynamic compliance ( $C_{dyn}$ ) in anesthetized dogs.

| Variable                                            | Initial estimate | Initial SE | Initial $p$ -value | Corrected mean estimate | Estimate 95%CI   | Robust SE | Corrected $p$ -value |
|-----------------------------------------------------|------------------|------------|--------------------|-------------------------|------------------|-----------|----------------------|
| Intercept                                           | −3.078           | 2.416      | 0.203              | −3.011                  | [−7.962, 1.539]  | 2.511     | 0.221                |
| Body mass                                           | +1.166           | 0.046      | <0.001             | +1.164                  | [1.049, 1.298]   | 0.066     | <0.001               |
| ETT_ID (medium)                                     | +5.971           | 1.088      | <0.001             | +6.015                  | [4.010, 7.837]   | 0.994     | <0.001               |
| BCS (Low)                                           | +9.293           | 3.010      | 0.002              | +9.251                  | [5.157, 13.834]  | 2.288     | <0.001               |
| BCS (Medium)                                        | +3.705           | 1.002      | <0.001             | +3.708                  | [1.707, 5.740]   | 1.035     | <0.001               |
| Inspiratory time (in seconds)                       | +4.708           | 1.148      | <0.001             | +4.681                  | [2.081, 7.572]   | 1.436     | 0.001                |
| Sensor (Other)                                      | −4.506           | 1.650      | 0.007              | −4.538                  | [−7.676, −1.222] | 1.677     | 0.007                |
| Sensor (Pedi-Lite)                                  | −4.992           | 1.336      | <0.001             | −5.028                  | [−7.129, −2.799] | 1.142     | <0.001               |
| FIO <sub>2</sub> >80% for at least 10 minutes (Yes) | −2.933           | 1.186      | 0.014              | −2.951                  | [−5.259, −0.548] | 1.206     | 0.015                |

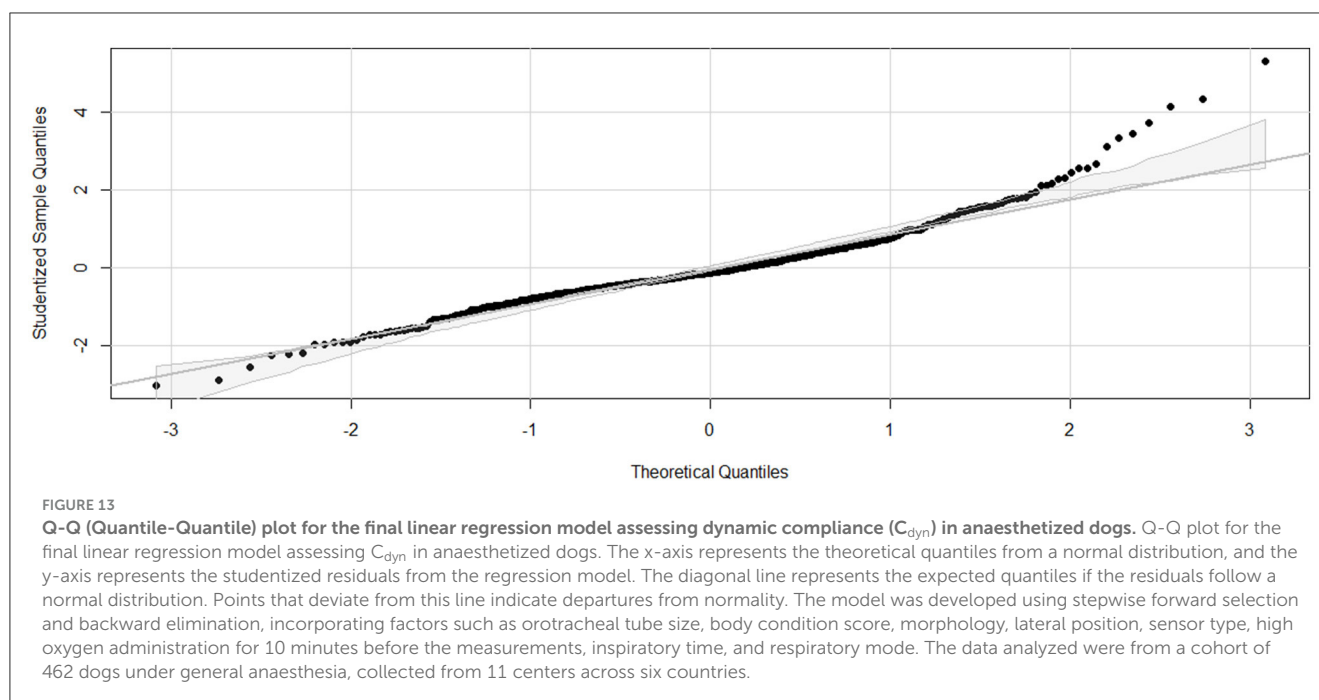
Final model for  $C_{dyn}$  per body mass, derived using stepwise forward selection and backward elimination techniques. The models incorporate additional factors to improve fit, including orotracheal tube smaller than 7% of the predicted internal diameter for that body mass, body condition score, morphology, lateral position, sensor used to determine  $C_{dyn}$ , administration of >80% oxygen for at least 10 minutes before the measurements, inspiratory time, and respiratory mode. Data were analyzed from a cohort of 462 dogs under general anesthesia, collected from 11 centers across six countries. Anesthetic management was at the discretion of the local anesthesia team, and the dogs were undergoing clinical procedures based on their individual conditions. Corrected mean estimates and their confidence intervals (95% CI) were obtained from bootstrapping ( $n = 10,000$ ). Robust standard errors (SE) and corrected  $p$ -values were obtained using Davidson and Mackinnon heteroscedasticity-consistent estimators.



volumes (10 mL/kg) and PEEP (5 cmH<sub>2</sub>O) with both modes and measured airway pressure. This contrasts with how veterinary anesthetists typically set pressure-controlled ventilation, where pressure is most commonly targeted (1). The reasons for the observed differences are unclear, although variations in the settings of ventilation modes could be a contributing factor. Future studies employing more standardized ventilation strategies could further clarify this aspect. It is worth noting that the influence of inspiratory time on  $C_{dyn}$  has the potential to vary significantly

between volume-controlled and pressure-controlled ventilation, which may contribute to explaining the discrepancies observed in our results.

Our study did not investigate thoracic shape and BCS in the same manner as Asorey et al. (12). The 20% inspiratory pause set in their study precludes direct comparison with our findings. However, they highlighted a reduction in compliance in overweight and “barrel-chested” dogs. Since our data collection began before their publication, we could not make a direct comparison of



thoracic shapes. Although there is some overlap in the morphology categories (brachymorphic, dolichomorphic, and mesomorphic), direct comparison was not feasible. However, BCS remained in our model as in theirs. Our results indicated that the effect of morphology on  $C_{dyn}$  was not retained in the multivariable analysis, possibly because it did not provide additional relevance beyond the internal diameter of the orotracheal tubes. There was no correlation between morphology and the internal diameter of the orotracheal tubes used in our study, so this relationship was not investigated further.

This study has several limitations. Firstly, while a variety of spirometry technologies and monitors are commonly used in veterinary anesthesia (1), near-patient spirometers using Ped-lite or D-lite flow sensors (Datex Ohmeda/GE Healthcare) were overrepresented. Additionally, several commonly available monitors were not used in this data collection. Unfortunately, no conclusions can be drawn regarding the impact of some monitors that were either underrepresented or not included in this study. Nevertheless, our model demonstrated an effect of technology used to determine  $C_{dyn}$  in this study and thus support the importance of considering the type of sensor when measuring compliance.

Secondly, while we acknowledge the potential for clustering due to the multicentre nature of the study, our primary aim was to assess dynamic compliance across a broad, representative sample rather than focus on center-specific effects. Incorporating a center variable would have required additional adjusting for the variability in machines used across centers, complicating the analysis without contributing significant clinical insight. Nonetheless, future studies could benefit from evaluating clustering effects, especially in contexts where center-based differences are of clinical relevance.

Thirdly, although calibration check of the monitors and correction of the data were originally planned, it proved practically impossible. It is likely that some of the monitors used in this study were not calibrated. However, this seems to represent typical

veterinary anesthesia practice (1) thus the results similar expected findings in this environment.

Fourthly, although our survey among veterinary anesthetists documented the potential effect of some categories on  $C_{dyn}$  a few of them were not included in the analysis because they were not sufficiently represented (Trendelenburg; breathing system type; the administration of etomidate, desflurane, and intravenous lidocaine). Additionally, the limited number of cases in some categories may have caused certain variables, like PEEP levels, to appear insignificant due to under-representation, despite their expected effect on  $C_{dyn}$ . Further study is required to determine their possible effects on models used to calculate  $C_{dyn}$ .

Fifthly, the absence of preoperative imaging studies to assess for underlying respiratory diseases may limit the interpretation of the results, as undetected respiratory conditions could influence  $C_{dyn}$  measurements.

Finally, the diagnostic tests performed on our multiple linear regression model yielded mixed results. The assumption of linearity was confirmed, indicating that the relationship between the predictor variables and the response variable was appropriately modeled as linear. Additionally, the independence of residuals was verified, suggesting that there are no significant autocorrelation issues. Importantly, multicollinearity was not a concern, ensuring that the predictor variables are not highly correlated, and the regression coefficients remain stable. However, the tests indicated violations in both homoscedasticity and the normality of residuals. These findings suggest that the variance of the residuals is not constant, and that the residuals do not follow a normal distribution, respectively. These violations may affect the efficiency and validity of our model's estimates and hypothesis tests. To address potential bias in the linear regression coefficient estimates, bootstrapping was applied, and confidence intervals were calculated. This approach is commonly used to provide more robust estimates and mitigate the impact of violations in residual normality. Furthermore, due

to the presence of heteroscedasticity, robust standard errors were calculated, and *p*-values accordingly adjusted. While caution is warranted when extrapolating the presented results, the application of these calculations has yielded more reliable estimates for further inference.

## 5 Conclusion

Many veterinary anesthetists employ P-V loops and specifically monitor respiratory system compliance (1). This study revealed that  $C_{dyn}$  should be evaluated relative to body mass. While a definitive reference interval was not established and may lack clinical utility, the study demonstrated that  $C_{dyn}$  was significantly influenced by several factors: the internal diameter of orotracheal tubes, BCS, inspiratory time settings, the specific sensor used for  $C_{dyn}$  determination, and exposure to  $FIO_2$  levels exceeding 80% for at least 10 minutes before assessment. Minimal inspiratory setting characteristics (such as inspiratory time, or inspiratory-to-expiratory ratio and set respiratory rate) should be considered when clinically comparing  $C_{dyn}$  over time and systematically reported in research.

## Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found at: The datasets analyzed for this study can be found in the BORIS (Bern Online Repository and Information System (<https://boris-portal.unibe.ch/handle/20.500.12422/33611>)).

## Ethics statement

An overall ethical approval was granted by the Ethical Review Group of the Association of Veterinary Anesthetists (2019-007). This approval was sufficient for the following centers: Southern Counties Veterinary Specialists, Davies Veterinary Specialists, Manchester Veterinary Specialists, Small Animal Hospital of the University of Glasgow, University of California, and VetAgro Sup. The project was further approved by the relevant local Ethical Committees at Murdoch University (R3186/19), the University of Bristol (VIN/18/032), the University of Sydney (2019/1617), and Vetsuisse Faculty Bern & Zürich (BE78/18). The studies were conducted in accordance with the local legislation and institutional requirements.

## Author contributions

MR: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing. MM: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing. AR: Supervision, Writing – review & editing. AA: Conceptualization, Investigation, Writing – review

& editing. GB: Investigation, Writing – review & editing. FD: Investigation, Writing – review & editing. CH: Investigation, Writing – review & editing. PM: Conceptualization, Investigation, Writing – review & editing. KP: Investigation, Writing – review & editing. JR: Investigation, Writing – review & editing. JS: Data curation, Investigation, Methodology, Writing – review & editing. BS: Investigation, Writing – review & editing. EW: Investigation, Writing – review & editing. OL: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

KP declared that she was an editorial board member of Frontiers at the time of submission. This had no impact on the peer review process or the final decision.

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## Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fvets.2024.1490494/full#supplementary-material>

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