

RESEARCH PAPER

Measurement of respiratory system compliance and respiratory system resistance in healthy dogs undergoing general anaesthesia for elective orthopaedic procedures

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Abstract

Objective The aim of this study was to investigate normal values for the dynamic compliance of the respiratory system (Crs) and respiratory system resistance (Rrs) in mechanically ventilated anaesthetized dogs.

Study design Prospective clinical study.

Animals Forty healthy dogs undergoing elective orthopaedic surgery. Body weight was (mean ± SD) 26.8 ± 10.7 kg (range: 1.9–45.0 kg), age 4.7 ± 2.9 years (range: 0.1–10.6 years).

Methods Dogs were premedicated with acepromazine and methadone administered intramuscularly and anaesthesia induced with propofol intravenously. After endotracheal intubation the dog's lungs were connected to an appropriate breathing system depending on body weight and isoflurane in oxygen administered for maintenance of anaesthesia. The lungs were ventilated mechanically with variables set to maintain normocapnia (end-tidal carbon dioxide concentration 4.7–6.0 kPa). Peak inspiratory pressure, Crs, Rrs, tidal volume, respiratory rate and positive end-expiratory pressure were recorded at 5, 30, 60, 90 and 120 minutes after start of mechanical ventilation. Cardiovascu-

lar variables were recorded at time of collection of respiratory data.

Results General additive modeling revealed the following relationships: Crs = [0.895 × body weight (kg)] + 8.845 and Rrs = [−0.0966 × body weight (kg)] + 6.965. Body weight and endotracheal tube diameter were associated with Crs ($p < 0.001$ and $p = 0.002$ respectively) and Rrs ($p = 0.017$ and $p = 0.002$ respectively), body weight being linearly related to Crs and inversely to Rrs.

Conclusion and clinical relevance Body weight was linearly related to Crs while Rrs has an inverse linear relationship with body weight in mechanically ventilated dogs. The derived values of Crs and Rrs may be used for monitoring of lung function and ventilation in healthy dogs under anaesthesia.

Keywords airway resistance, anaesthesia, dogs, dynamic compliance, lung, mechanical ventilation.

Introduction

Compliance and resistance are two variables used in respiratory mechanics to describe lung function (Cohen & Pittard 2006).

Respiratory system compliance, often measured in respiratory physiology is the sum of the compliance

of the lungs and chest wall. Lung compliance is defined as the change in lung volume per unit change in transmural (intrapleural to alveolar) pressure. Chest wall compliance is described as the change in lung volume per unit change in intrapleural to ambient pressure. For the calculation of both variables measurement of intrapleural pressure is required using an intrathoracic oesophageal balloon catheter.

Respiratory system resistance is more indicative of large airway function and is made up of tissue (chest wall and lung, R_{tissue}) and airway resistance, which is affected by gas flow within the airways. Gas flow will change when airway diameter and geometry are affected by changes in the volume and shape of the lungs and thoracic wall during the respiratory cycle (King et al. 2005).

For calculation of compliance of the respiratory system (C_{rs}) and resistance of the respiratory system (R_{rs}) during anaesthesia, spirometry is utilised, measuring pressure differences, volumes and flow, negating the requirement for intrapleural pressure measurement. These values can be calculated on a breath by breath basis provided mechanical ventilation with positive pressure is employed for measurement of airway pressures. At the end of inspiration and expiration, pressures within the alveoli, airways and breathing system and therefore monitoring system are equal due to a lack of flow in either direction. Therefore correct measurements of C_{rs} and R_{rs} require short no-flow periods at the end of inspiration and expiration. The difference between the pressure measured by the monitoring system plus the measurement of tidal volume (V_{t}) allows C_{rs} to be calculated. The measured pressures and the flow during lung inflation are used to calculate the R_{rs} . The software in modern spirometry devices can derive the values for C_{rs} and R_{rs} via linear regression techniques multiple times per breath. A recursive least squares method is then used to generate pressure, volume and flow values (Iotti et al. 1995).

C_{rs} and R_{rs} are highly lung volume dependent (Westbrook et al. 1973; Hedenstierna 2009). As anaesthesia causes a reduction in functional residual capacity both variables are affected by anaesthesia itself as well as changes in lung parenchyma and airway properties. Together they may provide more accurate information to guide ventilation strategies during anaesthesia and long-term ventilation (Albaiceta et al. 2008; Zanella et al. 2010).

Body weight and obesity also influence lung mechanics. An increase in lean body weight correlates with an increased lung volume and therefore lung compliance. Obesity has also been shown to decrease compliance and increase resistance in humans by decreasing lung volume (Littleton 2012).

No normal clinical values for C_{rs} and R_{rs} are available in the anaesthetized dog. Furthermore, extrapolated human data may not allow for appropriate clinical decisions regarding alteration of ventilator settings to be made. The aim of this study was to obtain values of C_{rs} and R_{rs} in mechanically ventilated, healthy, anaesthetized dogs.

Methods

This prospective clinical trial was approved by the Veterinary Research Ethics Committee of the University of Liverpool (VREC15).

Animals

Forty healthy dogs comprising a range of breeds, age 4.7 ± 2.9 years (range: 0.1–10.6 years) were recruited from clinical elective orthopaedic cases over a 2 month period. All dogs underwent pre-anaesthetic clinical examination prior to general anaesthesia with special focus on the evaluation of the respiratory tract. Body condition score (BCS) was assessed according to the Nestle Purina system (2013) which is a scale of 1 to 9, 9 being the most obese. Those graded I or II on the American Society of Anesthesiologists (ASA) physical status classification were included in the study. Informed owner consent was gained prior to commencement of data collection. Dogs were excluded from the study if extra sedation was required in addition to the standard protocol, due to poor effect or temperament. Dogs were also excluded from the study if ventilator-patient asynchrony was detected.

Anaesthesia

A standard anaesthetic protocol was used for all dogs: pre-anaesthetic medication was achieved with acepromazine (ACP 2 mg mL⁻¹ injection, Novartis, UK) 0.02 mg kg⁻¹ and methadone (Methadone, Martindale Pharmaceuticals, UK) 0.3 mg kg⁻¹ given intramuscularly. After 30 minutes an intravenous (IV) cannula was placed into a peripheral vein and anaesthesia induced with IV propofol (Vetofol, Norbrook Laboratories, UK) injection,

$4.6 \pm 1.2 \text{ mg kg}^{-1}$ (range 1.4–6.9 mg kg^{-1}) until endotracheal intubation was possible. The anaesthetist in charge of the case selected the size of the endotracheal tube, choosing as large an internal diameter as possible without causing any damage to upper airway structures. The internal diameter was recorded. After endotracheal intubation the patient was connected to an appropriate breathing system and isoflurane (Isoflo; Abbott Laboratories, UK) in oxygen 100% administered for maintenance of anaesthesia. Meloxicam (Metacam injection; Boehringer-Ingelheim, UK) 0.2 mg kg^{-1} and amoxicillin clavulanic acid (Augmentin; Glaxo Smithkline, UK) 20 mg kg^{-1} were both administered IV prior to surgery. Fluid therapy consisted of Hartmann's solution (Aqupharm No.11; Animalcare, UK) administered during anaesthesia at $10 \text{ mL kg}^{-1} \text{ hour}^{-1}$ IV. After the patient was moved into theatre and a stable plane of anaesthesia achieved, the lungs of all dogs were mechanically ventilated with a time cycled, flow/volume controlled ventilator (Pneupac; Smiths Medical, St Paul), with an initial tidal volume (V_T) of 12–15 mL kg^{-1} . Dogs' lungs were ventilated to maintain normocapnia, adjusting respiratory rate (f_R) as necessary to an end tidal carbon dioxide concentration ($P_{E'}\text{CO}_2$) of 4.7–6.0 kPa (35–45 mmHg). If heart rate or arterial blood pressure increased by 20% from pre-surgical baseline for more than 30 seconds then a $1 \mu\text{g kg}^{-1}$ bolus of fentanyl (Fentanyl citrate, Martindales, UK) was administered IV. Recumbency in theatre was dependent on the type of surgery being performed and therefore not randomised for each patient.

Monitoring

Measurements of lung physiology variables and cardiovascular data were collected using a Cardio-cap AS-5 equipped with spirometry (Datex Ohmeda; GE Healthcare, UK). Compliance (Crs) and resistance (Rrs) were measured utilising a double pitot tube, differential pressure constant cross-sectional area system. The spirometry module was calibrated by the manufacturer prior to first use and retrospectively on a *post-hoc* basis using a calibrated syringe. A $\pm 5\%$ error was found for the pedi-lite sensor and a $\pm 3\%$ error for the D-lite sensor respectively. The D-lite sensor was used in dogs greater than 20 kg and the Pedi-lite sensor in dogs below 20 kg. Variables recorded included heart rate (HR), f_R , oxygen saturation of arterial haemoglobin, non-invasive arterial blood pressure measurement,

peak inspiratory pressure (PIP), $P_{E'}\text{CO}_2$, Crs, Rrs, tidal volume, minute volume and positive end expiratory pressure (PEEP). PEEP was set to zero, but if values higher than zero were registered, it was recorded during the procedure. All variables were recorded after 5 minutes of mechanical ventilation (T5), and, depending on the duration of anaesthesia, after 30 minutes (T30), 60 minutes (T60), 90 minutes (T90) and 120 minutes (T120).

At the end of the procedure all dogs were disconnected from the mechanical ventilator and ventilation assisted manually until spontaneous ventilation recommenced. At this point the dog was transferred for post-operative radiography if required, after which isoflurane administration was discontinued and the patient allowed to recover from anaesthesia.

Statistics

The covariates body weight and endotracheal tube internal diameter were considered and used in the statistical analysis to ascertain any influence on the measured respiratory variables.

Measurements of compliance and resistance were assessed for normality using graphical methods including Q-Q analysis. The effect of body position on both dependent variables (Crs and Rrs) at each time point was then investigated using *t*-tests and a general linear model. Linear regression was used to assess the effect of each covariate on both compliance and resistance. All data were analysed using SPSS version 19 (IBM, UK), with further investigation of the relationship between covariates and dependent variables performed using General Additive Model (GAM) plots generated using R. Linear regression including curve analysis was used to assess the effect of each covariate on both compliance and resistance. A repeated measures ANOVA was used to assess changes in HR and MABP and a Bonferroni *post-hoc* test performed where appropriate.

Data are represented as mean \pm SD (range) if normally distributed and median and inter-quartile range (IQR) if not.

Results

A total of 45 dogs of various breeds were recruited to the study. Three were excluded due to additional sedation required for intravenous cannula placement. A further two were excluded due to ventilator-patient asynchrony. Results are therefore

presented for 40 dogs. The most commonly represented large and small dogs being the Labrador retriever ($n = 10$) and Terrier ($n = 4$) respectively. Body weight was 26.8 ± 10.7 kg (range: 1.9–45.0 kg), age 4.7 ± 2.9 years (range: 0.1–10.6 years), BCS 5.3 ± 1.4 (range: 3–8).

Twenty-nine dogs were positioned in dorsal recumbency and 11 dogs in lateral recumbency. In two dogs weighing <8 kg a Mapleson D breathing system was used instead of a circle re-breathing system.

GAM plots of compliance (Fig. 1) and resistance (Fig. 2) against body weight at the first measurement point (T5) showed a linear and inverse linear relationship, respectively. The equations for Crs and Rrs revealed from the GAM were:

$$\text{Crs} = [0.895 \times \text{bodyweight}(\text{kg})] + 8.845 \quad (1)$$

$$\text{Rrs} = [-0.0966 \times \text{bodyweight}(\text{kg})] + 6.965 \quad (2)$$

Results of Crs, Rrs and the other respiratory variables for the time points T5 to T120 are summarised in Table 1.

Total anaesthesia time was 150 ± 58 minutes (range: 55–380 minutes). PIP was 10.0 ± 2.3 cmH₂O (range: 4–16 cmH₂O), median PEEP was 0.0 cm H₂O, IQR 0.0–0.0 (range: 0–1 cm H₂O), V_T 365 ± 146 mL (range: 49–730 mL), P_eCO₂ 5.3 ± 0.53 kPa (range 3.7–6.8) kPa (40 ± 4 mmHg) (range: 28–51 mmHg) and minute volume 5.7 ± 2.1 L minute⁻¹ (range: 1.0–10.5 L minute⁻¹). Median internal diameter of endotracheal

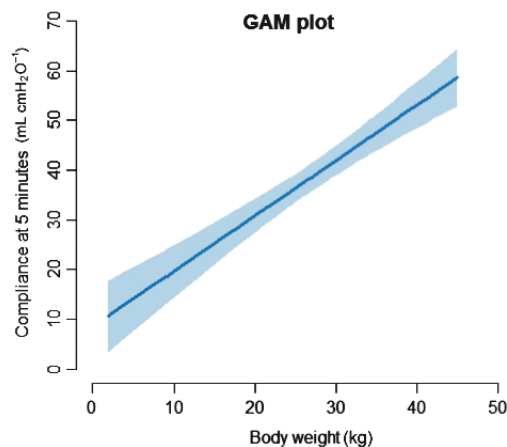


Figure 1 Respiratory system compliance (Crs) was linearly related to body weight ($n = 40$). Data are presented as a general additive model (GAM) plot of dynamic compliance at time point T5; line of best fit shown; shaded area is the 95% CI.

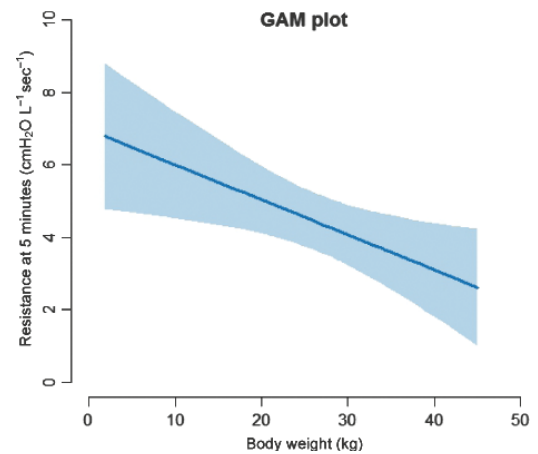


Figure 2 Respiratory system resistance (Rrs) was inversely related to body weight ($n = 40$). Data are presented as a general additive model (GAM) plot of airway resistance at time point T5; line of best fit shown; shaded area is the 95% CI.

tube (ETT) used was 10 mm, IQR 9–11 (range: 4.5–12 mm) and length was 310 ± 80 mm (range: 95–440 mm).

No significant difference in Crs and Rrs were observed at any time point between lateral and dorsal recumbency, after body weight was considered as a covariate in a general linear model. There was a trend of decreased Crs and increased Rrs over time, although this was not found to be significant between time points (Table 1).

A significant influence was found for body weight and ETT internal diameter (Crs: body weight $p < 0.001$, ETT $p = 0.002$; Rrs: body weight $p = 0.017$, ETT $p = 0.002$). Since ETT diameter was probably dependent upon body size and therefore body weight, only body weight was investigated further by general additive modeling.

Mean Crs was 16.4 ± 6.6 mL cmH₂O⁻¹ for the smaller dogs ($n = 8$ dogs) where the Pedi-lite sensor was used, and 41.2 ± 12.0 mL cmH₂O⁻¹ for the larger dogs ($n = 32$ dogs) where the D-lite sensor was used. Median Rrs was 5 cmH₂O L⁻¹ second, IQR 3–10.5 (range: 1–15) and 3 cmH₂O L⁻¹ second, IQR 3–4 (range: 1–15) for the small dogs (Pedi-lite) and larger dogs (D-lite) sensor respectively.

With regard to the measured cardiovascular variables, there was a significant difference between mean arterial blood pressure at T5 and T30 ($p = 0.025$), T60 ($p = 0.009$) and T90 ($p = 0.006$). There were no differences at any time point for HR.

Table 1 Respiratory and ventilatory variables over time

	T5		T30		T60		T90		T120	
	A (n = 32)	P (n = 8)	A (n = 32)	P (n = 8)	A (n = 28)	P (n = 6)	A (n = 13)	P (n = 4)	A (n = 6)	P (n = 3)
Cr _s (mL cmH ₂ O ⁻¹)	43.3 ± 10.7	17.1 ± 7.3	40.5 ± 11.7	16.8 ± 6.9	40.6 ± 13.1	15.3 ± 7.3	41.2 ± 12.4	16.3 ± 6.3	37.3 ± 16.3	16.0 ± 8.2
R _r s (cmH ₂ O L ⁻¹ second)	4.1 ± 2.4	6.1 ± 3.4	4.3 ± 2.6	6.1 ± 3.6	3.8 ± 2.5	7.2 ± 5.3	4.1 ± 3.4	6.0 ± 5.4	5.2 ± 5.0	6.3 ± 6.7
PIP (cmH ₂ O)	9.3 ± 1.7	8.5 ± 2.2	10.1 ± 2.0	9.3 ± 2.4	10.6 ± 2.6	10.2 ± 2.8	10.9 ± 2.0	10.5 ± 3.3	11.8 ± 1.2	10.3 ± 4.0
V _T (mL)	412 ± 95	150 ± 60	414 ± 95	147 ± 61	427 ± 103	143 ± 70	426 ± 132	163 ± 72	430 ± 168	150 ± 87
MV (L minute ⁻¹)	6.7 ± 1.3	2.6 ± 0.8	6.4 ± 1.4	2.9 ± 1.0	6.5 ± 1.8	4.8 ± 2.1	6.3 ± 1.6	3.0 ± 0.9	6.0 ± 1.7	3.1 ± 1.2
f _R (breaths minute ⁻¹)	16 ± 3	18 ± 2	16 ± 3	19 ± 3	17 ± 5	19 ± 4	16 ± 4	19 ± 4	16 ± 5	19 ± 3

A, D-lite sensor; P, Pedi-lite sensor; Cr_s, respiratory system compliance; R_rs, respiratory system resistance; PIP, peak inspiratory pressure; V_T, tidal volume; MV, minute ventilation; f_R, frequency of ventilation.

Data are presented as mean ± SD for each time point; n = number of cases with data at that time point.

Discussion

This study revealed a wide range for Cr_s and R_rs for healthy dogs during isoflurane anaesthesia, with a linear relationship of Cr_s and an inversely linear relationship of R_rs to body weight. The equations we have derived will allow the anaesthetist to estimate normal values for Cr_s and R_rs in anaesthetized, mechanically ventilated dogs. These values were only derived at time point T5 because there was no statistical difference between time points with respect to Cr_s and R_rs.

In a clinical setting Cr_s and R_rs can be estimated using simplified forms of our equations: 'Cr_s = body weight + 9' and 'R_rs = [body weight × -0.1] + 7'. Calculation of these values and comparison with monitored variables may allow the anaesthetist to evaluate ventilatory changes associated with events during anaesthesia such as changes in patient position, depth of anaesthesia or retraction of viscera.

Compliance has been suggested as a predictor of morbidity for certain surgical procedures (Jansen et al. 1999). Not acting on changes in compliance and resistance may lead to the development of atelectotrauma and barotrauma even if ventilator settings are deemed suitable for the size and shape of patient (Gillette & Hess 2001). A number of conditions may affect compliance such as recumbency, a change in recumbency under anaesthesia, a change in resistance and lung disease (Manna et al. 2005; Nam et al. 2010). Changes in or abnormal airway resistance can help to identify different obstructive lung pathology and also aid in evaluating the response to treatment (Blonshine & Goldman 2008). As documented with compliance, resistance may be altered by many conditions relevant to anaesthesia such as bronchoconstriction, airway stenosis, change in body position, ETT problems such as mucus-plugging, kinking and cuff over-inflation (Manna et al. 2005; Nam et al. 2010), and pneumoperitoneum for laparoscopic surgery (Dumont et al. 1997). However, due to the fact that no normal values for dogs are currently available, the clinical relevance of the changes in Cr_s and R_rs discussed above need to be proven in future studies.

The values of Cr_s recorded in the present study tended to be lower than the values for lung compliance (C_L) reported in other canine studies with 32 to 72 mL cmH₂O⁻¹ (Darowski et al. 1989; Lee 1991; Katoh & Ikeda 1994). This is because Cr_s is a representation of total compliance, while C_L

only represents lung compliance without taking chest wall compliance into account. Reported values for Crs in humans under anaesthesia are 70–80 mL cmH₂O⁻¹ (Lu & Rouby 2000). The fact that our reported values for Crs in dogs were lower than values reported in people is not surprising because of the difference in size (body weight) and therefore lung volume between the two species.

Reported values for tissue (lung and chest wall) resistance (R_{tissue}) in dogs in an experimental setting are 2.2 to 4.6 cmH₂O L⁻¹ second, which is lower than the values we measured in our dogs (Darowski et al. 1989; Lee 1991; Katoh & Ikeda 1994). However, the measurement techniques vary between our study and the aforementioned experimental canine studies, which complicate any comparison. The experimental studies derived R_{tissue} from oesophageal balloon pressure measurements, whereas our study determined R_{rs} from airway pressures. Resistance of the respiratory system should be greater than R_{tissue} (R_{rs} = R_{aw} + R_{tissue}), which fits well with the results described in this study.

The differences in both compliance and resistance may also be explained by comparative scaling of lung mechanics, which, in humans, shows that lung compliance has an isometric or linear relationship to body weight^{1.0}, whereas R_{aw} has an allometric or power relationship to body weight^{-0.819} (Bennett & Tenney 1982). During analysis, both a power relationship and a linear model were shown to have a very similar goodness of fit to describe the relationship between compliance and body weight with an *F* test demonstrating the latter to be marginally superior. Both models were shown to have a relationship achieving statistical significance. It should be noted that the exponent of the power relationship was -0.32, and therefore quite different from that previously reported. Biologically, a power relationship is arguably more relevant due to the asymptotic nature of the curve at the *y*-axis; however, for body weights above approximately 5 kg the curve is approximately linear. Using a parsimonious approach a linear model was therefore selected as this also correlates well with the generalised additive model, which applies a line of best fit by means of smoothing splines rather than creating a mathematical relationship to fit the data. With a population containing more low body weight individuals it is possible that a power relationship might be a better model of the data.

As body weight increases, so do lung volume, individual alveolar volume and total compliance of the respiratory system, while airway pressure remains relatively similar over a wide range of body weight, decreasing slightly with increasing size. This is due to the lower pressure required to expand larger diameter alveoli (with a greater compliance) as patient size and total lung volume increase, therefore a similar pressure is needed irrespective of body weight (Leith 1983). When using spirometry during monitoring of anaesthesia, particular attention should be paid to the size of the patient before analysing the respiratory variables, as a marked difference will be observed depending on body weight. Based on our study, only an equation and not a reference range for Crs and R_{rs} dependent on body weight could be documented statistically, because there were too few dogs within each proposed body weight group. Future studies with a larger population will allow for development of a reference range, removing the need for an equation.

In our study the internal diameter of the ETT had an influence on Crs and R_{rs}. There was a statistically significant decrease in Crs and increase in R_{rs} as ETT diameter decreased, but ETT size was influenced by body weight. Both of these effects can be explained by the physical laws of airway mechanics, as airway resistance ($\Delta P/\text{flow}$) can be calculated by combining Poiseuille's equation ($\Delta P = V \times 8L \times \eta/\pi r^4$, where ΔP is pressure gradient along the tube, *V* is volume flow rate, *L* is length of the tube, η is viscosity and *r* is radius of the tube) and flow. From this equation it becomes obvious that a decrease in ETT radius will amplify resistance and therefore R_{rs} by the fourth power. This explains the significance of our findings regarding the diameter of ETT.

The covariate, BCS had no significant effect on Crs or on R_{rs}, in contrast to what had been expected. Body condition score has been shown to decrease dynamic compliance in humans (Littleton 2012). As BCS increases, total lung capacity and functional residual capacity decrease, due to a reduced expiratory reserve volume, as a result of increased intra-abdominal fat (Littleton 2012). Obesity has been shown to decrease oxygenation in sedated dogs while ventilation remained unaffected (Iff et al. 2011). Even though we investigated a fairly wide range of BCS it is still possible that there were insufficient dogs included in our study to confirm our hypothesis and dogs at both ends of the BCS range (and especially BCS 9/9, the fattest/most

obese) were not recruited. It may also be possible that there is no influence of BCS in mechanically ventilated healthy dogs. Further studies with a larger number of dogs are required to confirm this result.

There are a number of limitations associated with this study. Of significant importance is our selection criterion for the spirometry sensor. This was based on patient body weight, as used in human anaesthesia. Therefore any patient under 20 kg body weight had the Pedi-lite sensor used for data recording. Retrospectively this criterion should not have been used and sensor selection should have been based on ETT diameter. The Datex Ohmeda technical reference manual confirms that the Pedi-lite should be used in patients with an ETT of 3 to 6mm internal diameter. Further statistical analysis of our data excluding any patient utilising the Pedi-lite sensor with an ETT of greater than 6.5 mm internal diameter did not change the results and significance of body weight on both Crs and Rrs. Future studies should therefore utilise this criterion for sensor selection and not base it on body weight. The majority of dogs enrolled were large dogs undergoing stifle surgery, positioned in dorsal recumbency which may have an affect on our results. Further studies are warranted with larger numbers of dogs utilising different anaesthetic protocols, body position during anaesthesia, health statuses, measurement devices and surgical procedures to determine their effects on compliance and resistance.

The measured respiratory variables reported in this study, Crs and Rrs, may be easily calculated in healthy, anaesthetized, mechanically ventilated dogs and follow a predictable pattern related to body weight. Spirometry is a simple, non-invasive technique for measuring Crs and Rrs and warrants further investigation. Future work will allow for a better understanding of changes in Crs and Rrs in higher risk patients under anaesthesia, potentially improving outcome measures.

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Erratum

In the publication 'Assessment of the variation in American Society of Anaesthesiologists Physical Status Classification assignment in small animal anaesthesia' by McMillan M and Brearley J, an error was made in the title (McMillan & Brearley 2013). The name of the Society should be the 'American Society of Anaesthesiologists'.

Reference

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