Pre-anaesthetic clinical examination influences anaesthetic protocol in dogs undergoing general anaesthesia and sedation

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OBJECTIVES: Identify whether pre-anaesthetic clinical examination influences anaesthetic and analgesic agents and techniques protocol in dogs presented for general anaesthesia and sedation at a large referral hospital.

MATERIALS AND METHODS: In this prospective clinical audit, 554 dogs, undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures were included. Multiple attending anaesthetists completed a questionnaire divided into four sections (American Society of Anesthesiologists physical status classification, anaesthetic and analgesic agents and techniques protocol, pre-anaesthetic clinical examination findings and changes made to the anaesthetic protocol). The attending anesthetist was able to review the patient’s history before planning the anaesthetic and analgesic agents and techniques protocol. The patients were examined and changes in American Society of Anesthesiologists physical status classification or anaesthetic protocol were recorded.

RESULTS: The initial anaesthetic and analgesic agents and techniques protocol was altered in 23.3% (n=129/554) of cases following a pre-anaesthetic clinical examination, but American Society of Anesthesiologists physical status reclassification occurred in only 8.0% (n=37/464) of cases. Multivariable logistic regression analysis showed that pre-anaesthetic clinical examination performed by European College of Veterinary Anaesthesia and Analgesia diplomates (odds ratio 5.8, 95% confidence interval 2.0 to 17.2), compared to anaesthesia interns, and the presence of an audible heart murmur (odds ratio 2.4, 95% confidence interval 1.4 to 4.4) were factors linked to changes in anaesthetic and analgesic agents and techniques protocol, whereas for each one kilogram increase in patient’s weight, the odds of a change in anaesthetic and analgesic agents and techniques protocol to occur decreased by 1.7% (odds ratio 0.98, 95% confidence interval 0.97 to 1.0).

CLINICAL SIGNIFICANCE: Pre-anaesthetic clinical examination has impact on American Society of Anesthesiologists physical status classification, therefore estimation of patient’s anaesthetic risk, and influences anaesthetic and analgesic agents and techniques protocol choice.
INTRODUCTION

The pre-anaesthetic assessment of an animal’s health status is crucial to estimate peri-anaesthetic risks and improve anaesthetic safety (Grubb et al. 2020) The American Animal Hospital Association advises all practitioners to perform and document a thorough physical examination before anaesthesia (Grubb et al. 2020). It has been shown that a thorough pre-anaesthetic assessment of a patient’s health status decreases anaesthetic-related mortality in dogs and cats (Brodbelt et al. 2007, Matthews et al. 2017).

In order to evaluate a patient’s health status, the American Society of Anesthesiologists (ASA) physical status classification (American Society of Anesthesiologists 2014) has been widely used and accepted in veterinary medicine and is particularly useful to predict peri-anaesthetic morbidity and mortality based on physical findings (Hosgood & Scholl 2002, Brodbelt et al. 2008).

The pre-anaesthetic examination (PAE) consists of a thorough physical examination that should be completed and documented before anaesthesia. It is rapid to perform, low-cost and may reduce or minimise complications during anaesthesia by identifying co-morbidities that may have a significant impact on the ASA physical status classification and therefore alter the patient’s anaesthetic risk (Gil & Redondo 2013). Pre-existing co-morbidities may reduce the therapeutic index of certain anaesthetic agents administered, defined as the ratio of the dose of an agent that produces death or toxicity to the dose of that same agent required to produce the desired therapeutic response (Brodbelt et al. 2008, Gil & Redondo 2013). Pre-existing co-morbidities may also alter the animal’s compensatory mechanisms to anaesthesia, which may lead to cardiopulmonary depression and ultimately death (Brodbelt et al. 2008, Gil & Redondo 2013). If a condition is identified during pre-anaesthetic assessment the patient can be medically stabilised before anaesthesia, and the anaesthetic and analgesic agents and techniques protocol (AP) can be altered in order to decrease the likelihood of anaesthetic-related mortality (Bille et al. 2014, de Vries & Putter 2015, Grubb et al. 2020).

The objective of this prospective clinical audit was to assess the clinical significance of PAE and their influence on AP in dogs undergoing general anaesthesia (GA) and/or sedation at the University of Liverpool Small Animal Teaching Hospital. We hypothesise that PAE produces clinically significant changes, defined by a change in AP in more than 20% of dogs undergoing general anaesthesia or sedation at our institution. The secondary objective of this prospective clinical audit was to report the proportional change of ASA physical status reclassification due to PAE in dogs undergoing GA and/or sedation at the University of Liverpool Small Animal Teaching Hospital.

MATERIALS AND METHODS

Study design

This prospective clinical audit was conducted between June 2018 and February 2019 at the University of Liverpool Small Animal Teaching Hospital and was based on a questionnaire including 14 closed, semi-closed and open questions given to the multiple attending anaesthetists. The questionnaire was divided into four sections (ASA physical status classification, AP, PAE findings and changes made to the AP) and is available as Data S1.

A sample size calculation (https://www.sealedenvelope.com/) determined that 385 cases were required to have a 95% power of detecting, as significant at the 5% level, a clinically significant change in AP due to PAE, assuming a prevalence of change in AP of 20% or more.

The questionnaire, related to changes made in the anaesthetic and analgesic agent choice, was presented to a variety of attending anaesthetists (European College of Veterinary Anaesthesia and Analgesia [ECVAA] diplomates, ECVAA residency trained anaesthetists, ECVAA residents, anaesthesia interns, non-anaesthesia residents or interns and registered veterinary nurses). Signalment, procedure to be performed and a brief clinical history (including the patient’s clinical signs, known co-morbidities and relevant laboratory, imaging or electrodiagnostic findings as well as the patient’s previous anaesthetic history) were available to be consulted before completion of the questionnaire. All data referring to clinical examinations performed during the concurrent referral appointment were not available. Once the anaesthetist reviewed all these elements an ASA physical status classification was attributed, and an AP was drafted. Subsequently, a PAE was performed by the attending anaesthetist.

The second part of the questionnaire was completed after the PAE was performed. Relevant findings of the PAE were recorded as well as any changes made to the previously formulated AP. Reasons for modifications as well as any ASA physical status reclassifications were recorded in the questionnaire (Fig 1).

Animals

All client-owned dogs presented for general anaesthesia or sedation required to perform surgical, diagnostic or imaging procedures at the University of Liverpool Small Animal Teaching Hospital were eligible to participate in the clinical audit. Patients were included in the study only if a PAE was able to be performed safely after the first part of the questionnaire was completed.

Data collection

The questionnaire consisted of information regarding signalment, type of anaesthesia performed (GA or sedation), ASA physical status classification, pre-anaesthetic medication, induction and maintenance of anaesthesia, intraoperative analgesia, locoregional anaesthesia techniques and recovery management. Specific anaesthetic and analgesic agent, route of administration and dosage were specified. Relevant PAE findings related to the PAE were recorded, these included: temperament, demeanour and body condition score; lung and heart auscultation for assessment of the heart rate, rhythm and murmurs as well as evaluation of the lung fields and respiratory effort; pulse quality; mucous membrane appearance and capillary refill time, temperature; abdominal palpation; integument inspection and brief neurological examination.

Other independent dichotomous variables were recorded including: previous anaesthetic history available (yes or no); type of procedure to be performed (surgical or diagnostic/imaging);
cardiac murmur present (yes or no); Continuous independent variables were also recorded: weight (kilograms) and age (months). Other independent covariables were grouped in categories: breed; sex; age categories; weight categories; anaesthetist experience level; heart murmur grade (Levine 6-level classification scheme), timing of diagnosis of the audible cardiac murmur (no audible murmur, diagnosed at the time of the PAE, previously diagnosed) and ASA physical status classification.

In order to investigate the key reasons for changes in AP due to PAE, data were coded in groups according to their nature: influence of the PAE on the anaesthetic phase (premedication, induction, locoregional anaesthesia techniques, maintenance, recovery and analgesia), influence of the PAE on the specific anaesthetic circumstances (type of anaesthetics and analgesic agent, dosage, route of administration and locoregional anaesthetic techniques) and reasoning for anaesthetic and analgesic agent and techniques protocol modification (related to findings in the PAE). To investigate how interventions might have changed AP, the data were analysed descriptively to illustrate the reasons that were reported to account for AP modification.

### Statistical methods

Statistical analysis was performed using SPSS Statistic version 25 for Windows. Normality of the data was evaluated using the Shapiro–Wilk test. Normally distributed variables are reported as mean (±standard deviation) and non-normally distributed data as median [interquartile range (IQR)]. Categorical variables were summarised as proportions with 95% confidence intervals (CI).

The outcome variable was changed in anaesthetic and analgesic agents and techniques protocol due to PAE (with odds ratio (OR) >1 indicating greater odds of change in anaesthetic and analgesic agents and techniques protocol and OR <1 indicating reduced odds of change in anaesthetic and analgesic agents and techniques protocol).

All categorical and continuous variables collected were screened for association with outcome (change to the AP due to PAE) using a univariable logistic regression model for continuous and categorical variables with an alpha level of 0.05. For categorical variables, reference categories were attributed to the highest number of occurrences in such category. Pearson's rank correlation was used to establish strength of association and significance between covariables. For highly correlated covariables (Pearson's rank correlation >0.7) only those with the smallest P-values were selected.

A backward stepwise elimination procedure was used to determine the final multivariable logistic regression model; all covariables with univariable P-values <0.2 were incorporated, with retention of covariables with Wald P-values <0.05 at each step, in order to determine which explanatory variables would be included in the final model. The fit of the final multivariable model was assessed using the Hosmer–Lemeshow goodness-of-fit test. Linear relationship between variables and the outcome was tested using ANOVA and tests of linearity. Specificity and sensitivity (95% CI) were calculated via a classification table using the predicted values produced by the final multivariable model and the observed values (change or no change to the AP due to PAE).

Multivariable logistic regression analysis was not performed for the secondary outcome as a result of the low proportional change in ASA physical status classification due to PAE.

### RESULTS

#### Case details

A total of 554 client-owned dogs, undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures at the University of Liverpool Small Animal Teaching Hospital, were included in this prospective clinical audit. Summary of the demographic information is included as Table S1.

#### Modifications in ASA physical status classification

ASA physical status classification was available in both parts of the questionnaire (before and after PAE) in 464 cases of the 554
Modifications in anaesthetic and analgesic agent protocol

The initial AP was altered in 129 out of 554 cases following a PAE corresponding to 23.3% (95% CI 19.8 to 27.0) of cases.

Pre-anaesthetic medication was the anaesthetic phase more often affected by the PAE (n=121/129, 93.8%, 95% CI 88.2 to 97.3) (Table S2). The reasons for such changes were commonly associated with aggressive or excitable temperament of the animals (n=34/129, 26.4%, 95% CI 19.0 to 34.8) (Table S3). Information obtained from PAE resulted in dosage adjustments of anaesthetic and analgesic agents in 85 out of 129 cases (65.9%, 95% CI 57.0 to 74.0) and in 68 out of 129 cases (52.7%, 95% CI 43.7 to 61.6) the PAE resulted in a variation in the type of agent used (Table S4).

A cardiac murmur was present in 60 out of 554 cases (10.8%, 95% CI 8.4 to 13.7), but only in 10 out 60 cases (16.7%, 95% CI 8.3 to 28.5) the AP was modified because of the cardiac murmur present. The modifications made to the AP in the presence of a cardiac murmur were administration of acepromazine instead of medetomidine in the premedication phase (n=1/10, 10.0%, 95% CI 0.25 to 44.5). Administration of medetomidine instead of acepromazine in the premedication phase (n=10, 19.0%, 95% CI 0.25 to 44.5).

The results obtained from univariable logistic regression analysis, based on pre-anaesthetic variables with an outcome of change in anaesthetic and analgesic agents and techniques protocol, are presented as supplementary information (Table S5).

The final multivariable logistic regression model based on pre-anaesthetic variables with an outcome of change in anaesthetic and analgesic agents and techniques protocol is shown in Table 1. The results obtained from univariable logistic regression analysis, based on pre-anaesthetic variables with an outcome of change in anaesthetic and analgesic agents and techniques protocol, are presented as supplementary information (Table S5).

Three variables remained significantly associated with modifications in anaesthetic and analgesic protocol: weight, anaesthetist experience level and presence of audible cardiac murmur. The results showed that the PAE is performed by an ECVAA diplomate the odds of a change in AP to occur increase by 5.8 times when compared to patients examined by anaesthesia interns (OR 5.8, 95% CI 2.0 to 17.2, P=0.001). When an audible cardiac murmur is present at the time of PAE the odds of a change in AP increase by 2.4 times when compared to patients without an audible cardiac murmur at the time of PAE (OR 2.4, 95% CI 1.4 to 4.4, P=0.003). A linear effect between weight, as a continuous variable, and change in AP was detected. For each one kilogram increase in patient's weight, the odds of a change in AP to occur decreased by 1.7% (OR 0.98, 95% CI 0.97 to 1.0, P=0.04).

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The Hosmer and Lemeshow test indicated no evidence of poor fit for the model (P=0.69). The model was able to predict change in anaesthetic and analgesic agents and techniques correctly in 77.8% of cases (95% CI 74.1 to 81.2) with a sensitivity of 10.1% (95% CI 5.5 to 16.6) and specificity of 98.4% (95% CI 96.6 to 99.3).

DISCUSSION

This prospective clinical audit showed that PAE influenced anaesthetic and analgesic agents and techniques protocol formulation in a clinically significant proportion of cases (more than 20% of patients included) undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures in a referral veterinary hospital population. In some of these patients, the PAE resulted in medetomidine dose (n=2/10, 20.0%, 95% CI 2.5 to 55.6) and administration of medetomidine instead of acepromazine in the premedication phase (n=10, 19.0%, 95% CI 0.25 to 44.5).

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The Hosmer and Lemeshow test indicated no evidence of poor fit for the model (P=0.69). The model was able to predict change in anaesthetic and analgesic agents and techniques correctly in 77.8% of cases (95% CI 74.1 to 81.2) with a sensitivity of 10.1% (95% CI 5.5 to 16.6) and specificity of 98.4% (95% CI 96.6 to 99.3).

Table 1. Multivariable logistic regression model for pre-anaesthetic variables associated with modifications in anaesthetic and analgesic agents and techniques protocol for 554 dogs presented for general anaesthesia or sedation required to perform surgical, diagnostic or imaging procedures at the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019

| Outcome | Pre-anaesthetic variable | P value | Odds ratio | 95% CI for odds ratio |
|---------|--------------------------|---------|------------|----------------------|
| Change in anaesthetic and analgesic agent protocol | Weight (kg) | 0.04 | 0.98 | 0.97 1.0 |
| Anaesthetist level of experience | Continuous | 0.001 | 5.8 | 2.0 17.2 |
| | ECVAA diplomate | 0.91 | 1.1 | 0.44 2.5 |
| | ECVAA residency trained | 0.63 | 0.64 | 0.40 1.0 |
| | ECVAA resident | 0.06 | 3.0 | 0.96 9.4 |
| | Registered veterinary nurse | 0.79 | 1.1 | 0.51 2.4 |
| | Non-anaesthesia intern/resident Anaesthesia intern | 0.003 | 2.4 | Reference |
| | Audible cardiac murmur | Yes | 1.4 | 4.4 |
| | No | <0.001 | Reference | |

CI Confidence interval, ECVAA European College of Veterinary Anaesthesia and Analgesia
Influence of pre-anaesthetic examination in dogs

in ASA physical status reclassification, potentially altering the estimation of the patient’s peri-anaesthetic risk.

The multivariable logistic regression model described that changes made to anaesthetic and analgesic agent protocols were associated with the level of experience of the attending anaesthetist and the presence of an audible cardiac murmur. The model also explained that these modifications were less likely to occur as the dogs’ weight increased.

Other procedures performed as part of the pre-anaesthetic assessment, such as blood analysis, were also investigated in terms of impact on anaesthetic protocols (Alef et al. 2008, Davies & Kawaguchi 2014, Mitchell et al. 2018). Findings in pre-anaesthetic blood haematology and biochemistry resulted in 4% and 9% of retrospective changes in the anaesthetic protocol for dogs and cats, respectively (Davies & Kawaguchi 2014). In another retrospective study, five anaesthetists reviewed blood analysis and case records of 100 dogs undergoing general anaesthesia. In 79% of cases, the AP was modified, although in 64% of cases the alterations in AP were made by only one evaluator and unanimous decisions was achieved in only 3% of the cases (Mitchell et al. 2018). Prospective studies, focusing on a population of healthy dogs, revealed that in 0.2% of cases changes would have been made to anaesthetic protocols due to findings in routine pre-anaesthetic blood analysis (Alef et al. 2008). This study has also shown that in 0.8% of cases, anaesthesia would have been postponed, and in 1.5% of cases additional therapy before anaesthesia would have been required (Alef et al. 2008).

Our results suggest that the physical findings observed during PAE have an impact in ASA physical status reclassification and estimation of a patient’s anaesthetic risk. These results are similar to others where the ASA physical status classification was modified in 8% (Alef et al. 2008) and 13% of cases (Mitchell et al. 2018) following interpretation of pre-anaesthetic blood analysis. These outcomes suggest that signalment, previously identified co-morbidities and clinical history as well as PAE and blood analysis may play a significant role in estimating anaesthetic risk in dogs.

In the final model, three variables remained significantly associated with modifications in anaesthetic and analgesic agent and techniques protocol: anaesthetist experience level, presence of audible cardiac murmur and weight.

ECVAA diplomates were significantly more likely to alter an anaesthetic protocol due to PAE of a patient when compared to anaesthesia interns. It could be that the greater clinical experience of senior anaesthetists makes them more aware of subtle abnormalities during clinical examination when compared to more junior personnel. It is also possible that when an abnormality is detected on PAE an experienced anaesthetist would be more likely to change their AP due to an understanding of the risks or complications this may lead to. Another possible explanation is that experienced anaesthetists may be more comfortable using different AP than junior personnel and therefore are more likely to make that change if they see fit.

The presence of an audible cardiac murmur was associated with an increased likelihood of AP modifications. This highlights the importance of thoracic auscultation during the PAE. It has been suggested that when advanced cardiac disease is missed before general anaesthesia or intravenous fluid therapy, unforeseen signs of congestive heart failure are likely to occur (Côté et al. 2015). The most common modifications in the AP in dogs with an audible cardiac murmur were administration of acepromazine instead of medetomidine or a reduction in medetomidine dose in the premedication phase. Medetomidine is contraindicated in dogs with degenerative mitral valve disease and dilated cardiomyopathies as they decrease cardiac index, cause bradycardia and increase systemic vascular resistance (Saponaro et al. 2013). Medetomidine produced a significant reduction of heart rate and cardiac index when compared with acepromazine (Saponaro et al. 2013). Therefore, acepromazine has been recommended for sedation of patients with degenerative mitral valve disease (Keene et al. 2019) and its judicial use can be beneficial in cases of dilated cardiomyopathy, as mild vasodilation reduces afterload and increases myocardial contractility (Scarabelli & Bradbrook 2016).

Our data suggest that heavier patients are less likely to experience changes in the anaesthetic protocol formulated prior to pre-anaesthetic clinical examination. Commonly, anaesthetists dose sedatives (α2-adrenoceptor agonists and acepromazine) using a milligram per kilogram regime, but larger breeds have a higher bodyweight to surface area compared with smaller breeds and therefore a body surface area regime is more appropriate (Pyndop & Verstegen 2000). When using similar dosages in a milligram per kilogram regime, large breed dogs are more reliably sedated than small breed dogs (Boveri et al. 2013, Kushnir et al. 2017). In this clinical audit, patient’s aggressive, excitable or calm temperament was the most common reason for changes in the AP and the premedication plan was changed more often than any other anaesthetic phase. This decision often resulted in an increase or decrease of drug dosages or the attending anaesthetist opted for different premedication agents. Anxious patients often require higher doses of premedication agents than quieter or depressed animals (Grubb et al. 2020). Various authors have suggested that temperament has an impact on sedation scores and dosages of sedative and induction agents (England & Clarke 1989, Maddern et al. 2010, Raszpiewicz et al. 2013). Therefore, we hypothesise that in the presence of an aggressive, excitable heavier patient, less adjustment of premedication agents is required to produce the desired sedative effect when compared to smaller patients due to a milligram per kilogramme dosage regime. Temperament assessment is an important part of the PAE, but as this variable was not included in the final multivariable regression model further studies are required to evaluate the impact of temperament on the decision-making process of the anaesthetist when it comes to formulating an anaesthetic protocol.

A weak correlation between cardiac disease and weight was observed, but both variables were significant at multivariable logistic regression level therefore their effect is considered independent. While weight has been correlated with degenerative mitral valve disease (Martin et al. 2015), there is no evidence of an association between weight and the presence of cardiac murmurs associated with canine cardiovascular diseases other than degenerative mitral valve disease.
The final multivariable logistic regression model had a high specificity, meaning that the explanatory variables obtained are useful to predict which patients will not require a change in AP after a PAE has been performed. Although due to a low sensitivity of the model, the explanatory variables obtained are not as useful to predict which patients will require a change in AP after a PAE has been performed.

One of the limitations of this clinical audit is that no monitoring of the outcome of these anaesthetic protocol changes was performed. With the data available we cannot determine if such changes improved the safety of the protocol used.

Even though the attending anaesthetist was blinded to clinical examinations performed during the concurrent appointment, the same cannot be said for clinical examinations which may have occurred and been documented in previous appointments, referring veterinary surgeon clinical history and previous anaesthetic records. Although, an effect was still observed despite this limitation.

Another limitation of the study is that the ASA physical status classification has been shown to have a poor inter-observer agreement (Mak et al. 2002, McMillan & Brearley 2013) therefore the decision of changing the ASA physical status classification in a specific case, based on physical examination, may vary between attending anaesthetists.

In conclusion, when a PAE is performed, identified findings are of clinical relevance and can result in important changes to the anaesthetic and analgesic agent and techniques protocol as well as ASA physical status classification resulting in adjustments to the estimation of patient’s peri-anaesthetic risk.

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Conflict of interest
None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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Supporting Information
The following supporting information is available for this article: Data S1. Questionnaire presented to multiple attending anaesthetists in order to audit the impact of the pre-anaesthetic examine (PAE) in anaesthetic and analgesic agents and techniques protocol (AP) of 554 patients undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures presented to the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019. This questionnaire includes fourteen closed, semi-closed and open questions, and is divided into four sections (American Society of Anaesthesiologists (ASA) physical status classification, AP, PAE findings and changes made to the AP). GÀ: general anaesthesia; TIVA: total intravenous anaesthesia.

Table S1. Demographic variables of 554 patients undergoing general anaesthesia or sedation for surgery, diagnostic or imaging procedures presented to the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019. All continuous variables are normally distributed and are presented as mean (± SD).
Table S2. Influence of the pre-anaesthetic examination on the anaesthetic phase in 129 of 554 patients undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures presented to the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019. The 95% confidence interval relates to percentage of change to the anaesthetic protocol due to pre-anaesthetic examination.

Table S3. Reasons for anaesthetic and analgesic agent and techniques protocol modification due to the pre-anaesthetic examination in 129 of 554 patients undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures presented to the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019. The 95% confidence interval relates to percentage of change to the anaesthetic protocol due to pre-anaesthetic examination.

Table S4. Influence of the pre-anaesthetic examination on the specific anaesthetic circumstances changed in 129 of 554 patients undergoing general anaesthesia or sedation for surgical, diagnostic or imaging procedures presented to the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019. The 95% confidence interval relates to percentage of change to the anaesthetic protocol due to pre-anaesthetic examination.

Table S5. Univariable logistic regression model for pre-anaesthetic variables associated with modifications in anaesthetic and analgesic agents and techniques protocol for 554 dogs presented for general anaesthesia or sedation required to perform surgical, diagnostic or imaging procedures at the University of Liverpool Small Animal Teaching Hospital between June 2018 and February 2019.