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The incidence of hypoxemia in dogs recovering from general anesthesia detected with pulse-oximetry and related risk factors

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ABSTRACT

The postoperative period is critical for the development of complications, including hypoxemia. To detect hypoxemia early and provide appropriate care, continuous monitoring of saturation is necessary: pulse oximetry is an easily accessible and simple method for this purpose. However, a SpO_2 cut-off value to detect hypoxemia in dogs recovering from general anesthesia is lacking in the veterinary literature. The objectives of this clinical study are to validate the room air SpO_2 test (SpAT), to identify a cut-off value to discriminate hypoxemia (Phase 1), and to apply the SpAT to study the incidence of transient postoperative hypoxemia (TPH) (Phase 2) in dogs with healthy lungs recovering from general anesthesia. Phase 1: 87 dogs recovering from general anesthesia with an arterial line were included. After extubation, SpAT was performed simultaneously with arterial blood sampling. A $PaO_2 < 80$ mmHg was considered hypoxemia. Phase 2: 654 dogs were enrolled. They underwent general anesthesia with different ventilation settings for different procedures. After extubation, dogs were classified as hypoxemic if the SpO_2 was lower than the cut-off obtained in phase 1. Phase 1 showed that the SpO_2 cut-off is < 95% (sensitivity 100%, specificity 97.4%; area under the curve, AUC = 0.996; 95% Confidence Interval = 0.944–1; $P<0.0001$). In Phase 2, 169 dogs were hypoxemic. Body Condition Score (BCS) > 3/5, dorsal recumbency, FiO_2 1, absence of Positive End-Expiratory Pressure (PEEP) had a significant odds ratio to induce TPH (5.8, 1.9, 3.7, 1.7, respectively). These results showed that $SpO_2 < 95\%$ indicates $PaO_2 < 80$ mmHg in dogs and TPH occurs in up to 28% of cases. Identification of associated risks could be useful to prevent and to increase awareness for monitoring and treatment.

Introduction

Postoperative hypoxemia may reflect the presence of respiratory dysfunction due to changes induced by anesthesia and/or surgery (transient postoperative hypoxemia, TPH). It may also be a sign of more severe pulmonary complications, such as acute respiratory failure, pneumonia, and acute respiratory distress syndrome (ARDS) (Canet and Gallart, 2014). Transient postoperative hypoxemia can be a significant issue in dogs, as it is in humans. Reduced postoperative tissue oxygenation can cause subclinical injury to tissues (Jonsson et al., 1987; Gill et al., 1992; Gögenur et al., 2004; Bojesen et al., 2019). Also, maintaining adequate tissue oxygen tension has been shown to be critical for proper wound healing and infection prevention (Knighton et al., 1984; Hopf and Sessler, 1994). During the early postoperative period, TPH may increase the risk of long-term adverse events, such as respiratory, renal and cardiovascular complications, as well as prolonged hospitalization and postoperative intensive care unit admission (Rostin et al., 2019). This risk escalates with the duration of hypoxemia, as noted by Rostin et al. (2019). In a recent study, in a population of 34 dogs, the continuous monitoring of SpO_2 allowed to detect TPH in 62% of dogs during recovery from general anesthesia, with 20% of them being severely hypoxemic ($SpO_2 < 90\%$) (Stabile et al., 2021). Campbell et al. (2003) found a 20% incidence of TPH in healthy dogs in the postoperative period, using intermittent arterial blood gas analysis. Factors contributing to the occurrence of TPH may be multiple and are related to patient characteristics, anesthesia, and surgery. It has been found that, in human patients undergoing surgery for acute type A aortic dissection, individual-specific risk factors include the general health of the patient

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(presence of systemic diseases), the functionality of specific systems (respiratory, cardiovascular, neuromuscular, renal), age, and obesity (Zhou et al., 2021; Song et al., 2022).

The gold standard test for verifying gas exchange efficiency is arterial blood gas analysis, but it is sometimes less practical to perform and, most importantly, does not allow for continuous monitoring. Thus, alternative methods of assessment may be required. Visible clinical signs associated with hypoxemia, such as cyanotic mucous membranes, changes in heart and respiratory rates, and the appearance of respiratory effort, have been found to be inaccurate in humans for early assessment of mild and moderate stages of hypoxemia (Dripps and Comroe, 1946; Comroe and Botelho, 1947). In contrast, the use of pulse oximetry has been shown to be reliable and accurate in identifying these conditions, with a good correlation between SpO_2/FiO_2 and PaO_2/FiO_2 values (Calabro et al., 2013). However, there is a lack of knowledge in the veterinary literature regarding the sensitivity and specificity of using SpO_2 cut-off values to determine hypoxemia in the recovery period.

More frequent use of pulse oximetry has revealed a tendency to desaturate (to an $SpO_2 < 90\%$) during recovery from general anesthesia and in the postoperative period (Campbell et al., 2003). Several studies have reported that drugs used during the various stages of general anesthesia and for intra- or postoperative analgesia (i.e., opioids, especially pure mu agonists) influence the occurrence of postoperative hypoxemia (Abdul-Rasool and Ward, 1989; Warner, 2000; Campbell et al., 2003; Henao-Guerrero and Riccò, 2014; Iizuka et al., 2017). The residual effects of drugs on central inhibition and muscle relaxation on the upper airways (hypoglossal nerve), respiratory muscles and diaphragm (phrenic nerve) predispose to the onset of postoperative respiratory deficit (Canet and Gallart, 2014). During anesthesia in humans, the occurrence of hypoxemia resulted to be influenced by the respiratory setting used. This includes the type of ventilation (mechanical mode or spontaneous breathing), the oxygen concentration delivered (FiO_2, Fraction of inspired Oxygen) and the use of a Positive End-Expiratory Pressure (PEEP) (Miskovic and Lumb, 2017). In veterinary medicine, a recent study of mechanical ventilation in dogs compared low (8 ml/kg) to high (15 ml/kg) tidal volumes, with or without 5 cmH_2O of PEEP. The study showed that the use of a tidal volume of 15 ml/kg and the addition of 5 cmH_2O of PEEP prevented both hypoaeration and atelectasis and improved lung compliance. The results of the study suggest that higher tidal volumes and the addition of PEEP may be used to improve lung function in dogs undergoing mechanical ventilation (De Monte et al., 2018). The effects of administering different fractions of FiO_2 on hypoxemia are conflicting in the veterinary literature (Staffieri et al., 2007; Martin-Flores et al., 2020).

During O_2 supplementation, pulse oximetry loses reliability in assessing a patient's true oxygenation status due to the flattening of the upper portion of the haemoglobin curve as PaO_2 values rises above approximately 90–100 mmHg (Tusman et al., 2017). An oxyhaemoglobin saturation of less than 85% is considered the critical lower limit of this parameter as it has been associated with significant visual, cognitive and electroencephalographic dysfunction in humans (Hanning and Alexander-Williams, 1995). Determining peripheral oxygen saturation (SpO_2) while breathing room air (SpO_2 air test, SpAT) provides a more accurate assessment of oxygenation status, eliminating the bias associated with supplemental oxygen (Gruber et al., 1995; Tusman et al., 2017; Ferrando et al., 2017; Stabile et al. 2021). Thus, it could be useful to use the SpAT to detect early the presence of any saturation problems, as in the case of TPH, and take the most appropriate measures to prevent negative consequences.

The first objective of this study is to validate the efficacy and reliability of SpAT as a replacement for arterial blood gas analysis in detecting hypoxemic states in dogs during the recovery period and to define an SpO_2 cut-off value for hypoxemia. In addition, this study aims to assess the incidence of TPH and its associated risk factors by monitoring SpO_2 during recovery from general anesthesia.

Materials and methods

The study was approved by the Ethical Committee of Clinical and Zootechnical Studies on Animals of the Department of Emergency and Organ Transplantation (DEOT) of the University of Bari, Italy (Approval number, 03–2017; Approval date, 15 January 2017). It was conducted at the Section of Veterinary Clinics and Animal Production of the DEOT and consisted of two phases:

- Phase 1: Validation of the AirTest in dogs through identification of the SpO_2 cut-off for hypoxemia, defined as PaO_2 <80 mmHg (Sumner and Rozanski, 2013).
- Phase 2: Detect hypoxemic dogs by monitoring SpO_2 using the AirTest to assess the incidence of TPH and identify associated risk factors.

This prospective, randomized clinical study followed the Consolidated Standards of Reporting Studies Statement 2010 for the presentation of randomized clinical trials (Moher et al., 2012). Dogs with different characteristics regarding age, sex, body weight (BW), Body Condition Score (BCS), breed, type of procedure (diagnostic or surgical), and associated recumbency, for which they underwent general anesthesia were included in the study. BCS was scored on a 5-point scale, with BCS = 3 representing ideal body condition and BCS > 3 representing overweight/obese dogs. BCS was assessed by visualization of the dog's silhouette and palpation of the thorax, spine, abdomen, and lumbar region (Lund et al., 2006). Written informed consent was obtained from each pet owner prior to enrollment. Inclusion criteria were American Society of Anesthesia (ASA) physical status I-III (based on history, clinical, and laboratory assessment), BW > 5 kg and duration of anesthesia less than 3 h. Exclusion criteria were cardiovascular and respiratory disease, and thoracic surgery. Prior to anesthesia, each dog underwent a comprehensive physical examination as well as haematological and biochemical tests.

The anesthetic protocol was established by the clinician and tailored to the health condition of each dog and the type of procedure being performed. The usual protocol at the institution included sedation with intramuscular (IM) acepromazine (0.005–0.010 mg/kg; Prequillan 1%, Fatro) or dexmedetomidine (0.002–0.005 mg/kg, Dexdomitor 0.5 mg/ml, Vetoquinol) and/or opioids (methadone 0.3 mg/kg, Semfortan 10 mg/ml or buprenorphine 0.010 mg/kg, Buprefelican 0. 3 mg/ml; Dechra), an induction of anesthesia with intravenous (IV) propofol (Proposure 10 mg/ml; Merial) and, after intubation, anesthesia was maintained with isoflurane (Vetflurane 250 ml; Virbac) or infusion of propofol (0.2–0.6 mg/kg/min, Smith et al., 2017) in combination with other adjuvants (fentanyl, dexmedetomidine, lidocaine) as needed. Locoregional anesthesia was also used in some cases. Prior to induction, all dogs received supplemental oxygen for 3 min via a face mask delivering 100 ml/kg/min of 100% oxygen (McNally et al., 2009). After intubation using an appropriately sized cuffed endotracheal tube, all dogs were connected to a rebreathing circuit of a COMEN AX-500 anesthesia machine (Foschi, DEMAS) and ventilation was established according to the randomization scheme (see below). The FiO_2 was measured with a side stream oxygen analyzer with the sampling line placed at the end of the orotracheal tube of the dog. By convention, in this study, we indicate FiO_2=1 when providing 100% oxygen; however, it should be noted that in dogs receiving inhalational anesthesia FiO_2 was slightly lower, depending on the amount of inhalational agent administered, and was approximately 0.9. Throughout anesthesia, standard physiological parameters of the dogs were monitored: heart rate (HR, beats/min), respiratory rate (RR, breaths/min), systolic, mean, and diastolic blood pressures by noninvasive oscillometric system or direct arterial catheterization (SAP, MAP, DAP, mmHg, respectively), percentage of oxygen saturation in peripheral hemoglobin (SpO_2%), arterial oxygen partial pressure (PaO_2, mmHg), arterial carbon dioxide partial pressure ($PaCO_2$, mmHg), end-tidal carbon dioxide tension

($EtCO_2$, mmHg), end-tidal isoflurane concentration (EtIso%), tidal volume (VT, ml), peak inspiratory pressure (Ppeak, cmH_2O), and rectal temperature (T, °C). At the end of the procedure, isoflurane and additional anesthetic/analgesic drugs were discontinued and dogs were allowed to recover. Once it was observed that the dogs had regained their swallowing reflex, they were extubated. Antibiotics, anti-inflammatory drugs, fluid therapy, and opioids were administered to dogs as needed for the disease or procedure. During recovery, temperature was continuously monitored, and a rewarming device was used to increase body temperature around 37°C in case of low values (<37°C). Oxygen status monitoring and oxygen supplementation were performed during recovery according to the study protocol (see below). For the purposes of this study, the recovery period from anesthesia was considered to be the 1 h interval after extubation, a time during which sequelae of general anesthesia-related effects may occur. The postoperative period was instead considered to be 24–48 h from the end of anesthesia, although in general the concept of the postoperative period has a longer and variable duration depending on the pathology and type of surgery performed.

Execution of AirTest

For the purpose of this study, the AirTest was performed as described by Stabile et al. (2021). Briefly, while the dogs were breathing room air ($FiO_2 = 0.21$) the pulse oximetry probe (MASIMO Rainbow 87 pulse oximeter) was placed on one of the following sites: tongue, lip, foreskin, vulva, interdigital space, skin fold, nipple (Huss et al., 1995). The signal quality was assessed using the perfusion index (PI > 1%) and the SpO_2 value was recorded after 1 min of reading with an adequate quality signal (Hood and Wilson, 2011).

Phase 1

This part of the study included dogs requiring invasive blood pressure monitoring for clinical reasons and undergoing general anesthesia for various surgical procedures. Dogs admitted during the period April - June 2018 were recruited into the study. At the end of surgery, between 10 min and 20 min after extubation with animals breathing room air (FiO_2 =0.21), an arterial blood sample was taken with 1 ml heparinized syringes and processed using the blood gas analyzer i-STAT1 and CG8+ cartridges (Abbott Point of Care Inc., USA): PaO_2 and $PaCO_2$ values were recorded. The site used for blood sampling to obtain the PaO_2 value was the dorsal pedal artery, which was catheterized for monitoring purposes (i.e., invasive blood pressure). The SpO_2 value was recorded simultaneously with the blood sampling and considered for the study.

Dogs were categorized according to PaO_2 values into Normoxemic (PaO_2 > 80 mmHg) and Hypoxemic (PaO_2 < 80 mmHg). Finally, SpO_2 ranges were determined for each of these classes.

Dogs that were found with low values of oxygenation (PaO_2 < 80 mmHg) were properly managed with face mask oxygenation and/or intubation soon after sampling.

Based on the data collected, the SpO_2 cut-off value capable of discriminating between normoxemia and hypoxemia was determined using the appropriate statistical analysis.

Phase 2

For this phase, dogs were monitored during the recovery period and the SpO_2 and other physiological parameters were measured. Under general anesthesia, dogs underwent different types of surgical procedures and the respiratory setting was adjusted based on a randomization scheme considering the following options: volume-controlled mechanical ventilation (VCM) or spontaneous breathing (SB); FiO_2:0.4 or 1 (delivered by mixing 100% oxygen with medical air or by using 100% oxygen alone, respectively); addition or omission of 5 cmH_2O PEEP during mechanical ventilation. More specifically, the combinations were

- SB at FiO_2 of 0.4 (SB0.4)
- SB at FiO_2 of 1 (SB1)
- VCM at FiO_2 of 0.4 without PEEP (VCM0.4)
- VCM at FiO_2 of 0.4 with PEEP (VCM0.4 PEEP)
- VCM at FiO_2 of 1 without PEEP (VCM1)
- VCM at FiO_2 of 1 with PEEP (VCM1 PEEP)

In cases receiving VCM, ventilator settings were as follows: tidal volume of 12 ml/kg, I/E=1:2, inspiratory pause of 30% of inspiratory time, and respiratory rate adjusted based on $EtCO_2$ (35–45 mmHg), with 5 cmH_2O of PEEP added if required by randomization. Allocation concealment was maintained using opaque envelopes, a random assignment was conducted utilizing a sequence generator available at http://www.random.org/. The randomization ratio among the different settings of ventilation was 1:1:1:1:1:1. However, at the facility of the study, two locations (diagnostic imaging and one soft tissue operating theater) were equipped with anesthetic workstations not able to provide air/oxygen mixture and PEEP. Thus, in these cases randomization was only between SB1 or VCM1.

At the end of general anesthesia the AirTest was performed with the animals in sternal recumbency. Specifically, SpO_2 values were recorded when dogs were still intubated after being disconnected from the breathing circuit and allowed to breathe room air (INTUB), 5 min after the extubation which was performed after the occurrence of the swallowing reflex (EXT), and 5 min later (POST). SpO_2 measurements were performed as described in the "*Execution of AirTest*" section. In cases of SpO_2 values below 85% at INTUB the endotracheal tube was maintained and dogs were supported as required, these cases were excluded from the study. Similarly, in cases where SpO_2 values < 85% were detected any time after extubation, dogs were re-intubated and supported with invasive ventilation. Also these cases dogs were excluded from the study. Considering the results obtained in phase 1 of the study, dogs were classified as normoxemic (SpO_2 > 95%) and hypoxemic (SpO_2 < 95%) based on the SpO_2 value at POST. SpO_2 monitoring was then continued for 1 h, and non-invasive respiratory support treatment was warranted for the hypoxemic cases. Specifically, hypoxemic dogs were supported with helmet CPAP (Continuous Positive Airway Pressure), high flow nasal cannula, or face mask until normoxemia was restored. Data from this phase of the study will be part of another publication.

Statistical methods

Data collected in both phases of the study were analyzed (MedCalc 1.9 software) for normal distribution using the Shapiro-Wilk test. The mean, standard deviation (SD) and 95% confidence interval (CI) were calculated for all data. The values of PaO_2, $PaCO_2$, SpO_2, weight and age of the dogs were analyzed using descriptive statistics. For phase 1 of the study, a receiver operating characteristic (ROC) curve was used to evaluate the ability of SpO_2 to predict hypoxemia. The required sample size for phase 1 of the study was estimated to be 64 dogs, considering a type 1 error (alpha) of 0.05, a type 2 error (beta) of 0.10, a hypothesized area under the curve (AUC) of 0.725, a null AUC hypothesis of 0.5, and a ratio of sample sizes in negative/positive groups of 1. The area under the ROC curve (AUC) was determined as previously described (DeLong et al., 1988). The best cut-off value to discriminate between normoxemia and hypoxemia was defined by a point on the ROC curve determined by the maximum YOUDEN index value (sensitivity + specificity −1). (Ray et al., 2010). For the data collected in the Phase 2 study, the incidence of hypoxemia was calculated in the population and compared within the different ventilation groups using multiple comparisons *t*-test with Bonferroni correction. A post-hoc power analysis was performed between ventilation groups, using a z test calculator considering a significance level of 0.05. Multivariate binary regressions were performed to determine the existence of an association between risk factors (BCS, dorsal recumbency, spontaneous breathing, NO PEEP, and high FiO_2 during anesthesia) and hypoxemia. Odds ratio, 95% CI and *P* values were reported for each factor. P <0.05 was considered statistically significant.

Results

Phase 1

Eighty-seven dogs participated in this phase of the study and 12 were excluded due to problems with blood sampling and/or SpO_2 measurement during recovery. A total of 75 cases completed the study, of which 40 were found to be normoxemic and 35 were found to be hypoxemic. Arterial blood gas analysis revealed that normoxemic dogs had a $PaO_2 =$ 96.87 (94.08–99.67, 95%CI) mmHg and a $PaCO_2 =$ 44.92 (42.13–47.73, 95%CI) mmHg. Pulse oximetry showed that this group had an $SpO_2 =$ 97.02 (96.30–97.75, 95%CI) %. In the hypoxemic group, PaO_2 was 59.69 (56.32–63.06, 95%CI) mmHg and $PaCO_2$ was 40.29 (37.68–42.9, 95%CI) mmHg. In this group, SpO_2 was 86.09 (84.19–87.99) %. ROC curve analysis showed that the cut-off value of SpO_2 was 95%, with 100% sensitivity and 97.4% specificity for predicting hypoxemia by pulse oximetry. The AUC of the SpO_2 ROC curve was 0.996 (95% IC= 0.944–1) with a significance level of P<0.0001. (Fig. 1)

Phase 2

During this phase of the study, 654 dogs were enrolled, of which 54 were excluded because they did not meet the inclusion criteria (lack of SpO_2 measurement during procedures, duration of anesthesia, or intraoperative complications). The remaining 600 dogs completed the study without complications (Fig. 2). Breeds are listed in Table S1 (see Supplementary material). Dogs underwent diagnostic (n=105), upper airway (n=29), orthopedic (n=197), spinal (n=24), abdominal (n=136), ophthalmic (n=15), and minor skin mass removal (n=94) procedures. Considering SpO_2 values at POST, 72% (n=431, 95%CI: 65%-79%) of the dogs were normoxemic and 28% (n=169, 95%CI: 24%-32%) were hypoxemic. There were no cases of SpO_2 < 85% at any time during the study. Therefore, none of the dogs in our population were reintubated.

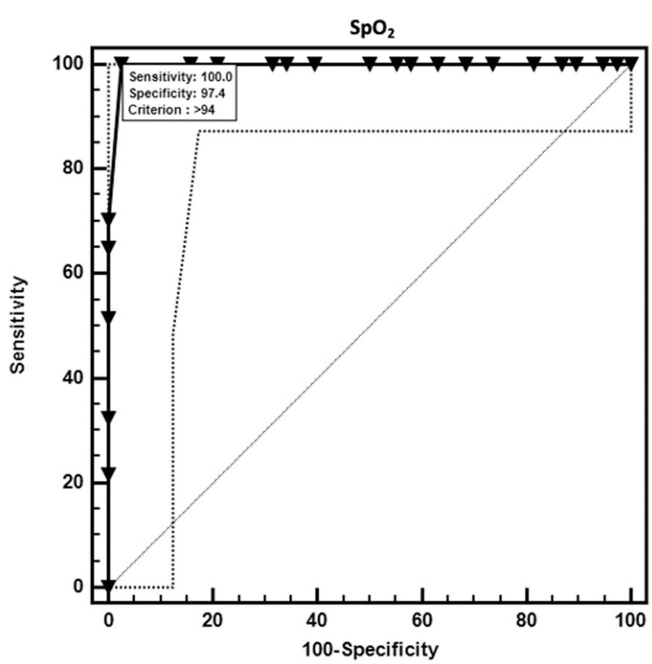

Fig. 1. Receiver operating characteristic (ROC) curve showing the ability of SpO_2 (measured by a MASIMO Rainbow 87 pulse-oximeter) to detect hypoxemia. The triangles indicate the mean SpO_2 values, and the dotted line indicates the 95% CI. The area under the curve (AUC) is 0.996 (95% Confidence Interval= 0.944–1) with a significance level of P<0.0001.

BW, age, and BCS data were not statistically different between the two groups and are shown in Table 1. The mean and 95% CI of the SpO_2 values of the two groups recorded at each time point of the study are shown in Table 2. SpO_2 trends of both normoxemic and hypoxemic groups during the monitoring period of the study are shown in Fig. 3. Differences between SpO_2 values between groups were statistically significant at each time point: INTUB (P = 0.002), EXT (P = 0.001), POST (P = 0.002). The SpO_2 trend of the hypoxemic group did not show any improvement over time. The factors found to be associated with TPH were: BCS, recumbency, and a respiratory setting with high FiO_2 and absence of PEEP during general anesthesia (Table 3). Fig. 2 shows the number and percentage of normoxemic and hypoxemic dogs for each ventilation group. Regarding the different ventilation modes, the SB1 group had a higher incidence of TPH than the VCM0.4 (P = 0.0005, power 0.93), VCM0.4PEEP (P = 0.0003, power 0.92), and SB0.4 (P = 0.0001, power 0.89) groups; the SB0.4 group had a lower incidence of TPH than the VCM1 (P = 0.0012, power 0.93) and VCM1PEEP (P = 0.0022, power 0.83) groups; the VCM1 group had a higher TPH incidence than the VCM0.4 (P = 0.0112, power 0.96) and VCM0.4PEEP (P = 0.0067, power 0.95) groups; in the VCM1PEEP group, the incidence of TPH is higher than in the VCM0.4PEEP group (P = 0.0142, power 0.86). Supplementary Tables S2 and S3 show the incidence and 95% CI of TPH for each group and the P values for comparing the incidence of TPH between the different ventilation groups.

Discussion

This study showed that in dogs recovering from general anesthesia: (1) pulse oximetry is an effective method for detecting hypoxemia during the AirTest, (2) the SpO_2 cut-off for hypoxemia is < 95%, and (3) the incidence of TPH in a population of 600 dogs is 28%. Moreover, dorsal recumbency, BCS > 3, and a ventilatory setting with high FiO_2 (1) and/or absence of PEEP are the main risk factors for TPH.

In this study, the AirTest was used to measure SpO_2 levels with a MASIMO pulse oximeter, and an SpO_2 <95% was found to be a sensitive and specific marker of hypoxemia. Arterial blood gas (ABG) is currently considered the "gold standard" test for detecting hypoxemia, although it is invasive and requires specialized skills and equipment (Shiroshita et al., 2000). Furthermore, PaO_2 measured by ABG is a point-in-time assessment and does not provide continuous monitoring of oxygenation. On the contrary, pulse oximetry is considered a valid tool to obtain a non-invasive and continuous assessment of peripheral hemoglobin saturation. Calabro et al. (2013) evaluated the correlation between the PaO_2/FiO_2 ratio and the SpO_2/FiO_2 ratio in dogs spontaneously breathing room air and affected by various diseases. They found that there is a good correlation between the two parameters, so that SpO_2 can be considered as a non-invasive surrogate for the assessment of oxygenation in dogs. The Phase 1 results found a very high sensitivity and specificity of the SpO_2 cut-off value of 95% obtained by ROC curve analysis (100% and 97.4%, respectively) that could allow an early assessment of a hypoxemic state by the use of the room air SpO_2 test (SpAT). With this type of monitoring, it would be possible to promptly support dogs with supplemental oxygen therapy in order to rapidly intervene when TPH occurs. It is important to note that changes in temperature, pH, pCO_2, and 2,3-diphosphoglycerate levels, as well as anemia, can alter the SpO_2/PaO_2 relationship and shift the oxy-hemoglobin dissociation curve (Clerbaux et al., 1993). The reader must take these factors into account when interpreting the results.

By demonstrating the reliability of pulse oximetry during the AirTest and establishing the SpO_2 cut-off achieved in Phase 1, Phase 2 was able to show that there was a 28% incidence of transient hypoxemia in our population during the post-operative period. Transient hypoxemia is one of the postoperative pulmonary complications that have been reported in 22% of dogs undergoing laparotomy (Alwood et al., 2006). In a study conducted by Campbell et al. (2003), 20% of a population of 20 healthy dogs that underwent general anesthesia for elective ovariohysterectomy

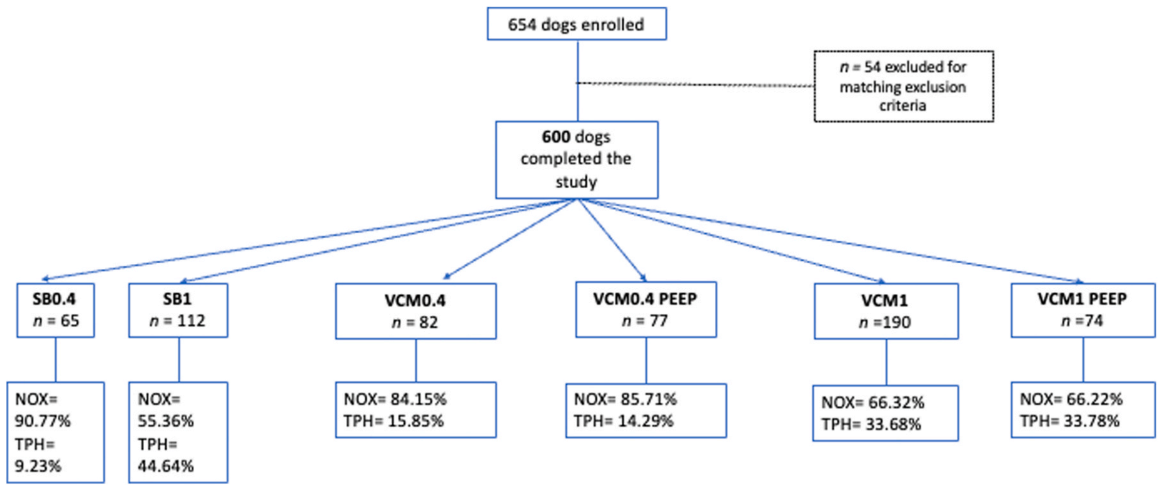

Fig. 2. The flow-diagram shows the number of dogs for each mode of ventilation they underwent during general anesthesia. The percentage of normoxemic (NOX) and transient postoperative hypoxemic (TPH) dogs at POST (10 min after extubation) are also represented for each group. (Modes of ventilation: SB0.4, spontaneous breathing at FiO_2 of 0.4; SB1, spontaneous breathing at FiO_2 of 1; VCM0.4, volume-controlled mechanical ventilation at FiO_2 of 0.4 without PEEP; VCM0.4 PEEP, volume-controlled mechanical ventilation at FiO_2 of 0.4 with 5 cmH_2O of PEEP; VCM1, volume-controlled mechanical ventilation at FiO_2 of 1 without PEEP; VCM1 PEEP, volume-controlled mechanical ventilation at FiO_2 of 1 with 5 cmH_2O of PEEP. FiO_2, Fraction of inspired Oxygen; PEEP, Positive End-Expiratory Pressure).

Table 1
Data about age, body weight and Body Condition Score (BCS) reported as mean ± SD (standard deviation) of dogs assigned to the Normoxemic and Hypoxemic groups at POST (10 min after extubation).

	Normoxemic (mean ± SD)	Hypoxemic (mean ± SD)
n	431 (72%)	169 (28%)
Age (months)	71 ± 48	68.68 ± 46.77
Body weight (Kg)	20.4 ± 13.2	23.35 ± 16.29
BCS (1–5)	3 ± 0.6	3.64 ± 0.75

SD, standard deviation; BCS, Body Condition Score.

Table 2
Mean SpO_2 values of the Normoxemic and Hypoxemic groups registered at each time-point of the study (INTUB, EXT, POST). *P* values showed a statistically significant difference between SpO_2 values of the two groups at each time-point.

	Normoxemic(n=431) (95% CI)	Hypoxemic (n=169) (95% CI)	*P*
SpO_2 INTUB	97.2241 (97.07–97.38)	92.7091 (92.18–93.24)	0.002
SpO_2 EXT	96.7034 (96.55–96.86)	91.7725 (91.28–92.26)	0.001
SpO_2 POST	97.2181 (97.09–97.35)	91.8876 (91.49–92.29)	0.002

95% CI, 95% confidence interval; SpO2 INTUB, values recorded after disconnection from the breathing circuit when dogs were still intubated; SpO2 EXT, values recorded 5 min after extubation; SpO2 POST, values recorded 10 min after extubation (5 min after EXT time-point).

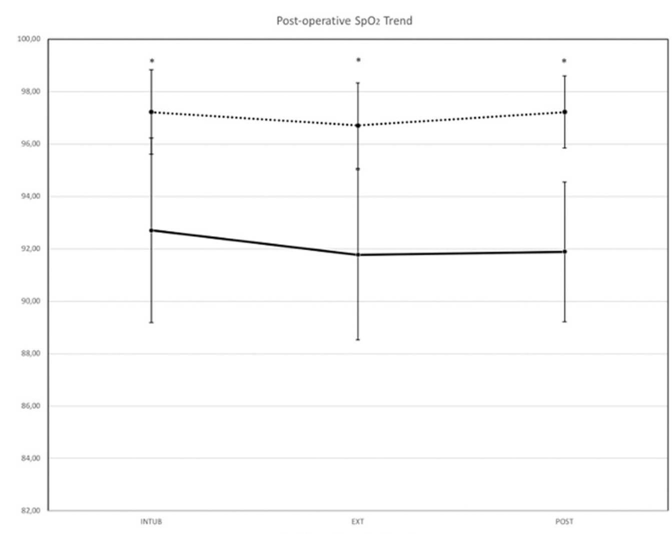

Fig. 3. SpO_2 trends of both Normoxemic and Hypoxemic groups. (*) Differences between SpO_2 values among groups resulted statistically significative at each time-point: INTUB (P =0.002), EXT (P =0.001), POST (P =0.002). SpO_2 trend of the Hypoxemic group did not showed any improvement over time. (INTUB, after disconnection from the breathing circuit when dogs were still intubated; EXT, 5 min after extubation; POST, 10 min after extubation).

or castration presented TPH, which resulted to be associated with the use of hydromorphone in their protocol.

Firulete et al. (2018) observed a 50% incidence of TPH in dogs recovering from general anaesthesia, while Stabile et al. (2021) reported a higher incidence of 62%, using pulse oximetry and applying our same SpO_2 cutoff. However, it is important to note that the previous studies differ from the present study in terms of sample size and lack of consideration for recumbency, FiO_2, BCS, and respiratory setting.

Several risk factors contribute to the occurrence of TPH. Among them, recumbency, especially in the dorsal position, was found to be a significant risk factor for hypoxemia. Our findings are consistent with previous experimental studies in dogs under general anesthesia, which have shown that oxygenation efficiency is lower in the supine position than in the prone position due to an increased ventilation-perfusion mismatch (Beck et al., 1992). A clinical study in conscious dogs in an intensive care unit found that dogs, regardless of the presence of respiratory disease, had higher PaO_2 values and lower alveolar-arterial oxygen difference when placed in sternal recumbency than in lateral recumbency (McMillan et al., 2009). In our study, in agreement with Beck et al. (1992), dorsal recumbency was associated with a higher incidence of TPH; this may be due to the pressure of abdominal viscera on the diaphragm in this position, which, combined with muscle relaxation due to general anesthesia, causes impaired ventilation. This can result in a ventilation/perfusion mismatch and atelectasis, leading to hypoxemia in the recovery period. Thus, to improve pulmonary oxygen uptake, as demonstrated by McMillan et al. (2009), all dogs were kept in the sternal position during recovery.

Table 3
Factors associated with transient postoperative hypoxemia (TPH) among dogs undergoing general anesthesia.

Risk factors	Odds ratio (95% CI)	*P*
BCS > 3 (out of 5)	5.8084 (3.9238–8.5983)	< 0.0001
Dorsal recumbency	1.9285 (1.334–2.788)	= 0.0005
FiO_2 1	3.7927 (2.4479–5.8762)	< 0.0001
no PEEP	1.7749 (1.1828–2.6636)	< 0.0056

95% CI, 95% confidence interval; BCS, Body Condition Score; FiO2, Fraction of inspired Oxygen; no PEEP, mechanical ventilation without the application of any Positive End-Expiratory Pressure

Another important risk factor for TPH development was a BCS > 3. Overweight and obesity are patient-specific risk factors that affect respiratory function. Such dogs typically have a decreased functional residual capacity and tidal volume, with an increased respiratory rate compared to fit dogs (Bach et al. 2007; Love and Cline, 2015). This condition can also lead to impaired respiratory function during sedation (Mosing et al. 2013). Araos et al. (2021), in a CT evaluation of the lungs of obese dogs, found that they have extensive hypoareated areas in the caudo-dorsal region of the lungs. In fact, body fat percentage is positively correlated with lung, chest wall, and airway elastance and negatively correlated with functional residual capacity (Araos et al., 2021). Furthermore, the PaO_2/FiO_2 ratio has been shown to decrease with increasing age and body mass index (BMI) in overweight human patients. Poor oxygenation in these subjects is due to shunting (primarily caused by atelectasis) and alveolar regions with a low ventilation/perfusion ratio (Hedenstierna et al., 2019).

The occurrence of hypoxemia may also depend on the type of ventilation setting (mechanical or spontaneous), the oxygen concentration delivered during anesthesia, the use of PEEP, and the development of atelectasis during the procedure (Staffieri et al., 2007; De Monte et al., 2013). This study found a significant association between 100% oxygen administration during general anesthesia and a higher incidence of TPH. High FiO_2 concentrations have a dual effect in terms of hypoxemia: to mask hypoxemia and to promote atelectasis. High oxygen percentages correspond to the flat part of the hemoglobin dissociation curve, where hyperoxia can hide the actual presence of a gas exchange problem. This can make saturation values appear to be good, even when there is an underlying issue. Furthermore, administering 100% oxygen can cause alveolar collapse due to the highly diffusible nature of oxygen molecules. In contrast, administering a lower percentage of oxygen by mixing it with medical air can prevent alveolar collapse due to the gas (nitrogen in medical air) being less diffusible and remaining in the alveolus for longer. Staffieri et al. (2007) performed a CT (computed tomography) evaluation of lung aeration in dogs under general anesthesia during mechanical ventilation at two different FiO_2s: 0.4 and 1. This study showed that maintaining anesthesia with FiO_2 of 0.4 can provide better lung aeration and gas exchange compared to using pure oxygen (FiO_2 =1), so this is a way to prevent alveolar atelectasis (Staffieri et al., 2007). Our study is in accordance with this finding, as FiO_2 1 was found to be significantly associated with TPH. In contrast, Martin-Flores et al. (2020) found no benefit for postoperative oxygenation in dogs under general anesthesia with a FiO_2 of 0.4, due to a higher incidence of hypoxemia compared to dogs with an intraoperative $FiO_2 >$ 0.9. (Martin-Flores et al., 2020). Although the dogs in this study were also subjected to intermittent positive pressure ventilation, it is important to note that there were several differences in the conditions compared to the study conducted by Flores et al. Specifically, the ventilation mode used in their study was solely volume-controlled IPPV without PEEP. In our study, we tested various respiratory settings, including spontaneous breathing and the use of positive end-expiratory pressure (PEEP). We found a higher incidence of TPH in all settings when using high FiO_2. In the previous study, the number of enrolled cases was limited to 20, all of which were in dorsal recumbency, which, based on our data, was found to be the least favorable position. Furthermore, three cases with high FiO_2 did not complete the study. Martin-Flores et al. (2020) analyzed blood gases at fixed intervals during recovery. Although this methodology is considered the gold standard for gas exchange assessment, it is limited by its point-in-time nature. This may have resulted in the loss of short-lived episodes of TPH.

This study also found that the absence of 5 cmH_2O of PEEP during mechanical ventilation was a risk factor associated with an increased incidence of TPH. During general anesthesia, airway closure and alveolar atelectasis can be prevented by applying PEEP, which counteracts atelectasis, improves V/Q ratio, and increases airway volume (Hedenstierna et al., 2019). It has been reported in the literature that PEEP can be used to re-expand collapsed alveoli to improve dynamic lung compliance, lung aeration and gas exchange, either in combination with a recruitment maneuver or alone. (Staffieri et al., 2010; Canfràn et al., 2012). Martin-Flores et al. (2022) evaluated the effects of three different volume-controlled ventilation modes ($FiO_2$1 with PEEP, FiO_2 1 without PEEP, and FiO_2 0.4 with PEEP) on oxygenation in dogs by analyzing arterial blood samples up to 4 h postoperatively. In agreement with previous studies from our group (De Monte et al., 2013), they found that the use of FiO_2 of 0.4 and PEEP reduced the lung shunt fraction (F-shunt) during anesthesia. On the contrary, their results regarding the recovery period contrast with ours. They did not find any difference in postoperative oxygenation among the three groups of dogs, instead in this study the VCM group with FiO_2 of 0.4 and PEEP had a lower incidence of hypoxemia than the mechanically ventilated group with FiO_2 of 1 and PEEP. More specifically, in our study, by comparing the incidence of TPH among the six different ventilation groups, it was found that administering a FiO_2 of 0.4, both in SB or in VCM, with or without PEEP, reduced the occurrence of hypoxemia in the recovery period. These results were also confirmed by comparing the SB0.4, VCM0.4 and VCM0.4PEEP groups, which showed no significance on the occurrence of TPH. Thus, there is a discordance in the results of the postoperative period between the two studies; however, the number of dogs in the Martin-Flores study was smaller (n=30) than ours (n=600), and the authors stated that some arterial catheters failed during postoperative monitoring, further reducing the sample size.

De Monte et al. (2013) found that after an alveolar recruitment maneuver, both the use of PEEP (5 cmH_2O) and low FiO_2 (0.4) were effective in reducing anesthesia-induced atelectasis. This statement is consistent with our study; both PEEP and FiO_2=0.4 may have prevented alveolar collapse during anesthesia, resulting in improved oxygenation during recovery.

The clinical nature of the study can be considered a limitation that did not allow a more standardization of the groups also in terms of drugs, procedures and body conformation. All these aspects should be clarified in future studies. The MASIMO Rainbow 87 pulse oximeter was used to measure SpO_2. The use of pulse oximeters other than those that have been demonstrated to be equivalent may result in inaccurate results that could not align with the findings of this study. The use of 80 mmHg as a cut-off to identify hypoxemia was based on recent literature investigating the incidence of this condition in clinical cases (Campbell et al., 2003; Stabile et al., 2021). It should also be considered that the intention of this study was to identify an early sign of deterioration in oxygenation for immediate case management and prevention of major complications. The classical definition of hypoxemia of less than 60 mmHg PaO_2 refers more to the objective identification of a state of low arterial oxygen tension, which identifies a specific pathological condition. The higher number of cases with a FiO_2 of 1 in both SB and VCM could have created a bias in the impact of these modes of ventilation on our results. Therefore, these data should be taken with caution. We have not analyzed in our data the influence that brachycephalic conformation and upper airway surgery may have had on our results. The number of brachycephalic dogs in the hypoxemic group was only 10 and the number of upper airways surgeries was only 3. Thus, we thought that our caseload regarding brachycephalic dogs and surgeries was not representative of a normal population and for this reason we decided to not include this analysis in our study.

Conclusions

This study demonstrated that TPH is a significant event in clinical practice, affecting up to 28% (95%CI: 24%-32%) of healthy dogs undergoing general anesthesia. Another important finding relates to pulse oximetry, which showed a reliable method for early detection of hypoxemia identified by $SpO_2 < 95\%$ while breathing room air. This could allow appropriate management of dogs in the post-operative period with non-invasive respiratory support if required. Furthermore, the identification of risk factors for TPH could be of great benefit in veterinary clinical practice: although it is not possible to modify BCS and recumbency (which depend on the animal's condition and surgical needs), it might be possible to operate on the ventilatory setting. In fact, the use of low FiO_2 and 5 cmH_2O PEEP could reduce the incidence of TPH and should be preferred, especially when the other two risk factors are present.

CRediT authorship contribution statement

C. Piemontese: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **M. Stabile:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **C. Di Bella:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **A. Scardia:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **C. Vicenti:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **C. Acquafredda**: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **A. Crovace:** Writing – review & editing, Writing – original draft, Methodology Investigation. **L. Lacitignola:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **F. Staffieri:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tvjl.2024.106135.

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