

1 **Title:**

2 Impact of flow and temperature on non-dyspnoeic dogs' tolerance undergoing high-flow oxygen  
3 therapy

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7 **Abstract**

8 **Objectives:** To prospectively describe the impact of gas flow rate and temperature on dog's  
9 tolerance of high-flow nasal oxygen therapy (HFNOT) during recovery from anaesthesia,  
10 hypothesizing that higher flow rates and temperatures will decrease tolerance.

11 **Methods:** Twelve non-dyspnoeic client-owned dogs recovering from general anaesthesia  
12 were included in this study. After extubation, a nasal cannula was positioned and HFNOT was  
13 initiated. Two flow rates (two or four time the theoretical minute ventilation: HF2 and HF4),  
14 each of them combined with two temperatures (31 and 37°C: T31 and T37), were randomly  
15 applied (four conditions *per* dog). For each condition, cardiovascular and respiratory  
16 parameters (heart rate, respiratory rate, arterial systolic blood pressure, and pulse oximeter  
17 oxygen saturation), sedation score, and tolerance score were recorded at initiation (T<sub>0</sub>) and  
18 after 10 minutes of accommodation (T<sub>10</sub>).

19 **Results:** Sedation scores were not significantly different between the four conditions.  
20 Cardiovascular and respiratory parameters were not significantly different between any  
21 condition at both T<sub>0</sub> and T<sub>10</sub>. Tolerance scores were good and not significantly different  
22 between any flow rate or temperature (HF2-T31: 4 (2-4), HF4-T31: 4 (2-4), HF2-T37: 4 (2-4),  
23 HF4-T37: 4 (1-4)).

24 **Clinical significance:** The gas flow rates and temperatures studied have no impact on  
25 tolerance during the recovery period of non-dyspnoeic dogs, and HFNC is well tolerated.  
26 Further studies are required to confirm these results in dyspnoeic dogs.

27

28 **Keywords:** Hypoxaemia, High-flow oxygen therapy, Dyspnoea, Mechanical Ventilation,  
29 Nasal cannula

30

31

## 32 **Introduction**

33 Oxygen supplementation is often the first line, lifesaving, treatment for hypoxaemic dogs. In  
34 veterinary medicine, oxygen therapy is mostly delivered by non-invasive techniques such as  
35 flow-by, nasal prongs or oxygen cages. These methods are known as conventional oxygen  
36 therapy (COT). They deliver oxygen as a cold dry gas, and can achieve variable fractions of  
37 inspired oxygen (FIO<sub>2</sub>) ranging from 30 to 70% (Guenther 2018). Delivery of cold gas could  
38 cause patient discomfort at higher rates, desiccation of the nasal mucosa, airway constriction,  
39 impairment of the mucociliary function, and increased risk of infection (Dunphy *et al.* 2002;  
40 Kallstrom 2002; Kopelman & Holbert 2003; Kilgour *et al.* 2004).

41 Since the early 2000s, an advanced oxygen delivery method, called high flow nasal oxygen  
42 therapy (HFNOT) has received growing attention in human medicine (Guenther 2018). High-  
43 flow nasal oxygen therapy uses an air-oxygen blender connected to a flow meter, an active  
44 humidifier and heater, a warmed breathing circuit, and a specific bilateral nasal cannula  
45 (Pouzot-Nevoret *et al.* 2019). Respiratory support delivered with HFNOT machines is  
46 achieved by administration of humidified air/oxygen blends, using high flow rates up to 60  
47 L/min, adjustable fraction of inspired oxygen (FIO<sub>2</sub>) from 21 to 100%, and precise  
48 temperature, between 31 and 37°C (Mauri *et al.* 2018). Heated and moistened air inspired  
49 through the high flow nasal cannula (HFNC) improves comfort and compliance of the  
50 dyspnoeic human patient (Stefan *et al.* 2018).

51 High-flow nasal oxygen therapy recommendations settings for paediatric patients are a flow  
52 rate from 1 to 2 L/kg/min and a temperature of 34°C (Milési *et al.* 2018; Yurtseven *et al.*  
53 2019). In adult patients, clinicians use flow rates from 50 to 60 L/min, independently of the  
54 weight, considering that lung capacities are almost equivalent from one individual to another.  
55 Several studies have suggested that an increase in the flow rate may decrease the work of  
56 breathing in patients with acute respiratory distress, although this may also impact the  
57 patient's comfort (Milési *et al.* 2013; Weiler *et al.* 2017). Recently, the influence of flow rate

58 and temperature on patient comfort using HFNOT was evaluated (Mauri *et al.* 2018). In this  
59 study, adult dyspnoeic patients were more comfortable with the temperature set at 31°C than  
60 37°C, with the HFNOT set at both 30 and 60 L/min. However, in the subgroup of patients  
61 with  $\text{FIO}_2 \geq 45\%$ , both lower temperature (31°C) and higher flow rate (60 L/min) led to  
62 higher comfort, highlighting the importance of flow rate and temperature on patient's  
63 comfort.

64

65 In veterinary medicine, feasibility, tolerance and safety of HFNOT have already been proven  
66 in healthy and hypoxaemic dogs (Daly *et al.* 2016; Keir *et al.* 2016; Daly *et al.* 2017; Pouzot-  
67 Nevoret *et al.* 2019; Jagodich *et al.* 2020). Its efficacy in increasing the arterial partial  
68 pressure of oxygen ( $\text{PaO}_2$ ) compared to COT has also been demonstrated (Daly *et al.* 2016;  
69 Keir *et al.* 2016; Jagodich *et al.* 2019; Pouzot-Nevoret *et al.* 2019; Jagodich *et al.* 2020).  
70 Described flow rates in dogs range from 0.2 to 2.5 L/kg/min (Jagodich *et al.* 2019; Pouzot-  
71 Nevoret *et al.* 2019; Jagodich *et al.* 2020) or predefined flow rates of 20 to 30 L/min (Daly *et*  
72 *al.* 2017) all derived from human medicine (Kernick & Magarey 2010; Mayfield *et al.* 2014;  
73 Mauri *et al.* 2018; Yurtseven *et al.* 2019). However, a flow rate above 2 L/kg/min is not well  
74 tolerated in healthy dogs (Jagodich *et al.* 2019). A search on the Pubmed Database with the  
75 following keywords: “High flow oxygen” and “dog” was performed on 19th August 2020 and  
76 revealed no study reporting the impact of temperature on dogs' tolerance of HFNOT.

77 The objective of this study was to evaluate the impact of the combination of two different  
78 flow rates and temperatures on the tolerance of HFNOT in healthy dogs. We hypothesized  
79 that higher flow rates and temperature might reduce tolerance in healthy dogs.

80

## 81 **Material and methods**

### 82 ***Ethical statement***

83 This study protocol was approved by the VetAgro Sup Ethics committee (number 1849).

84

85 ***Study design and inclusion criteria***

86 Written owner informed consent was obtained during the pre-surgery consultation. Client-  
87 owned dogs undergoing general anaesthesia for surgery or diagnostic procedures were  
88 enrolled in this prospective blinded randomized crossover study, from January to April 2019.  
89 All dogs were deemed healthy prior to the study on the basis of a complete physical  
90 examination.

91 At the end of the procedure, all dogs were transferred into the emergency and critical care unit  
92 (SIAMU, VetAgro Sup) for experimental convenience and were extubated when the  
93 swallowing reflex was recovered. In all dogs, type of procedure, duration of anaesthesia (from  
94 induction to discontinuation of isoflurane administration) and extubation time were recorded.

95 The person assessing patient tolerance scores was blinded to the machine settings which were  
96 determined through random order draws and set by another person.

97

98 ***Exclusion criteria***

99 Exclusion criteria at enrolment included dogs below 9.5 kg. This exclusion criteria was due to  
100 paediatric manufacture settings of the HFNOT equipment, as paediatric mode of the Airvo™  
101 2 System is preset to 34°C and thus, did not meet the study model. Other exclusion criteria at  
102 enrolment were abnormal findings at physical examination, aggressive or agitated dogs.

103

104 ***High-flow nasal cannula settings***

105 The HFNOT was provided with the Airvo™ 2 System in adult mode (Fisher & Paykel  
106 Airvo™ 2 System, Fisher & Paykel Healthcare), using soft silicone bilateral nasal cannula  
107 (Optiflow™+ nasal high flow canula, Fisher & Paykel Healthcare) as the interface to the  
108 patient. Nasal cannulas are available in 7 sizes (4 paediatrics and 3 adults). Depending on the

109 dog size and morphology, a cannula was chosen as to occlude a maximum of 50% of the  
110 opening of the nares (Figure 1). The adult mode allows adjustable flow rates from 10 to 60  
111 L/min, with a possible increase by steps of 1L from 10 to 25L, and by steps of 5L from 25 to  
112 60L, and with adjustable temperature of 31, 34 or 37°C. The FIO<sub>2</sub> was maintained at 21% as  
113 all study dogs were deemed healthy.

114

### 115 ***Experimental procedure***

116 In order to assure the delivery of the predetermined FIO<sub>2</sub>, the flow rate of HFNOT should be  
117 set above the minute ventilation (MV) of the dog (MV = respiratory rate (bpm) x tidal volume  
118 (mL/kg)) (Helviz & Einav 2018, Pouzot-Nevoret *et al.* 2019). For each dog, theoretical MV  
119 was calculated with a standard respiratory rate of 20 bpm and a tidal volume of 20 mL/kg  
120 considering these dogs were healthy (Testa *et al.* 2014; Helviz & Einav 2018; Milési *et al.*  
121 2018; Jagodich *et al.* 2019). The MV was then multiplied by 2 (High Flow x 2: HF2) or by 4  
122 (HF4), depending on the tested flow rate. When calculated flow rate was under 10 L/min  
123 (minimum limit of the Airvo<sup>TM</sup> 2 System), flow rates of 10 L/min (HF2) and 20 L/min (HF4)  
124 were selected. Each dog underwent, in a random order, four 10-minutes steps:

125 A. Flow rate MV x 2 and temperature 31°C (HF2-T31)

126 B. Flow rate MV x 4 and temperature 31°C (HF4-T31)

127 C. Flow rate MV x 2 and temperature 37°C (HF2-T37)

128 D. Flow rate MV x 4 and temperature 37°C (HF4-T37)

129 Transition between each step was done automatically and gradually by the Airvo<sup>TM</sup> 2 System,  
130 and equilibration at each flow rate and temperature couple occurred for 10 minutes prior to  
131 each subsequent recording.

132

### 133 ***Monitoring***

134 Three-lead electrocardiogram, pulse oximetry (SpO<sub>2</sub>), and non-invasive systolic arterial blood  
135 pressure (SBP) were monitored during the whole study protocol (Dynascope DS-7100,  
136 Fukuda Denshi) (Figure 1).

137

### 138 *Data collection*

139 Immediately after extubation, baseline parameters (heart rate (HR), respiratory rate (RR),  
140 SBP, SpO<sub>2</sub> and temperature) were recorded by the same operator (CH). Then, the nasal  
141 cannula attachment was gently tightened behind the neck. Sedation score (SS, Table S1),  
142 tolerance score (TS, Table 1) and vital parameters (HR, RR, SBP and SpO<sub>2</sub>) were recorded,  
143 before the beginning of HFNOT (PreHF). The tubing of the nasal cannula was connected to  
144 the Airvo™ 2 System circuit and the first phase of the protocol was started. For each step,  
145 flow rate and temperature were determined by randomized drawing and set by a second  
146 operator (AF), different from the one assessing TS and SS. For each separate setting, HR, RR,  
147 SBP and SpO<sub>2</sub> were recorded at the beginning (T<sub>0</sub>) and at the end (T<sub>10</sub>) of the ten minutes  
148 (Figure 2).

149

### 150 *Scoring systems*

151 Dogs were all recovering from general anaesthesia. No additional anaesthetic was used. Given  
152 that sedation could influence our results, SS was evaluated at each step of the protocol. The  
153 SS was assessed by an experienced observer (CH) using a visual sedation scale validated by  
154 Wagner *et al.* (2017), with a score of 0 indicating no sedation, and 21 indicating deep sedation  
155 (Table S1). The SS used is based on the dog's mentation, palpebral reflex, ocular position,  
156 jaw and tongue tone, response to clapping, posture and tolerance of lateral recumbency.  
157 Sedation was evaluated during PreHF, at the initiation of each setting (T<sub>0</sub>) and after the 10-  
158 minutes accommodation period (T<sub>10</sub>) for each setting.

159 The TS to HFNOT was blindly assessed by the same experienced observer, using a simple  
160 descriptive scale (Table 1; Pouzot-Nevoret *et al.* 2019). This scale ranges from 1 (least  
161 tolerant) to 4 (most tolerant). For the specific aim of the study, if a TS of 1 was recorded,  
162 there was an immediate change to the next flow rate-temperature setting. If a TS of 1 was  
163 recorded a second time, the dog was excluded from the study.

164

### 165 *Outcome*

166 Primary outcome of the study was the evolution of TS under the different HFNOT conditions.  
167 Evolution of vital parameters (HR, RR, SBP, SpO<sub>2</sub>) under the different HFNOT conditions  
168 was the secondary outcome.

169

### 170 *Statistical analysis*

171 Prior to study enrolment, a power analysis was performed to determine minimum sample size  
172 to detect a clinically meaningful difference of 2 points TS between HF2 at a temperature of  
173 31°C and HF4 at a temperature of 37°C. Using an effect size of 0.80 (moderate effect) and  
174 significance level ( $\alpha$ ) of 0.05, the inclusion of 4 dogs was estimated to find a significant  
175 effect.

176 Statistical analyses were carried out with JMP version 13.1 (SAS Institute) and envelop  
177 number pull was used as randomization method. Data were tested for normal distribution with  
178 the Shapiro-Wilk test. For all collected data, the mean  $\pm$  standard deviation (parametric data)  
179 or the median and range (nonparametric data) were calculated. Nonparametric data (duration  
180 of anaesthesia, RR and TS) were tested with a Friedman test. Parametric data (HR, SBP, SpO<sub>2</sub>  
181 and SS) were compared with a one-way ANOVA. *P* values lower than 0.05 were considered  
182 statistically significant.

183

184 **Results**

185 *Animals*

186 Sixteen dogs were initially eligible for the protocol (Figure 2). Two of them had to be  
187 excluded at enrolment: one because of aggressiveness and one because the owner declined to  
188 participate.

189 Fourteen dogs were therefore enrolled in the study. Two of them had to be excluded because  
190 of a TS of 1 in two successive HFNOT settings, associated with a dysphoric anaesthesia  
191 recovery. They were very agitated before placement of the cannula and extra sedation would  
192 have been necessary to make them tolerate HFNC.

193 Twelve dogs were in the final study enrolment: 5 females (2 intact and 3 spayed) and 7 males  
194 (1 intact and 6 neutered). Breeds included 2 Mixed Breeds, 2 Labradors retrievers, 1 German  
195 shepherd, 1 Dogo Argentino, 1 Beagle, 1 Bernese Mountain Dog, 1 Chow-Chow, 1 American  
196 Bully, 1 Brittany and 1 Braque Français. The mean age and mean body weight were  $5.8 \pm 4.0$   
197 years and  $29.3 \pm 11.8$  kg, respectively. Type of procedures included 4 orthopaedic surgeries  
198 (2 tibial plate levelling osteotomies, 1 pelvic limb amputation and 1 removal of osteosynthesis  
199 implant), 1 ventral slot, 1 perineal hernia repair, 1 mass removal, 2 castrations, 1 ovariectomy,  
200 1 pericardiocentesis and 1 CT scan. Median duration of aesthesia was 137.5 minutes (40-400  
201 minutes).

202 Eleven dogs completed all phases of the study. One dog did not tolerate HF4-T37, leading to  
203 a change to the next step of the protocol and achievement of three conditions over four.

204 Median flow rate was 24 L/min (10-35 L/min) for the HF2 condition (0.8 L/kg/min), and 47.5  
205 L/min (20-60 L/min) for the HF4 condition (1.6 L/kg/min).

206

207 *Sedation status*

208 Mean  $\pm$  SD sedation scores were  $11 \pm 6$  for PreHF,  $6 \pm 3$  for HF2-T31,  $7 \pm 4$  for HF4-T31, 8  
209  $\pm 5$  for HF2-T37 and  $8 \pm 4$  for HF4-T37 (Figure 3).

210 Global mean  $\pm$  SD sedation score of the HFNOT conditions was  $8 \pm 4$  and there was no  
211 significant difference between any of the HFNOT conditions ( $p = 0.711$ ).

212

### 213 *Vital parameters*

214 Median (range) temperature at inclusion was  $37.8^{\circ}\text{C}$  ( $36.4 - 38.4^{\circ}\text{C}$ ).

215 PreHF vital parameters were: HR:  $114 \pm 38.8$  bpm; RR: 40 (16-250) bpm; SBP:  $102.8 \pm 27.2$   
216 mm Hg and SpO<sub>2</sub>:  $95 \pm 3\%$ .

217 There was no effect of flow rate or temperature on vital parameters (HR, RR, SBP, SpO<sub>2</sub>) at  
218 T<sub>0</sub>, and T<sub>10</sub> (Figure 4 and Table 2).

219

### 220 *Effects of flow rate and temperature on tolerance*

221 PreHF TS was 4 (2-4). Tolerance score was not significantly different between any of the  
222 HFNOT conditions (Table 3).

223

### 224 **Discussion**

225 Based on the literature search performed, this is the first veterinary study evaluating the  
226 impact of a combination of different flow rates and temperatures on healthy dogs' tolerance of  
227 HFNOT. The study design was based on Mauri et al. (2018)'s clinical trial investigating  
228 dyspnoeic human patients. Their study revealed improved patient comfort with the  
229 administration of lower gas temperatures. This comparison had never been performed in dogs.

230 In our study, we were not able to show any difference in the dogs' tolerance between HFNOT  
231 at  $31^{\circ}\text{C}$  or  $37^{\circ}\text{C}$ , by using a tolerance scale. However, all median scores were high, whatever  
232 the setting, confirming the good tolerance of this oxygen therapy technique in dogs. Only one  
233 dog did not tolerate the first step of the protocol (HF4-T37) but tolerated every other step. A

234 dysphoric waking could have explained this intolerance. Association of highest flow rate  
235 and temperature could have also led to this intolerance. Two dogs had to be excluded from the  
236 study because of nasal cannula intolerance for 2 conditions. However, these dogs were highly  
237 agitated since the beginning of the recovery period and would have needed extra sedation to  
238 tolerate nasal cannula. Sedation is often used in dyspnoeic dogs undergoing oxygen therapy.  
239 As this study was conducted during the anaesthetic recovery period and sedation score was  
240 part on the initial assessment, no additional interventions were administered.

241 Absence of difference between conditions could be related to the choice of the tolerance  
242 score. This score has never been validated but was described in the clinical trial of Staffieri *et*  
243 *al.* (2014), in which the objectives were comparable to ours. Between the time our study was  
244 designed and the end of the clinical trial, Jagodich *et al.* (2019) published a study using  
245 another tolerance score, based on the dog's number of attempts to remove the cannula. This  
246 score might be more sensitive as long as they were able to highlight an alteration of tolerance  
247 with higher flow rates. This scoring system could be used in future studies. Finally, the dogs  
248 in this study were not in respiratory distress and therefore did not need HFNOT. Further  
249 studies assessing tolerance of differing gas temperatures in dyspnoeic dogs would be useful.

250 Given the infancy of HFNOT in veterinary medicine, there is no consensus as to ideal flow  
251 rate settings. In human medicine, flow rates of 2-8 L/min (~0.4-3.2 L/kg/min) in neonates and  
252 15-60 L/min (~0.2-1 L/kg/min) in adults are generally used (Kernick & Magarey 2010;  
253 Mayfield *et al.* 2014; Mauri *et al.* 2018; Yurtseven *et al.* 2019; Koga *et al.* 2020). The first  
254 studies published in dogs used flow rates without considering a dog's bodyweight or  
255 respiratory rate (20 L/min and 30 L/min, (Daly *et al.* 2017)). In order to avoid recruitment of  
256 air or oxygen from the surrounding air and assure the delivery of the predetermined FIO<sub>2</sub>, the  
257 flow rate should be fixed above the MV of the patient (Helviz & Einav 2018). In our study,  
258 we have chosen higher flow rates and attempted to determine a limit to tolerance. The

259 calculated flow rates were equivalent to 0.8 and 1.6 L/kg/min in this study. In the recent study  
260 of Jagodich *et al.* (2019), tolerance score appears to be worsened only above 2 L/kg/min. This  
261 study, not available at the time of protocol conception, could explain our results showing no  
262 significant difference in tolerance for our flow rates range. However, the lower flow rates  
263 used in this study were based on previous data showing they could be effective in increasing  
264 PaO<sub>2</sub> in dyspnoeic dogs (Pouzot-Nevoret *et al.* 2019).

265 This study was conducted in non-dyspnoeic dogs recovering from anaesthesia, so sedation  
266 could have influenced TS. Randomization of machine settings order, median sedation score in  
267 the lower range and absence of difference of sedation scores between all conditions suggest  
268 that sedation had a minor influence, at most, on our tolerance evaluation. However, further  
269 studies in non-sedated dogs would be required.

270 The 10-minutes period for each setting was chosen based on our clinical experience and  
271 previous studies in dyspnoeic dogs. While using HFNOT in dyspnoeic dogs, we noticed that  
272 they were generally either compliant from the beginning or never compliant to HFNOT.  
273 Tolerance scores stayed the same during the 10-minutes period, confirming this observation.  
274 This duration was decided in the light of the various recent studies. In similar protocols,  
275 Mauri *et al.* (2018) in human medicine, and Staffieri *et al.* (2014) in veterinary medicine, used  
276 20-minutes steps, whereas Jagodich *et al.* (2019) used 8-minutes periods of time. However, a  
277 longer time frame of assessment could have changed the tolerance, especially considering the  
278 effect of gas temperature on body temperature. Indeed, Gilardi *et al.* (2020) suggested in a  
279 preliminary report that median time of rewarming was shorter in hypothermic non-dyspnoeic  
280 patients treated with HFNOT, highlighting the influence of heated air administration on body  
281 temperature in people. Tolerance evaluation of different temperature in pyrexia or severely  
282 hypothermic dogs is indicated.

283 We experienced some technical constraints with the Airvo™ 2 System, especially the  
284 impossibility to use paediatric cannulas in our protocol. Indeed, they can be used only with  
285 the paediatric mode in which temperature cannot be changed. These cannulas have a different  
286 shape depending on whether they are adult or junior size. We had an excellent general  
287 tolerance to HFNOT in our study, using exclusively adult interfaces. Paediatric cannulas are  
288 described to be very comfortable, easier to place and with a better accommodation to the  
289 facial structure of dogs (Jagodich et al. 2019, Jagodich et al. 2020), suggesting the same  
290 results. Moreover, dog's normal rectal temperature is 38.5°C, and the Airvo™ 2 System  
291 temperature set up is optimal for human with a normal temperature of 37.5°C. Setting the  
292 temperature of the device at 38.5°C could have changed the tolerance. Although we only had  
293 access to the Airvo™ 2 System, other devices are available on the market. For example,  
294 Precision Flow® Plus system (Vapotherm® Precision Flow® Plus, Vapotherm® inc) can be  
295 adjusted by 1-degree intervals, at all flow rates, independently of the cannula size (paediatric  
296 or adult). Further studies would be interesting to determine if a precise regulation of the gas  
297 temperature influence dog's tolerance.

298 There are some limitations in this current study. First, the protocol included only dogs with no  
299 respiratory issues, recovering from general anaesthesia. Further studies are required to  
300 evaluate the degree of HFNOT tolerance in fully conscious dogs and for longer periods.  
301 Moreover, the efficacy of this system in different pathological conditions should be supported  
302 by further studies. Second, the impact of flow rates and temperatures on PaO<sub>2</sub> has not been  
303 evaluated in this protocol. Daly et al. (2017) showed that HFNOT significantly improved  
304 PaO<sub>2</sub> versus COT but there was no significant difference in PaO<sub>2</sub> between rates of 20 L/min  
305 and 30 L/min. Jagodich *et al.* (2019) highlighted that HFNOT significantly improved PaO<sub>2</sub>  
306 compared to baseline and PaO<sub>2</sub> was significantly higher at rate of 1 L/kg/min or more,  
307 compared to 0.4 L/kg/min. The potential impact of temperature on oxygenation has never

308 been investigated and further studies will be necessary. Third, clinical complications  
309 associated with HFNOT, like gastric dilation, have not been evaluated in our study. However,  
310 none of our twelve dogs showed any clinical abdominal distension or discomfort. Finally,  
311 non-cooperative or aggressive dogs could not be included in the study because frequent head  
312 manipulations were necessary which could represent a bias.

313

#### 314 **Conclusion**

315 This study is the first in veterinary medicine to evaluate the combined impact of flow rate and  
316 temperature on non-dyspnoeic dogs' tolerance of HFNOT and shows no significant difference  
317 between 31 and 37°C. It also confirms the high degree of tolerance of HFNOT in healthy  
318 dogs of varied body sizes and gives practical information on its use in this species. No clear  
319 recommendation for flow rate and temperature settings could be determined based on our  
320 results, and user should combine available data in veterinary literature with evaluation of  
321 tolerance and efficacy on their patients to guide settings of non-invasive respiratory support  
322 by HFNOT.

323

324 Conflict of Interest statement: The Authors declare no conflict of interest.

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## Figure legends

Figure 1: High-flow nasal oxygen therapy (Fisher-Paykel Airvo™ 2 System, Fisher & Paykel Healthcare) on a dog with full cardiorespiratory monitoring.

Figure 2: Experimental protocol. Conditions 1 to 4 are applied in a randomized order.

SS: Sedation score, TS: Tolerance score, HR: Heart rate, RR: Respiratory rate, SBP: Systolic blood pressure, SpO<sub>2</sub>: Pulse oximetry.

Figure 3: Sedation scores during PreHF and the end (T<sub>10</sub>) of the 4 HFNOT conditions.

Figure 4: Mean values of heart rate (A), systolic blood pressure (C) and SpO<sub>2</sub> (D), and median values of respiratory rate (B) in the 12 dogs, at the initiation of each condition (T<sub>0</sub>) and after 10 minutes of accommodation (T<sub>10</sub>).

<b>SEDATION SCORE</b>		<b>Score</b>
<b>Spontaneous posture</b>	Standing	0
	Tired but standing	1
	Lying but able to rise	2
	Lying but difficulty rising	3
	Unable to rise	4
<b>Palpebral reflex</b>	Brisk	0
	Slow but with full corneal sweep	1
	Slow but with only partial corneal sweep	2
	Absent	3
<b>Eye position</b>	Central	0
	Rotated forwards/downwards but not obscured by third eyelid	1
	Rotated forwards/downwards and obscured by third eyelid	2
<b>Jaw and tongue relaxation</b>	Normal jaw tone, strong gag reflex	0
	Reduced tone, but still moderate gag reflex	1
	Much reduced tone, slight gag reflex	2
	Loss of jaw tone and no gag reflex	3
<b>Response to noise (handclap)</b>	Normal startle reaction (head turn towards noise/ cringe)	0
	Reduced startle reaction (reduced head turn/ minimal cringe)	1
	Minimal startle reaction	2
	Absent reaction	3
<b>Resistance when laid into lateral recumbency</b>	Much struggling, perhaps not allowing this position	0
	Some struggling, but allowing this position	1
	Minimal struggling/ permissive	2
	No struggling	3
<b>General appearance/attitude</b>	Excitable	0
	Awake and normal	1
	Tranquil	2
	Stuporous	3
	<b>Total /21</b>	

Table S1: Sedation score (Wagner *et al.* 2017).