

1 **Prospective pilot study for evaluation of High-flow Oxygen Therapy in**  
2 **dyspneic dogs: the HOT-DOG study**

3

4 C. Pouzot-Nevoret<sup>1,2</sup>, DV, PhD, Dipl ECVECC, L. Hocine<sup>1,2</sup>, **DV, MSc**, J. Nègre<sup>2,3</sup>, PT, I. Goy-  
5 Thollot<sup>1,2</sup>, DV, PhD, Dipl ECVECC, A. Barthélémy<sup>1,2</sup>, DV, PhD, E. Boselli<sup>2</sup>, MD, PhD, J.M.  
6 Bonnet<sup>2</sup>, DV, PhD, B. Allaouchiche<sup>2,3</sup>, MD, PhD

7

8 <sup>1</sup> Intensive Care Unit (SIAMU), Université de Lyon, VetAgro Sup, APCSe, F-69280, Marcy  
9 l'Etoile, France

10 <sup>2</sup> Université de Lyon, VetAgro Sup, APCSe, F-69280, Marcy l'Étoile, France

11 <sup>3</sup> Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Service de Réanimation, F-69310,  
12 Pierre-Bénite, France

13

14 **Corresponding author:** Céline Pouzot-Nevoret DVM, MS, PhD, Intensive Care Unit (SIAMU),

15 VetAgro Sup, Campus Vétérinaire de Lyon, 1 avenue Bourgelat, 69280 Marcy l'Étoile, France

16 Cell: +336 82 74 34 05

17 Email: [celine.pouzotnevoret@vetagro-sup.fr](mailto:celine.pouzotnevoret@vetagro-sup.fr)

18

19 No conflicts of interest have been declared.

20

21 **Keywords:** Hypoxemia, High-flow oxygen therapy, Dyspnoea, Mechanical Ventilation, Nasal  
22 cannula

23

24 **Acknowledgment**

25 The authors would like to thank Dr Mathieu Taroni for the realisation of the Figure 1.

26

## 27 **Abstract**

28 **Objectives:** To describe the use, effectiveness and tolerance of high-flow oxygen therapy in  
29 dyspneic dog.

30 **Methods:** Prospectively, dogs in acute respiratory distress admitted to the ICU between January  
31 and May 2018 that failed to respond to nasal oxygen therapy and medical stabilization after 30  
32 minutes were transitioned to high-flow oxygen therapy and included in the study. High-flow  
33 oxygen therapy, delivering an inspired oxygen fraction of 100%, was carried out using an  
34 air/oxygen blender, active humidifier, single heated tube, and specific nasal cannula. Respiratory  
35 rate (RR), pulse oxymetry (SpO<sub>2</sub>), heart rate (HR), and tolerance score were assessed every 15  
36 minutes from T<sub>0</sub> (under nasal oxygen) to 1 hour (T<sub>60</sub>), and PaO<sub>2</sub> and PaCO<sub>2</sub> at T<sub>0</sub> and T<sub>60</sub>.  
37 Complications were recorded for each dog.

38 **Results:** Eleven dogs were included. At T<sub>60</sub>, PaO<sub>2</sub>, flow rate, and SpO<sub>2</sub> were significantly greater  
39 than at T<sub>0</sub> (171 ±123 mmHg *vs* 73 ±24 mmHg; P=0.015; 18 ±12 L minute<sup>-1</sup> *vs* 3.2 ±2.0 L minute<sup>-1</sup>,  
40 P<0.01; 97.7 ±2.3% *vs* 91.6 ±7.2%, P=0.03, respectively). There was no significant difference in  
41 PaCO<sub>2</sub>, RR, HR between T<sub>0</sub> and T<sub>60</sub>. Tolerance score was excellent, and no complication  
42 occurred.

43 **Clinical significance:** This study established that high-flow oxygen therapy improves markers of  
44 oxygenation in dyspneic dogs and confirms that this technique deliver effective oxygen with  
45 comfort and minimal complications in this population.

46

47

## 48 **Introduction**

49 Supplemental oxygen administration is the first supportive measure provided to dyspneic  
50 dogs upon admission to an emergency facility. In veterinary medicine, oxygen therapy is mostly  
51 delivered by non-invasive techniques such as flow-by, nasal prongs, or oxygen cages. These  
52 methods are known as conventional oxygen therapy (COT) and can achieve variable fractions of  
53 inspired oxygen (FIO<sub>2</sub>) ranging from 21 to 70% (Sumner & Rozanski 2013). When patients  
54 remain hypoxemic despite COT, clinicians may choose among more advanced oxygen delivery  
55 methods. One option is mechanical ventilation, which however requires prolonged general  
56 anaesthesia, continuous advanced care and is associated with frequent complications, high costs,  
57 and, depending on the underlying disease, a guarded prognosis - often leading the owner to a  
58 decision of euthanasia (Hopper *et al.* 2007, Mueller 2007). In human medicine, non-invasive  
59 ventilation (NIV) is a popular method to avoid intubation. Continuous positive airway pressure  
60 (CPAP) is a NIV mode that has been validated in dogs (Briganti *et al.* 2010, Staffieri *et al.* 2014,  
61 Meira *et al.* 2018). Continuous positive airway pressure is effective to improve arterial partial  
62 pressure of oxygen (PaO<sub>2</sub>) in companion animals when used with devices such as masks or  
63 helmets (Briganti *et al.* 2010, Staffieri *et al.* 2014, Meira *et al.* 2018) and can be used in dyspneic  
64 animals.

65 In human medicine, a non-invasive oxygen delivery technique known as high-flow oxygen  
66 therapy (HOT) has emerged as an alternative to COT (Helviz *et al.* 2018). This system allows for  
67 delivery of heated and fully humidified gas with high flow rates of up to 60 L minute<sup>-1</sup> through a  
68 specific high-flow nasal cannula, with a FIO<sub>2</sub> ranging from 21% to 100% (Frat *et al.* 2015). Such  
69 high flow rates are not achievable with COT because of technical limitations (flowmeters rates,  
70 diameter of the nasal prongs). Furthermore, administration of a partially humidified, cold gas  
71 could cause patient discomfort, desiccation of the nasal mucosa, airway constriction, impairment

72 of the mucociliary functions, and increased risk of infection if delivered at similar rates (Kallstrom  
73 2002, Dunphy *et al.* 2004, Kilgour *et al.* 2004, Kopelman & Holbert 2003).

74 High-flow oxygen therapy uses an air-oxygen blender connected to a flow meter, an active  
75 humidifier and heater, a heated breathing circuit, and a specific nasal cannula (Nishimura 2016)  
76 (Figure 1). Warm and adequately humidified gas delivered at high flow rates has apparent  
77 beneficial physiological effects that are increasingly recognized in humans. These include: good  
78 tolerance (Sztrymf *et al.* 2012) and comfort (Roca *et al.* 2010, Frat *et al.* 2015), decreased  
79 mismatch between the oxygen flow and the patient's inspiratory flow (Sztrymf *et al.* 2012),  
80 allowing precise setting by the clinician; generation of a low level of positive airway pressure  
81 (Groves & Tobin 2007, Parke *et al.* 2011), decreased anatomical dead space by washing the  
82 expired volume of carbon dioxide from the airway and replacing it with oxygen-enriched gas  
83 (Helviz *et al.* 2018, Hernández *et al.* 2017, Millar *et al.* 2014), and decreased ventilatory drive and  
84 work of breathing in obstructive human patients (Di Mussi *et al.* 2018), allowing the use of HOT  
85 in hypoxemic and hypercapnic respiratory failure.

86 High flow oxygen therapy has recently been studied in veterinary medicine. It has been  
87 shown to be a safe and effective method for oxygen delivery in sedated and awake healthy dogs  
88 (Daly *et al.* 2017; Jagodich *et al.* 2019), and a preliminary retrospective study described its  
89 successful use in six hypoxemic dogs (Keir *et al.* 2016). No prospective study reporting the use of  
90 HOT in dyspneic dogs has been conducted. The objective of this pilot study was to prospectively  
91 describe the use, tolerance and potential complications of HOT in dyspneic dogs.

92

## 93 **Materials and Methods**

### 94 **Ethical statement**

95 The study protocol was approved by the VetAgro Sup Ethics committee (number 1730).

96

97 **Animals**

98           This prospective pilot study was conducted between January and May 2018 in the  
99 emergency and critical care unit (SIAMU, VetAgro Sup) on client-owned dogs admitted for acute  
100 respiratory distress. Respiratory distress at admission was defined as a respiratory rate (RR) above  
101 40 breaths minute<sup>-1</sup> associated with an abnormal respiratory pattern or laboured breathing at rest.

102

103 **Inclusion**

104           After admission, all respiratory distressed patients received 100% oxygen delivered via a  
105 single nasal cannula at 150 mL kg<sup>-1</sup> minute<sup>-1</sup> (Dunphy *et al.* 2002, Mazzaferro 2015), using a  
106 standard wall water humidifier (COT). Standard therapy for stabilization of the respiratory distress  
107 was administered based on the most likely diagnosis, at the discretion of the attending clinician,  
108 independently from the study. After 30 minutes of medical stabilization, dogs non-responsive to  
109 nasal oxygen therapy were transitioned to HOT and prospectively enrolled in the study. Dogs non-  
110 responsive to nasal oxygen therapy (inclusion criteria) were defined as persisting respiratory  
111 distress as previously defined or a SpO<sub>2</sub><95% under nasal oxygen at the end of the 30-minute  
112 stabilization period. Owner consent was obtained prior to transition from nasal oxygen therapy to  
113 HOT.

114

115 **Exclusion criteria**

116           The exclusion criteria were a body weight below 2 kg, adequate response to COT defined  
117 as respiratory distress improvement and SpO<sub>2</sub>>95%, or criteria for immediate intubation, defined  
118 as excessive respiratory effort with impending respiratory fatigue or failure, severe hypoxemia  
119 despite oxygen therapy (SpO<sub>2</sub><90% or PaO<sub>2</sub><60 mmHg), or a severe hypercapnia (arterial partial  
120 pressure of carbon dioxide (PaCO<sub>2</sub>)>60 mmHg).

121 Early termination criteria were failure to tolerate HOT (defined by a tolerance score (TS) equal to  
122 4, Table 1) and fulfilment intubation criteria (as defined above). Dogs with a do-not-intubate order  
123 remained on HOT despite being intubation candidates.

124

### 125 **High-flow oxygen technique description**

126 High flow oxygen therapy was delivered by a commercially available unit connected to a  
127 specific nasal cannula interface (Optiflow®, Fisher&Paykel Healthcare). The system is composed  
128 of an air-oxygen blender connected to oxygen wall source, a flow meter, an active humidifier and  
129 heater, a heated breathing circuit, and a specific nasal cannula (Figure 1). The nasal cannula is a  
130 soft silicone bilateral nasal prong with tubing that connects to the heated breathing circuit (Figure  
131 2). The system allows for administration of humidified and warmed gas with a FIO<sub>2</sub> between 21  
132 and 100%. Continuous humidification was ensured by a water chamber connected to a sterile  
133 water bag. Temperature was set at 37°C and administered to the patient via the heated breathing  
134 tube.

135 The nasal cannula was chosen according to the size of the dog's nostrils, so that the  
136 cannula diameter would not exceed 50% of the diameter of the nostril and therefore allowed  
137 exhalation with minimal resistance (Daly *et al.* 2017). Seven different sizes were available (4  
138 junior, 3 adult). Once the size of the nasal cannula was chosen, they were gently tightened behind  
139 the neck, and eventually secured with tape and sutured in place next to each nare (Figure 2).

140 In order to avoid recruitment of oxygen from the surrounding air and assure the delivery of  
141 the predetermined FIO<sub>2</sub>, the oxygen flow rate was set to be equivalent to the dog's minute  
142 ventilation (MV=RR\*tidal volume) (Helvis *et al.* 2018). For homogeneity, tidal volume was set at  
143 10 mL kg<sup>-1</sup> (Grimm *et al.* 2015). For example, a 30 kg dog with a RR of 80 breaths minute<sup>-1</sup> had a  
144 flow rate with HOT of 10\*30\*80=24 L minute<sup>-1</sup> (compared to a flow rate of 4.5 L minute<sup>-1</sup> with  
145 nasal oxygen therapy). The FIO<sub>2</sub> was set at 100% and the gas temperature at 37°C during the 60-

146 minute protocol. Once setting was ready, the patient was connected to the heated breathing tube.  
147 At the end of the 60-minute protocol period, the FIO<sub>2</sub> was adjusted to the lowest level possible to  
148 maintain SpO<sub>2</sub>>95%.

149

## 150 **Data recording**

151 The RR, SpO<sub>2</sub>, heart rate (HR), TS (Table 1), flow rate, need for additional sedation, type  
152 and dose of sedative agent used and complications during HOT were recorded by the same  
153 operator (LH). Each of these parameters was recorded right after the 30-minute stabilization  
154 period (T<sub>0</sub>), when dogs were still receiving nasal oxygen therapy. The oxygen delivery technique  
155 was then changed from nasal oxygen therapy to HOT and the parameters were recorded  
156 immediately at 15, 30, 45 and 60 minutes after T<sub>0</sub> (T<sub>15</sub>, T<sub>30</sub>, T<sub>45</sub>, and T<sub>60</sub>, respectively). A catheter  
157 was inserted in the dorsal pedal artery to allow drawing of arterial blood samples and evaluate  
158 PaO<sub>2</sub> and PCO<sub>2</sub> at T<sub>0</sub> (under nasal oxygen therapy) and T<sub>60</sub> (under HOT). Arterial blood gases  
159 measurements were performed on fresh whole arterial blood collected in a heparinized syringe  
160 according to the manufacturer's instructions using an on-site VetStat (IDEXX Laboratories Inc.).

161 An APPLE<sub>fast</sub> scale (0-50 score, calculated from glucose, albumin, lactate, platelet count,  
162 and mentation score) was used in each dog at inclusion to stratify illness severity by mortality risk  
163 as previously described (Hayes *et al.* 2010).

164

## 165 **Outcomes**

166 The evolution of PaO<sub>2</sub>, PaCO<sub>2</sub> and flow rate between T<sub>0</sub> and T<sub>60</sub>, and evolution of RR,  
167 tolerance score, SpO<sub>2</sub> and HR every 15 minutes during the 60-minute protocol were recorded. The  
168 occurrence of complications due to the oxygen delivery technique during the protocol,  
169 requirement for escalation to intubation within 24 hours after admission and in-hospital mortality  
170 were also recorded.

171

## 172 **Statistical method**

173 Statistical analyses were carried out with JMP® version 13.1 (SAS institute). All  
174 individual data were described with a spaghetti plot graphic. Data were tested for normal  
175 distribution with the Shapiro-Wilk test. Continuous variables were compared with paired t-tests.  
176 Data were expressed as mean  $\pm$  standard deviation (SD) with 95% confidence intervals (CI). A  
177 value of  $P < 0.05$  was considered as statistically significant.

178

## 179 **Results**

### 180 **Animals**

181 During the study period, 11 dogs were included in the high flow oxygen therapy protocol.  
182 The breeds of dogs included were three Golden Retriever, two King Charles Spaniel, two  
183 Dachshunds and one each of Australian Shepherd, German Wirehaired Pointer, Jack Russell  
184 Terrier and Pomeranian. Four dogs were female neutered and seven were male neutered, with  
185 mean  $\pm$ SD weights of  $28.3 \pm 12.3$  kg (range, 4.8 to 43.0 kg) and ages  $7.8 \pm 3.8$  years (range, 2 to 13  
186 years).

187 Five dogs had a diagnosis of aspiration pneumonia, and one of each: cardiogenic  
188 pulmonary oedema, non-cardiogenic oedema following cluster seizures, leptospirosis infection,  
189 pulmonary haemorrhages following a car accident, pulmonary hypertension of unknown origin,  
190 and pericardial effusion. The mean  $\pm$ SD APPLE<sub>fast</sub> score was  $27.0 \pm 4.4$

191

### 192 **Recorded data**

193 Dogs were receiving nasal oxygen therapy at T<sub>0</sub> and HOT at T<sub>15</sub>, T<sub>30</sub>, T<sub>45</sub> and T<sub>60</sub>.

194

195 *PaO<sub>2</sub>*

196 High-flow oxygen therapy allowed a significant increase in mean PaO<sub>2</sub> at T<sub>60</sub> (171 ±123  
197 mmHg) compared to nasal oxygen therapy at T<sub>0</sub> (73 ±24 mmHg; P=0.015, 95% CI: 23 to 172  
198 mmHg).

199 Individual data are presented in Figure 3. For every dog, PaO<sub>2</sub> increased after HOT  
200 initiation. Of the 7 dogs with PaO<sub>2</sub><80 mmHg at COT, 5 had a resolution of their hypoxemia one  
201 hour after HOT initiation.

202

203 *Flow rate (Figure 4)*

204 The mean oxygen flow rate was significantly greater with HOT (18 ±12 L minute<sup>-1</sup>) than  
205 in nasal oxygen technique (3.2 ±2.0 L minute<sup>-1</sup>, P<0.01, 95% CI: 8.0 to 22.5 L minute<sup>-1</sup>). Flow  
206 rate with HOT ranged from 2 to 37 L minute<sup>-1</sup>. Flow rate with nasal oxygen technique ranged  
207 from 0.7 to 6.5 L minute<sup>-1</sup>.

208

209 *Respiratory rate*

210 Individual data are presented in Figure 5. Six dogs had a decrease in RR between T<sub>0</sub> and  
211 T<sub>60</sub>. However, only 2 dogs reached our criteria of respiratory distress of less than 40 breaths  
212 minute<sup>-1</sup> at T<sub>60</sub> despite the use of HOT.

213

214 *SpO<sub>2</sub>, HR and PaCO<sub>2</sub>*

215 The mean SpO<sub>2</sub> was significantly greater at T<sub>60</sub> (97.7 ±2.3%) than at T<sub>0</sub> (91.6 ±7.2%,  
216 P=0.03, 95% CI: 0.7 to 11.5%). There was no significant difference at any time for HR or PaCO<sub>2</sub>.

217 All individual data are showed in figure 6, 7, and 8 (supplemental material).

218

219 *Tolerance score*

220 The TS remained low during the entire protocol. Only one animal displayed a TS of 3  
221 when setting the HOT device, requiring additional sedation that lowered its TS to 2 or 1  
222 depending on the protocol time. Another dog displayed a TS of 2 at two occurrences but did not  
223 need any additional sedation. Every other dog had a TS of 1 at every protocol time.

224

### 225 *Complications*

226 No complications due to the oxygen delivery technique occurred during the study. Nasal  
227 cannulas were easy to fix and to use. No injuries occurred due to the nasal cannula.

228

### 229 *Intubation within 24 hours and mortality in hospitalisation*

230 Five of the 11 dogs (45%) developed a need for intubation within 24 hours after  
231 admission. Due to financial reasons, only 3 of them (27%) were intubated. Six of 11 dogs (54%,  
232 including the 5 that presented intubation criteria) died during hospitalization. Death were due to  
233 deteriorating clinical state leading to cardiac arrest in 5 dogs and 1 euthanasia for prognostic  
234 reason.

235

## 236 **Discussion**

237 This is the first prospective clinical trial evaluating the effectiveness and tolerance of HOT  
238 in respiratory distress dogs. Our study shows the potential for HOT to be an efficient, safe and  
239 well-tolerated alternative to COT with nasal oxygen therapy to deliver oxygen. This technique  
240 allows for a significant increase in PaO<sub>2</sub> in dogs, with the PaO<sub>2</sub> more than doubling between nasal  
241 oxygen therapy and HOT within only one hour. This finding is consistent with the human  
242 (Sztrymf *et al.* 2012, Frat *et al.* 2015, Makdee *et al.* 2017), and the veterinary literature. Indeed,  
243 Daly *et al.* (2017) and Jagodich *et al.* (2019) in healthy dogs, and Keir *et al.* (2016) in hypoxemic  
244 dogs showed this PaO<sub>2</sub> improvement after HOT. With such an increase in PaO<sub>2</sub> during a short

245 period of time, HOT raised concern for oxygen toxicity if continued for a long time. For  
246 homogeneity in the study design, the authors chose to keep the FIO<sub>2</sub> up to 100% during the 60-  
247 minute protocol, but FIO<sub>2</sub> was decreased immediately at the end of the protocol to the lowest  
248 required FIO<sub>2</sub> to reach a SpO<sub>2</sub>>95%. As high-flow devices offer multi-configurable solutions for  
249 flow and FIO<sub>2</sub>, these two parameters can be changed easily to fit patient's demand. Once the  
250 targeted oxygenation parameters are reached and plateaued, the FIO<sub>2</sub> should be decreased under  
251 60% as soon as possible to avoid oxygen toxicity (Guenther 2019).

252 In the present study, flow rates with HOT ranged from 2 to 37 L minute<sup>-1</sup> and resulted in  
253 an increase in PaO<sub>2</sub> in all cases (Figure 3). By delivering higher flow rates, HOT systems are less  
254 prone to allow inhalation of room air during patient inspiration than traditional oxygenation  
255 systems (Helvis *et al.* 2018). Different systems exist for high-flow delivery: Precision flow  
256 (Vapotherm), Optiflow (Fisher&Paykel Healthcare), Airvo system (Fisher&Paykel Healthcare).  
257 Each of them has specific characteristics and has to be used with their specific nasal cannula to  
258 ensure appropriate flow rate, temperature, and FIO<sub>2</sub>. In our study, we used the Optiflow system  
259 which was easy to use and offer a multi-configurable solution for patients requiring HOT. This  
260 system relies on an O<sub>2</sub>/air blender, and FIO<sub>2</sub> of 100% is obtained with use of oxygen wall not  
261 mixed with air. No internal system was available to ensure that the delivered FIO<sub>2</sub> at the nasal  
262 cannula was at 100%. We were not able to measure the delivered FIO<sub>2</sub> in our study, and some  
263 dogs were panting during measurements, so we could not ensure that we were delivering the pre-  
264 set FIO<sub>2</sub>. Moreover, a recent study with the same system showed that, when delivering a FIO<sub>2</sub> of  
265 100%, the effective delivered FIO<sub>2</sub> increases with flow rate and varies between 72.2% and 95%  
266 for flow rate from 0.4 L kg<sup>-1</sup> minute<sup>-1</sup> to 2.5 L kg<sup>-1</sup> minute<sup>-1</sup> (Jagodich *et al.* 2019). In our study,  
267 flow rate ranged from 0.44 to 1.84 L kg<sup>-1</sup> minute<sup>-1</sup>, so we can hypothesise that the effective FIO<sub>2</sub>  
268 did not reach 100%. Despite this limitation, our study confirms that HOT allows increase in PaO<sub>2</sub>  
269 in clinical settings.

270 In human medicine, several studies have showed a significant decrease of RR after  
271 initiation of HOT (Roca *et al.* 2010, Sztrymf *et al.* 2011, Sztrymf *et al.* 2012, Makdee *et al.* 2017).  
272 In our study, six dogs had a decrease in RR between T<sub>0</sub> and T<sub>60</sub>, but with very variable evolution  
273 among time (Figure 5). The dogs were included in this study because of respiratory distress with  
274 failure to respond to nasal oxygen therapy, that could reasonably not resolve in one hour,  
275 especially as our population mainly had principally respiratory distress secondary to aspiration  
276 pneumonia. Finally, they were treated with HOT early in the course of their respiratory distress  
277 (30 min after admission), meaning that other treatments, such as diuretics, antibiotics, etc., did not  
278 have time to be effective. Mackdee *et al.* (2017) showed a significant decrease in RR after one  
279 hour in the HOT group compared to COT group in human patients with cardiogenic pulmonary  
280 oedema. Another study comparing RR between patients under nasal oxygen therapy or HOT in a  
281 more homogeneous population would be of great interest to differentiate between effects of time  
282 versus effects of treatment.

283 By enhancing the heating and humidification of nasal cavities, HOT has been shown to  
284 improve patient comfort in human medicine (Roca *et al.* 2010, Boyer *et al.* 2011, Sztrymf *et al.*  
285 2012). In one veterinary study in hypoxemic dogs, HOT intolerance requiring sedation was  
286 noticed in 1/6 dogs (Keir *et al.* 2016). However, no TS was used in this study. Jagodich *et al.*  
287 (2019), using a different TS associated with a respiratory score, showed that HOT tolerance was  
288 inversely proportional to flow rate, and flow rate above 2.5 L minutes<sup>-1</sup> were not well tolerated. In  
289 this study, the HOT administered with specific nasal cannula was easily tolerated and displayed  
290 very low TS during all the study period. It would have been interesting to compare tolerance of  
291 COT and HOT, but it was not the purpose of this study, and more studies on HOT tolerance are  
292 therefore needed. Moreover, one study in human medicine showed that temperature seems to  
293 significantly impact the comfort of dyspneic patients with high flows: for equal flow, patient

294 comfort was significantly higher at 31°C compared to 37°C (Mauri *et al.* 2018). The impact of  
295 temperature was not evaluated in our pilot study and could be assessed in a larger population.

296 No clinically relevant complications related to the oxygen therapy technique were noted  
297 during our study, which therefore supports previously published studies of HOT safety in dogs  
298 (Keir *et al.* 2016, Daly *et al.* 2017, Jagodich *et al.* 2019). Jagodich *et al.* (2019) showed that at  
299 flow rates above 2 L kg<sup>-1</sup> minute<sup>-1</sup>, dogs became less tolerant. Our study showed that lower flow  
300 rate allowed improvement of oxygen parameters with good tolerance. However, in the study of  
301 Daly *et al.* (2017), one dog had radiographic evidence of gastric distension, and in the study of  
302 Jagodish *et al.* (2019), 8 out of 8 dogs had aerophagia noted on radiographs. As our dogs were  
303 dyspneic, we did not perform any abdominal radiographs to evaluate the incidence of gastric  
304 distension. Nevertheless, we did not notice any abdominal distension during physical examination.  
305 Moreover, the potential long-term complications could not be assessed with our study design.

306 Given the inclusion criteria of severely dyspneic dogs, the mortality rate in our population  
307 was high. In the study of Keir *et al.* (2016), 3 out of 6 dogs died, of those, 2 died as a result of  
308 worsening hypoxemia. Our study population included various primary pulmonary disease  
309 processes, that have a different prognosis (Hopper *et al.* 2007). However, both in Keir *et al.*  
310 (2016) and in our study, aspiration pneumonia was the main diagnosis. Larger population is  
311 needed to compare influence on mortality rate of HOT.

312 Some limitations should be noted in the current study. The biggest limitations are the small  
313 sample size and the absence of control group that limits interpretation of the results. Our study  
314 was designed as a pilot study for a future randomised controlled study. Adding the result of a  
315 control group, treated with standard medical stabilisation and nasal oxygen therapy would have  
316 been of great interest to provide context for the magnitude of improvement in recorded parameters  
317 (i.e. effects of time versus treatment type). However, the dogs included in our study were severely  
318 dyspneic, and not adding HOT to their therapeutic plan could have raised ethical concerns.

319 Second, HOT has been showed to have several physiological effects allowing improvement of  
320 PaO<sub>2</sub>. In dogs, Jagodish *et al.* (2019) showed that HOT provides CPAP and predictable oxygen  
321 support in healthy dogs. As our study was a clinical study, it was not possible to use more invasive  
322 monitoring to differentiate between a positive effect on PaO<sub>2</sub> related to a therapeutic effect of the  
323 HOT on respiratory mechanic or related to enrichment of inspired oxygen. Third, the long-term  
324 implications of HOT were not evaluated, and our results (especially tolerance and complication)  
325 should be validated in a longer study. Finally, the inclusion of patients with different respiratory  
326 distress causes could have change the results, as some patients could benefit more or less from  
327 HOT.

328

## 329 **Conclusion**

330 This study is the first in veterinary medicine to prospectively confirm that HOT could  
331 deliver effective oxygenation and comfort with minimal complications in dyspneic dogs, and  
332 gives practical information on HOT use in dogs.

333

334 **Bibliography**

335 Boyer, A., Vargas, F., Delacre, M., *et al.* (2011) Prognostic Impact of High-Flow Nasal Cannula  
336 Oxygen Supply in an ICU Patient with Pulmonary Fibrosis Complicated by Acute Respiratory  
337 Failure. *Intensive Care Medicine* 37, 558-559

338 Briganti, A., Melanie, P., Portela, D., *et al.* (2010) Continuous positive airway pressure  
339 administered via face mask in tranquilized dogs. *Journal of Veterinary Emergency and Critical*  
340 *Care* 20, 503-508

341 Brown, J.E., Bersenas, A.M.E., Mathews, K.A., *et al.* (2009) Noninvasive ventilation in cats.  
342 *Journal of Veterinary Emergency and Critical Care* 19, 416-425

343 Daly, J.L., Guenther, C.L., Haggerty, J.M., *et al.* (2017) Evaluation of oxygen administration with  
344 a high-flow nasal cannula to clinically normal dogs. *American Journal of Veterinary Research* 78,  
345 624-630

346 Di mussi, R., Spadaro, S., Stripoli, T., Volta, C.A., Trerotoli, P., Pierucci, P., Staffieri, F., Bruno,  
347 F., Camporota, L., Grasso, S. (2018) High-flow nasal cannula oxygen therapy decreases  
348 postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive  
349 pulmonary disease. *Critical Care* 22, 180

350 Dunphy, E., Mann, F.A., Dodam, J., Branson, K., Wagner-Mann C., Johnson P., Brady M. (2002)  
351 Comparison of unilateral versus bilateral nasal catheters for oxygen administration in dogs.  
352 *Journal of Veterinary Emergency and Critical Care* 12, 245–251

353 Frat, J.P., Thille, A.W., Mercat, A., *et al.* (2015) High-flow oxygen through nasal cannula in acute  
354 hypoxemic respiratory failure. *The New England Journal of Medicine* 372, 2185-2196

355 Guenther, C.L. (2019) Oxygen therapy In: Textbook of small animal emergency medicine. 1st  
356 edn. Eds K. Drobatz, K. Hopper; E. Rosanski and D. Silverstein. Wiley-Blackwell, Hoboken. pp  
357 1177-1182

358 Grimm, K., Lamont, L., Tranquilli, W., *et al.* (2015) Anesthesia equipment. In: Veterinary  
359 anesthesia and analgesia. 5th ed. Ames, Iowa, Wiley Blackwell. pp 23-85

360 Groves, N., Tobin, A. (2007) High flow nasal oxygen generates positive airway pressure in adult  
361 volunteers. *Australian Critical Care: Official Journal of the Confederation of Australian Critical*  
362 *Care Nurses* 20, 126-131

363 Hayes, G., Mathews, K., Doig, G., *et al.* (2010) The acute patient physiologic and laboratory  
364 evaluation (APPLE) score: a severity of illness stratification system for hospitalized dogs. *Journal*  
365 *of Veterinary Internal Medicine* 24, 1034-1047

366 Helviz, Y., Einav, S. (2018) A Systematic Review of the High-flow Nasal Cannula for Adult  
367 Patients. *Critical Care* 22, 71

368 Hernández, G., Roca, O., Colinas, L. (2017). High-flow nasal cannula support therapy: new  
369 insights and improving performance. *Critical Care* 21, 62

370 Hopper, K., Haskins, S.C., Kass, P.H., *et al.* (2007) Indications, management, and outcome of  
371 long-term positive-pressure ventilation in dogs and cats: 148 cases (1990-2001). *Journal of the*  
372 *American Veterinary Medical Association* 230, 64-75

373 Jagodich, T., Bersenas, A., Bateman, S., Kerr, C. (2019) Comparison of high flow nasal cannula  
374 oxygen administration to traditional nasal cannula oxygen therapy in healthy dogs. *Journal of*  
375 *Veterinary Emergency and Critical Care* DOI: 10.1111/vec.12817

376 Kallstrom, T.J. (2002) AARC Clinical Practice Guideline: oxygen therapy for adults in the acute  
377 care facility--2002 revision & update. *Respiratory Care* 47, 717-720

378 Keir, I., Daly, J., Haggerty, J., *et al.* (2016) Retrospective evaluation of the effect of high flow  
379 oxygen therapy delivered by nasal cannula on PaO<sub>2</sub> in dogs with moderate-to-severe hypoxemia.  
380 *Journal of Veterinary Emergency and Critical Care* 26, 598-602

381 Kilgour, E., Rankin, N., Ryan, S., *et al.* (2004) Mucociliary function deteriorates in the clinical  
382 range of inspired air temperature and humidity. *Intensive Care Medicine* 30, 1491-1494

383 Kopelman, A.E., Holbert, D. (2003) Use of Oxygen Cannulas in Extremely Low Birthweight  
384 Infants is Associated with Mucosal Trauma and Bleeding, and Possibly with Coagulase-negative  
385 Staphylococcal Sepsis. *Journal of Perinatology* 23, 94-97

386 Makdee, O., Monsomboon, A., Surabenjwong, U., *et al.* (2017) High-flow nasal cannula versus  
387 conventional oxygen therapy in emergency department patients with cardiogenic pulmonary  
388 edema: A Randomized Controlled Trial. *Annals of Emergency Medicine* 70, 465-472

389 Mazzaferro, E.M. (2015) Oxygen therapy. In: Small animal critical care medicine. 2nd edn. Eds  
390 K. Hopper and D. Silverstein. W.B. Saunders, Philadelphia. pp 77-80

391 Meira, C., Joerger, F.B., Kutter, A.P.N., Waldmann, A., Ringer, S.K., Böehm, S.H., Iff, S.,  
392 Mosing, M. (2018) Comparison of three continuous positive airway pressure (CPAP) interfaces in  
393 healthy Beagle dogs during medetomidine-propofol constant rate infusions. *Veterinary*  
394 *Anaesthesia Analgesia* 45,145-157

395 Millar, J., Lutton, S., O'Connor, P. (2014) The use of high-flow nasal oxygen therapy in the  
396 management of hypercarbic respiratory failure. *Therapeutic Advances in Respiratory Disease* 8,  
397 63-64

398 Mueller, E.R., (2007) Suggested Strategies for Ventilatory Management of Veterinary Patients  
399 with Acute Respiratory Distress Syndrome. *Journal of Veterinary Emergency and Critical Care*  
400 11, 191-198

401 Parke, R.L., Eccleston, M.L., McGuinness, S.P. (2011) The effects of flow on airway pressure  
402 during nasal high-flow oxygen therapy. *Respiratory Care* 56, 1151-1155

403 Staffieri, F., Crovace, A., De Monte, V. *et al.* (2014) Noninvasive continuous positive airway  
404 pressure delivered using a pediatric helmet in dogs recovering from general anesthesia. *Journal of*  
405 *Veterinary Emergency and Critical Care* 24, 578-585

406 Sumner, C., Rozanski, E. (2013). Management of respiratory emergencies in small animals. *The*  
407 *Veterinary Clinics of North America Small Animal Practice* 43, 799-815

408 Sztrymf, B., Messika, J., Bertrand, F., *et al.* (2011) Beneficial effects of humidified high flow  
409 nasal oxygen in critical care patients: a prospective pilot study. *Intensive Care Medicine* 37, 1780-  
410 1796

411 Sztrymf, B., Messika, J., Mayot, T., *et al.* (2012). Impact of high-flow nasal cannula oxygen  
412 therapy on intensive care unit patients with acute respiratory failure: A prospective observational  
413 study. *Journal of Critical Care* 27, 324.e9-13

1	The patient is calm, comfortable; no agitation; no attempts to remove the nasal cannula
2	The patient tolerates the nasal cannula, but looks stressed and afraid; no attempts to remove the nasal cannula
3	The patient is agitated and tries to remove the nasal cannula; it is still possible to keep the nasal cannula on by gently restraining the patient
4	The patient does not tolerate the nasal cannula, is agitated, attempts to pull the nasal cannula; additional sedation is required to tolerate the oxygen delivery device

Table 1 : Oxygen delivery device tolerance score (adapted from Staffieri *et al.* 2014)

Figure 1: Schematic representation of a high-flow oxygen device and its components (Drawing Dr Mathieu Taroni).

Figure 2: Dog with the specific high-flow nasal cannula

Figure 3: Change in Arterial Partial Pressure of Oxygen ( $\text{PaO}_2$ ) for individual patients. HOT: High-flow oxygen therapy. In figures 3, 4, 5 and supplemental material, the same dog is represented by the same colours.

Figure 4: Change in flow rates for individual patients. HOT: High-flow oxygen therapy.

Figure 5: Change in respiratory rates (RR) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Supplemental material

Figure 6: Change in pulse oxymetry ( $\text{SpO}_2$ ) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Figure 7: Change in heart rates (HR) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Figure 8: Change in arterial partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>) for individual patients. HOT: High-flow oxygen therapy.

**Conflicts of interest statement**

No conflicts of interest have been declared.