

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Respiratory variation in aortic blood peak velocity and caudal vena cava diameter can predict fluid responsiveness in anaesthetised and mechanically ventilated dogs

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1691494> since 2022-07-05T17:35:07Z

Published version:

DOI:10.1016/j.tvjl.2017.08.004

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

1 **Original Article**

2

3

4 **Respiratory variation in aortic blood peak velocity and caudal vena cava diameter can predict**
5 **fluid responsiveness in anaesthetised and mechanically ventilated dogs**

6

7

8 M. Bucci^{a,*}, R. Rabozzi^b, C. Guglielmini^a, P. Franci^a

9

10 ^a*Department of Animal Medicine, Production and Health, University of Padua, Viale*
11 *dell'Università, 16, Legnaro 35020, Italy*

12 ^b*Clinica Veterinaria Roma Sud, Via Pilade Mazza, Rome 00173, Italy*

13

14

15

16

17 * Corresponding author. Tel.: +39 049 8272608

18 *E-mail address: massimobucci@inwind.it (M. Bucci)*

19 **Abstract**

20 Dynamic preload indices, such as systolic pressure variation (SPV), aortic flow peak velocity
21 variation (ΔV_{peak}) and distensibility index of the caudal vena cava (CVCDI), are reliable indices
22 for predicting fluid responsiveness in humans. This study aimed to investigate the ability of these
23 indices to predict fluid response in healthy dogs undergoing general anaesthesia and mechanical
24 ventilation. The study included 24 dogs. ΔV_{peak} , CVCDI, and SPV were calculated before and
25 after volume expansion (5 mL/kg bolus of lactated Ringer's solution). Dogs were considered
26 responders (group R, n = 9) when the aortic velocity time integral (VTI) increase was $\geq 15\%$ and
27 non-responders (group NR, n = 15) when the increase was $< 15\%$. ΔV_{peak} , CVCDI, and SPV before
28 volume expansion were higher in group R than in group NR ($P = 0.0009$, $P = 0.0003$, and $P =$
29 0.0271 , respectively). Receiver operating characteristic (ROC) curves were plotted for the three
30 indices. The areas under the ROC curves for SPV, ΔV_{peak} , and CVCDI were 0.91 (CI 0.73–0.99; P
31 $= 0.0001$), 0.95 (CI 0.77–1; $P = 0.0001$), and 0.78 (CI 0.56–0.92; $P = 0.015$), respectively. The best
32 cut-offs were 6.7% for SPV (sensitivity, 77.78%; specificity, 93.33%), 9.4% for ΔV_{peak}
33 (sensitivity, 88.89%; specificity, 100%), and 24% for CVCDI (sensitivity, 77.78%; specificity,
34 73.33). In conclusion, ΔV_{peak} , CVCDI, and SPV are reliable predictors of fluid responsiveness in
35 dogs undergoing general anaesthesia and mechanical ventilation.

36

37 *Keywords:* Anaesthesia; Dog; Fluid responsiveness; Mechanical ventilation; Preload indices

38 **Introduction**

39 One of the major task for the anaesthetist, in order to optimize cardiac output and tissues
40 perfusion, is to evaluate the perioperative fluid responsiveness which is commonly defined as an
41 increase in the stroke volume by 15% after intravenous administration of an adequate bolus of IV
42 fluid, and a responder is considered as a subject who reacts to such an increase. Stroke volume (SV)
43 monitoring and prediction of fluid responsiveness are crucial to optimised hemodynamic and to
44 avoid a detrimental fluid overload in non-responder subjects (Vellet et al., 2013).

45
46 Dynamic indices of preload, such as systolic pressure variation (SPV), aortic flow peak
47 velocity variation (ΔV_{peak}), and distensibility of the inferior vena cava, are associated with heart-
48 lung interactions (Jardin et al., 1983; Pinsky, 1997), allow beat-to-beat monitoring, and have been
49 shown to be reliable predictors of fluid responsiveness in subjects undergoing general anaesthesia
50 and controlled mechanical ventilation (CMV) (Gan et al, 2013;Rabozzi and Franci, 2014;
51 Desgranges et al., 2016). The literature concerning the use of these dynamic indices in dogs is quite
52 scarce and incomplete. Recently, SPV has been studied in anaesthetised dogs undergoing CMV at 8
53 cm H₂O of airways pressure and has been shown to be a good predictor of fluid responsiveness
54 (Rabozzi and Franci, 2014).

55
56 Ideally, an index of fluid responsiveness should be sensitive to changes in ventricular
57 preload, predictive of fluid responsiveness, reproducible, simple to use, non-invasive, and widely
58 available, in order to be conveniently used in the operating theatre or in the intensive care unit
59 (Michard and Teboul, 2002; Marik et al., 2009). Echography offers the possibility to obtain indices
60 correlated with preload, with many of these desired characteristics. Unfortunately, none
61 sonographic index of fluid responsiveness can be currently used in dogs in clinical practice because
62 the lack of validated cut-off values in this specie.

63

64 As mentioned above monitoring of SV is a mandatory aspect of studying indices of fluid
65 responsiveness. Sonography has also been used as a non-invasive, painless and widely available
66 method for beat-to-beat monitoring of the variation of stroke volume (SV) in experimental setting.
67 Authors measured the aortic velocity time integral (VTI), using its percentage variation (Δ VTI) in
68 the same subject after a fluid challenge, as a surrogate for SV variation (Pereira de Souza Neto et
69 al., 2011; Brun et al., 2012; de Oliveira et al., 2016). In a pulsatile and accelerated flow detected
70 with Doppler trace, the VTI (expressed in cm) is the integral under the velocity-time curve and
71 represents the length covered by a systolic ejection flow. Previous studies have shown a high
72 correlation between VTI variation, measured with transthoracic echocardiography (TTE), and SV
73 variation in the same human subject measured by invasive methods (Lewis et al., 1984; Nguyen et
74 al., 2006).

75

76 The present study aimed to evaluate the ability of SPV, ΔV_{peak} , and of the caudal vena cava
77 distensibility index (CVCDI) to predict an increase equal to or greater than 15% in Δ VTI, after a
78 fluid challenge, in mechanically ventilated dogs under general anaesthesia.

79

80 **Materials and Methods**

81 This prospective clinical study was approved by the Ethics Committee of the University of
82 Padua (protocol no. 2422824). This study investigated 24 client-owned dogs, who were referred to
83 the Veterinary Teaching Hospital of the University of Padua for elective surgeries. Written informed
84 consent was obtained from each owner.

85

86 Preoperative physical examination and routine blood analysis (packed cell volume,
87 haemoglobin, total protein, creatinine, urea, and electrolytes) were performed in each dog. The dogs
88 were aged greater than 12 months, and dogs with arrhythmia, a history or clinical signs of
89 cardiovascular or thoracic diseases, and systemic diseases were excluded.

90

91 After inserting a venous catheter into the cephalic vein, general anaesthesia was induced with
92 fentanyl (Fentanest, Pfizer, Latina, Italy) administered at 0.003 mg/kg, followed by propofol
93 (Vetofol, Norbrook, Carlisle, UK) administered to effect. Once intubated, each dog was maintained
94 in left lateral recumbency and the tracheal tube was connected to an anaesthesia machine (ADU,
95 Datex-Ohmeda, Helsinki, Finland). CMV was immediately started, and the tidal volume was set such
96 that a plateau pressure of 10 cmH₂O was maintained. No positive end-expiratory pressure or
97 inspiratory pause was applied. Anaesthesia was maintained with an infusion of propofol (18–25
98 mg/kg/h) using a syringe pump (3500, Graseby, Watford, UK). The respiratory rate was set such that
99 a partial pressure of end-tidal CO₂ (PE'CO₂) between 4.6 and 6 kPa was maintained. The inspired
100 fraction of oxygen was set between 35% and 40%.

101

102 Electrocardiography (three derivations), pulse oximetry, rectal temperature monitoring,
103 capnography (side-stream system), and spirometry (pitot based) were performed throughout the
104 entire procedure (AS/5, Datex-Ohmeda). Arterial blood pressure was measured invasively using an
105 arterial catheter placed in the dorsal pedal artery, and the arterial line transducer was zeroed and
106 maintained at the level of the right atrium.

107

108 After ensuring that the dog had completely adapted to mechanical ventilation and confirming
109 the absence of spontaneous inspiratory effort on the spirometry trace, the maximum and minimum
110 systolic arterial pressures (SAPmax and SAPmin) were measured over three respiratory cycles.

111 For measuring the SAPmax and SAPmin, we used the 'wedge pressure' menu of the Datex-
112 Ohmeda AS/5 monitor, which allows the freezing of the arterial pressure trace, as performed by
113 Rabozzi and Franci (2014). Median values over three respiratory cycles were used to calculate SPV
114 using the following formula (Perel et al., 1987):

115
$$\text{SPV (\%)} = (\text{SAPmax} - \text{SAPmin}) / ([\text{SAPmax} + \text{SAPmin}] / 2) \times 100$$

116

117 Maximum Vpeak (Vpeak max) and minimum Vpeak were measured over three respiratory
118 cycles using a cardiological probe (Z One Ultra, Zonare Mountain View, CA) at a frequency of 4-8
119 MHz. A standard subxifoid diaphragmatico-hepatic long axis view allowed to visualize the left
120 ventricular outflow tract (LVOT) and aorta in order to obtain a pulsed Doppler traces over three
121 respiratory cycles. Aortic valve and aortic annulus were identified as landmarks. The median values
122 were used to calculate ΔV_{peak} using the following formula (Feissel et al., 2001): $\Delta V_{\text{peak}} (\%) =$
123 $(V_{\text{peak max}} - V_{\text{peak min}}) / ([V_{\text{peak max}} + V_{\text{peak min}}] / 2) \times 100$

124

125 VTI was measured as the median value over three respiratory cycles. ΔVTI was calculated as
126 follows: $\Delta VTI (\%) = ([VTI \text{ after volume expansion} - VTI \text{ before volume expansion}] / VTI \text{ before}$
127 $\text{volume expansion}) \times 100.$

128

129 CVC image was obtained using a 4-9 MHz convex probe (Z One Ultra, Zonare Mountain
130 View, CA) at the level of the tenth to twelfth intercostal space, just few centimetres ventrally to the
131 vertebral column, in the lateral short axis view in order to obtain a good image of the porta hepatis.
132 Aorta, CVC and portal vein cross sections were identified as landmarks. In this view CVC appears
133 slightly elliptical. The short axe calibre was measured according to the approach presented by
134 Meneghini et al. (2015). Maximum CVC diameter (CVCmax) and minimum CVC diameter
135 (CVCmin) were measured from the recorded cine-loop images of three respiratory cycles. The
136 median values were used to calculate the caudal vena cava distensibility index (CVCDI) using the
137 following formula (Feissel et al., 2004): $CVCDI (\%) = (CVC_{\text{max}} - CVC_{\text{min}}) / ([CVC_{\text{max}} +$
138 $CVC_{\text{min}}] / 2) \times 100.$

139

140 A volume expansion was performed with a bolus of 5 mL/kg of lactated Ringer's solution
141 administered intravenously over one minute using preloaded 50 mL syringes. One minute later,

142 systolic pressure, Doppler aortic trace, and cine-loop images of the caudal vena cava were again
143 obtained and stored.

144

145 All measurements (before and after volume expansion) were taken for three respiratory
146 cycles, and the median values were recorded for statistical analyses and calculation of haemodynamic
147 indices. Synchronization of the measurements with the inspiratory and expiratory phases of the
148 respiratory cycles was verified with the trace of airway pressure and the capnogram. After obtaining
149 all measurements, the dog was positioned as required to perform the scheduled surgical procedure.

150

151 *Statistical methods*

152 The distribution of normality for each variable was assessed using the visual inspection of the bar
153 graph and performing the Shapiro-Wilk test. Data that were not normally distributed are expressed
154 as median and interquartile range (25th-75th percentiles). Normally distributed variables are
155 expressed as mean \pm standard deviation (SD). Fisher's exact test was used for categorical data, the
156 independent Student's *t*-test for continuous normally variables while Wilcoxon rank-sum test was
157 used to assess changes of not normally distributed variables.

158

159 The effects of VE on haemodynamic parameters were assessed using a non-parametric
160 Wilcoxon rank-sum test. Assuming that a 15% increase in the VTI was needed for clinical
161 significance, dogs showing a Δ VTI \geq 15% after VE were classified as responders (R) and those
162 showing a Δ VTI $<$ 15% were classified as non-responders (NR). Receiver operating characteristic
163 (ROC) curves were plotted for SPV, Δ V_{peak}, and CVC_{DI} in order to evaluate their ability to predict
164 fluid responsiveness. A *P*-value $<$ 0.05 was considered significant.

165

166 All measurements were performed by the same operator (MB). Intra-observer and inter-
167 observer variabilities of echographic measurements were determined through repetition of

168 measurements (VTI, V_{peak}, and CVC diameters) in eight randomised dogs by the same operator and
169 by a second operator. The second observer was an expert sonographer (CG).

170

171 **Results**

172 This study included 24 dogs (female, 14; male, 10). The median age of the dogs was 27 (16–
173 52) months, and the median weight was 8.2 (7.5–12.6) kg. All dogs were ventilated at a plateau
174 pressure of 10 cmH₂O, and the median tidal volume per kg was 14 (13.8–15.4) mL. VE induced a
175 VTI increase of ≥15% in nine dogs (group R) and <15% in 15 dogs (group NR). There were no
176 significant differences in baseline characteristics between groups R and NR (Table 1). The effects of
177 volume expansion on haemodynamic parameters are summarised in Table 2. Before volume
178 expansion, heart rate, systolic pressure, and mean arterial pressure were not significantly different
179 between groups R and NR. SPV (Fig. 1), ΔV_{peak} (Fig. 2), and CVCDI (Fig. 3) before volume
180 expansion were higher in group R than in group NR ($P = 0.0009$, $P = 0.0003$, and $P = 0.0271$,
181 respectively). ROC curves for SPV, ΔV_{peak}, and CVCDI are presented in Fig. 4. The areas under the
182 ROC curves for SPV, ΔV_{peak}, and CVCDI were 0.91 (CI 0.73–0.99; $P = 0.0001$), 0.95 (CI 0.77–1;
183 $P = 0.0001$), and 0.78 (CI 0.56–0.92; $P = 0.015$), respectively. The best cut-offs were 6.7% for SPV
184 (sensitivity, 77.78%; specificity, 93.33%), 9.4% for ΔV_{peak} (sensitivity, 88.89%; specificity, 100%),
185 and 24% for CVCDI (sensitivity, 77.78%; specificity, 73.33%).

186

187 For VTI, V_{peak}, and CVC diameters, the inter-observer variabilities (expressed as the mean
188 percent errors and SDs) were $3.8 \pm 3\%$, $3.5 \pm 3.2\%$, and $5.7 \pm 4.6\%$, respectively, and the intra-
189 observer variabilities were $5.5 \pm 4\%$, $4.8 \pm 3.7\%$, and $6 \pm 3.8\%$, respectively.

190

191 **Discussion**

192 To our knowledge, this is the first study to show that the preload dynamic indices ΔV_{peak}
193 and CVCDI can predict the response to a fluid bolus in anaesthetised adult dogs undergoing

194 mechanical ventilation.

195

196 All three indices tested in this study can be used to predict the fluid responsive status of an
197 anaesthetized and mechanically ventilated dog, as it has been proposed in humans (Feissel et al.,
198 2001; Feissel et al., 2004; Barbier et al., 2004; Pereira de Souza Neto et al., 2011). The ΔV_{peak} had
199 the best predictive value of the three indexes. The best performance of ΔV_{peak} may be explained,
200 on one hand, by the fact that arterial compliance has a lower influence on this index than on other
201 dynamic indices (Durand et al., 2008). On the other, V_{peak} can be a major component of the VTI,
202 especially when left ventricle ejection time is short. CVCDI had the worst performance as index of
203 fluid responsiveness in this study. One reason which may explain this performance is that CVCDI
204 measurement may be influenced by movements of the area to be scanned during ventilation, which
205 can result in measurement errors. The fact that the ultrasound scanning of the vena cava in dog can
206 be difficult in some subjects may have been another source of error.

207 Based on this study SPV can be regarded as an excellent predictor of fluid responsiveness. This is
208 the first study which tests SPV as index of fluid responsiveness using a SV measurement or a
209 surrogate of it. Previously, the HR or MAP variation, comparing baseline and post fluid challenge
210 values, were used to analyse the ability of the baseline SPV to predict 10% decrease in HR or
211 increase in MAP (Rabozzi & Franci 2014). Considering the important difference regarding the
212 response variables between this study and the previous on SPV, not surprisingly, two differences
213 cut-off values were found: 4.5% Vs 6.7%. The higher SPV cut-off value found in this study can be
214 even partially explained by the higher airway pressure of ventilation used. Studies have shown that
215 a higher airway pressure is associated with a greater cut-off value that is able to discriminate
216 between responders and non-responders (da Silva Ramos et al., 2011; Michard, 2005).

217

218 Even though, there are reports which suggest that SPV is less accurate than pulse pressure
219 variation (ΔPP), in our opinion it retains one important practical advantage over others dynamic

220 indices. In clinical veterinary practice it is uncommon to have monitors which provide dynamic
221 index values to the clinician. In order to measure them one has to use the modality presented by
222 Rabozzi & Franci (2014) and used in this paper, which is already rather time consuming for SPV.
223 Pulse pressure variation needs twice the manual measurements than SPV.

224

225 In our study, there were not significant differences of the heart rate and mean arterial pressure
226 in the two groups (R and NR). This implies that the monitoring of blood pressure or heart rate may
227 not be a reliable way to evaluate preload-dependence of an anaesthetized and ventilated subject.

228

229 The dynamic indices considered in this study are based on cyclical interactions between the
230 heart and lungs during mechanical ventilation, and the extent of their variations is proportional to
231 the magnitude of hypovolaemia. The inspiratory phase of positive-pressure ventilation causes a
232 decrease in both the venous return from the CVC and the ventricular preload (Pinsky, 1997; Luecke
233 and Pelosi, 2005). From this point of view, mechanical ventilation itself can be considered as a
234 rhythmic volaemic challenge. For this reason, the above-mentioned preload indices can better
235 predict fluid responsiveness in subjects fully adapted to mechanical ventilation, because all the
236 aspects of the breathing cycle are predetermined and constantly maintained breath-by-breath..

237

238 In this study, the VTI was measured as a SV surrogate both before and after volume
239 expansion to evaluate the SV variation in the same dog. In several studies in humans, the VTI has
240 been used as a SV surrogate to measure the variation of left ventricular ejection in the same subject
241 (Pereira de Souza Neto et al., 2011; Brun et al., 2012; de Oliveira et al., 2016). This approach to
242 monitor cardiovascular function has several advantages both in clinical and experimental settings in
243 veterinary medicine. It provides non-invasive beat-to-beat monitoring of SV, without further pain
244 and distress.

245

246 Although SPV is an invasive index, its use is advantageous during the intraoperative period.
247 In the majority of surgical procedures, monitoring ΔV_{peak} or CVCDI is not feasible owing to
248 incorrect positioning or difficulties in reaching the body area for scanning. In some dogs, it might
249 be difficult to obtain good images of the CVC owing to rhythmic interposition of the lungs, and
250 both ΔV_{peak} and CVCDI can be difficult to evaluate in large dogs with a profound chest. The cut-
251 off values identified are of value only within the clinical setting presented, as different airway
252 pressures will produce different cut-off values. Respiratory diseases, which cause relevant changes
253 in chest and/or lung compliance or are associated with lung hyperinflation and the development of
254 auto-PEEP, can reduce the clinical applicability of the data obtained in this study. Dynamic indices
255 of fluid responsiveness are difficult to use in dogs with respiratory diseases, as well as dogs with
256 cardiac conditions that impede venous return or aortic blood flow and dogs with profound alteration
257 of the Frank-Starling curve owing to end-stage myocardial degeneration. CVCDI should not be
258 used with increased abdominal pressure, as the CVC size can reduce in this condition. Moreover, all
259 conditions that cause direct mechanical action, such as restriction, compression, and thrombosis of
260 the CVC, may invalidate the applicability of CVC ultrasound to estimate fluid responsiveness (Via
261 et al., 2016).

262

263 Decisions with regard to fluid therapy, irrespective of the clinical setting, are among the
264 most important tasks that veterinarians face daily, considering that hypervolaemia and
265 hypovolaemia can increase the risk of mortality (Han et al., 2003; Rosenberg et al., 2009; Boyd et
266 al., 2011). The only reason for a fluid challenge is to increase the SV. When an animal is a non-
267 responder, a fluid challenge should be potentially harmful, at least in the most fragile animals.
268 Careful fluid administration should be considered even in anaesthetised animals, as there is
269 evidence that anaesthesia can cause a drastic change in fluid distribution across the body (Hahn,
270 2010). In this clinical setting, there is a steep increase in the amount of administered fluids
271 distributed in the interstitial space, and this can be more pronounced and detrimental in

272 hypervolaemic or ill animals (Lee and Slutsky, 2010; Bruegger et al., 2005). Therefore, the
273 advantages of a fluid challenge should be well weighted against the potential risks. Further studies
274 recruiting a larger number of dogs could be useful in understanding whether the use of indices of
275 fluid responsiveness to manage fluid therapy in the perioperative period can improve the outcome in
276 subjects undergoing surgical procedures.

277

278 **Conclusion**

279 SPV, Δ PV and CVCDI are reliable predictors of fluid responsiveness in dogs undergoing general
280 anaesthesia and mechanical ventilation.

281

282 **Conflict of interest statement**

283 The authors have no conflicts of interest to declare.

284

285 **Acknowledgments**

286 This study was presented in part at the Italian Society of Ultrasonography in Medicine and Biology
287 (SIUMB) National Congress, Rome, November 2015.

288

289 **References**

- 290 Barbier, C., Loubieres, Y., Schmit, C., Hayon, J., Ricome, J.L., Jardin, F., Vieillard-Baron, A.,
291 2004. Respiratory changes in inferior vena cava diameter are helpful in predicting fluid
292 responsiveness in ventilated septic patients. *Intensive Care Medicine* 30, 1740-1746.
293
- 294 Bruegger, D., Jacob, M., Rehm, M., Loetsch, M., Welsch, U., Conzen, P., Becker, B.F., 2005.
295 Atrial natriuretic peptide induces shedding of endothelial glycocalyx in coronary vascular bed
296 of guinea pig hearts. *American Journal of Physiology. Heart and Circulatory Physiology* 289,
297 H1993-1999.
298
- 299 Brun, C., Zieleskiewicz, L., Textoris, J., Muller, L., Bellefleur, J.P., Antonini, F., Turrett, M.,
300 Ortega, D., Vellin, A., Lefrant, J.Y. et al., 2013. Prediction of fluid responsiveness in severe
301 preeclamptic patients with oliguria. *Intensive Care Medicine* 39, 593-600.
302

303 da Silva Ramos, F.J., de Oliveira, E.M., Park, M., Schettino, G.P., Azevedo, L.C., 2011. Heart-lung
304 interactions with different ventilatory settings during acute lung injury and hypovolaemia: an
305 experimental study. *British Journal of Anaesthesia* 106, 394-402.
306

307 de Oliveira, O.H., Freitas, F.G., Ladeira, R.T., Fischer, C.H., Bafi, A.T., Azevedo, L.C., Machado,
308 F.R., 2016. Comparison between respiratory changes in the inferior vena cava diameter and
309 pulse pressure variation to predict fluid responsiveness in postoperative patients. *Journal of*
310 *Critical Care* 34, 46-49.
311

312 Desgranges, F.P., Desebbe, O., Pereira de Souza Neto, E., Raphael, D., Chassard, D., 2016.
313 Respiratory variation in aortic blood flow peak velocity to predict fluid responsiveness in
314 mechanically ventilated children: a systematic review and meta-analysis. *Paediatric*
315 *Anaesthesia* 26, 37-47.
316

317 Durand, P., Chevret, L., Essouri, S., Haas, V., Devictor, D., 2008. Respiratory variations in aortic
318 blood flow predict fluid responsiveness in ventilated children. *Intensive Care Medicine* 34,
319 888-894.
320

321 Feissel, M., Michard, F., Faller, J.P., Teboul, J.L., 2004. The respiratory variation in inferior vena
322 cava diameter as a guide to fluid therapy. *Intensive Care Medicine* 30, 1834-1837.
323

324 Feissel, M., Michard, F., Mangin, I., Ruyet, O., Faller, J.P., Teboul, J.L., 2001. Respiratory changes
325 in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic
326 shock. *Chest* 119, 867-873.
327

328 Gan, H., Cannesson, M., Chandler, J.R., Ansermino, J.M., 2013. Predicting fluid responsiveness in
329 children: a systematic review. *Anesthesia and Analgesia* 117, 1380-1392.
330

331 Hahn, R.G., 2010. Volume kinetics for infusion fluids. *Anesthesiology* 113, 470-481.
332

333 Jardin, F., Farcot, J.C., Gueret, P., Prost, J.F., Ozier, Y., Bourdarias, J.P., 1983. Cyclic changes in
334 arterial pulse during respiratory support. *Circulation* 68, 266-274.
335

336 Lee, W.L., Slutsky, A.S., 2010. Sepsis and endothelial permeability. *The New England Journal of*
337 *Medicine* 363, 689-691.
338

339 Lewis, J.F., Kuo, L.C., Nelson, J.G., Limacher, M.C., Quinones, M.A., 1984. Pulsed Doppler
340 echocardiographic determination of stroke volume and cardiac output: clinical validation of
341 two new methods using the apical window. *Circulation* 70, 425-431.
342

343 Luecke, T., Pelosi, P., 2005. Clinical review: positive end-expiratory pressure and cardiac output.
344 *Critical Care* 9, 607-621.
345

346 Marik, P.E., Cavallazzi, R., Vasu, T., Hirani, A., 2009. Dynamic changes in arterial waveform
347 derived variables and fluid responsiveness in mechanically ventilated patients: a systematic
348 review of the literature. *Critical Care Medicine* 37, 2642-2647.
349

350 Meneghini, C., Rabozzi, R., Franci, P., 2016. Correlation of the ratio of caudal vena cava diameter
351 and aorta diameter with systolic pressure variation in anesthetized dogs. *American Journal of*
352 *Veterinary Research* 77, 137-143.
353

354 Michard, F., 2005. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 103,
355 419-428; quiz 449-445.
356

357 Michard, F., Teboul, J.L., 2002. Predicting fluid responsiveness in ICU patients: a critical analysis
358 of the evidence. *Chest* 121, 2000-2008.
359

360 Nguyen, H.B., Losey, T., Rasmussen, J., Oliver, R., Guptill, M., Wittlake, W.A., Corbett, S.W.,
361 2006. Interrater reliability of cardiac output measurements by transcutaneous Doppler
362 ultrasound: implications for noninvasive hemodynamic monitoring in the ED. *The American*
363 *Journal of Emergency Medicine* 24, 828-835.
364

365 Pereira de Souza Neto, E., Grousseau, S., Duflo, F., Ducreux, C., Joly, H., Convert, J., Mottolise, C.,
366 Dailier, F., Cannesson, M., 2011. Predicting fluid responsiveness in mechanically ventilated
367 children under general anaesthesia using dynamic parameters and transthoracic
368 echocardiography. *British Journal of Anaesthesia* 106, 856-864.
369

370 Perel, A., Pizov, R., Cotev, S., 1987. Systolic blood pressure variation is a sensitive indicator of
371 hypovolemia in ventilated dogs subjected to graded hemorrhage. *Anesthesiology* 67, 498-502.
372

373 Pinsky, M.R., 1997. The hemodynamic consequences of mechanical ventilation: an evolving story.
374 *Intensive Care Medicine* 23, 493-503.
375

376 Rabozzi, R., Franci, P., 2014. Use of systolic pressure variation to predict the cardiovascular
377 response to mini-fluid challenge in anaesthetised dogs. *Veterinary Journal* 202, 367-371.
378

379 Vallet, B., Blanloeil, Y., Cholley, B., Orliaguet, G., Pierre, S., Tavernier, B., 2013. Guidelines for
380 perioperative haemodynamic optimization. *Annales Françaises d'Anesthésie et de Réanimation*
381 32. 151-158
382

383 Via, G., Tavazzi, G., Price, S., 2016. Ten situations where inferior vena cava ultrasound may fail to
384 accurately predict fluid responsiveness: a physiologically based point of view. *Intensive Care*
385 *Medicine* 42, 1164-1167.
386
387

388 **Table 1**

389 Baseline characteristics of the dogs

	Total	R	NR	<i>P</i> -value
No. of dogs	24	9	15	
Sex (male/female)	10/14	4/5	6/9	0.280*
Age (months)	27 (16–52)	26 (18–48)	30 (16–52)	0.445**
Weight (kg)	8.2 (7.5–12.6)	9.2 (6.8–11.8)	7.8 (7.2–12.6)	0.322**
Type of surgery (No.)	Ovariectomy (10)	Ovariectomy (3) Orthopaedic surgery (TPLO) (4)	Ovariectomy (7) Orthopaedic surgery (TPLO) (5)	
	Orthopaedic surgery (TPLO) (9)	Skin surgery (2)	Skin surgery (3)	
TV/kg (mL/kg)	14 (13–15)	13 (12–16)	14 (13–15)	0.932**
Respiratory rate (breaths/min)	14 (12–14)	14 (12–14)	14 (12–14)	1**
Plateau pressure (cmH ₂ O)	10	10	10	
I:E ratio	1:2	1:2	1:2	

390

391 Data are presented as median (25th-75th percentiles) or numbers.

392 *Fisher's exact test; **Independent Student's *t*-test

393 R, Responders; NR, Non-responders; TV, Tidal volume; TPLO, Tibial plateau levelling osteotomy

394 **Table 2**

395 Haemodynamic parameters in group R and group NR before and after volume expansion

Group	Before fluid challenge		<i>P</i> -value*	After fluid challenge		<i>P</i> -value*
	R	NR		R	NR	
Dogs (No.)	9	15		9	15	
HR (beats/min)	91 (76–105)	78 (65–90)	0.0889	81 (70–98)	75 (60–83)	0.4732
SAP (mmHg)	98 (96–101)	110 (94–112)	0.189	105 (101–108)	114 (102–118)	0.2201
DAP (mmHg)	58 (57–63)	54 (50–62)	0.2616	61 (60–76)	55 (50–62)	0.0828
MAP (mmHg)	71 (70–72)	71 (68–79)	1	74 (74–77)	76 (70–79)	0.8812
SPV (%)	6.9 (6.8–7.1)	5.2 (4.5–6.3)	0.0009	2.9 (2.2–3.4)	4.4 (3.8–5.6)	0.0031
ΔV_{peak} (%)	11 (10.7–12.2)	7.3 (6.3–8.9)	0.0003	6.8 (4–7.5)	7 (4.6–8.3)	0.9286
CVCDI (%)	33 (30–38)	21 (19–30)	0.0271	25 (15–30)	19 (12–22)	0.2201

396

397 Data are presented as median (25th-75th percentiles) or numbers.

398 *Wilcoxon rank-sum test

399 R, Responders; N, Non-responders; HR, Heart rate; SAP, Systolic arterial pressure; DAP, Diastolic

400 arterial pressure; SPV, Systolic arterial Pressure; ΔV_{peak} , Aortic flow peak velocity variation;

401 CVCDI, Caudal vena cava distensibility index

402 **Figure Legends**

403 Fig. 1

404 Box-plot of the systolic pressure variation (SPV) index before volume expansion (VE), comparison
405 between responders and non-responders group ($P=0.0009$)

406

407 Fig. 2

408 Box-plot of the aortic flow peak velocity variation (ΔV_{peak}) index before volume expansion (VE),
409 comparison between responders and non-responders group ($P=0.0003$)

410

411 Fig. 3

412 Box-plot of the caudal vena cava distensibility index (CVCDI) before volume expansion (VE),
413 comparison between responders and non-responders group ($P=0.0271$)

414

415 Fig. 4

416 Receiver operating characteristic (ROC) curves comparing the ability of the ΔV_{peak} , CVCDI and
417 SPV to predict fluid responsiveness. The area under the curve is 0.95 (CI 0.77–1; $P = 0.0001$)
418 for the ΔV_{peak} , 0.91 (CI 0.73–0.99; $P = 0.0001$) for the SPV and 0.78 (CI 0.56–0.92; $P =$
419 0.015) for the CVCDI.

420