



# Cardiopulmonary effects of a new inspiratory impedance threshold device in acute hemorrhagic shock in dogs

Alessio Vigani, DVM, PhD; Andre C. Shih, DVM, DACVA; Gareth J. Buckley, MA, VetMB, DACVECC, MRCVS; Leonel Londoño, DVM and Carsten Bandt, DVM, DACVECC

## Abstract

**Objective** – To compare cardiovascular and respiratory effects of an inspiratory impedance threshold device (ITD) in dogs before and after induction of acute hemorrhagic shock.

**Study Design** – Prospective experimental randomized study.

**Animals** – Eight healthy adult dogs.

**Methods** – Dogs were anesthetized and maintained on spontaneous ventilation. Tidal volume ( $V_T$ ), systolic, mean and diastolic arterial blood pressure (SAP, MAP, DAP), central venous pressure (CVP), gastric  $P_{CO_2}$  (GBF) as an indicator of gastric perfusion, cardiac index (CI), systemic vascular resistance (SVR), oxygen delivery ( $DO_2$ ), and plasma lactate were monitored. To monitor respiratory compliance (RC) and respiratory resistance (ResR), animals were briefly placed on mechanical ventilation. Dogs were studied under 4 different conditions: (1) baseline (euvoletic state) (MAP > 60 mm Hg) with and without the ITD and (2) acute hemorrhagic shock (hypovolemic state) (target MAP of 40 mm Hg) with and without ITD. These 4 conditions were performed during one anesthetic period, allowing time for stabilization of parameters for each condition. Data were analyzed by ANOVA for repeated measure mixed models.

**Results** – No cardiovascular changes were detected between groups with and without use of ITD during euvoletic states. During acute hemorrhagic hypovolemic state, CI and  $DO_2$  were higher with the ITD ( $2.9 \pm 0.6$  L/min/m<sup>2</sup>) and ( $326.5 \pm 86.8$  mL/min) compared with no ITD ( $1.8 \pm 0.6$  L/min/m<sup>2</sup>) and ( $191.3 \pm 58.1$  mL/min), respectively. The use of ITD during hypovolemia also increased SAP and MAP. There was an increase in ResR and decreased RC with the ITD in both euvoletic and hypovolemic states.

**Conclusion and clinical relevance** – The use of an ITD in dogs during acute hemorrhagic hypovolemic shock improved cardiovascular parameters but had negative effects on RC and ResR.

(J Vet Emerg Crit Care 2011; 21(6): 618–624) doi: 10.1111/j.1476-4431.2011.00692.x

**Keywords:** canine, cardiac output, hypovolemic shock, ITD

## Introduction

Hemorrhagic shock remains one of the leading causes of death following multiple system trauma.<sup>1,2</sup> Untreated,

severe hypovolemia leads to circulatory collapse and organ failure,<sup>2</sup> making the maintenance of appropriate cardiac output (CO) and oxygen delivery ( $DO_2$ ) critical in preventing multiple organ ischemic injury and mortality.<sup>3–5</sup> The value of aggressive large volume replacement to improve CO in trauma patients has been questioned, especially in those patients with hemorrhagic shock. Fluid resuscitation that is too vigorous (eg, excessive volume or too rapid) may result in a bleeding diathesis and ultimately decrease oxygen-carrying capacity.<sup>2</sup> A therapeutic method that could improve CO without the need for large volume fluid administration would be beneficial for treatment of hemorrhagic shock.

Breathing exerts a significant influence on venous return to the heart, and one of the body's natural responses to hypotension is to harness the respiratory effect on

From the Departments of Large Animal Clinical Sciences (Vigani, Shih) and Small Animal Clinical Sciences (Buckley, Londoño, Bandt), College of Veterinary Medicine, University of Florida, Gainesville, FL 32610.

Funded in part by the University of Florida, College of Veterinary Medicine Consolidated Faculty Research Development Grant.

The authors declare no conflict of interest.

Preliminary data presented at the 2010 International Veterinary Emergency Critical Care Symposium, San Antonio, TX.

Address correspondence and requests to Dr. Carsten Bandt, 2015 SW 16th Ave, College of Veterinary Medicine, Gainesville, FL 32610, USA.

Email: bandtc@ufl.edu

Submitted March 12, 2011; Accepted September 30, 2011.

venous return to improve hemodynamics.<sup>6</sup> An increase in airway resistance leads to a reduction in pleural pressure and increases systemic venous return,<sup>6,7</sup> improving CO without the need for fluid administration.

Impedance threshold devices (ITDs) are noninvasive, disposable, small plastic devices that fit on the endotracheal tube. They are composed of a one-way valve with a set opening pressure referred to as “cracking pressure.” ITDs generate a momentary airway resistance and therefore, augment negative intrathoracic pressure and improve venous return.<sup>8</sup> Depending upon the set cracking pressure, ITDs are designed for use in cardiopulmonary resuscitation (eg, high cracking pressure) or for spontaneous breathing (eg, low cracking pressure).<sup>2</sup> A high cracking pressure of  $-12$  cm H<sub>2</sub>O found in ITDs such as the *ResQPod*, may be useful in CPR. The *ResQGuard*<sup>9</sup> instead is a new ITD designed with a low cracking pressure (eg,  $-7$  cm H<sub>2</sub>O) to be used in spontaneously breathing patients to aid in the treatment of hypovolemia.<sup>9</sup>

The use of ITDs increased CO and blood pressure in a pediatric porcine model of hemorrhagic hypovolemia.<sup>2</sup> An ITD device could be useful for the treatment of hypovolemic shock reducing the total amount of fluid required for resuscitation, or by buying time while fluid therapy is administered or surgery is planned. The ITD has also been used to treat isoflurane-induced hypotension due to high doses of isoflurane in anesthetized dogs.<sup>10</sup> To the best of the authors' knowledge, this is the first study using ITD in dogs during acute hemorrhagic shock.

In the present study, we hypothesized that ITD will significantly affect hemodynamic parameters, respiratory variables, and gastric blood flow during euvoolemia and acute hypovolemia in anesthetized dogs.

## Materials and Methods

This study was approved by the University of Florida Institutional Animal Care and Use Committee.

### Animals

Eight healthy cross-breed dogs were used in this study. Dogs enrolled in this study were older than 1 year of age and were healthy based on physical examination, complete blood count, and serum biochemistry profiles. Animals were fasted for 12 hours prior to each experiment but had free access to water.

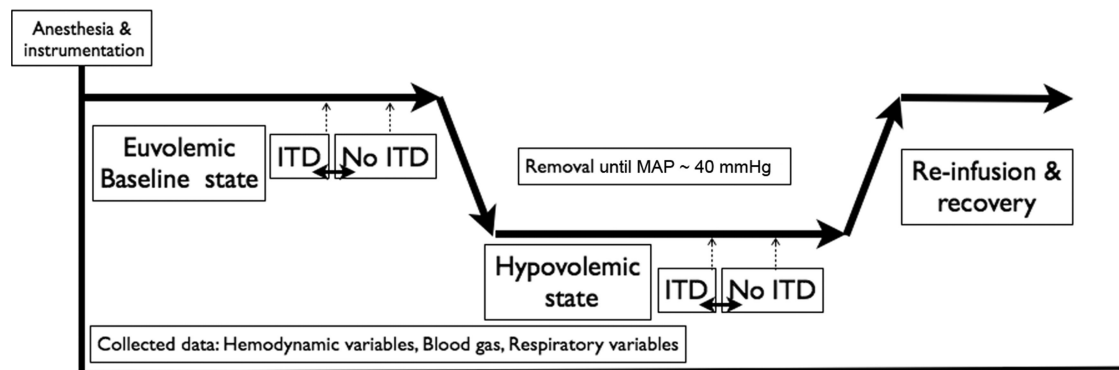
### Animal preparation

A 20-Gauge, 1-inch length over-the-needle catheter was aseptically placed in the cephalic vein and anesthesia was induced with IV propofol<sup>b</sup> given to effect (calcu-

lated dose 10 mg/kg). An endotracheal tube was placed and the cuff inflated to eliminate air leak around the tube at 20 cm H<sub>2</sub>O. Anesthesia was maintained with isoflurane<sup>c</sup> vaporized in oxygen and delivered via a circle breathing system. Animals were placed in right lateral recumbency. A 7-Fr 30 cm, double lumen catheter<sup>d</sup> was placed in the jugular vein and its tip directed to the junction of the cranial vena cava and right atrium. Length of the catheter was premeasured (mid neck to right atrial chamber) and placement confirmed by examination of the pressure waveform. A 20-G, 1.88-inch catheter was placed in the right medial metatarsal artery. Animals were instrumented<sup>e,f</sup> for continuous monitoring of end tidal CO<sub>2</sub> (PE'CO<sub>2</sub>), end tidal isoflurane (Et<sub>Iso</sub>), tidal volume (V<sub>T</sub>), direct systolic, mean, diastolic arterial pressure (SAP, MAP, DAP, respectively), central venous pressure (CVP), heart rate (HR), and respiratory rate (f<sub>R</sub>). Plasma lactate, blood hemoglobin, arterial and central venous blood gas, and oxyhemoglobin content were also measured.<sup>8</sup> Arterial DO<sub>2</sub> was calculated at each experimental stage using the formula:  $DO_2 = CO \times (1.34 \times Hb \times SPO_2) + (0.003 \times PaO_2)$ . The atmospheric pressure value used in the experiment was a default sea level of 760 mm Hg. Rectal temperature was maintained between 37° and 38°C with the help of a circulating, warm-water blanket.

CO was measured by the LidCO-lithium dilution method.<sup>h</sup> Lithium chloride (0.003 mmol/kg) was injected IV via the CVP. CO was derived from the concentration versus time curve as described by Corley et al.<sup>11</sup> Stroke volume (SV) and systemic vascular resistance (SVR) were calculated by the LiDCO computer.<sup>i</sup> The SV was calculated as  $CO/HR \times 1000$  and SVR was calculated as  $([MAP - CVP] \times 80)/CO$ . Each dog's height (cm) was determined by measuring from the tip of the nose to the anus.<sup>12</sup> Body surface area (BSA) was determined by the modified DuBois equation:  $BSA (m^2) = 0.0072 \text{ Height (cm)}^{0.725} \times \text{Weight (kg)}^{0.425}$ . CO was divided by BSA to calculate cardiac index (CI).

A gastric tonometry catheter<sup>j</sup> was inserted by mouth into the gastric cavity to estimate visceral blood perfusion (GBF). The length of the tube was premeasured (tip of the nose to the stomach) and the gastric tonometry tube was placed blindly. Gastric tonometry estimates mucosal perfusion by measuring the amount of CO<sub>2</sub> produced by the gastric mucosa.<sup>13,14</sup> The rationale for this approach is that inadequate DO<sub>2</sub> to the stomach results in an increase of lactic acid and gastric CO<sub>2</sub> formation. Increased CO<sub>2</sub> indirectly reflects a decrease in tissue perfusion.<sup>13-15</sup> The gastric-to-arterial carbon dioxide gap reflects the mucosal blood supply to metabolic demand balance and is considered a marker of gastric perfusion.<sup>14</sup> The gastric tonometry module was calibrated using a CO<sub>2</sub> calibration gas<sup>k</sup> of known concentration (5%).



**Figure 1:** Experimental protocol assessing hemodynamic effects with and without impedance threshold device (ITD) during hemorrhagic shock.

Animals were allowed to breathe spontaneously throughout the experiment and were mechanically ventilated only for the determination of respiratory compliance (RC) and respiratory resistance (ResR). The ventilator setting was trying to mimic the patients' respiratory rate (RR) and  $V_T$ . The ventilator was set at volume control with a respiratory pause;  $f_R$  and  $V_T$  equal to each of the patients' previous spontaneous breathing pattern. The pressure difference measured between 2 Pitot tubes facing in opposite directions during inspiration and expiration was used to calculate air-flow velocity,  $V_T$ , RC, and ResR<sup>e</sup> with atmospheric pressure as the comparison pressure. Three to 4 breath cycles were usually needed to measure RC and ResR.

### Experimental protocol

After instrumentation, dogs were evaluated during 2 volumetric states, baseline euvoolemia and hypovolemia. To achieve the euvolemic state animals were kept at end tidal isoflurane of approximately 1.4% (baseline). Following this, a hemorrhagic hypovolemic state was obtained by actively withdrawing blood using a 60-mL syringe connected to a 3-way stopcock, until the MAP was stable at  $40 \pm 5$  mm Hg (hypovolemia). Blood volume was calculated as  $80 \text{ mL/kg}$ .<sup>16</sup> Blood was collected from the central venous catheter and stored in citrate-phosphate-dextrose-adenine solution<sup>1</sup> in a 37°C incubator. Blood was withdrawn at a constant rate over approximately 30 minutes. Once the target MAP of  $40 \pm 5$  mm Hg was reached, a timer was initiated and animals were maintained at a stable hemodynamic plane (MAP of  $40 \pm 5$  mm Hg) for a minimum of 10 minutes prior to data collection. If a physiologic compensatory mechanism developed and MAP increased above the target values, more blood was removed to restore the MAP back to  $40 \pm 5$  mm Hg and the timer reinitiated for a new equilibration period of 10 minutes prior to data collection. At each

state, measurements were performed in duplicate with at least 3 minutes between measurements. If any 2 measurements for a given method varied by more than 20%, a third measurement was taken and the measurement outside the 20% variation was discarded. Cardiopulmonary variables, lactate, gastric tonometry, and peripheral perfusion were recorded with and without the ITD in place. Animals were kept in a euvolemic baseline state first and then a hypovolemic state was induced. A random sequence generator determined the order of treatment (ITD vs. no ITD). All animals received both treatments at each volumetric state (Figure 1). Blood withdrawn was returned to the patient at the end of the experiment. Animals were allowed to recover from anesthesia.

### Statistical analyses

Data were analyzed by ANOVA for repeated measures determined by least square analysis of variance, using the General Linear Modules procedures of SAS.<sup>m</sup> For all analyses,  $P < 0.05$  was considered significant. Data are expressed as mean  $\pm$  SD.

### Results

A total of 8 dogs were used. Body weight ranged from 18.5 to 31 kg, with a mean of  $21.1 \pm 4.9$  kg. To determine CO by LidCO a total  $1.3 \pm 0.5$  mmol of lithium chloride was used, no signs of lithium overdose were observed. End tidal isoflurane concentration was maintained constant at  $1.4 \pm 0.3\%$  throughout the procedure. The total amount of blood removed to induce the hypovolemic state was  $(36.12 \pm 10.37 \text{ mL/kg})$  equal to  $(45.16 \pm 12.96\%$  of total blood volume). All animals recovered without complications from the study.

There were no significant changes in any of the parameters (SAP/MAP/DAP, CVP, CI, HR, SVR, SV, SVR,  $\text{DO}_2$ , and GBF) ( $P > 0.05$ ), when using the ITD was

**Table 1:** Comparison of cardiovascular variables: heart rate (HR) in bpm, direct systolic, mean, diastolic arterial pressure (respectively, SAP, MAP, DAP) in mm Hg, central venous pressure (CVP) in mm Hg, cardiac index (CI) in L/min/m<sup>2</sup>, systemic vascular resistance (SVR) in dynes/s/cm<sup>5</sup>, and blood lactate concentration (Lactate) in mmol/L studied under 4 different conditions: (1) euvoemia without impedance threshold device (euvo no ITD), (2) euvoemia with ITD (euvo ITD), (3) hypovolemia without impedance threshold device (hypovol no ITD), and (4) hypovolemia with ITD (hypovol with ITD).

Treatment	HR	SAP*†	MAP*†	DAP*	CVP	CI*†	SVR	Hb	Lactate
Euvo no ITD	96 ± 15	107.8 ± 19.1	67.7 ± 12.5	54.4 ± 12.9	-0.75 ± 1.4	4.12 ± 1.4	1,435 ± 342	13.9 ± 1	1.0 ± 0.6
Euvo ITD	99 ± 20	101.9 ± 19.1	60.8 ± 12.5	40.2 ± 12.4	-2.6 ± 1.4	3.9 ± 1.3	1,424 ± 34	13.9 ± 2	1.0 ± 0.5
Hypovol no ITD	91 ± 8	56.3 ± 3.7	39.1 ± 1.9	32.5 ± 1.7	-5.25 ± 1.4	1.8 ± 0.6	1,863 ± 865	10.4 ± 2	1.3 ± 0.5
Hypovol ITD	99 ± 12	85.4 ± 16.3	55 ± 8.5	44.1 ± 5.8	-4.6 ± 2.6	2.9 ± 0.6	1,791 ± 352	10.6 ± 1	1.1 ± 0.3

\*Statistical significance between states (euvoemia vs. hypovolemia).

†Statistical significance between treatments (ITD vs. no ITD) in hypovolemic state with  $P < 0.05$ .

**Table 2:** Comparison of the variables: Respiratory rate (RR) in bpm, end tidal CO<sub>2</sub> (PE'CO<sub>2</sub>) in mmHg, end tidal isoflurane (E'ISO) in percent, tidal volume (V<sub>T</sub>) in mL, respiratory resistance (ResR) in cm H<sub>2</sub>O L/s, respiratory compliance (RC) in mL/cm H<sub>2</sub>O, oxygen delivery (DO<sub>2</sub>) in mL/min, gastric CO<sub>2</sub> tonometry (GBF) in mm Hg, and arterial oxygen tension (PaO<sub>2</sub>) in mm Hg in studied under 4 different conditions: (1) euvoemia without impedance threshold device (euvo no ITD), (2) euvoemia with ITD (euvoemia ITD), (3) hypovolemia without impedance threshold device (hypovol no ITD), and (4) hypovolemia with ITD (hypovol with ITD).

Treatment	RR	PaCO <sub>2</sub>	V <sub>T</sub>	RC*	ResR*	DO <sub>2</sub> *	GBF	PaO <sub>2</sub>
Euvo no ITD	10 ± 3	46.6 ± 4	257 ± 53	32.2 ± 5.4	3.1 ± 1.2	583.0 ± 226.6	5.4 ± 1.6	499 ± 22
Euvo ITD	15 ± 5	40 ± 3.4	255 ± 40	18.3 ± 6	15.5 ± 2	449 ± 242.8	5.7 ± 1.6	411 ± 23
Hypovol no ITD	15 ± 6	42.2 ± 5	252 ± 84	29.3 ± 5.5	2.6 ± 1.2	191.3 ± 58.1	6.4 ± 3.8	461 ± 73
Hypovol ITD	16 ± 3	46 ± 4	266 ± 67	17.4 ± 3.6	14.6 ± 1.4	326.5 ± 86.8	5.4 ± 4.0	447 ± 90

\*Statistical significance between states (euvoemia vs. hypovolemia).

compared to no ITD during baseline euvoemic state (Tables 1 and 2). There was, however, a significant increase in ResR ( $3.1 \pm 1.2$  vs.  $14.7 \pm 1.4$  cm H<sub>2</sub>O/L/s;  $P < 0.01$ ) and decrease in RC ( $32.0 \pm 5.3$  vs.  $17.5 \pm 3.6$  mL/cm H<sub>2</sub>O;  $P < 0.01$ ) with the ITD versus without ITD, during baseline euvoemic dogs. No changes in minute ventilation ( $f_R \times V_T$ ) or occurrence of hypoventilation (PaCO<sub>2</sub>) ( $46.6 \pm 4$  vs.  $40.0 \pm 3.4$  mm Hg;  $P > 0.05$ ) were observed with use of ITD at either experimental stage.

When euvoemic state was compared to hypovolemic state without ITD there was a significant decrease in SAP ( $107.8 \pm 19.1$  vs.  $56.3 \pm 3.7$  mm Hg;  $P = 0.001$ ), MAP ( $67.7 \pm 16.5$  vs.  $39 \pm 1.8$  mm Hg;  $P = 0.001$ ), DAP ( $54.4 \pm 12$  vs.  $32 \pm 1.6$  mm Hg;  $P = 0.001$ ), CI ( $4.1 \pm 1.3$  vs.  $1.8 \pm 0.5$  L/min/m<sup>2</sup>;  $P = 0.004$ ), and DO<sub>2</sub> ( $583.0 \pm 226.6$  vs.  $191.3 \pm 58.1$  mL/min;  $P = 0.001$ ).

During hemorrhagic hypovolemic state, the use of ITD significantly increased CI by 37.9% ( $1.8 \pm 0.5$  vs.  $2.9 \pm 0.6$  L/min/m<sup>2</sup>;  $P = 0.003$ ) and DO<sub>2</sub> by 70.6% ( $191.3 \pm 58.1$  vs.  $326.5 \pm 86.8$  mL/min;  $P = 0.003$ ) (Table 1). The ITD improved SAP by 34% ( $56.3 \pm 3.7$  vs.  $85 \pm 16.3$  mm Hg;  $P = 0.02$ ) and MAP by 29% ( $39.1 \pm 1.8$  vs.  $55 \pm 8.4$  mm Hg;  $P = 0.006$ ), but not DAP. HR, SVR, and gastric tonometry CO<sub>2</sub> did not change significantly ( $P > 0.05$ ). There was an increase in ResR by 560% ( $2.6 \pm 0.7$  vs.  $14.62 \pm 1.4$  cm H<sub>2</sub>O/L/s;  $P = 0.02$ ) and a decrease in compliance by 40% ( $29.3 \pm 5.4$  vs.  $17.5 \pm 3.5$  mL/cm H<sub>2</sub>O;  $P < 0.01$ ) with

the ITD. At the end of the study prior to retransfusion of shed blood the MAP was  $49.7 \pm 5.8$  mm Hg.

## Discussion

The main results of this investigation support the concept that inspiratory impedance threshold device may be valuable in the initial treatment of hypotension secondary to hypovolemia in dogs. The use of the ITD during spontaneous ventilation enhanced arterial blood pressure and CI during acute hemorrhagic shock. Since there was no change in SVR or HR, the improvement in CI was likely secondary to the decrease in intrathoracic pressure resulting in improved venous return and consequently CO and finally blood pressure. This in part explains why the use of the ITD significantly increased SAP and MAP but not DAP. The ITD improves venous return but does not dramatically change vascular tone and consequently SVR.<sup>9</sup> During hemorrhage, the use of ITD correlated with a significantly higher DO<sub>2</sub> compared to no ITD. Giving that there was no difference in Hb concentration ( $10.4$  vs.  $10.6$  g/dL) nor in SpO<sub>2</sub> values (99 vs. 99%) between ITD and no ITD during hypovolemia, the difference in DO<sub>2</sub> can be explained by the higher CO in the ITD group ( $2.25$  vs.  $1.33$  L/min).

The current study did not detect a change in GBF by gastric tonometry with use of the ITD. Gastric

tonometry is still a controversial method to assess visceral perfusion,<sup>17</sup> but despite this, it is still widely used in people as an assessment of intestinal mucosal perfusion<sup>14,15</sup> and of splanchnic perfusion.<sup>18</sup> Two conclusions could be drawn from our finding. One is that ITD improved central blood flow, diverting blood preferentially from peripheral compartments instead of splanchnic circulation. A second explanation would be that gastric tonometry technology was not sensitive enough to detect changes in GBF. A type II error due to the small study population may be an explanation for the lack of statistical difference and high SD in the gastric tonometry results. Moreover, the high SD found could also be related to difference in food intake and gastric pH of each animal.<sup>13</sup> The gastric pH was not evaluated in our study and cannot be ruled out as a source of variation. All dogs were fed the same diet on the same schedule, fasted overnight and were not on any medication that would alter stomach acid production. The physiologic gastric juice pH of fasted dogs is reported to be approximately 2.<sup>19</sup> In a human study triggered by the same controversies on the reliability of gastric tonometry, it has been shown that a reduction in interindividual variability in the parameters measured by gastric tonometry can be achieved only when the gastric juice pH is artificially raised to values above 4.<sup>20</sup> In the present study, gastric pH was not artificially manipulated and physiological values were used instead.

Other technologies such as laser Doppler flowmetry and contrast-enhanced ultrasonography to assess gastrointestinal perfusion are now available.<sup>21</sup> In human medicine both are used widely to evaluate gastric mucosal blood flow, but they require expensive equipment and specialized operators. Neither of these devices was available to us at the time of the experiment.

This investigation suggests that the ITD does not affect hemodynamic values in normotensive, euvolemic patients. Previous work performed by our group<sup>10</sup> determined ITD to be helpful in treating euvolemic hypotension induced by high doses of isoflurane anesthetic.<sup>10</sup> Thus, ITD may be useful in dogs for treating hypotension independent of its cause. An exception and absolute contraindication to the use of ITD is a pre-existing condition of heart failure. In such patients, the sudden augmentation of preload induced by ITD could lead to pulmonary overperfusion and possible myocardial decompensation. Further studies are warranted to demonstrate if those findings can be exploited in clinical situations.

The results in our study are in agreement with work done by Marino *et al*<sup>2</sup> and by Sigurdsson *et al*,<sup>22</sup> in which the use of an ITD resulted in a rapid increase in CI and blood pressure in a piglets hemorrhagic model. Sigurdsson reported keeping the ITD in place for up to 45 minutes.<sup>22</sup> The current study evaluated ITD for a

much shorter period of time (at least 10 minutes in each state). The improvement in blood pressure and CI may be short lived; however, even a temporary improvement would allow the clinician time to institute more definitive therapy. It is important to state that the ITD offers a palliative solution and ultimately, fluid resuscitation and correction of the cause of blood loss is critical to maintain long-term viability during hypovolemic shock.<sup>2</sup>

Unlike volume replacement with saline or colloids that may result in dilution of clotting factors and a decrease in oxygen-carrying capacity, the ITD increases venous return by harnessing the energy involved in spontaneous ventilation.<sup>2</sup> During spontaneous breathing, increasing the rate and depth of respiration promotes venous return and therefore enhances CO by a mechanism referred to as "abdomino-thoracic or respiratory pump."<sup>7</sup> During inspiration, the chest wall expands and the diaphragm descends. This makes the pleural pressure become more negative and consequently causes the intravascular (eg, CVP) and intracardiac pressures (eg, right atrial pressure) to temporarily fall.<sup>7</sup> Furthermore, as right atrial pressure falls during inspiration, the pressure gradient for venous return to the right ventricle increases. In the spontaneously breathing patient, the ITD creates a momentary transient inspiratory resistance and creates an even greater negative intrathoracic pressure and greater transthoracic gradient from the extrathoracic to intrathoracic great veins, resulting in increased venous return into the right atrium each time the patient takes a breath.<sup>21</sup> This can be at the same time an advantage and disadvantage. The harnessed energy can lead to increase work of breathing (WOB) and ventilatory collapse. The benefit of ITD assisted breathing must be weighted against the potential increase in WOB over time.<sup>2</sup> For an ITD to be clinically useful, the effort for breathing through the device should not demand excessive energy.<sup>23</sup>

This study suggests that spontaneously ventilating patients breathing through an ITD will encounter increased resistance during inspiration resulting in decreased chest compliance. In agreement with previous reports,<sup>10</sup> subjective observations noticed that the animals would breathe with more abdominal effort when ITD was in place but we did not detect signs of decreased minute ventilation ( $V_T \times f_R$ ) or hypoventilation when ITD was compared to no ITD. The determination of increased effort of breathing was based on the subjective observation by the blinded investigator, regarding abdominal component and chest excursion during the respiratory cycle. The use of a quantitative determination instead of a subjective observation would provide a more consistent evaluation of the "effort of breathing."

Animals in this study were healthy without any respiratory disease and were breathing through the ITD for

a short period of time. The energy available for breathing can be significantly diminished in ill and injured patients. Thus, ITD should be avoided in animals with pulmonary disease or injury, respiratory distress, or any compromise to the chest wall integrity.<sup>10</sup> If an ITD is to be used, it is important that signs of ventilation and muscle fatigue be monitored and this device should be removed as soon as the patient is unable to adequately ventilate,<sup>24</sup> as indicated by hypercapnia, decrease in  $V_T$  or increased effort of breathing.

There are some limitations to the current study. The small study sample size may have hampered our ability to detect differences between study groups. The study was also not designed to evaluate long-term organ function, including neurologic function after recovery. Additionally, CO was determined by lithium dilution and not pulmonary thermodilution (TD). The pulmonary TD method has been accepted as the gold standard for CO monitoring for many years.<sup>11,25</sup> However, measurement of CO via lithium dilution is comparable to TD,<sup>26</sup> and is currently one of the most commonly used methods in anesthetized dogs.<sup>26,27</sup> Also, this study was not set up to determine preload and afterload parameters such as left ventricular end diastolic volume and SV variation. Further studies looking at the ITD effect on real time beat-to-beat contractility and aortic impedance would be beneficial.

In conclusion, the ITD improved CI and arterial blood pressure in hypotensive dogs by an increase in ResR. The major drawback of ITD use consisted of a significant decrease in RC. Each individual clinical case would need to be evaluated to ensure that the advantages gained by improving cardiovascular function are balanced against the known negative effects on respiratory function. Further studies are needed to evaluate the benefits of ITD in veterinary medicine under a wide variety of conditions.

### Acknowledgement

The authors would like to thank Mr. Hunter Schrank for technical assistance in the execution of the study.

### Footnotes

- <sup>a</sup> ResQGard, Advanced Circulatory Systems Inc, Roseville, MN.
- <sup>b</sup> Propoflo, Abbott Animal Health, Chicago, IL.
- <sup>c</sup> Isoflo, Abbott Animal Health.
- <sup>d</sup> Mila International Inc, Denver, CO.
- <sup>e</sup> Spirometry 88956 Kit, Datex-Ohmeda, Tewksbury, MA.
- <sup>f</sup> AS/5 Monitor Datex-Ohmeda, Tewksbury, MA.
- <sup>g</sup> ABL 660 COoxymeter and Blood Gas Analyzer, Radiometer Inc, Copenhagen, DK.
- <sup>h</sup> LidCOplus, LidCO LTD.
- <sup>i</sup> LidCO CM 31-01 LiDCO LTD, London, UK.
- <sup>j</sup> Datex Naso-gastric Tonometry Catheter, Datex-Ohmeda.
- <sup>k</sup> Datex-Ohmeda.
- <sup>l</sup> CPDA-1 blood collection bag, Terumo Corp Teruflex, Tokyo, Japan.
- <sup>m</sup> SAS for Windows, version 9.3, SAS Institute Inc, Cary, NC.

### References

1. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. *J Trauma* 1995; 38(2):185–193.
2. Marino BS, Yannopoulos D, Sigurdsson G, et al. Spontaneous breathing through an inspiratory impedance threshold device augments cardiac index and stroke volume index in a pediatric porcine model of hemorrhagic hypovolemia. *Crit Care Med* 2004; 32(9 Suppl):S398–S405.
3. Tantalean JA, Leon RJ, Santos AA, et al. Multiple organ dysfunction syndrome in children. *Pediatr Crit Care Med* 2003; 4(2):181–185.
4. Hatherill M, Waggle Z, Purves L, et al. Mortality and the nature of metabolic acidosis in children with shock. *Intensive Care Med* 2003; 29(2):286–291.
5. Kim JJ, Dreyer WJ, Chang AC, et al. Arterial pulse wave analysis: an accurate means of determining cardiac output in children. *Pediatr Crit Care Med* 2006; 7(6):532–535.
6. Courmand A, Motley H, Werko L. Physiological studies of the effects of intermittent positive pressure breathing on cardiac output in man. *Am J Physiol* 1948; 152:162–174.
7. Guyton AC, Lindsey AW, Abernathy B, et al. Venous return at various right atrial pressures and the normal venous return curve. *Am J Physiol* 1957; 189(3):609–615.
8. Lurie KG, Voelckel WG, Zielinski T, et al. Improving standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve in a porcine model of cardiac arrest. *Anesth Analg* 2001; 93(3):649–655.
9. Lurie KG, Barnes TA, Zielinski TM, et al. Evaluation of a prototypic inspiratory impedance threshold valve designed to enhance the efficiency of cardiopulmonary resuscitation. *Respir Care* 2003; 48(1):52–57.
10. Shih AC, Vigani A, Loring N, et al. Cardiopulmonary effects of a new inspiratory impedance threshold device in anesthetized hypotensive dogs. *Vet Anaesth Analg* 2010; 37(3):215–221.
11. Corley KT, Donaldson LL, Furr MO. Comparison of lithium dilution and thermodilution cardiac output measurements in anaesthetised neonatal foals. *Equine Vet J* 2002; 34(6):598–601.
12. Cowgill R, Drabkin D. Determination of a formula for the surface area of the dog together with a consideration of formulae available for other species. *Am J Physiol* 1926; 81:36–61.
13. Sanchez LC, Giguere S, Javscas LH, et al. Effect of age, feeding, and omeprazole administration on gastric tonometry in healthy neonatal foals. *J Vet Intern Med* 2008; 22(2):406–410.
14. Cerny V, Cvachovec K. Gastric tonometry and intramucosal pH-theoretical principles and clinical application. *Physiol Res* 2000; 49(3):289–297.
15. Grum CM, Fiddian-Green RG, Pittenger GL, et al. Adequacy of tissue oxygenation in intact dog intestine. *J Appl Physiol* 1984; 56(4):1065–1069.
16. Finsterer U, Prucksunand P, Brechtelsbauer H. Critical evaluation of methods for determination of blood volume in the dog. *Pflugers Arch* 1973; 341(1):63–72.
17. Uusaro A, Ruokonen E, Takala J. Gastric mucosal pH does not reflect changes in splanchnic blood flow after cardiac surgery. *Br J Anaesth* 1995; 74(2):149–154.
18. Masai T, Taniguchi K, Kuki S, et al. Usefulness of continuous air tonometry for evaluation of splanchnic perfusion during cardiopulmonary bypass. *Asaio J* 2003; 49(1):108–111.
19. Sagawa K, Li F, Liese R, et al. Fed and fasted gastric pH and gastric residence time in conscious beagle dogs. *J Pharm Sci* 2009; 98(7):2494–2500.
20. Brinkmann A, Glasbrenner B, Vlatten A, et al. Does gastric juice pH influence tonometric PCO<sub>2</sub> measured by automated air tonometry? *Am J Respir Crit Care Med* 2001; 163(5):1150–1152.
21. Kamino D, Hata J, Haruma K, et al. Real-time visualization and quantitation of canine gastric mucosal blood flow by contrast-enhanced ultrasonography. *Scand J Gastroenterol* 2006; 41(7):856–861.
22. Sigurdsson G, Yannopoulos D, McKnite SH, et al. Effects of an inspiratory impedance threshold device on blood pressure and short term survival in spontaneously breathing hypovolemic pigs. *Resuscitation* 2006; 68(3):399–404.

23. Idris AH, Convertino VA, Ratliff DA, et al. Imposed power of breathing associated with use of an impedance threshold device. *Respiratory care* 2007; 52(2):177–183.
24. Lurie KG, Mulligan KA, McKnite S, et al. Optimizing standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve. *Chest* 1998; 113(4):1084–1090.
25. Tibby SM, Murdoch IA. Monitoring cardiac function in intensive care. *Arch Dis Child* 2003; 88(1):46–52.
26. Chen HC, Sinclair MD, Dyson DH, et al. Comparison of arterial pressure waveform analysis with the lithium dilution technique to monitor cardiac output in anesthetized dogs. *Am J Vet Res* 2005; 66(8):1430–1436.
27. Cooper ES, Muir WW. Continuous cardiac output monitoring via arterial pressure waveform analysis following severe hemorrhagic shock in dogs. *Crit Care Med* 2007; 35(7):1724–1729.