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RESEARCH PAPER

Pulse pressure variation as a guide for volume expansion in dogs undergoing orthopedic surgery

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Abstract

Objective To investigate whether pulse pressure variation (PPV) can predict fluid responsiveness in healthy dogs during clinical surgery.

Study design Prospective clinical study.

Animals A total of 33 isoflurane-anesthetized dogs with arterial hypotension during orthopedic surgery.

Methods Fluid challenge with lactated Ringer's solution (15 mL kg^{-1} in 15 minutes) was administered in mechanically ventilated dogs (tidal volume 10 mL kg^{-1}) with hypotension [mean arterial pressure (MAP) < 65 mmHg]. The volume expansion was considered effective if cardiac output (CO; transesophageal Doppler) increased by ≥ 15%. Cardiopulmonary data were analyzed using two-way ANOVA, receiver operating characteristics (ROC) curves and Spearman coefficient; $p < 0.05$ was considered significant.

Results Effective volume expansion, mean ± standard deviation 42 ± 4% increase in CO, ($p < 0.0001$) was observed in 76% of the dogs, resulting in a decrease in PPV ($p < 0.0001$) and increase in MAP ($p < 0.0001$), central venous pressure (CVP; $p = 0.02$) and ejection fraction ($p < 0.0001$) compared with before the fluid challenge. None of these changes occurred when volume expansion resulted in a nonsignificant CO increase of 4 ± 5%. No significant differences were observed in blood gas analysis between responsive and nonresponsive dogs. The increase in CO was correlated with the decrease in PPV ($r = -0.65$; $p < 0.0001$) but absolute values of CO and PPV were not correlated. The PPV performance (ROC curve area: 0.89 ± 0.06, $p = 0.0011$) was better than that of CVP (ROC curve area: 0.54 ± 0.12) and MAP (ROC curve area: 0.59 ± 0.13) to predict fluid responsiveness. The best cut-off for PPV to distinguish responders and nonresponders was 15% (50% sensitivity and 96% specificity).

Conclusions and clinical relevance In mechanically ventilated, healthy, isoflurane-anesthetized dogs, PPV predicted fluid responsiveness to volume expansion, and MAP and CVP did not show such applicability.

Keywords arterial blood pressure, central venous pressure, echocardiography, fluid therapy, hypotension.

Introduction

Circulating blood volume is a major focus of therapeutic management in cases of arterial hypotension during anesthesia (Cecconi et al. 2011). A decision on whether fluids or other treatments, such as vasopressors, are necessary should be made once hypoperfusion is identified (Carsetti et al. 2015). The correct and early diagnosis must be accurately and rapidly established to determine the optimal strategy to prevent hypoperfusion related to volume depletion

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or adverse effects from unnecessary fluid overload (Auler et al. 2008a). However, identification of the volume status is not possible under clinical conditions when intravascular volume cannot be measured and, therefore, the hemodynamic function is estimated through monitoring of changes in cardiac output (CO) in response to fluid infusion (Marik 2009). The ventricles of patients that are on the ascending portion of the Frank–Starling curve respond to fluid infusion by increasing CO (i.e. they have a preload reserve; responders), while fluid infusion has little effect on CO of those that are near the *flat* part of the curve (nonresponders) (Marik et al. 2009).

The techniques to measure CO may be invasive and time-consuming, and are often not available in the clinical setting (Descorps-Declere et al. 1996). Therefore, fluid management has been monitored through static pressure indices, such as arterial pressure and central venous pressure (CVP; preload), stroke volume (SV), and more recently with dynamic indices, such as pulse pressure variation (PPV) (Berkenstadt et al. 2005; Marik et al. 2009). Pulse pressure variation results from the difference between the maximum and minimum arterial pressure [systolic (SAP) and diastolic (DAP) arterial pressures] variations over a single respiratory cycle, divided by the mean of the maximum and minimum variations and expressed as a percentage. In mechanically ventilated patients, positive pressure ventilation promotes cyclical changes in SV, and is coupled with arterial pulse pressure changes (Auler et al. 2008a). Therefore, SV and arterial pulse pressure rise during inspiration and SV decreases during expiration (Michard et al. 2000). In human patients, a PPV < 12–13% indicates minimal effect of ventilation on venous return whereas patients with a PPV > 13% may be relatively hypovolemic and respond with an increase in SV after fluid infusion (Michard et al. 2000; Huang et al. 2008; Marik et al. 2009). In animals, PPV was shown to be accurate for predicting fluid responsiveness in a canine model of hemorrhagic shock (Berkenstadt et al. 2005; Klein et al. 2016), and in pig models of hemorrhage with endotoxemia (Noel-Morgan et al. 2013) and normovolemic hemodilution (Sant'Ana et al. 2012).

At the time of writing, there are no published clinical studies investigating the ability and threshold values of PPV for assessing fluid responsiveness in dogs during anesthesia for surgical procedures. Given that animals undergoing surgery are often monitored by using a catheter for invasive arterial pressure, more information could be available from the automated and continuous measurement of PPV in real time from multiparametric monitors. Therefore, the aims of this study were to assess whether PPV can predict fluid responsiveness, and to compare PPV with other markers of volume expansion, such as mean arterial pressure (MAP), CVP and SV, in dogs with arterial hypotension during isoflurane anesthesia for orthopedic surgery, and to determine the best cut-off value for PPV that could distinguish responders from nonresponders to fluid loading. The hypothesis was that PPV can predict fluid responsiveness as a marker of volume expansion, and that the best cut-off value would be 10–15%.

Material and methods

Animals

This was a prospective clinical study using client-owned healthy dogs undergoing orthopedic surgery in the Veterinary Hospital of Faculdade de Medicina Veterinária e Zootecnia of Universidade de São Paulo. The study was approved by the Ethical Committee on Animal Use (Comissão de Ética no Uso de Animais) at our institution (no. 19362010). Client consent was obtained before entry of any dog into the study. Prior to inclusion in the study, each animal's medical history was taken and a physical examination conducted. Animals were only included in the study if they had no known cardiopulmonary abnormalities detected after a complete physical examination, electrocardiogram evaluation and complete blood count and serum biochemical analysis.

Anesthesia and surgery

Food was withheld for 12 hours and water for 8 hours before anesthesia. All dogs were administered meperidine (2 mg kg^{-1}; Dolosal; Cristália Produtos Químicos Farmacêuticos Ltda, Brazil) and atropine (0.03 mg kg^{-1}; Pasmodex; Isofarma Industrial Farmacêutica, Brazil) by intramuscular (IM) injection as premedication. After 20 minutes, a 20 gauge catheter (Angiocath; BD, Brazil) was placed in the right cephalic vein, and propofol to achieve relaxation of mandibular muscles (3–5 mg kg^{-1}; Propovan; Cristália Produtos Químicos Farmacêuticos Ltda) was administered intravenously (IV) through the catheter for induction of anesthesia. After orotracheal intubation, animals were positioned in dorsal recumbency on a heated mat (ChillBuster VET; ThermoGear Inc., OR, USA) and anesthesia was maintained with an end-tidal isoflurane

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