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Original Contribution

A mini-fluid challenge of 150 mL predicts fluid responsiveness using Modelflow^R pulse contour cardiac output directly after cardiac surgery

Annemieke Smorenberg, MSc [a,*], Thomas G.V. Cherpanath, MD, PhD [b], Bart F. Geerts, MD, PhD [a], Robert B.P. de Wilde, PhD [c], Jos R.C. Jansen, MSc, PhD [c], Jacinta J. Maas, MD, PhD [c], A.B. Johan Groeneveld, MD, PhD, FCCP, FCCM [d,1]

[a] Department of Anesthesiology, Amsterdam Medical Center, 1109 AZ Amsterdam, The Netherlands
[b] Department of Intensive Care, Amsterdam Medical Center, 1109 AZ Amsterdam, The Netherlands
[c] Department of Intensive Care, Leiden University Medical Center, 2333 ZA Leiden, The Netherlands
[d] Department of Intensive Care, Erasmus Medical Center, 3015 CE Rotterdam, The Netherlands

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ABSTRACT

Study objective: The mini-fluid challenge may predict fluid responsiveness with minimum risk of fluid overloading. However, the amount of fluid as well as the best manner to evaluate the effect is unclear. In this prospective observational pilot study, the value of changes in pulse contour cardiac output (CO) measurements during mini-fluid challenges is investigated.
Design: Prospective observational study.
Setting: Intensive Care Unit of a university hospital.
Patients: Twenty-one patients directly after elective cardiac surgery on mechanical ventilation.
Interventions: The patients were subsequently given 10 intravenous boluses of 50 mL of hydroxyethyl starch with a total of 500 mL per patient while measuring pulse contour CO.
Measurements: We measured CO by minimal invasive Modelflow^R (COm) and PulseCO^R (COli), before and one minute after each fluid bolus. We analyzed the smallest volume that was predictive of fluid responsiveness. A positive fluid response was defined as an increase in CO of >10% after 500 mL fluid infusion.
Main results: Fifteen patients (71%) were COm responders and 13 patients (62%) COli responders. An increase in COm after 150 mL of fluid >5.0% yielded a positive and negative predictive value (+PV and −PV) of 100% with an area under the curve (AUC) of 1.00 ($P < 0.001$). An increase in COli >6.3% after 200 mL was able to predict a fluid response in COli after 500 mL with a +PV of 100% and −PV of 73%, with an AUC of 0.88 ($P < 0.001$).
Conclusion: The use of minimal invasive Modelflow^R pulse contour CO measurements following a mini-fluid challenge of 150 mL can predict fluid responsiveness and may help to improve fluid management.

1. Introduction

Fluid therapy is essential in the treatment of shock and hypoperfusion. A restrictive fluid policy has been shown to result in fewer complications compared to a more liberal fluid strategy [1–3]. After cardiac surgery, fluid overloading may contribute to pulmonary oedema and is associated with an increase in mortality and morbidity [4,5]. Fluid boluses have been shown to notably contribute to a positive fluid balance after cardiac surgery and could be reduced without increasing renal complications using a protocolled algorithm for fluid administration [6,7]. Predicting fluid responsiveness may minimize harmful fluid overloading in intensive care patients, especially in patients after cardiac surgery [8–10]. Additionally, a mini-fluid challenge may predict fluid responsiveness and concomitantly limit fluid loading in unresponsive patients [11–14]. Mallat et al. has shown that only 100 mL of colloid infusion may be sufficient in a mainly septic patient population, using the change in stroke volume variation (SVV) and pulse pressure variation (PPV) to predict fluid responsiveness [15]. The use of these dynamic parameters to accurately predict a positive response to fluid administration, however, may be restricted to mechanically ventilated patients with tidal volumes >8 mL/kg and having regular heart rates [16–18]. Furthermore, transthoracic echocardiography allows for the assessment of the aortic velocity time index (VTI) variations, and can be used to assess and predict fluid responses after infusion of only 50–100 mL of colloids [19,20]. However, VTI measurements can be technically

* Corresponding author at: Anesthesiology, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
E-mail addresses: a.smorenberg@amc.nl (A. Smorenberg), t.g.cherpanath@amc.uva.nl (T.G.V. Cherpanath), b.f.geerts@amc.uva.nl (B.F. Geerts), R.B.P.de_Wilde@lumc.nl (R.B.P. de Wilde), j.j.maas@lumc.nl (J.J. Maas).
[1] Deceased.

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demanding and cannot provide continuous registration. Thus, several hemodynamic parameters and methods have been opted when using a mini-fluid challenge, with their own limitations as stated above. A minimal invasive parameter providing continuous registration during a mini-fluid challenge may be preferred.

Cardiac output (CO) by modified Modelflow^R (COm) and by PulseCO^R (COli) are minimal invasive and use arterial pressure pulse contour analysis to derive CO measurements. Modelflow CO measurement estimates CO using the three-element Windkessel model. It accounts for the aorta resistance to volume increase and pulsatile inflow and peripheral vascular resistance. PulseCO on the other hand uses an autocorrelation algorithm to calculate stroke volume using a pressure/volume relationship with calibration. COm and COli have been shown to compare reasonably well to thermodilution CO measurements, with COm showing the lowest bias and limits of agreement [21–23]. Previous research has shown that both pulse contour analyses are able to predict fluid responsiveness during passive leg raising [23].

The hypothesis of the current study was that the COm and COli can lower the amount of fluid that is needed to predict fluid responsiveness by mini-fluid challenges. We therefore studied the two pulse contour CO methods and analyzed the smallest amount of fluid needed to predict fluid responsiveness in mechanically ventilated patients after elective cardiac surgery.

2. Methods

2.1. Patients and methods

This study was conducted according to the principles of the Helsinki declaration. Ethical approval for this study was provided by the Medical Ethics Committee of the Leiden University Medical Center, Leiden, The Netherlands, ISRCTN37554354. In this pilot study, twenty-one consecutive patients undergoing elective coronary artery bypass grafting and/or valve replacement were included into the study after written informed consent was obtained prior to surgery. Exclusion criteria were: previous myocardial infarction, congestive heart failure (NYHA class IV), aortic aneurysm, extensive peripheral arterial occlusive disease, postoperative valvular insufficiency, irregular heart rhythm, and use of a cardiac assist device. According to institutional standards, anesthesia was continued with propofol (dosage mean: 2.7 mg/kg/h, standard deviation (SD): 1.1 mg/kg/h) and sufentanil (dosage mean: 0.1 mcg/kg/h, SD: 0.1 mcg/kg/h) intravenously upon arrival in the intensive care unit (ICU) after surgery based upon level of sedation and comfort.

Mechanical ventilation was applied to achieve normocapnia (arterial pCO_2 between 40 and 45 mm Hg) with mean tidal volumes of 8 mL/kg (SD: 1 mL/kg) and a positive end-expiratory pressure (PEEP) of 5 cm H_2O. During the study protocol ventilator settings and vasoactive medication were not changed. Before ICU admission, each patient had received a 20G radial artery catheter to measure arterial pressure (Prad) and a pulmonary artery catheter (IntelliCath, Edwards Lifesciences; Irvine CA, USA) inserted into the pulmonary artery via the right jugular vein to measure central venous pressure (CVP) and thermodilution CO. Patients maintained a supine position and pressure transducers were referenced to the level of the tricuspid valve and zeroed to atmospheric pressure after calibration. Prad and CVP data were continuously recorded with a resolution of 0.125 mm Hg at a sample frequency of 200 Hz and stored on a personal computer for analysis and documentation. From Prad we calculated CO using two different arterial waveform (i.e. pulse contour) methods; modified Modelflow^R (COm, FMS, Amsterdam, the Netherlands) and PulseCO^R (COli from LiDCO Ltd., London, UK). Both methods are extensively described elsewhere [22]. COm was measured beat-to-beat and averaged over 30 s, while COli was calculated over 20 s. The PulseCO^R device was calibrated with the averaged value of three thermodilution measurements (COtd) prior to start of the protocol, while the Modelflow^R was not calibrated [22,23]. No additional thermodilution measurements were done. It was not the objective to compare COm and COli to thermodilution CO measurements, as this was done previously [22,23]. Simultaneously, heart rate (HR), mean arterial pressure (MAP), and CVP were determined and the systemic vascular resistance (SVR) was calculated with either COm or COli. While PPV was calculated using PulseCO^R arterial waveform analysis, the SVV was calculated by both PulseCO^R (SVVli) and Modelflow^R (SVVm) pulse contour methods.

2.2. Study protocol

All measurements were carried out within 2 h after arrival in the ICU with patients in supine position. At baseline, hemodynamic measurements were performed. All patients received fluid administration as part of the research protocol irrespective of further baseline hemodynamic measurements. In each patient, a total of 10 consecutive 50 mL fluid boluses with hydroxyethyl starch solution (Voluven®, Fresenius Kabi, Bad Homburg, Germany) were administered intravenously through the central venous catheter. After baseline measurements, a bolus was infused in 30 s and measurements were repeated 1 min after infusion. Thirty seconds later (and 2 min after the start of the first fluid step), the second bolus was given. The sequence was repeated for the ten boluses, so that in 20 min a total of 500 mL of colloid was administered.

2.3. Statistical analysis

For statistical analysis SPSS 20.0 (SPSS Institute, Chicago, IL, USA), and MedCalc (V9, Mariakerke, Belgium) were used. A positive fluid response was defined by a 10% increase in COm or in COli after 500 mL of fluid loading [9]. The Kolmogorov-Smirnov test showed non-normality for various hemodynamic parameters, therefore, non-parametric tests were used for analysis. The Fisher's exact was used to compare groups for categorical dichotomous variables and the Mann-Whitney *U* test was used for continuous variables. Spearman's correlation coefficient r_s was applied to quantify relations between continuous variables. To correct for multiple comparisons, the Bonferroni correction was used to identify statistical significance [24]. The area under the receiving operator curve (AUC) was calculated to assess predictive value in our study population. Positive and negative predictive values (+PV and −PV) were calculated according to standard formulas. We looked for the minimum amount of fluid necessary when either the COm or COli method was used, to yield an increase in CO >5% (roughly conform the precision of our thermodilution method) with a +PV, −PV, or both of 100% for fluid responsiveness to 500 mL. Data is shown as median [25th–75th percentile], or number (percentage), where appropriate. Median [range] will be given when the amount of patients in the group analyzed is three or less. A $P < 0.05$ was considered statistically significant. Exact *P* values are given unless $P < 0.001$. A power calculation was not performed prospectively since 50% of fluid responses are common in most studies on fluid responsiveness of similar size as our current study [9,25]. Retrospectively, a power calculation was performed using PASS12 (NCSS, Kaysville, Utah, USA). A total of 18 patients with a response rate of 50% (or allocation ratio of 1) achieved 82% power to detect a difference of 0.350 between the AUC under the null hypothesis of 0.500 and an AUC under the alternative hypothesis of 0.850.

3. Results

3.1. Overall study population

Twenty-one patients (5 women) were included with baseline characteristics shown in Table 1. No significant bleeding (>50 mL/h) occurred during the study period. Patient characteristics did not differ between fluid responders and non-responders. CVP, HR, and MAP or their change during fluid loading did not differ between groups