Journal of Critical Care 29 (2014) 992–996

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Pulse pressure variation–guided fluid therapy after cardiac surgery: A pilot before-and-after trial☆

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ARTICLE INFO

Keywords:
Pulse pressure variation
Fluid therapy
Cardiac surgery
Intensive care
Cardiac output

ABSTRACT

Purpose: The aim of this study is to study the feasibility, safety, and physiological effects of pulse pressure variation (PPV)–guided fluid therapy in patients after cardiac surgery.
Materials and methods: We conducted a pilot prospective before-and-after study during mandatory ventilation after cardiac surgery in a tertiary intensive care unit. We introduced a protocol to deliver a fluid bolus for a PPV ≥13% for at least >10 minutes during the intervention period.
Results: We studied 45 control patients and 53 intervention patients. During the intervention period, clinicians administered a fluid bolus on 79% of the defined PPV trigger episodes. Median total fluid intake was similar between 2 groups during mandatory ventilation (1297 mL [interquartile range 549-1968] vs 1481 mL [807-2563]; $P = .17$) and the first 24 hours (3046 mL [interquartile range 2317-3982] vs 3017 mL [2192-4028]; $P = .73$). After adjusting for several baseline factors, PPV-guided fluid management significantly increased fluid intake during mandatory ventilation ($P = .004$) but not during the first 24 hours ($P = .47$). Pulse pressure variation–guided fluid therapy, however, did not significantly affect hemodynamic, renal, and metabolic variables. No serious adverse events were noted.
Conclusions: Pulse pressure variation–guided fluid management was feasible and safe during mandatory ventilation after cardiac surgery. However, its advantages may be clinically small.

1. Introduction

Fluid management is an important and challenging daily aspect of intensive care unit (ICU) therapy because hypovolemia and hypervolemia may both contribute to morbidity [1,2]. Thus, fluid therapy optimization is of clinical interest, particularly in patients after cardiac surgery. In these patients, compromised myocardial function [3] and/or systemic inflammation induced by cardiopulmonary bypass (CPB) and/or surgical injury itself rapidly and unpredictably decrease cardiac preload and make optimization of preload particularly difficult [4]. Such difficulty persists despite the invasive measurement of cardiac output or cardiac or pulmonary static filling pressures.

Despite routine measurement, static filling pressures such as central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), or pulmonary arterial pressure (PAP) are all unreliable measures of cardiac preload and fluid responsiveness in mechanically ventilated patients [5-9]. In contrast, variations in arterial waveform-derived variables or in stroke volume induced by mandatory mechanical ventilation such as pulse pressure variation (PPV), systolic pressure variation (SPV), and stroke volume variation (SVV) are reasonably accurate predictors of fluid responsiveness in these patients [8-11]. The use of PPV, SPV, or SVV in clinical practice, however, has been held back by the lack of automated calculation and display on bedside monitors and/or the need to apply novel measurement technologies and specific additional monitors. Moreover, interventional studies in high-risk surgery and major abdominal surgery have had conflicting results [12,13]. Finally, the feasibility, safety, and physiological effects of fluid therapy guided by a dynamic measurement of fluid responsiveness have not been evaluated in patients after cardiac surgery.

Accordingly, we conducted a prospective before-and-after trial to assess the feasibility, safety, and physiological effect of PPV-guided therapy on the total amount of fluid given to patients after cardiac surgery. We hypothesized that fluid management guided by PPV

☆ Funding: Austin Hospital Intensive Care Trust Fund.
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http://dx.doi.org/10.1016/j.jcrc.2014.07.032
0883-9441/

would be feasible and safe and that it would increase the amount of fluid administered immediately after cardiac surgery. We further hypothesized that such targeted fluid therapy would lead to improved hemodynamics and/or improved renal and metabolic status.

2. Methods

We performed a prospective before-and-after pilot study in the 22-bed multidisciplinary ICU of the Austin Hospital, a tertiary care hospital affiliated with The University of Melbourne, Australia. The control period ran from January 11 to May 17, 2012; the intervention period from September 17, 2012, to February 6, 2013, separate by a period of education for medical and nursing staff.

The study was approved by the Austin Hospital Human Research Ethics Committee with a waiver for informed consent (approval no. H2012/04846) and was registered with ClinicalTrial.gov (NCT01681758).

2.1. Patients

Adult patients admitted to the ICU after cardiac surgery and receiving mandatory ventilation were eligible. Patients were ineligible if they had atrial fibrillation [14,15] or required reoperation. During mandatory ventilation, patients were sedated and volume control adjusted to tidal volumes of 8 to 10 mL/kg. A positive end-expiratory pressure of 5 cmH_2O was applied.

2.2. Hemodynamic measurements

As part of our routine monitoring, in all patients, a pulmonary artery catheter (Edwards Lifesciences, Irvine, Calif) and a peripheral arterial catheter (Arrow International, Reading, Pa) were inserted before cardiac surgery. Pressure transducers were zeroed at the mid chest level to atmospheric pressure. Arterial blood pressure (ABP), PAP, and CVP were continuously monitored.

Pulse pressure variation was calculated and displayed in real time by IntelliVue MP70 monitors (Philips Healthcare, Eindhoven, Netherlands). The algorithm used has been previously published [16,17].

2.3. Study design

During both periods, patients did not receive any "maintenance" infusion of fluids. During the control period, fluid management for each patient was prescribed at the discretion of bedside clinicians, and all clinicians were kept strictly unaware of the study as data were collected. After a phase-out/education period that included education and preparation of all medical and nursing ICU staff, the intervention period commenced with screening of all consecutive admissions. When an eligible patient had PPV 13% or higher for at least 10 minutes during mandatory ventilation, clinicians were instructed to deliver a fluid bolus. However, if clinicians had any concerns about giving a fluid bolus (eg, presence of poor gas exchange, radiological pulmonary edema, very high PAOP), they were allowed to withhold it. All other management including mechanical ventilation, sedation, and administration of vasopressors remained unchanged. The PPV protocol did not prevent clinicians from giving fluid at other times, should they feel that other indications justified intervention (eg, sudden hypotension, oliguria, rising lactate levels, rising noradrenaline requirements).

2.4. Data collection

We started data capture within 30 minutes of arrival in the ICU. Every 15 minutes, we recorded heart rate, ABP, PAP (if applicable), CVP, and PPV as stored in the monitor until the patient was weaned from mandatory ventilation. Every hour, we recorded cumulative fluid intake and output, cardiac index (CI), and use of vasoactive drugs. Simultaneously, we also collected blood lactate and creatinine concentration from blood gas analysis. Blood gas analysis was performed with ABL800 FLEX (Radiometer, Copenhagen, Denmark). We collected these data over the first 24 hours or until ICU discharge (whichever occurred first). We also collected information on age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) III score, type of surgery, and time on CPB. Clinical outcomes such as length of stay (LOS) in ICU and hospital and survival status were also collected.

2.5. Outcome

The primary outcome measures were the amount of fluid administered during mandatory ventilation and in the first 24 hours after ICU admission. Secondary outcomes included fluid balance, CI, and blood lactate concentration. We also assessed the effect of the intervention on other hemodynamic parameters including ABP, PAP, and CVP, and renal function including urine output serum creatinine level and the incidence of acute kidney injury (AKI) according to the risk, injury, failure, loss, and end-stage renal failure (RIFLE) criteria. Feasibility was assessed by protocol compliance. Safety was assessed by clinical outcomes and the development of serious adverse events including severe hypotension, myocardial failure, and pulmonary edema [18].

2.6. Statistical analysis

We estimated that a minimum of 45 patients per group (90 patients total) were required to detect a difference of 0.6 SDs of fluid administration in the first 24 hours after ICU admission between the 2 groups with an α of .05 and 80% power. Target recruitment was set at 50 patients per group.

Continuous data are reported as means (SD) or medians [interquartile range], depending on the underlying data distribution. Comparisons were made using Student t test or Wilcoxon rank sum test when appropriate. Categorical data are reported as proportions and compared with the χ^2 test.

To evaluate adherence to the PPV-guided fluid management protocol, we identified episodes of PPV 13% or higher and assessed whether fluid bolus was given during the episodes. A fluid bolus was defined as an episode where any of the following were prescribed: (1) any crystalloid of 250 mL or greater or (2) any amount of 4% albumin or 20% albumin.

Multivariable linear regression analyses were conducted to assess the relationship between the PPV-guided fluid therapy and the relevant outcomes, after adjusting for APACHE III score, type of surgery, and time on CPB.

All analyses were performed using SPSS version 19.0 (SPSS Inc, Chicago, Ill). To account for multiple comparisons and further reduce the chance of a type I error, a two-sided P value of .01 was used to indicate statistical significance.

2.7. Sensitivity analysis

We assessed the impact of PPV-guided fluid therapy by measuring the response of hemodynamic parameters to the fluid bolus. We regarded a fluid bolus episode with at least one PPV value 13% or higher in the last 1 hour as a PPV-triggered fluid bolus episode. We compared hemodynamic parameters 1 hour before each episode between groups. The response of hemodynamic parameters to a fluid bolus episode was expressed as relative percentage change from the before value to the value 1 hour after the fluid bolus episode. We also assessed how many fluid boluses were associated with a 15% or higher increase in CI over such 1-hour periods [10]. In addition, to better describe the clinical effects of fluid boluses, we used more strict definitions of fluid bolus episode: 250 to 500 mL of crystalloid or albumin, and the same analysis was repeated.