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Cardiac output responses in a flow-driven protocol of resuscitation following cardiac surgery☆,☆☆

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Abstract

Objective: Determine the role of cardiac output and central venous pressure (CVP) measurements in the clinical decisions that were based on the algorithm used in a randomized trial that compared a colloid to a crystalloid solution in the management of patients early after cardiac surgery (FACS trial, NCT00337805, Crit Care Med 2010; 38:2117).

Methods: We analyzed the changes in CVP and cardiac index (CI) in 729 fluid challenges from the FACS trial in which 119 patients were randomized to colloid and 118 to crystalloid boluses in a flow-based protocol. A fluid challenge was defined as being positive if CI increased by $\geq$0.3 L/min^{-1}m^{-2} and negative if CI increased by <0.3 L/min^{-1}m^{-2} but CVP increased by $\geq$2 mmHg.

Results: As defined in the protocol, 26% of boluses were given for a low CI (<2.2 L/min^{-1}m^{-2}). CI did not increase in 20% of boluses despite an adequate increase in CVP; in the protocol this meant that further volume boluses were not given. In another 34% of boluses in which CI did not increase, CVP increased by < 2 mmHg, which meant that volume responsiveness could not be ruled out and another bolus was indicated. 43% of the boluses were given for hypotension, but surprisingly in 90% of these instances, CI was in the acceptable range indicating that the low arterial pressure was due to decreased systemic vascular resistance.

Conclusion: Measurement of cardiac output and CVP significantly influenced clinical decisions in the FACS algorithm.

1. Introduction

Fluid boluses are a fundamental component of resuscitation of patients with compromised circulatory function. The trigger for a fluid bolus is often a decrease in arterial pressure and success commonly is evaluated by restoration of the blood pressure. However, tissue perfusion and oxygen

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delivery are determined by cardiac output and the resistances distributing blood flow to different organs and not by arterial blood pressure per se. Although arterial pressure is a key determinant of regional flows, arterial pressure itself is determined by the product of cardiac output and systemic vascular resistance [1,2]. For example, consider the consequence of clamping the thoracic aorta; arterial pressure rises in the arms, but overall perfusion of the body does not improve. Thus, whenever feasible, it would make sense to base resuscitation protocols on a flow response rather than a pressure response. With this principle in mind, we recently used a flow-based protocol in a double-blind randomized trial in which we compared use of a colloid versus a crystalloid solution for resuscitation of patients after cardiac surgery (fluids after cardiac surgery [FACS]) [3]. The primary end-point in the trial, use of catecholamines the morning after surgery, was significantly reduced with the use of the colloid solution. There also were some positive trends in some secondary end-points such as a reduction in mediastinal and pulmonary infections and the proportion of patients still in the intensive care unit at 24 hours after surgery. A key part of the rationale for the trial was that a "flow-directed" protocol with decisions based on responses of cardiac output and central venous pressure (CVP) would avoid potential harmful effects from excessive use of colloids and thereby allow potential benefits to become evident. Indeed, we saw no increase in renal injury with the use of the colloid in the trial. A central concept was that if a fluid bolus does not increase cardiac output, then the clinician should not continue to use fluid boluses and a catecholamine should be used instead to correct the hemodynamic abnormality. All patients in this trial had pulmonary artery catheters in place as part of their routine care so that cardiac output could be used to drive therapy. There were over 700 fluid challenges in the trial, which provided us the opportunity to observe how often cardiac output itself was involved in the decision to give or not to give fluids. Secondly, we evaluated the consequent change in cardiac output in response to the standardized fluid challenges.

2. Methods

The detailed methods of the trial have previously been published [3]. In brief, the study was performed in the intensive care unit of the Royal Victoria Hospital in Montreal and approved by the institutional clinical research review board and registered with ClinicalTrials.gov (NCT00337805). We obtained an unrestricted grant from Bristol-Myers-Squibb to perform the study and they provided the pentastarch, which has a molecular weight of approximately 250 kd and is prepared as a 10% solution in 0.9% sodium chloride. All patients undergoing elective cardiac surgery were eligible for the study unless informed consent could not be obtained, the treating surgeon did not want the patient included, the patient had a known prior allergic reaction to starches (no patient was excluded on this basis), or there was no plan for a pulmonary artery catheter. Consent was obtained the night before surgery and randomization occurred after surgery once the presence of other exclusion criteria were ruled out, including the absence of a pulmonary artery floatation catheter, presence of an intra-aortic balloon pump, the use of a starch solution after the initial priming of the pump and prior to randomization, request by the surgeon to exclude the patient and, importantly, patients who were bleeding excessively immediately after surgery. Up to 1 L of either saline or the pentastarch in 250 mL unmarked bags were given. Thereafter, only saline boluses of 250 mL were used as directed in the protocol.

2.1. Protocol

There were four triggers for a volume bolus in the protocol: 1) cardiac index (CI) less than 2.2 $L/min^{-1}m^{-2}$; 2) systolic or mean arterial pressure below the prescribed values set by the treating team at the time of admission to the intensive care unit: 3) central venous pressure (CVP) less than 3 mmHg (transducer referenced to 5 cm below the sternal angle); and 4) urine output less than 20 ml/hr. Volume boluses were not given if the CI was greater than 4 $L/min^{-1}m^{-2}$; at these high values of CI, these patients were considered to have primarily a vascular resistance problem and were treated with vasoconstrictors. Volume also was not given if CVP was greater than 12 mmHg, for these patients are more likely functioning on the flat part of the cardiac function curve and not volume responsive, and even if they are volume responsive, the high CVP will increase capillary leak. Catecholamines thus are a potentially better therapeutic choice for these patients [4]. A key part of the protocol was that CVP and CI were again measured after each volume bolus and the four possible outcomes were re-assessed. Thus a unique component of the algorithm is that it is "responsive" to the hemodyanmic outcome of the fluid bolus. If CI increased by < 0.3 $L/min^{-1}m^{-2}$ and CVP increased by < 2 mmHg, the volume challenge was deemed to be inadequate to test fluid responsiveness, and if criteria for a volume bolus were still present, another bolus was given. If the CI increased by ≥ 0.3 $L/min^{-1}m^{-2}$, whether or not the CVP changed, the patient was considered fluid responsive and further boluses could be given if criteria for a volume bolus were still present. The fourth outcome was the most critical and its recognition sets this protocol apart from most other studies. If CI increased by < 0.3 $L/min^{-1}m^{-2}$ and CVP increased by ≥ 2 mmHg, the fluid challenge was considered adequate to test Starling's law and the lack of increase in CI indicated that the patient was not responsive to volume boluses. Hemodynamic abnormalities (i.e. CI $<$ 2 $L/min^{-1}m^{-2}$ or arterial pressure below the set target) then were treated with vasopressors or inotropic agents according to the predefined rules in the protocol.