Time to haemodynamic effect dissipation after a crystalloid fluid bolus in cardiac surgery patients: a prospective observational study

STUDY DESIGN

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Research Abstract

Introduction:

Fluid bolus therapy (FBT) is near ubiquitous in the management of the post-op cardiac surgical patient. Although its immediate hemodynamic effects are documented, the concept of haemodynamic effect dissipation time has not been defined and it has not been measured in the setting of day-to-day clinical practice.

Research Question:

In post-op cardiac surgical patients, what is the haemodynamic effect dissipation time of a 500ml bolus of crystalloid solution when measured using common vital parameters (mean arterial pressure (MAP), cardiac index (CI), central venous pressure (CVP) and pulmonary artery pressure (PAP))? In what percentage of patients has the haemodynamic effect dissipated at 30 minutes post FBT?

Study Design:

A prospective observational study of fluid bolus therapy in post op cardiac surgical patients. Patients will be observed for one hour following the completion of a 500mls crystalloid solution fluid bolus with continuous monitoring of haemodynamic parameters.

Outcome measures:

1. The time to haemodynamic effect dissipation post fluid bolus as determined using MAP, CI, CVP and PAP.
2. The percentage of patients in whom haemodynamic effect dissipation has occurred at 30 minutes post FBT.
Background and Rationale

Hypotension occurs frequently in the first few hours after cardiac surgery. Fluid bolus therapy (FBT) using crystalloid solutions is a common treatment in this situation. The physiologic rationale for FBT is that it will increase stroke volume via the Frank-Starling mechanism, and therefore increase both cardiac output and blood pressure.

The concept of fluid responsiveness is commonly used to determine the impact of FBT and patients are typically considered to be responders if there is an increase of at least 10% to 15% in their stroke volume after the administration of a fluid bolus. Currently however, there is no consensus as to what volume of fluid should be administered as a bolus, the timescale over which it should be administered and the time, post-bolus, at which fluid responsiveness should be assessed.

To date, the concept of “haemodynamic effect dissipation time” following fluid bolus therapy has not been defined. For this study, we have defined it as the time taken for the haemodynamic effects of a fluid bolus to return to values that are not considered to be clinically different from the baseline values pre-FBT.

Recent studies have suggested that the haemodynamic effect dissipation times of crystalloid fluid boluses may be short-lived and that patients who are considered to be responders at the end of a fluid bolus may be classed as non-responders in as little as ten minutes after the bolus. These studies have only reported short periods of continuous observation or longer periods of intermittent observation following FBT. Furthermore, the fluid boluses used in some cases have been relatively small (circa 3ml/kg).

FBT is normally part of a complex intervention that occurs in concert with numerous other haemodynamic confounders which makes assessment of the haemodynamic effect dissipation time challenging. Thus, to date, no studies have measured haemodynamic effect dissipation time in the setting of day-to-day clinical practice.
Accordingly, we aim to continuously measure the haemodynamic impact of a larger fluid bolus (500 ml) for as long as possible following completion of the bolus. We plan to quantify the haemodynamic effect dissipation time of crystalloid FBT for a number of haemodynamic variables with as much fidelity as possible whilst also minimizing the impact of haemodynamic confounders associated with usual clinical practice. We hypothesise that, in post-op cardiac surgical patients admitted to the ICU who are deemed to require FBT, the time to haemodynamic effect dissipation will be less than 30 minutes for most patients.
Plan of Investigation

Study Design

A prospective, single-centre, observational study performed in the cardiothoracic ICU of a tertiary university hospital ongoing from December 2016.

Patient Recruitment and Selection

All ventilated patients aged over 18 years who are admitted to the ICU following cardiac surgery will be considered for inclusion in the study. Patients will be included if the treating clinician decides to prescribe a bolus of fluid in the first 12 hours on arrival to the ICU and if a member of the research team is available at the bedside to observe the patient’s haemodynamic parameters for one hour post bolus. Patients will be excluded from the study if they do not have invasive blood pressure monitoring or a pulmonary artery (PA) catheter in-situ. Patients who are known to be pregnant or who require mechanical haemodynamic support (intra-aortic balloon pump or extracorporeal membrane oxygenation (ECMO) will also be excluded.

Ethical Approval

This study has been approved as a service evaluation by the Ethics Committee of the Austin Hospital in Melbourne, Australia (reference number LNR/16/Austin/358). The need for informed consent has been waived due to its purely observational nature.

Intervention

Fluid challenges will only be administered if deemed necessary by the clinical team but clinicians will be asked to use a bolus of 500 mls of crystalloid solution (Hartmann’s solution or Plasmalyte) unless there are clinical contraindications to this. The research team will record the indication for the fluid bolus according to a list of pre-defined indications.

All fluid boluses will be given at room temperature using a hand pump via an intravenous giving set connected to the patient’s central venous catheter or a large bore peripheral cannula. No guidelines will be given regarding the speed of fluid administration although patients will be excluded from further analysis if administration of the bolus takes greater than 30 minutes.
*Patient Care, Risks and Benefits*

Participation in this study will not affect patient treatment in any way except that the treating clinician who has decided to administer a fluid bolus will be asked to prescribe 500mls of crystalloid solution (unless there are contraindications to this). All other therapies and interventions will be administered at the discretion of the treating clinician.

Administration of intravenous boluses of crystalloid solutions is established clinical practice that is commonly used post cardiac surgery. The risks for patients included in this study are therefore minimal.

*Sample Size*

We will aim to analyse 25 patients who have at least 10 minutes of confounder-free haemodynamic observations following completion of the fluid bolus. Trial runs of the study protocol have suggested that 30% of patients enrolled in the study will be excluded due haemodynamic confounders with this criterion. We therefore plan to enrol 35 patients.

Defining the haemodynamic effect dissipation time using statistical tests for significance yields a measure of the dissipation time that is dependent on the sample size. We have therefore chosen a clinical definition for the haemodynamic effect dissipation time and accordingly our plan does not include a power analysis.

*Monitoring*

All patients will be monitored using Philips Intelliview MP70 (Philips Healthcare, Best, Netherlands) bedside monitors with continuous arterial blood pressure monitoring from either a radial or brachial artery catheter and continuous central venous pressure measurement via an internal jugular catheter. PA pressures and blood temperature will be recorded from PA catheters (Edwards Lifesciences, Irvine, CA) inserted via the internal jugular vein. Depending on the variety of PA catheter, intermittent or continuous measurements of cardiac output will be recorded using a thermodilution technique. In the case of intermittent cardiac output catheters, all measurements will be performed by the patient’s bedside nurse or a member of the research team. 10ml boluses of room temperature 0.9% saline will be used for each cardiac output measurement and the recorded values will be based on the average of three measurements (or
two measurements when there is less than 10% difference between the two values). All pressure measurements will be referenced to the intersection of the anterior axillary line and the fifth intercostal space.

**Data Collection**

Haemodynamic data will be recorded on a second-by-second basis using Medicollector data logging software (Medicollector LLC, Boston, MA) connected to the Phillips MP70 bedside monitors.

Baseline haemodynamic parameters will be recorded for a minimum of five minutes prior to commencement of the fluid bolus. Baseline ventilator parameters and the rates of any sedative and vasoactive infusions will also be noted. Arterial blood gas results from within two hours prior to the fluid bolus will be recorded.

A member of the research team will be present at the bedside throughout fluid bolus administration and for one hour afterwards. Following commencement of the fluid bolus, the clinical team will be asked to avoid any interventions (haemodynamic confounders) that may alter the patient’s haemodynamic status provided that doing so would not be detrimental to patient care. When this is not possible, the researcher will contemporaneously record the nature of the confounder by electronic annotation of the Medicollector datafile.

When patients do not have PA catheters that are capable of continuous cardiac output measurements, measurements of cardiac output will be performed within 15 minutes prior to the fluid bolus, immediately after completion of the bolus and then, as a minimum, at 30 minutes and 60 minutes post bolus.

**Data Analysis**

**Overall Approach**

The results will be analysed using the R statistical computing language. All data will be initially assessed for normality. Group comparisons will be performed using chi-square tests for equal
proportion, student t-tests for normally distributed data and Wilcoxon rank-sum tests otherwise, with results reported as n (%), mean (standard deviation) or median [interquartile range] respectively.

**Summarising of Haemodynamic Variables**

The second-by-second pressure, heart rate, oxygen saturation and temperature recordings will be collated into a 5-minute-long pre-bolus window, an intra-bolus window and 1-minute-long post-bolus windows. Cardiac index and systemic vascular resistance recordings will be collated into a 15-minute-long pre-bolus window, an intra-bolus window and 10-minute-long post-bolus windows. A mean value will be calculated for each window from the individual values included in it.

**Approach to Outliers and Confounders**

The frequency of data logging means that transient but extreme events (such as flushing of an arterial catheter) will inevitably be recorded. Therefore, heart rate, blood pressure and filling pressure data will be filtered for extreme outliers by excluding any value that is more than three standard deviations from the mean of the entire dataset.

Any haemodynamic confounders that occur during the period of observation will categorised as: additional fluid bolus, change in vasoactives, sedation/analgesia, muscle relaxation, pacing, ventilation changes or other significant confounders. When a confounder occurs, data will censored for that patient at that time point and further haemodynamic data from that patient will not contribute to the final analysis.

**Primary Outcome Measures: Haemodynamic Effect Dissipation Time**

The primary outcome measures will be the time taken for the haemodynamic effects of a fluid bolus to return to values that are not considered to be clinically different from the baseline values pre-FBT. These will be defined as follows:
1. For mean arterial pressure (MAP), central venous pressure (CVP) and pulmonary artery pressure (PAP): a value equal to or less than the baseline MAP pre-fluid bolus for two consecutive minutes.

2. For cardiac index (CI) and stroke volume (SV): the first time window post fluid bolus when the CI or SV are no longer greater than 5% above the baseline pre-fluid bolus.

3. Core temperature: a value equal to or greater than the baseline core temperature pre-fluid bolus for two consecutive minutes (we anticipate a cooling effect with room temperature fluid boluses).

Of note, for pressure and temperature measurements (1 & 3 above). We will determine the haemodynamic effect dissipation time from the start of the fluid bolus, from the end of the fluid bolus and from the time at which the peak effect occurs as a result of the fluid bolus. See table 3 below.

We hypothesise that the duration of haemodynamic effect dissipation time for MAP and CI following a fluid bolus of 500mls of fluid will be short (less than 30 minutes) for the majority of patients. We will therefore interrogate the data at 30 minutes post fluid bolus therapy to determine percentage of patients in whom haemodynamic effect dissipation has occurred at this point.

**Presentation of Results**

**Description of Proposed Tables**

**Table 1:** Demographic characteristics of the study population.

- Additional columns comparing the characteristics of patients in whom haemodynamic effect dissipation for MAP occurred at 30 minutes and those in whom it did not.

**Table 2:** Summary of FBT. Indications for FBT, duration of infusion, volume infused (ml/kg).

**Table 3.** A summary of haemodynamic effect dissipation times (for MAP, CVP, CI etc):

- Mean baseline value pre-fluid
- Peak change in parameter post fluid
• % of patients in which dissipation occurred within 30mins post FBT
• % in whom dissipation was not determined during confounder free observation
• Median time to haemodynamic effect dissipation from peak effect
• Median time to haemodynamic effect dissipation from the end of FBT
• Median time to haemodynamic effect dissipation from the start of FBT

Description of Proposed Figures

Figure 1: Flow chart of study enrolment and exclusions
Figure 2: A panel of box plots summarising the change in each haemodynamic variable for all patients with time post FBT.
Figure 3: A panel of correlation plots comparing magnitude of peak change in MAP, time of peak change in MAP and time to haemodynamic effect dissipation for MAP with duration of fluid bolus.

References

