

Perioperative Goal Directed Fluid and Hemodynamic Therapy with Echocardiography in Pediatric Congenital Heart Disease: A Study Protocol

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Abstract

Background: Echocardiography is a tool widely used in diagnostic and interventional cardiology. One retrospective study has demonstrated the impact of intraoperative transoesophageal echocardiography in pediatric and adults after surgical congenital heart disease repair in terms of reduced postoperative length of hospital stay. There are no pediatric studies concerning the impact of perioperative goal directed fluid and hemodynamic therapy with echocardiography on postoperative outcome. This study protocol was designed to determine the impact of perioperative goal directed fluid and hemodynamic therapy (PGDFHT) with echocardiography on postoperative outcome in children.

Objectives: The primary objective of this study protocol is to describe the trial which is in development and which will determine the impact of PGDFHT with echocardiography on postoperative outcome in terms of morbidity. The secondary objectives of the study are to clarify the impact of PGDFHT with echocardiography on postoperative length of stay in the intensive care unit, length of invasive or non invasive mechanical ventilation and postoperative length of hospital stay.

Methods: Patients will be randomized in two groups, one control and one experimental group. The study will be single blinded, mono or multicentric.

Patients: Patients aged less than 18 years old with congenital heart disease scheduled for surgical repair.

Statistical Analysis: Statistical analysis will be realized with XLSTAT 2018.3 or plus software.

Results: Are expected in the second semester of 2024.

Conclusion: This trial protocol was designed to describe the study in progress and development which will determine the impact of perioperative goal directed fluid and hemodynamic therapy with echocardiography on postoperative outcome in pediatric patients with congenital heart disease scheduled for surgical repair.

Keywords: Congenital Heart Disease; Children; Echocardiography; Goal Directed Fluid Hemodynamic Therapy; Postoperative Outcome

Introduction and Objectives

Perioperative goal directed fluid and hemodynamic therapy (PGDFHT) has been studied in adults [1-7]. This practice has demonstrated in adults its efficiency in terms of reduced postoperative complications and length of hospital stay (LOS)[1-7]. The objective of PGDFHT is to monitor fluid responsiveness and hemodynamic status with the aim to improve oxygen delivery to different systemic organs and to improve tissular perfusion [8].

Tissular hypoperfusion can have side effects in terms of organ failure. Unoptimal fluid and hemodynamic status (insufficient or plethoric) can alter tissular perfusion. That is why monitoring fluid responsiveness and hemodynamic status using tools to assess adequate cardiac output to maintain sufficient tissular oxygen delivery is mandatory.

There are no studies in children demonstrating the impact of PGDFHT with echocardiography on postoperative outcome.

Nonetheless, there are studies in pediatric cardiac surgery mostly which identified perioperative biomarkers of postoperative adverse outcome (9). These biomarkers were lactate levels, central venous oxygen saturation (SCVO₂), regional cerebral, renal, splanchnic oxygen saturation and veno-arterial carbon dioxide gradient. Unoptimal values of these biomarkers predicted adverse postoperative outcome in terms of mortality, morbidity and length of hospital stay (LOS) [9]. Concerning the tool to assess cardiac output, fluid responsiveness and hemodynamic status, transthoracic echocardiography is a non invasive mean which can bring solutions [10]. Echocardiography is an essential tool utilized in diagnostic and interventional cardiology. In children, there are no studies demonstrating the impact of PGDFHT with echocardiography on postoperative outcome in terms of morbidity.

There is one retrospective study in pediatric and adult cardiac surgery which showed that intraoperative trans-oesophageal echocardiography after surgical repair in congenital heart disease reduced LOS [11].

The primary objective of this study is to determine the impact of PGDFHT with echocardiography on postoperative outcome in terms of morbidity.

The secondary outcome is to determine the impact of PGDFHT with echocardiography on postoperative length of stay in the intensive care unit (LOSICU), postoperative length of invasive or non invasive mechanical ventilation (LMV) and postoperative length of hospital stay (LOS).

The primary outcome measures will be postoperative organ dysfunction until discharge from hospital.

The secondary outcome measures will be the number of postoperative days spent in the intensive care unit (ICU), the number of postoperative days spent on invasive or non invasive mechanical ventilation and the number of postoperative days spent in the conventional hospitalization ward.

Methods

This trial has been declared at the French National Agency of Drugs and Medications Security, ANSM (Agence Nationale de Sécurité du Médicament et des Produits de Santé) and registered under the number RCB : 2019-A02886-51. After approval from the Ethics Committee, after registration of the study to the CNIL (Commission Nationale de l'Informatique et des Libertés, National Commission for Computer Science and Liberties) and after written and informed consent from parents, patients will be randomized in two groups. The control group (CG) will be defined as the group managed using the local protocol if any exists or according to the local management or at the discretion of the medical doctor in charge of the patient. The experimental group (EG) will be defined as the group where perioperative fluid and hemodynamic therapy will be guided with echocardiography in the immediate perioperative period and in the ICU. The echo-

cardiographic hemodynamic parameters used in this study will be those validated in the pilot observational trial declared at the ANSM and registered under the number RCB : 2019-A02925-52 and entitled 'Perioperative Echocardiographic Hemodynamic parameters and postoperative outcome in pediatric congenital heart disease: A Descriptive Observational Prospective Pilot Study Protocol [12].

Patients will be blinded to the treatment.

Patients included will be children aged less than 18 years with congenital heart disease (CHD) scheduled for surgical repair. Parameters such as age, gender, type of CHD, surgery, elective or urgent surgery, re-dux, tri-dux or more, Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1), American Society of Anesthesiologists status (ASA), weight, height, prematurity, blood pressure, heart rate, pulse oxymetry, hemoglobin levels, platelet count, leucocyte count, activated thromboplastin, prothrombin time, fibrinogen, blood urea nitrogen, serum creatinin levels, c-reactive protein (crp), procalcitonin (PCT) levels, hepatic functional tests will be registered.

Preoperatively basal values of blood pressure, heart rate, core temperature, pulse oxymetry, mixed venous oxygen saturation ($ScVO_2$), lactate levels, cerebral (ScO_2) and renal oxygen saturation (SrO_2), venous to arterial carbon dioxide gradient will be registered prior to anesthesia and surgery and intraoperatively.

Intraoperative parameters registered will be time on cardiopulmonary bypass (CPB), aortic cross clamping, circulatory arrest, ultra-filtration during CPB, blood product transfusion (packed red blood cells (PRBC), fresh frozen plasma (FFP), concentrated platelet units (CUP), fibrinogen, cryoprecipitate, concentrated complex of prothrombin (CPP) or other blood product derivatives, crystalloids and colloids or other fluids administered, priming volume of the CPB, CPB output during surgery, blood loss, urinary output, quantity of inotropes administered and mechanical ventilation parameters.

Normal blood pressure and heart rate values are those defined according to the patient age [13].

Pulse oxymetry normal values will be considered according to the congenital heart disease (right to left shunts, left to right shunts), normal values of $ScVO_2$ will be considered $\geq 75\%$.

20% reduction of ScO_2 and SrO_2 under the basal levels will be considered abnormal [9].

Lactate levels above 2 mmol/L will be considered abnormal.

After weaning from CPB until discharge from the intensive care unit (ICU), the patient will be either managed according to the existing protocol or according to the PGDFHT protocol after preoperative randomization (see figure 1).

Postoperative parameters registered will be blood pressure, heart rate, core temperature, pulse oxymetry, mixed venous oxygen saturation ($ScVO_2$), lactate levels, cerebral (ScO_2) and renal oxygen saturation (SrO_2), venous to arterial carbon dioxide gradient, blood product transfusion (PRBC, FFP, CUP), fibrinogen, cryoprecipitate, concentrated complex of prothrombin other, blood product derivatives, crystalloids, colloids or other fluids administered, blood loss, urinary output, quantity of inotropes administered, mechanical ventilation parameters, hemoglobin, platelet, leucocyte levels, CRP, PCT, hepatic functional tests, blood urea nitrogen, serum creatinin levels.

Cardiac output measures will be realized with velocity time integral (VTI) at the aortic valve in the apical five chamber view. Normal values of aortic VTI have been defined in children [14].

Fluid responsiveness will be assessed with aortic peak velocity at the apical five chamber view with peak velocity variation (ΔV_{peak})

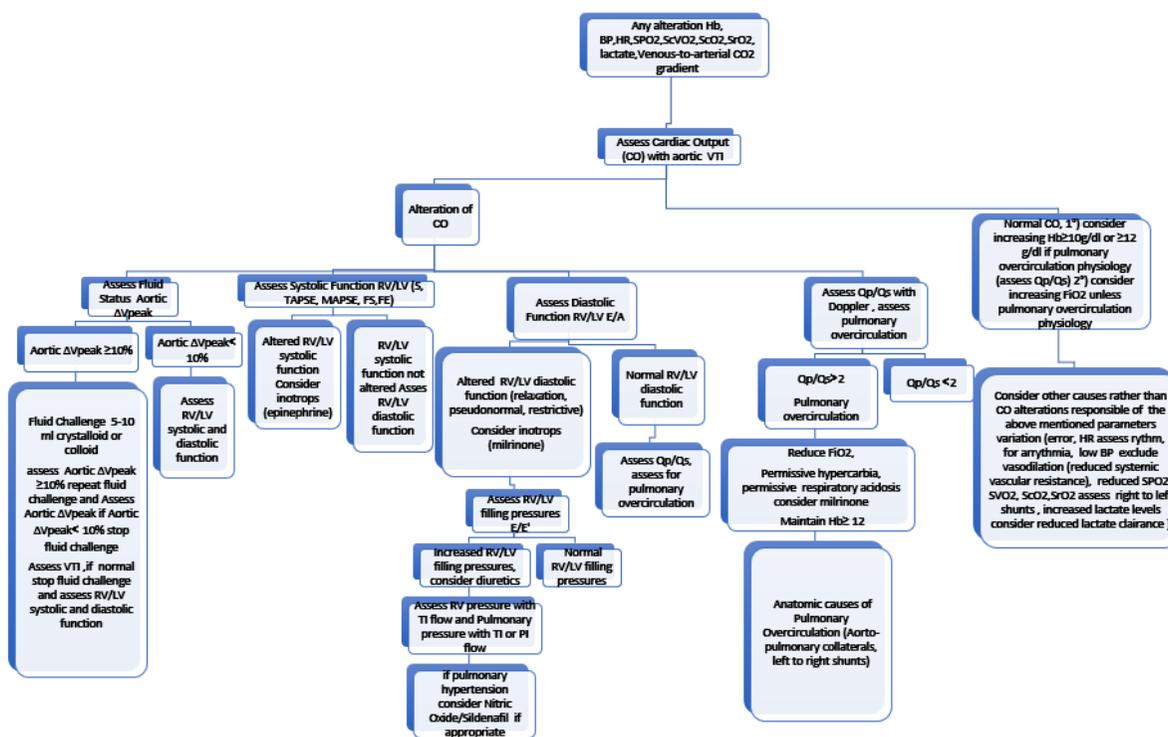


Figure 1: PGDFHT protocol.

of $\geq 10\%$ defining responders to fluid therapy.

ΔV_{peak} is defined as $(V_{max} - V_{min}) / (V_{max} + V_{min}) / 2 \times 100$ [10].

Right ventricular (RV) and left ventricular (LV) systolic function will be assessed in the apical four chamber view with lateral S (S_{lat}) wave velocity in tissue Doppler; mitral and tricuspid annular plane systolic excursion (MAPSE, TAPSE) in time motion mode (TM) and with ejection fraction (EF) with Simpson’s method. Normal MAPSE, TAPSE and S_{lat} values have been defined in children [15-20]. Fractional shortening (FS) will be assessed in the parasternal longitudinal axis view, normal values are the same as in adults (28-42%).

Right ventricular and left ventricular diastolic function will be assessed in the apical four chamber view at the tricuspid and mitral valves with pulsed Doppler to assess for E wave velocity, A wave velocity and E/A ratio. E/A ratios will be analyzed according to age [20-27]. To assess for normal, relaxation alteration, pseudonormal and restrictive profiles. Right and left filling pressures will be assessed with tissue Doppler at the apical four chamber view at the tricuspid and mitral valves to assess lateral E’ wave velocity and E/E’_{lat} ratio. Normal E/E’ and E_{lat} values have been defined in children [21-28].

To assess for pulmonary overcirculation, Q_p/Q_s ratio (where Q_p is pulmonary output and Q_s is systemic cardiac output) will be calculated using the formula $Q_p/Q_s = \text{Pulmonary VTI} \times \text{Area of the pulmonary annulus} \times \text{HR} / \text{Aortic VTI} \times \text{Area of the aortic annulus} \times \text{HR} = \text{VTI}_p \times \pi \times (D/2)^2 / \text{VTI}_{ao} \times \pi \times (D/2)^2$, where D is the diameter of the annulus and HR the heart rate [29].

Pulmonary VTI and pulmonary annulus diameter will be assessed at the parasternal transverse axis view.

Aortic VTI will be assessed at the apical 5 chamber view and the aortic annulus diameter at the parasternal longitudinal axis view.

Postoperative organ dysfunction until discharge from hospital will be registered to assess for primary outcome. The number of days spent in ICU, under invasive or non invasive mechanical ventilation and days in the conventional hospitalization ward postoperatively will be registered to assess for secondary outcomes.

Statistic analysis will be realized with XLSTAT 2018.3 or plus software. Normally distributed and non normally distributed variables will be compared using Student t test and Wilcoxon test respectively. Normally distributed variables will be expressed in terms of means with standard deviation. Non normally distributed variables will be expressed in terms of medians with interquartile ranges. Categorical variables will be compared with the exact Fisher's test or Chi squared test accordingly. Categorical variables will be expressed as percentages with confidence intervals. To assess for independent predictors of adverse postoperative outcome, multivariate analysis will be realized. A P-value ≤ 0.05 will be considered significative. Missing data will not be included

The study is expected to begin in the second semester of 2021 and will end first semester of 2024

The number of patients included will be 400 with 200 in each group. This number was calculated to assess for a significative difference between the two groups using the Case Control Chi squared test with Yates continuity correction.

The study will be mono or multicentric.

Results

Results are expected in the second semester of 2024.

Conclusion

This study protocol was designed to describe the trial which is in development and progress. This trial will clarify the impact of PGDFHT with echocardiography on postoperative outcome in terms of morbidity, LOSICU, LMV and LOS in children with CHD scheduled for surgical repair.

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There will be funding .

Conflict of Interest

The authors declare non conflict of interest.

Disclosure

This study is part of the Thesis entitled 'Do goal directed therapies improve postoperative outcome in children ? (Perioperative Goal Directed Fluid and Hemodynamic Therapy ; Transfusion goal directed therapy using viscoelastic methods and enhanced recovery after surgery and Postoperative outcome)' [30-32] Registered at <http://www.theses.fr/s232762>.

Addendum

This Research Study Protocol Has been accepted for presentation at the 5th World Congress on Advanced Clinical Trials and Clinical Research July 22-23, 2020 in Melbourne, Australia.

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