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Short Communication

Perioperative Goal Directed Fluid and Hemodynamic Therapy with Echocardiography in Children: A Study Protocol

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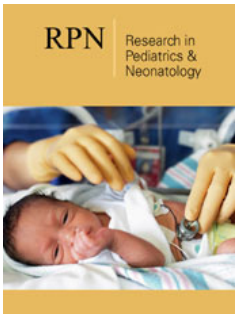

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Abstract

Background: Echocardiography is a tool widely used in diagnostic and interventional cardiology. 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 noninvasive 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 admitted for surgery. Statistical analysis will be realized with XLSTAT 2018.3 or plus software.

Result and 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 admitted for surgery.

Keywords: Children; Echocardiography; Perioperative goal directed fluid hemodynamic therapy; Postoperative outcome

Introduction

Perioperative goal directed fluid and hemodynamic therapy (PGDFHT) has been studied in adults [1-7]. This practice has demonstrated in adults it's efficacy 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 can alter tissular perfusion. Therefore, 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.

However, 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 ($SCVO_2$), 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 Stays (LOS) [9]. Concerning the tool to assess cardiac output, fluid responsiveness and hemodynamic status, transthoracic echocardiograpy 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. One retrospective study in pediatric and adult cardiac surgery showed that intra operative 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 Noninvasive Mechanical Ventilation (LMV), postoperative Length of Hospital Stay (LOS), intraoperative fluid therapy and intraoperative vasopressor inotropic score. 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, the number of postoperative days spent in the conventional hospitalization ward, the quantity of intraoperative fluid therapy and vasopressor-inotropic score.

Methods and Materials

This trial has been declared at the French National Agency of Drugs and Medications Security, ANSM (National Agency for The Safety of Medicines and Health Products) and registered under the number RCB: 2019-A03338-49. After approval from the Ethics Committee, after registration of the study to the CNIL (National Commission for Computer Science and Freedoms, 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 perioperative period.

The echocardiographic 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-A03256-51 and entitled 'Perioperative Echocardiographic Hemodynamic Parameters and Postoperative Outcome in Pediatric Surgical Patients: A Descriptive Observational Prospective Pilot Study' [12]. A similar protocol study has been elaborated for pediatric patients admitted for congenital heart disease surgical repair [13,14]. Patients will be blinded to the treatment. Patients included will be children aged less than 18 years admitted for surgery. Parameters such as age, gender, type of surgery, elective or urgent surgery, 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, Creative protein levels (CRP), procalcitonin (PCT) levels, hepatic functional tests will be registered.

Preoperatively basal values of blood pressure, heart rate, core temperature, pulse oxymetry, will be registered prior to anesthesia and surgery and intraoperatively hourly. Intraoperative parameters registered will be 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, blood loss, urinary output, quantity of inotropes administered and mechanical ventilation parameters, regional cerebral oxygen saturation, renal oxygen saturation and mixed venous oxygen saturation (if monitored) and lactate levels. Normal blood pressure and heart rate values are those defined according to the patient age [15]. Normal values of $ScVO_2$ will be considered ≥75%. 20% reduction of ScO_2 and SrO_2 under the basal levels will be considered abnormal [9]. Lactate levels above 2mmol/L will be considered abnormal. Intra-operatively, patients will be either managed according to the existing protocol or according to the PGDFHT protocol after preoperative randomization (Figure 1). Postoperative parameters registered will be blood pressure, heart rate, core temperature, pulse oximetry, mixed venous oxygen saturation ($ScVO_2$), lactate levels, cerebral (ScO_2) and renal oxygen saturation (SrO_2), 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 creatinine 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 [16]. Fluid responsiveness will be assessed with aortic peak velocity at the apical five chamber view with peak velocity variation (ΔV_{peak}) of ≥10% defining responders to fluid therapy. ΔV_{peak} is defined as V_{max}-V_{min} / [(V_{max}+V_{min})2] X100 [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 [17-22]. Fractional shortening (FS) will be assessed in the parasternal longitudinal axis view, normal values are the same as in adults (28-42%).

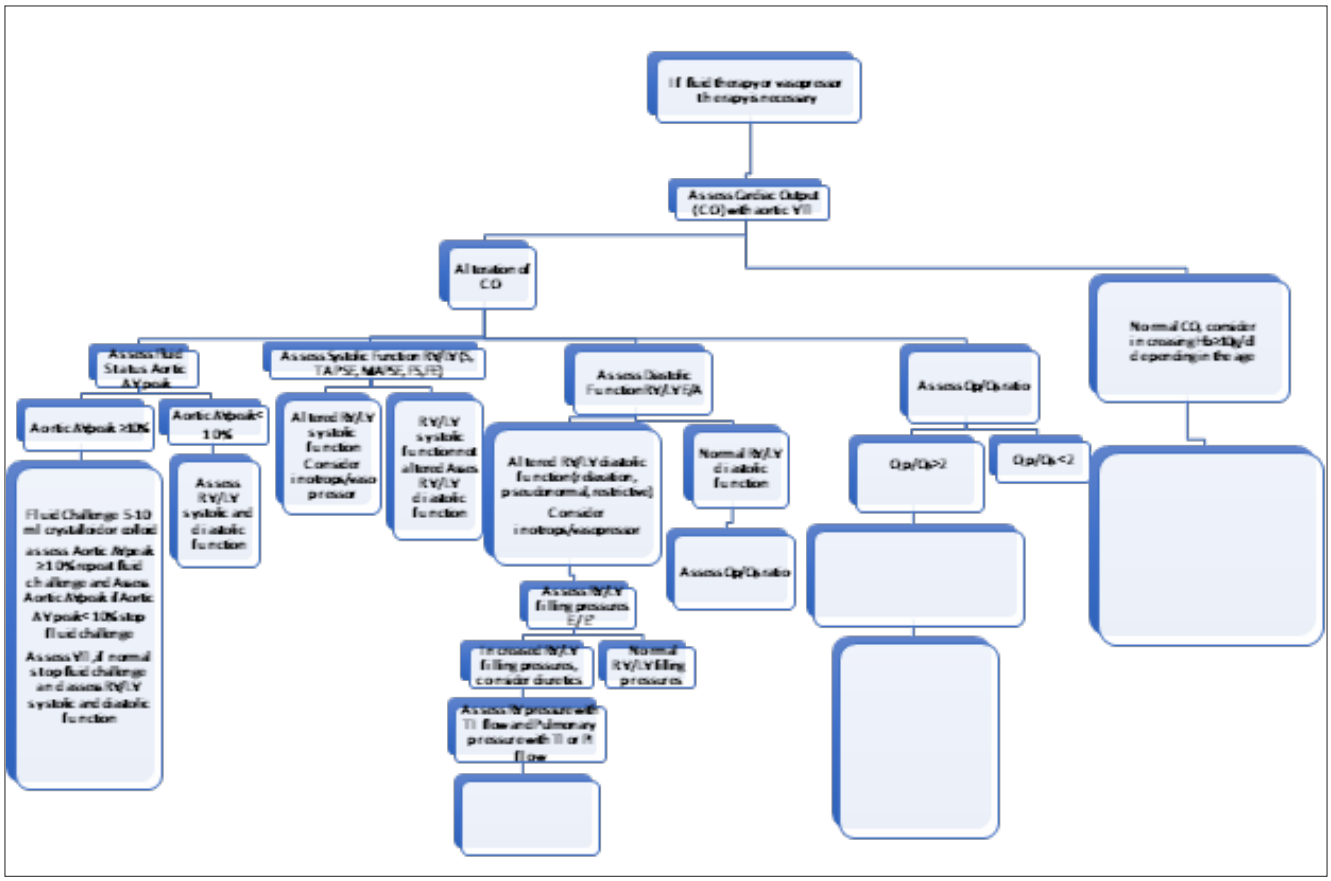

Figure 1. PGDFHT protocol.

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 [23-30]. To assess for normal, relaxation alteration, pseudo normal 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 [23-30]. To assess for Qp/Qs ratio (where Qp is pulmonary output and Qs is systemic cardiac output) the following formula will be calculated Qp/Qs=Pulmonary VTI x Area of the pulmonary annulus x HR /Aortic VTI x Area of the aortic annulus x HR=VTIp x II $(D/2)^2$/VTIao x II x $(D/2)^2$, where D is the diameter of the annulus and HR the heart rate [31]. 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. The inferior veina cava diameter (IVC) and the variation of the latter (**Δ** IVC) will be assessed at the subcostal view and will be defined as $\Delta\ IVC=[D_{max}-D_{min}/(D_{max}+D_{min}/2)]x100$. Where D_{max} is the maximum and D_{min} is the minimum diameter of the IVC.

Supra-hepatic Doppler waves velocity V, A, S, D and S/D ratios will be assessed in the subcostal view. Pulmonary Doppler waves velocity S, D, E, Ap and S/D ratios will be assessed in the apical four chamber 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 noninvasive mechanical ventilation, postoperative days spent in the conventional hospitalization ward, the amount of intraoperative and postoperative fluid therapy and intraoperative and postoperative vasopressor inotropic score will be registered to assess for secondary outcomes. Statistical 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 or Mann-Whitney test and Wilcoxon test or Kruksal-Wallis 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 squarred test accordingly. Categorical variables will be expressed as percentages with 95% 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 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.

Result and 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, LOS, intraoperative and postoperative fluid therapy and vasopressor-inotropic score in children admitted for surgery.

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)' [32-34]. This Thesis is registered at http://www.theses.fr/s232762.

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