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Review Article

Predicting Perioperative Fluid Responsiveness in Pediatric Patients; how it Differ from the Adults?

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ABSTRACT

Accurate Prediction of fluid responsiveness can be challenging, particularly in children. Although, fluid administration is the main stay of resuscitation during pediatric surgery associated with significant blood or third space loss, volume overload is frequently encountered in small children and is often associated with adverse outcomes. The parameters used to assess fluid responsive are basically classified into two categories, static and dynamic parameters. Static parameters like central venous pressure measurement are slowly becoming unpopular and are replaced by dynamic parameters which rely on the heart-lung interactions are more accurate predictors of fluid responsiveness. Unlike adults, there are insufficient data on the efficacy of dynamic variables for the prediction of fluid responsiveness in children. In this review article we discuss the strengths and limitations of both the static and dynamic parameters for assessing the fluid responsiveness in the perioperative period in pediatric patients.

Keywords: Fluid responsiveness; Pediatric surgery; Dynamic parameters; Static parameters

INTRODUCTION

Intravenous fluid therapy is an essential part of intraoperative anesthetic and perioperative surgical care. However, inappropriate fluid therapy can have significant perioperative outcomes [1-5]. The goals of perioperative fluid management are to restore and maintain blood volume and cardiac output to provide adequate perfusion to pertinent tissues and prevent hypoperfusion and tissue injury. On the other hand hypervolemia due to excess iatrogenic fluid loading has been associated with increased length of hospital stay, significant morbidity and mortality [6-7]. Predicting fluid responsiveness can be challenging, particularly in children especially when there is ongoing blood loss where estimation of blood loss and third space loss may be difficult. Clinical assessment of hemodynamic status based on physical examination and routine monitoring is inadequate, particularly in small children. These finding underline the need for more reliable predictors of fluid responsiveness [8-10].

Numerous hemodynamic variables have been proposed as predictors of fluid responsiveness. Static variables are based on observation against static time. This includes clinical observations such as heart rate and arterial blood pressure, preload pressures such as Central Venous Pressure (CVP) and pulmonary artery occlusion pressure. Dynamic indices of preload, which reflect heart-lung interaction through ventilation-induced cyclic changes in left ventricular stroke volume over a period of time. In this review article we discuss the reliability of these parameters in perioperative setting to detect fluid responsiveness in pediatric patients.

STATIC VARIABLES

Clinical parameters (Systolic Blood Pressure (SBP) and Heart Rate(HR))

SBP and HR under anesthesia are affected by confounding factors like depth of anesthesia or surgical simulations, so they are not very sensitive indicators for volume status. Studies in paediatric patients during period using the heart rate and SBP variability as a clinical predictor of volume status was not significant ($P > 0.5$) in most of the studies [11-13].

Central venous and pulmonary arterial wedge pressure: Numerical values of Central Venous Pressure (CVP) and values of Pulmonary Artery Wedge Pressure (PAWP), do not accurately measure the circulating blood volume or responsiveness to fluid challenge (an increase in Cardiac Output, reflected by predictable change in CVP after a bolus of fluid). A sophisticated approach of measuring separately total blood volume and circulating blood volume, using a dye dilution or thermodilution technique, also did not demonstrate consistent correlation between values of CVP and blood volume, either total or circulating blood volume [14,15]. In addition, these invasive techniques are associated with complication during insertion such as pneumothorax or hematoma formation [16].

Echocardiography and Doppler assessment of ventricular function: Use of Left Ventricular End Diastolic Area (LVEDA) and aortic Velocity-Time Integral Aortic Output (VTI -AO) (figure 1) as measured by trans esophageal or transthoracic Echocardiographic measurement was looking promising initially, but on meticulous re-

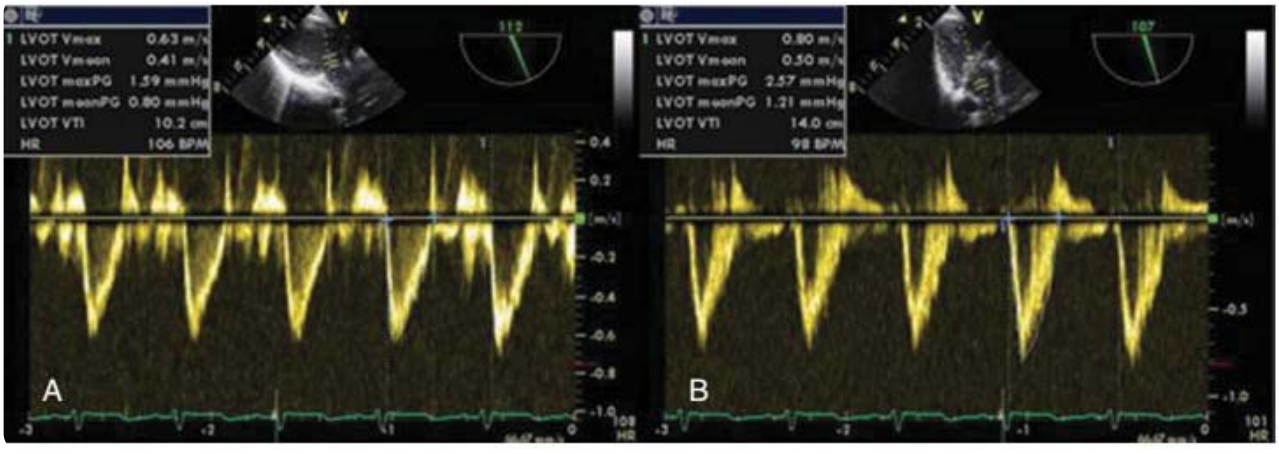

Figure 1: Measurement of Doppler velocity time integral in the LVOT (A) and in the ascending aorta (B) [44].

evaluation, it was found not that much useful tool to predict fluid responsiveness [11]; further, Echocardiography need special expertise and training for the operator and it may not be applicable in some surgical procedure limiting its usefulness as routine practice. Raux et al. [17] have shown Trans-Esophageal Doppler (TED)-derived parameters that included Stroke Volume Index (SVI); Corrected Flow Time (CFT); Peak Velocity (PV) during volatile anesthesia was useful to predict and follow Volume Expansion (VE) responsiveness in neonates and infants [17,18]. Trans esophageal Doppler has the advantage of being simple and relatively non-invasive technique unlike echocardiography, but, TED was not useful to detect FR (Fluid Responsiveness) in cardiac patients [19,20].

Thermodilution and Ultrasound Dilution technique: Saxena et al. [18] investigated the static variables (total end diastolic volume, active circulation volume, central blood volume, and total ejection fraction derived from trans pulmonary ultrasound dilution method (ultrasound transit time-based measurement of pulmonary blood flow) as predictors of FR defined by increase in SV by 15% [18]. The result of the study was that none of these markers discriminated adequately for volume responsiveness and all of them were comparable to CVP (AUC 0.41, 95% CI 0.26-0.55) [18].

Global End Diastolic Volume Index (GEDVI) measured by thermodilution failed to predict fluid responsive in patient with left to right shunt (VSD /ASA) (AUC: 0.59 P = 0.42) but its predictive value improved after repair of shunt (AUC: 0.77 P = 0.008 Cutoff: ≤ 400 ml) [20].

Laboratory based parameters

Hematocrit dilution: Hematocrit dilution is often based on changes in measured values from the baseline value and can only assess changes in the circulating part of the blood volume, ignoring a considerable non circulating portion of the plasma [21-23] but these changes take place over a certain period and do not immediately reflect acute changes in volume status. In addition, there is possibility of lag between the timing of result and timing of the blood sampling.

Urine Output (UO): Oliguria (UO < 0.5mL/kg per hour) is a commonly used general indicator of hypovolemia. However, perioperative oliguria alone is not a sufficient indication for fluid administration. Perioperative medication and anaesthetic drugs and techniques as well as surgical technique and manipulation may reduce UO. Administration of fluid to treat oliguria in a euvolemic state may lead to fluid overload [24,25].

Mixed venous (SVO2) and Central venous oxygen saturation (ScVO2): SVO_2 and $ScVO_2$ value can be obtained periodically from pulmonary artery catheter or central venous catheter through blood gas analysis or continuously using a fiber-optic catheter. Although SvO_2 and $ScVO_2$ are proportional to cardiac output, tissue perfusion, and tissue O_2 delivery, these measurements are also inversely proportional to tissue O_2 consumption. However, these changes may not reflect accurate changes in tissue perfusion during the perioperative period when regional perfusion and O_2 consumption may vary [26,27].

Base Deficit (BD) and serum lactate: Lactic acidosis on sequential arterial blood gases can be a surrogate marker of reduced global tissue perfusion. However, these laboratory values do not provide information regarding contemporaneous clinical intravascular volume status since they are measured intermittently and do not immediately reflect acute changes. In addition; the BD can be caused by intravenous infusion predominately normal saline. Moreover, base deficit as a surrogate for serum lactate can be confounded by renal dysfunction and ketoacidosis [28].

Dynamic variables

Dynamic indices of circulating fluid volume based on ventilation-induced (cardiopulmonary interaction) cyclic changes in Left Ventricular (LV) stroke volume have been shown to reliably predict the FR in adults [29-32]. During positive pressure ventilation; on inspiration - increase in intrathoracic pressure- reduces venous return and thereby reducing right ventricular stroke volume which is proportional to the degree of hypovolemia and is transmitted to the left heart after two or three beats (pulmonary vascular transit time [31,33]. These variables can be calculated through the direct arterial pressure trace.

Variable derived from the arterial pressure: The variable derived from the arterial pressure are SPV (Systolic Arterial Pressure Variation) and PPV (Pulse Pressure Variation) (Figure (2).

SPV is calculated using he maximal and minimal SAP (Systolic Arterial Pressure Variation) values measured in a single respiratory cycle

SPV (%) = (SAP max - SPB min)/ [(SAP max + SAP min)/2] × 100 [34].

PPV was defined as the difference between Pulse Pressure

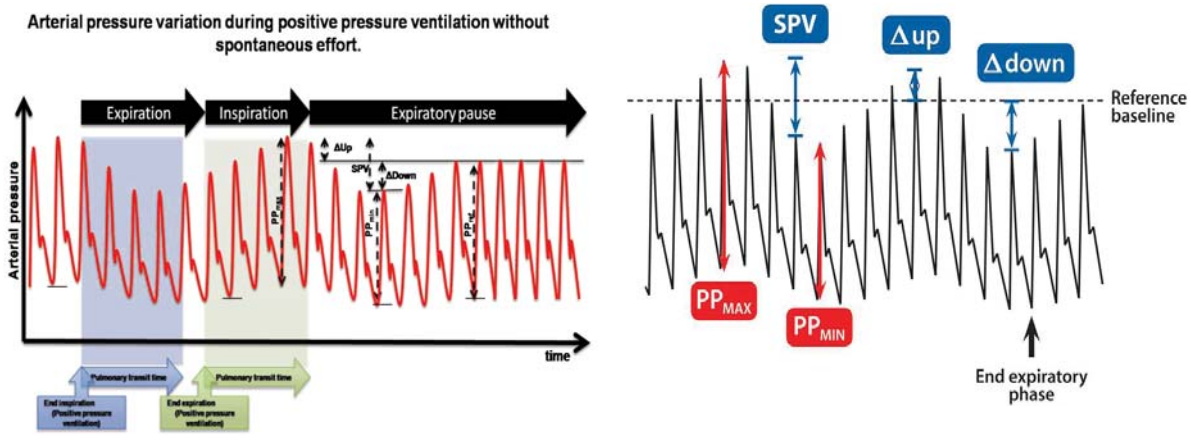

Figure 2: Arterial pressure variation, showing Systolic Pressure Variation, Pulse Pressure (PP) maximum and minimum.

(systolic minus diastolic pressure) Maximal (PP max) and minimal (PP min) values over mean pulse pressure were determined over the same respiratory cycle.

PPV = PP max-PP min/ PP mean

PPV (%) =100× (PP max - PP min)/ [(PP max +PP min)/2]]

PV is also calculated with PP using an analogous formula. An average is taken either over 3 consecutive down =SP ref- SP min, and up = SP max- SP ref. where is (SP ref) reference systolic pressure at the end expiratory pause (SP ref) at the end-expiratory pause [34,35].

In contrast to the strong evidence of predictive value of this variable in adult, the evidence in children is poor as almost all studies revealed that these dynamic parameters are not significant predictors of fluid responsiveness in children. There are several possible explanations for the difference in the predictive value of PPV between children and adults. Arterial elastance in children is low (compliance is high), therefore, pressures transmitted by an increase in stroke volume may be partially absorbed, and pressure variations caused by an increase in stroke volume may be absent from the arterial pressure waveform [35,36].

Variables derived of Plethysmography: Two variables derived from Plethysmography ΔPOP = Pulse Oximeter Plethysmography amplitude variation and PVI = Plethysmography Variability Index.

Red and infrared light are used by a pulse oximeter to measure oxygen saturation. A constant amount of light (DC) from the pulse oximeter is absorbed by skin, other tissues, and non-pulsatile blood, whereas a variable amount (AC) is absorbed by pulsatile arterial inflow. The PI (Perfusion Index) is calculated from the absorptions of red and infrared light, using: PI (%) = (AC/DC) ×100. AC and DC signals are extracted from the amplitude of the plethysmographic waveform. The dynamic change in perfusion index PI during a respiratory cycle results in the PVI, which was automatically calculated using: PVI =100 × (PI max-PI min)/PI max. PVI reflects respiratory variations in PI (Figure 3) [35]. The plethysmographic waveform amplitude is measured beat to beat as the vertical distance between peak and preceding valley in the output waveform. ΔPOP is then calculated using a formula analogue to that of SPV and PPV. Similar to the calculation of PPV, an average is usually taken over 3 consecutive respiratory cycles [36,37]. There is no evidence ΔPOP is predictor of fluid responsive in children but for PVI the results of the studies are variable [12,16,34,39].

FLOW BASED VARIABLES

These variables include respiratory variation in aortic blood flow peak velocity (ΔPeak), the aortic velocity, Time Integral (ΔVTI) and Inferior Vena Cava Diameter Variation (ΔIVCD). Unlike pressure based variable and Plethysmography based variable, flow based variable are not affected by high arterial compliance in children. ΔV peak is measured either transthoracic or Trans esophageal echo by Doppler at LVOT or ascending aorta. (Figure 1).

ΔV peak = (V peak max-V peak min)/ [(V peak max + V peak min)/2],

Where V is peak max and V peak min are the maximum and minimum aortic flow peak velocities over a single respiratory cycle, respectively.

ΔV peak has the strongest evidence as a predictor VR among all other dynamic and static variable. As the Area under the Curve (AUC) or ROC for all studies ranges from 0.8 to 1.00. [11,13,20]. However, only one study found ΔIVCD as reliable predictor of FR in pediatric intensive care unit PICU, [40] but other subsequent study failed to usefulness of vana caval diameter (IVCD) change as predictor of FR [13]. IVCD was measured from the subcostal view (2 cm from the right atrium) using M-mode. The maximum and minimum IVCD (IVCD max and IVCD min) over a single respiratory cycle are recorded. DIVCD was calculated as DIVCD (%) = 100 × (IVCD max + IVCD min) / [(IVCD max + IVCD min)/2] [13]. These technique have limitations that skilled operator is required for accurate measurements and interpretation.

Passive Leg Raising (PLR)

PLR induced changes in cardiac output reliably predicted the fluid responsiveness regardless of ventilation mode, underlying cardiac rhythm, and technique of measurement. PLR-induced changes in pulse pressure variation could be a viable alternative, but in children it has a lower predictive ability as Children have a lower leg-length to body-length ratio than adults, so the effect of PLR may be smaller [42]. Moreover, PLR may be not convenient or practical in Operating Room due to possibility of interruption of surgery. Lukito et al. [43] used PLR test to predict fluid responsiveness in pediatric

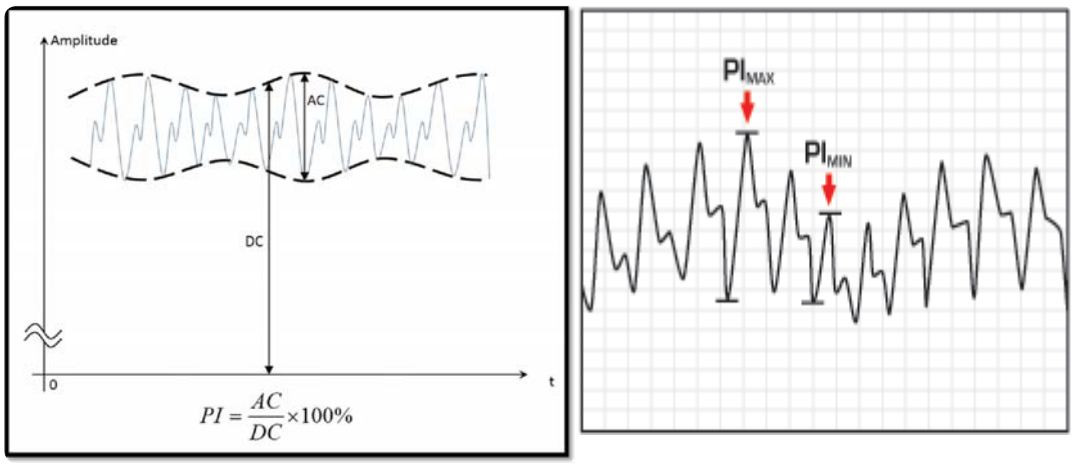

Figure 3: Plathysmographic Index.

intensive care unit patients and to get a cutoff value of cardiac index in predicting fluid responsiveness in pediatric patients. The study has shown that Cardiac Index (CI) increase by ≥ 10% induced by passive leg raising predicted preload-dependent status with sensitivity of 55% and specificity of 85% (area under the curve 0.71 ± 0.084, 95% confidence interval 0.546-0.874 [43].

LIMITATIONS OF DYNAMIC PARAMETERS IN PAEDIATRIC AGE GROUP

Unlike Adult, there are several factors that may play important role in paediatric population because of which many variables may not accurately reflect the FR in paediatric age group [44]. Dynamic parameters are more accurate in adults compared to static ones. There are many different types of dynamic parameters based cardio-pulmonary interaction, these dynamic variables are

1. Arterial pressure related variable
2. Plethysmography derived variable
3. Left ventricular outflow - aortic flow dependent variable
4. Passive leg raising - based on clinical parameters.

Arterial pressure trace is dependent on stroke volume and arterial elastance, as the arterial elastance is different in paediatric age group, arterial pressure trace and pulse wave velocity may not reflect like in adults. The pulse wave velocity increase non-linearly with age in arteries of arms and legs [45]. The non-linearity is due to change in both arterial wall thickness and change in elastance. Because of these changes may explained why pulse pressure and PPV may not predict fluid responsiveness in children between aged 6-14 years of age [45]. The basic of dynamic parameters is heart -lung interaction or Cardio-pulmonary interaction, which paediatric age group may be different than adults, lung compliance and chest wall rigidity, airway resistance, respiratory rate and tidal volume which may have difference impacts on the preload and after load unlike adults. Recently, it was reported that the significance of dynamic parameters in a ventilated may be influenced not only by tidal volume, but also by other ventilator settings. Kang et al. [46] observed significant difference in Stroke Volume Variation (SVV) in same patient with same volume status with different level of Peak Inspiratory Pressure (PIP) [46].

Obtaining accurate Pulse oxymetry trace may be challenging in small pediatric patients and is influenced by many factors like regional blood flow, temperature, electro-cautery, use of inotropes etc. Plethysmography derived parameters may not be as useful as PPV or SPV [47].

Unlike pressure based variable and Plethysmography based variable, flow based variable are not affected by high arterial compliance in children. ΔV peak is measured either transthoracic or Trans esophageal echo by Doppler at LVOT or ascending aorta, this may not be practical or feasible to obtained the image during intraoperative period. Moreover, use of echocardiography require special experience and training making its usefulness limited to few center with expertise in using it.

Passive Leg Raising (PLR) maneuver is a dynamic test to detect fluid responsiveness based on shifting of significant amount of blood to central compartment and thereby reflected by changes in cardiac output. This maneuver is not very popular because the blood volume shift with this maneuver may be small and variable depending on the ratio between leg and thorax, size and age of the patient. Other alternative dynamic tests such as end-expiratory occlusion may be of interest in this setting, which require further testing [48].

AUTHORS PREFERRED TECHNIQUES TO DETECT VOLUME RESPONSIVE IN PEDIATRIC SURGERY

Clearly, dynamic parameters are superior over the static variable to assess the fluid status and fluid responsiveness. Among the dynamic parameters, apart from flow variables which require special skills and special facilities, there is no evidence that any pressure variable dynamic parameters are reliable predictor of volume responsive if each used alone. Instead of relying on single variable, use of multiple variable significantly improved the sensitivity and specificity. Clinical assessment of intravascular volume begins with knowledge of age-related norms for heart rate and BP and then answer the following questions: Is the heart rate persistently increased, or does it vary with surgical stimulation? Is the pulse pressure narrow, or more ominously, is the BP reduced for age? Does it vary with positive-pressure breaths? Are there SAP (Systolic Arterial Pressure variation or ΔPOP (Pulse Oximeter Plethysmography amplitude variation)? Are the extremities warm? Is capillary refill brisk? What is the urine output? How low CVP? How low the hematocrit and hemoglobin level? Are these variables changing? What is the rate of the change? Is there evidence of blood loss in the surgical field? What is the result of blood gases? When hypovolemia is suspected, observing the response to a 10 to 20 mLkg bolus of isotonic crystalloid or colloid may test the hypothesis of hypovolemia and re check the change in this parameters.

CONCLUSION

Dynamic parameters are definitely better predictor of FR over static variables. So far, we don't have a single predictor to have highly sensitive and specific for fluid responsiveness. Instead of relying on single parameters, combing these multiple parameter along with clinical scenario may help to improve their sensitivity and specificity.

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