The Reliability of CVP in Predicting Fluid Responsiveness in Critically Ill Mechanically Ventilated Children

Seham Awad Elsherbiny Ali[1], Bassant Salah Saad Meligy[2], Ahmed Said Mohammed Behairy[3], Mohamed Salah Mohamed Eldoadoa[4]
[1] Professor of Pediatrics, Faculty of Medicine, Cairo University, Egypt.
[2] Assistant Professor of Pediatrics, Faculty of Medicine, Cairo University, Egypt.
[3] Lecturer of Pediatrics, Faculty of Medicine, Cairo University, Egypt.
[4] M.Sc., Pediatrics, Faculty of Medicine, Cairo University, Egypt.
Corresponding author: Mohamed Salah Mohamed Eldoadoa
Email: msm7690@gmail.com

Abstract
Background: The main goal of hemodynamic resuscitation is to achieve adequate tissue perfusion. This is initially attempted with intravascular volume expansion (VE). Although central venous pressure (CVP) role in prediction of fluid responsiveness is controversial, it remains the most commonly used parameter for detecting volume status in ICU patients. Methods: Forty-eight critically ill mechanically ventilated children considered for VE by clinical evaluation of circulatory status were prospectively included. Patients were divided in 2 age groups; group A:<24 months and group B: ≥24 months. Patients with Stroke volume variation (SVV) more than 10% after VE were categorized as volume responders. CVP values were noted before and after VE in the responder and non-responder groups. Results: For group A (<24 m); CVP had no statistical value in prediction of fluid responsiveness (p=0.083), however; in the total study population, and in group B (≥24m) it had value (p=0.001) in predicting responders with a sensitivity, specificity and cut off values of 88%,64% and ≤ 10 respectively in the total study population and 100%,88% and ≤11 respectively in group B. Also, both had good correlation with SVV that was better with group B (r=-0.778) than with total population (r=-0.454). Conclusion: CVP role in prediction of fluid responsiveness is un reliable in infant and young children (<24m), while in older children it is valuable in guiding fluid therapy together with the other dynamic variables.
Keywords: central venous pressure, CVP, fluid responsiveness, stroke volume variation (SVV)

1. Background

CVP is frequently used to assess the complex circulatory status of critically ill patients (Li et al.,2017). It continues to be widely used in guiding fluid therapy (Cecconi et al.,2015) and is recommended to guide fluid therapy in patients with septic shock (Dellinger et al.,2013).
CVP is a good approximation of right atrial pressure, and therefore it has been assumed as a good indicator of right ventricular preload and intravascular volume status (Berlin et al.,2015). Based on rationale provided by the Starling curves and Guyton model on cardiac function, CVP is determined by the interaction of cardiac function and venous return. An elevated CVP might indicate an impediment to the venous return and microcirculatory blood flow as well as accompanying lung edema and splanchnic congestion, which may further worsen the potential organ failure in critical patients (Vellinga et al.,2013).
But, many factors other than preload status can affect CVP measurements as congestive heart failure, constrictive pericardial disease, tension pneumothorax, positive pressure ventilation, place of central venous catheter tip and resuscitation/evacuation phases of septic shock, so, recent studies have challenged the validity of elevated CVP in critical care settings (Semler et al.,2016).
Extreme values of CVP are expected to have some predictive value in critical conditions and CVP may be considered the downstream pressure of venous return (Sondergaard et al.,2015). Along this line, a recent consensus statement recommended immediate fluid resuscitation in shock states associated with very low levels of preload parameters (e.g. CVP) (Cecconi et al.,2014)
Two European surveys and a Canadian survey reported that about 90% of intensivists use the CVP to monitor fluid resuscitation in patients with septic shock(McIntyre et al.,2007), (Kastrup et al.,2007).
Evaluating CVP in pediatric patients seems to be a tedious job, since many variables are considered; as the difficulty in inserting central lines for all patients, the difficulty of achieving the optimum line position due to short necks and wide variety in ages, weights and anatomy in pediatric population. Since the literature is scarce in pediatric studies evaluating CVP, we underwent this study to evaluate its role in the young children.

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2. Methods

Population of study & disease condition

We conducted the study in pediatric intensive care unit (PICU) in Cairo University Hospitals, on critically ill mechanically ventilated pediatric patients considered for volume expansion by clinical evaluation of circulatory status.

Study design: Prospective observational study.

Inclusion criteria

Critically ill mechanically ventilated children, 1 month to 13 years of age, considered for volume expansion by clinical evaluation of circulatory status e.g. prolonged capillary refill, tachycardia and hypotension.

Exclusion criteria

1. Ages below 1 month or more than 13 years.
2. Patient with refractory septic shock.
3. Patients with known congenital heart diseases.
4. Patients with status athmaticus.
5. Patients who are not mechanically ventilated.
6. Contraindication to fluid overload such as acute kidney injury.
7. Shocked patients who require immediate fluid resuscitation

Interventions

8. This was a single prospective study involving 48 patients admitted to pediatric intensive care unit from June 2020 December 2021.
9. Critically ill children fulfilling inclusion criteria who have received initial fluid resuscitation (40 ml/kg) but still showing signs of tissue hyopoxia will be assessed for CVP and Stoke volume (SV) before and after further volume expansion (VE).
10. Volume responders (R) will be patients showing SVV of at least 10%
11. Informed consent was obtained from all included patients by one of the legal guardians.

All patients who fulfilled the inclusion criteria were subjected to

Doppler Echocardiography Measurement

SV was assessed immediately before and after fluid challenge using echocardiography (GE vivid 7;GE Vingmed Ultrasound AS, N-3190, GE, Horten, Norway). In the left parasternal view, the diameter of the aorta was measured at the level of the aortic valve insertion. The left ventricular outflow tract (LVOT) area was measured using the following equation: (LVOT area= 0.785× [diameter of the aorta at the level of annuls]). Velocity time integral (VTI) of aortic blood flow is equivalent to the product of the mean velocity (obtained by tracing the spectrum of LVOT flow) and ejection time. Pulsed-wave Doppler signal from the five chambers' apical view was directed parallel to flow through the LVOT below the aortic valve and the velocity was recorded (cm/s). The SV was calculated by the device using the equation: (SV=VTI×LVOT area).

According to previous studies, we adopted that SVV ≥10% was valid to signify fluid responsiveness .

SVV is assessed by both systems using the following equation: SVV (%) = (SVmax - SVmin)/SVmean (Hofer et al.,2005).

Central venous pressure: manual measurement by disposable CVP manometer set, with zero point at the level of the right atrium(the 4th intercostal space in the mid-axillary line) while the patient is lying supine, each time at the same zero position.

Volume expansion: after measuring the previous variables, bolus fluid volume of 10 ml/kg crystalloids solution is administered over 10 minutes then all the variables are remeasured.

3. Results

For the total number of patients who had CVP readings(n=48)

Table (1):Comparison according to CVP between non-responders (SVV<10%) (n=14) and responders (SVV>10%) (n=34) before and after volume expansion (in the total study group who had CVP readings (n=48):

		Total (n = 48)	Fluid responsiveness		p
			Non-responders (n = 14)	Responders (n = 34)	
CVP	Before				
	Min. – Max.	1.0 –17.0	1.0 –17.0	2.0 –15.0	0.001*
	Mean ± SD.	8.35 ±3.53	10.79 ±3.70	7.35 ±2.97	
	Median (IQR)	8.0 (6.0 –11.0)	11.50 (9.0 –13.0)	8.0 (6.0 –9.0)	
	After				
	Min. – Max.	4.0 –19.0	5.0 –19.0	4.0 –17.0	0.003*
	Mean ± SD.	10.44 ±3.48	12.71 ±3.83	9.50 ±2.89	
	Median (IQR)	10.0 (8.0 –12.50)	12.50 (10.0 –16.0)	10.0 (8.0 –11.0)	
	(p_0)	,p_0<0.001*	p_0<0.001*	p_0<0.001*	

IQR: Inter quartile range, SD: Standard deviation, p:p value for comparing between non-responders and responders, p0: p value for comparing between before and after *: Statistically significant at p ≤ 0.05

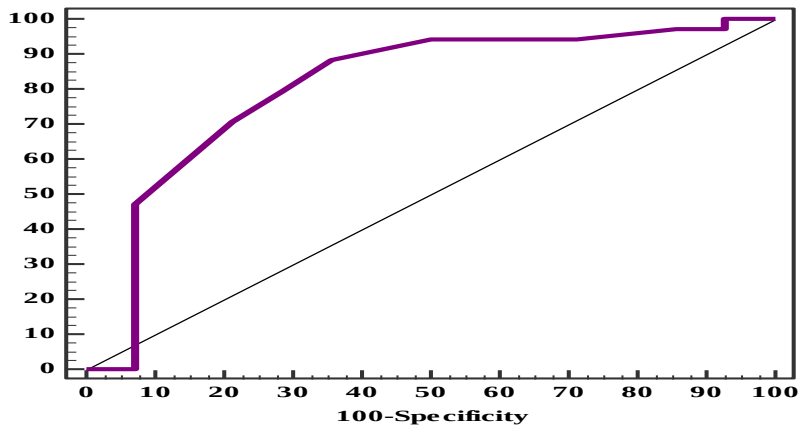

Figure (1): ROC curve for CVP and its ability of predicting volume responders (SVV>10%) (n=34) from non-responder (SVV<10%) (n=14) in the total study group who had CVP readings (n=48).

Table (2):validity (AUC, CI, cut off value, sensitivity, specificity, PPV and NPV) of CVP in predicting volume responders (SVV>10%) (n=34) from non-responder (SVV<10%) (n=14) in the total study group who had CVP readings (n=48).								
	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
CVP	0.807	0.001*	0.654 –0.960	≤10#	88.24	64.29	85.7	69.2
AUC: Area Under a Curve, p value: Probability value , CI: Confidence Intervals , NPV: Negative predictive value , PPV: Positive predictive value , *: Statistically significant at p ≤ 0.05								

For patients < 24 months who had CVP readings (n=29)

Table (3):Comparison according to CVP between non-responders (SVV<10%) (n=7) and responders (SVV>10%) (n=22) in patients who had CVP readings in group A(<24m) (n=29):			
	Fluid responsiveness		P
	Non-responders (n = 7)	Responders (n = 22)	
CVP			
Mean ± SD.	9.14 ±4.74	6.86 ±3.15	0.152
Median (Min. – Max.)	9.0 (1.0 –17.0)	7.0 (2.0 –15.0)	
SD: Standard deviation, p:p value for comparing between non-responders and responders, *: Statistically significant at p ≤ 0.05			

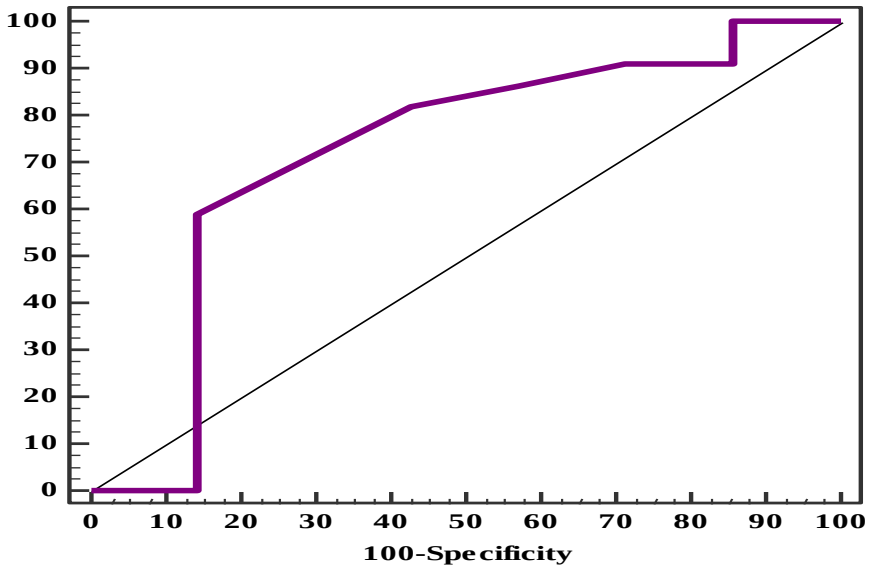

Figure (2): ROC curve for CVP and its ability of predicting volume responders (SVV>10%) (n=22) from non-responder (SVV<10%) (n=7) in patients who had CVP readings in group A(<24m) (n=29).

Table (4):validity (AUC, CI, cut off value, sensitivity, specificity, PPV and NPV) of CVP in predicting volume responders (SVV>10%) (n=22) from non-responder (SVV<10%) (n=7) in patients who had CVP readings in group A(<24m) (n=29).								
	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
CVP	0.721	0.083	0.468 –0.974					
AUC: Area Under a Curve, p value: Probability value , CI: Confidence Intervals , NPV: Negative predictive value , PPV: Positive predictive value , *: Statistically significant at p ≤ 0.05								

For patients ≥ 24 months who had CVP readings (n=19)

Table (5):Comparison according to CVP between non-responders (SVV<10%) (n=7) and responders (SVV>10%) (n=12) in patients who had CVP readings in group B(≥ 24m) (n=19):			
	Fluid responsiveness		P
	Non-responders (n = 7)	Responders (n = 12)	
CVP			
Mean ± SD.	12.43 ±0.98	8.25 ±2.49	0.001*
Median (Min. – Max.)	12.0 (11.0 –14.0)	8.50 (2.0 –11.0)	
SD: Standard deviation, p:p value for comparing between non-responders and responders, *: Statistically significant at p ≤ 0.05			

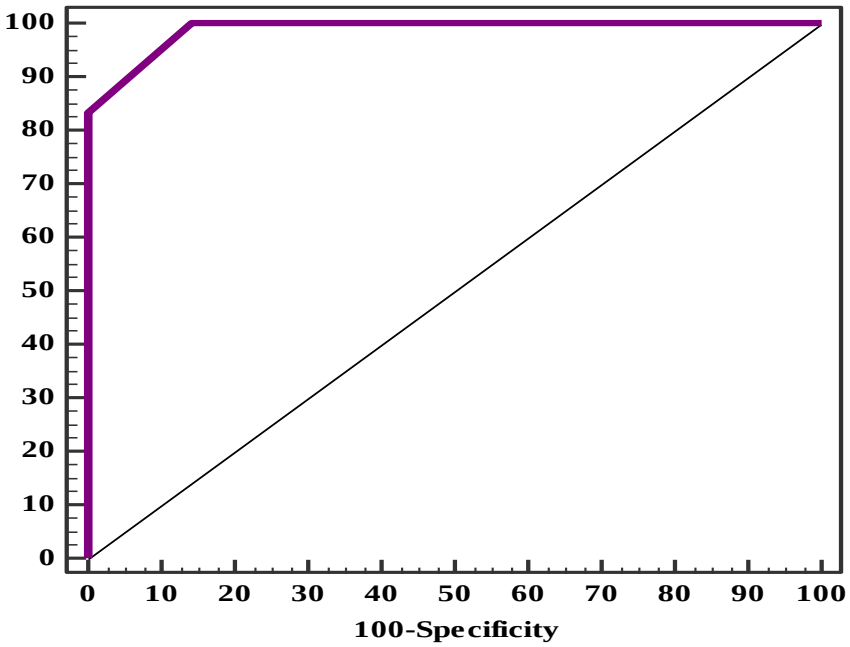

Figure (3): ROC curve for CVP and its ability of in predicting volume responders (SVV>10%) (n=12) from non-responder (SVV<10%) (n=7) in patients who had CVP readings in group B(≥ 24m) (n=19).

Table (6):validity (AUC, CI, cut off value, sensitivity, specificity, PPV and NPV) of CVP in predicting volume responders (SVV>10%) (n=12) from non-responder (SVV<10%) (n=7) in patients who had CVP readings in group B(≥ 24m) (n=19).								
	AUC	p	95% C.I	Cut off#	Sensitivity	Specificity	PPV	NPV
CVP	0.988	0.001*	0.951 –1.026	≤11	100.0	85.71	92.3	100.0
AUC: Area Under a Curve, p value: Probability value , CI: Confidence Intervals , NPV: Negative predictive value , PPV: Positive predictive value , *: Statistically significant at p ≤ 0.05								

For patients who had CVP readings in total study population (n=48), group A(<24m) (n=29) and group B (≥24m) (n=19)

Table (7):Correlation between SVV and CVP before fluid loading in patients who had CVP readings in total study population (n=48), in group A(<24m) (n=29) and group B (≥24m) (n=19)						
SVV% vs.	Total Sample (n = 48)		Age			
			<24 month (n = 29)		≥24 months (n = 19)	
	r_s	P	r_s	p	r_s	P
CVP	-0.454	0.001*	-0.292	0.124	-0.778	<0.001*
rs: Spearman coefficient , Statistically significant at p ≤ 0.05						

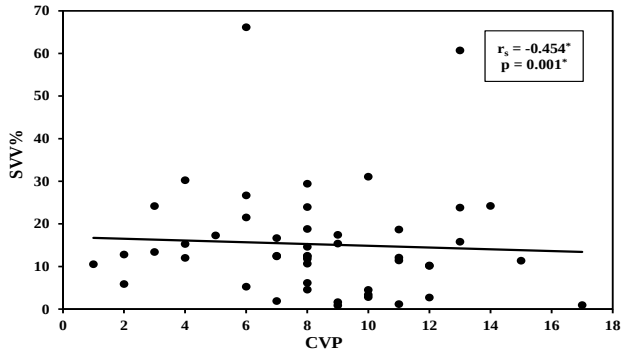

Figure (4): Correlation between SVV and CVP before fluid loading in patients who had CVP readings in total study population (n=48),

4. Discussion

For group A (<24 m); CVP had no statistical value in prediction of fluid responsiveness (p=0.083), however; in the total study population, and in group B (≥24m) it had value (p=0.001) in predicting responders with a sensitivity, specificity and cut off values of 88%,64% and ≤ 10 respectively in the total study population and 100%,88% and ≤11 respectively in group B. Also, both had good correlation with SVV that was better with group B (r=-0.778) than with total population (r=-0.454).

These results goes with Seung et al.,2018 who studied 226 patients aging 6 months to 14.4 years at PICU settings and found that patients with CVP > 12-mmHg had significantly greater mortality rates (50.0%, p = 0.002) than those with CVP <12mmHg (Seung et al., 2018).

Also, The European Society of Paediatric and Neonatal Intensive Care (ESPNIC) recommendations for hemodynamic monitoring for critically ill children strongly suggested the evaluation of CVP values and wave morphology as part of multi-modal hemodynamic monitoring not a solo-parameter to assess the intravascular volume and cardiac function with special focus on CVP trend in response to fluids and vasoactive therapy especially in refractory shock (Yogen et al.,2020).

Besides, 2 meta-analysis on adult patients showed the role of CVP in critical illness; Eskesen et al., 2016 meta-analysis included 1148 patient from 51 studies and showed that specific lower and higher CVP values had some positive and negative predictive value for fluid responsiveness, respectively, but none of the predictive values were above 66 % for any CVPs from 0 to 20 mmHg. There were less data on higher CVPs, in particular >15 mmHg, making the estimates on predictive values less precise for higher CVP, while Dong et al.,2017 included more than 9000 patients in his retrospective analysis and found that elevated central venous pressure level correlated with poor outcomes and prolonged treatment in critical care settings (Eskesen et al., 2016),(Dong et al.,2017).

Also, Biais et al., 2014 mentioned that the predictive value of extreme CVP readings (CVP < 6–8 mmHg and CVP > 12–15 mmHg) is satisfactory in his adult study (Biais et al., 2014).

On the other hand many pediatric studies found that CVP had no predictive value in children; Renner et al., 2012 conducted his study on 26 neonates and infants undergoing congenital heart surgery, Byon et al., 2013 had a study on 33 children below the age of 9 years undergoing neurosurgery, Sasidaran et al.,2012 had a total of 166 fluid boluses and CVP measurments Gan et al., 2013 had a systemic review that included 12 studies involving 501fluid boluses on children aging from 1 day to 17.8 years. All the data from the former studies came out suggesting the non-reliable role of CVP in pediatrics (Renner et al., 2012),(Byon et al., 2013),(Sasidaran et al.,2012),(Gan et al., 2013).

This variety in results regarding the role of CVP in prediction of fluid responsiveness in pediatrics may be attributed to the wide age spectrum of pediatric population in these different studies (from 1day to 17 years old patients).

Besides, the patients in the former studies were exposed to different settings while assessment of their CVPs; some patients were assessed during induction of anesthesia at different types of operations (open heart surgeries and neurosurgeries), others had septic shock and were assessed at PICU settings . Also, not all the patient were mechanically ventilated during their assessment.

These different circumstances may explain the contradictory results regarding CVP role in prediction of fluid responsiveness in pediatrics. But we recommend that CVP should be used together with other dynamic variables to guide fluid therapy in children at PICU especially in older children.

Refrences

Li DK, Wang XT, Liu DW. Association between elevated central venous pressure and outcomes in critically ill patients. Ann Intensive Care. 2017;7:83–89. doi: 10.1186/s13613-017-0306-1.

Cecconi M, Hofer C, Teboul JL, Pettila V, Wilkman E, Molnar Z, Della Rocca G, Aldecoa C, Artigas A, Jog S, Sander M, Spies C, Lefrant JY, De Backer D (2015) Fluid challenges in intensive care: the FENICE study: a global inception cohort study. Intensive Care Med 41:1529–1537

Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb S, Beale RJ, Vincent JL, Moreno R (2013) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 39:165–228.

Berlin DA, Bakker J. Starling curves and central venous pressure. Crit Care. 2015;19(1):1–8. doi: 10.1186/s13054-015-0776-1.

Vellinga NAR, Ince C, Boerma EC. Elevated central venous pressure is associated with impairment of microcirculatory blood flow in sepsis: a hypothesis

generating post hoc analysis. BMC Anesthesiol. 2013;13(1):1–7. doi: 10.1186/1471-2253-13-17.
Semler MW, Wheeler AP, Thompson BT, Bernard GR, Wiedemann HP, Rice TW. Impact of initial central venous pressure on outcomes of conservative versus liberal fluid management in acute respiratory distress syndrome. Crit Care Med. 2016;44(4):782–789.
Sondergaard S, Parkin G, Aneman A (2015) Central venous pressure: we need to bring clinical use into physiological context. Acta Anaesthesiol Scand 59:552–560
Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, Jaeschke R, Mebazaa A, Pinsky MR, Teboul JL, Vincent JL, Rhodes A (2014) Consensus on circulatory shock and hemodynamic monitoring. Task Force of the European Society of Intensive Care Medicine. Intensive Care Med 40:1795–1815
McIntyre LA, Hebert PC, Fergusson D, et al. A survey of Canadian intensivists' resuscitation practices in early septic shock. Crit Care 2007; 11: R74.
Kastrup M, Markewitz A, Spies C, et al. Current practice of hemodynamic monitoring and vasopressor and inotropic therapy in post-operative cardiac surgery patients in Germany: results from a postal survey. Acta Anaesthesiol Scand 2007; 51: 347–58.
Eskesen T. G., Wetterslev M., Perner A., Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Medicine volume 42, pages324–332 (2016).
Yogen Singh , Javier Urbano Villaescusa , Eduardo M da Cruz , Shane M Tibby , Gabriella Bottari , Rohit Saxena , Marga Guillén , Jesus Lopez Herce , Matteo Di Nardo , Corrado Cecchetti , Joe Brierley , Willem de Boode , Joris Lemson , Recommendations for hemodynamic monitoring for critically ill children-expert consensus statement issued by the cardiovascular dynamics section of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC), Crit Care,2020 Oct 22;24(1):620.
Sasidaran K, Jaishree M , Singhi S,Do we still accept central venous pressure measurements to assess preload responsiveness in children with septic shock? A single-center experience Critical Care volume 16, Article number: P87 (2012)
Hofer CK, Muller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. Chest. 2005;128:848–854. doi: 10.1378/chest.128.2.848.
Renner J, Broch O , Duetschke P , Scheewe J , Höcker J , Moseby M , O. Jung , Bein B,Prediction of fluid responsiveness in infants and neonates undergoing congenital heart surgery, British Journal of Anaesthesia Volume 108, Issue 1, January 2012, Pages 108-115
Byon HJ, Lim CW, Lee JH, et al. Prediction of fluid responsiveness in mechanically ventilated children undergoing neurosurgery. Br J Anaesth. 2013;110(4):586-91
Gan H, Cannesson M, Chandler JR, Ansermino JM. Predicting fluid responsiveness in children: a systematic review. Anesth Analg 2013;117:1380e92.
Biais M, Cottenceau V, Petit L, Masson F, Cochard JF, Sztark F. Impact of norepinephrine on the relationship between pleth variability index and pulse pressure variations in ICU adult patients. Critical Care. 2011;15:R168.
Seung Jun Choi, Eun-Ju Ha, Won Kyoung Jhang & Seong Jong Park, Elevated central venous pressure is associated with increased mortality in pediatric septic shock patients, BMC Pediatrics volume 18, Article number: 58 (2018)
Dong-kai Li, Xiao-ting Wang, and Da-wei Liu,Association between elevated central venous pressure and outcomes in critically ill patients, doi: 10.1186/s13613-017-0306-1Ann Intensive Care. 2017; 7: 83.