IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Correlation of Ultrasonographic Measurement of Inferior Vena Cava Collapsibility Index with Central Venous Pressure in Diagnosis and Management of Neonatal Shock

Yashwant Kumar Rao[1*], Sunisha Arora[1], Tanu Midha[2], NeerajRao[1]

1. Department of Pediatrics, G.S.V.M Medical College, Kanpur
2. Department of Preventive and Social Medicine, Government Medical College, Kannauj

ABSTRACT

Background: Neonatal intensive care unit (NICU)Conventionally, Central Venous Pressure (CVP) monitoring has been used by intensivists to measure intravascular volume. However, it is an invasive procedure resulting in many complications. Non-invasive ultrasonographic measurement of inferior vena cava collapsibility index (IVC-CI) is a promising alternative. Therefore, this study wasconducted to evaluate the correlation of central venous pressure with IVC-CIand establish the cut off valuesfor IVC-CI to diagnose and manage neonatal shock.

Methods: The current research was a prospective longitudinal study.All sick neonates requiring intensive hemodynamic monitoring were enrolled in the study and umbilical vein catheterization was performedto measure CVP. IVC diameters and IVC-CI were measured using ultrasound. Based on CVP, the patients were classified into three categories: hypovolemic (CVP<5 cmH_2O), euvolemic (CVP 5-8 cmH_2O), and hypervolemic (CVP>8 cmH_2O) and managed with intravenous fluid boluses and/or inotropes, accordingly. CVP and IVC-CI were again recorded after the intervention and compared with the previous values.

Results: A total of 76(62.3%) males and 46 (37.7%) females were included in the study with a mean age of 27.16±17.5 years. There was a strong negative correlation,which was statistically significant, between CVP and IVC-CI (r= -0.913, n=122, P<0.001). After fluid resuscitation in the hypovolemic group, CVP improved from 2.31±0.92 to 5.88±1.79 cmH_2O and IVC-CI changed from 62.39±6.005 to 33.02±2.64% which was statistically significant(P<0.001). After the administration of inotropes in the hypervolemic group, CVP dropped from 10.86±9.07 to 9.07±1.85cmH_2O and IVC-CI changed from 11.27±4.71 to 24.3±13.3% which was again statistically significant(P<0.001). The receiver operator characteristic (ROC) curve analysis indicated that the IVC-CI cut-off of 55% predicted CVP <5 cmH2O with 87.9% sensitivity, 82% specificity, 75.3%positive predictive value and 58.9% negative predictive value. IVC-CI cut-off of 20% predicted CVP >8 cmH2O with 91.1% sensitivity, 83.2% specificity, 71.8% positive predictive value and 50.6% negative predictive value.

Conclusion: The obtained results revealed an inverse correlation between CVP and IVC-CI, and it was concluded that IVC-CI can provide a useful guide in the diagnosis and management of shock in sick newborns.

Keywords: Central venous pressure(CVP), Management, Neonates, Shock, Ultrasound

Introduction

Shock is a "state of cellular energy failure resulting from an inability of tissue oxygen delivery to satisfy tissue oxygen demand" (1). This situation, if not corrected, will result in irreversible damage and ultimately death. There are three phases of shock (2): "Compensated Phase" where complex neuroendocrine and autonomic compensatory mechanisms maintain perfusion and oxygen delivery to the vital organs (heart, brain, and adrenals) at the expense of decreased perfusion to the remaining organs. If adequate treatment is not commenced, the infant

* *Corresponding author*: Yashwant Kumar Rao, Department of Pediatrics, G.S.V.M Medical College, Kanpur. Tel: 9919080807; Email: ykraoneo@yahoo.co.in

Please cite this paper as:
Kumar Rao Y, Arora S, Midha T, Rao N. Correlation of Ultrasonographic Measurement of Inferior Vena Cava Collapsibility Index with Central Venous Pressure in Diagnosis and Management of Neonatal Shock. Iranian Journal of Neonatology. 2020 Sep: 11(3). DOI: 10.22038/ijn.2020.44748.1743

will most likely develop hypotension due to the failure of compensatory mechanisms and shock enters its "Uncompensated Phase" where perfusion to all organs including vital organs becomes compromised. If treatment is ineffective in the uncompensated phase of shock, multiorgan failure develops and shock may enter its "Irreversible Phase", where permanent damage to the various organ systems occurs and further interventions will be ineffective in reversing the patient's condition (3). Neonatal shock may be due to lower vascular tone (distributive shock), inadequate blood volume (hypovolemic shock), decreased cardiac function (cardiogenic shock), restricted blood flow (obstructive shock), and inadequate oxygen delivery (dissociative shock). Shock remains an important cause of neonatal mortality and morbidity. Shock can lead to long term morbidity including severe neurological compromise. Therefore, recognizing shock promptly and initiating therapy to address the cause of shock and maintaining hemodynamic stability is essential. There exists no consensus on the gold standard in the diagnosis of circulatory compromise. Commonly used clinical signs, such as increased heart rate, slow skin capillary refill time, increased core-periphery temperature difference, and low blood pressure aid establishing the diagnosis; nonetheless, they have serious limitations. Traditionally, central venous pressure (CVP) has been extensively used as a guide to fluid management (4, 5). A survey carried out in Canada concluded that 90% of the intensivists use CVP to monitor fluid resuscitation in septic shock patients. High CVP is recognized to be associated with volume overload states, while low CVP is connected with volume-depleted states (5). nevertheless, measuring CVP in neonates requires umbilical venous cannulation which is an invasive procedure and is associated with various complications, such asbleeding, sepsis, portal venous thrombosis, and portal hypertension. With the advent of technology, the respiratory changes of the inferior vena cava (IVC) diameter measured by bedside ultrasound have demonstrated promising results as a guide to fluid therapy (6). IVC is a valveless highly compliant vessel. During inhalation, there is an increase in intra-abdominal pressure due to downward movement of the diaphragm causing the collapse of intra-abdominal IVC and vice-versa during exhalation.[7]

Therefore, the measurement of changes in IVC diameter can provide an indirect means of measuring CVP. However, there is a paucity of data on the correlation of CVP with inferior vena cava diameter and collapsibility index (IVC-CI) in newborns, especially in India. With this background in mind, the present study aimed to determine the correlation of IVC-CI with CVP in newborns and establish the cutoff values of IVC-CI as a guide in the diagnosis and management of shock.

Methods

Study design and Setting

This prospective longitudinal study was conducted in Sick Newborn Care Unit, Department of Pediatrics, Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, from December 2015 to July 2017. Written informed consent was obtained from parents/guardians. The study protocol was reviewed and approved by the Ethics Committee of GSVM Medical College, Kanpur.

Participants

A total of 122 critically ill consecutive newborns with clinical shock were selected for the study. Shock was defined as the presence of any two of the following criteria: peripheral cyanosis, tachycardia >160-180 beats/min, delayed capillary refill >2sec, mottling, and feeble peripheral pulse. Patients with omphalitis, necrotizing enterocolitis, peritonitis, and coagulation disorders were excluded from the study.

Sample size

The sample size was estimated using Medcalc statistical software (version 19.2.0). At 80% power, 95% level of significance, area under the curve 0.725, and null hypothesis 0.50, the minimum sample size was calculated as 57[8].Patients' characteristics and vital parameters were registered at baseline. Umbilical venous catheterization was performed under proper aseptic conditions using standardized graphs to estimate the length of catheter insertion,and anX-ray was performed to verify the position of the catheter. The rise of the blood column was noted in the catheter which represented the central venous pressure. IVC was examined from a subcostal view in a longitudinal section using an abdominal probe (2-6 MHz) in the ultrasound machine. The inspiratory (iIVC) and expiratory diameter (eIVC) of IVC were measured during a respiratory cycle, using M-mode, 2 cm caudal to the junction of the right atrium. Thereafter, IVC-CI was calculated using the formula: IVC-CI = (eIVC-iIVC)/eIVC * 100.

Based on the CVP values, the patients were

assigned to hypovolemic (CVP <5 cmH_2O), euvolemic (CVP 5-8 cmH_2O), and hypervolemic (CVP>8 cmH_2O) group. Fluid boluses were administered to hypovolemic patients, hypervolemic patients received inotropes to achieve hemodynamic stability under cardiopulmonary monitoring, and euvolemic patients received no intervention. CVP and IVC measurements were recorded again after carrying out appropriate intervention and compared with previous values.A receiver operator characteristic (ROC) curve was generated to determine the optimal cut-offs of IVC-CI for estimating low (<5 cmH2O) and high (>8 cmH2O) CVP.

Statistical Methods

Data was compiled using Microsoft Excel and analyzed in SPSS 21.0.0 (IBM Inc. Chicago, IL). A p-value less than 0.05was considered statistically significant. Quantitative variables were analyzed using mean and standard deviation. ANOVA was used to compare the three groups of patients with different intravascular status. Pearson correlation coefficient was applied to assess the significance of the relationship between CVP and IVC-CI. Paired t-tests were used to compare CVP and IVC-CI values before and after the intervention. A receiver operator characteristic (ROC) curve was generated to determine the optimal cut-offs of IVC-CI for estimating CVP. The sensitivity, specificity, positive predictive value and negative predictive value of IVC-CI were calculated to predict the CVP.

Results

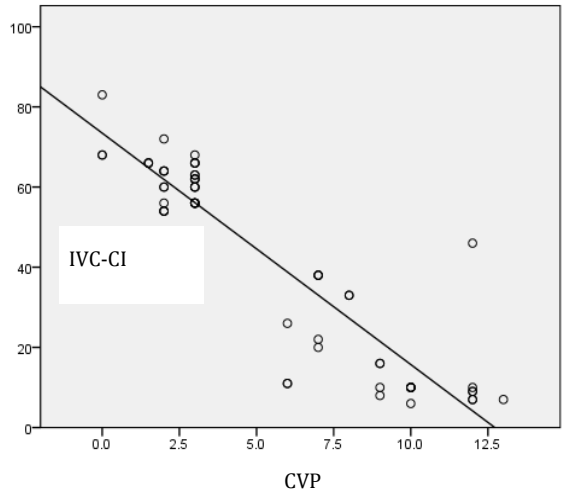
A total of 122 neonates were enrolled in the study with a mean age of 27.16±17.54 hours, mean gestational age 37.16±3.12 weeks, mean birth weight of 2460±790 grams. Among the study subjects,62.3% were male and 37.7% were female. Mean CVP was 5.284±3.87 cmH_2O and mean IVC-CI was found to be 42.36±24.16%. According to the CVP, the patients were stratified into three groups: 66 (54.1%) patients were hypovolemic (CVP <5 cmH_2O), 22 (18%) patients were euvolemic (CVP 5-8 cmH_2O), and 34 (27.9%) patients were hypervolemic (CVP >8 cmH_2O)

Table 1. Demographic characteristics of the study subjects

Age (hours) (mean±SD)	27.16±17.54
Gestational Age (weeks) (mean±SD)	37.16±3.12
Birth weight (grams) (mean±SD)	2460±790
Male	76 (62.3%)
Female	46 (37.7%)
Hypovolemic	66 (54.1%)
Euvolemic	22 (18%)
Hypervolemic	34 (27.9%)

(Table1). Pearson correlation coefficient was used to determine the relationship between CVP values and IVC-CI. As illustrated in Figure 1, a strong negative linear correlation was observed between CVP and IVC-CI (r= -0.913, n=122, P<0.001) which was statistically significant.

After receiving intravenous fluid boluses, mean CVP in the hypovolemic group increased from 2.318±0.92 to 5.88±1.79 cmH_2O and IVC-CI decreased from 62.39±6.005 to 33.02±12.64%, both of which were statistically significant (P<0.001). On the other hand, after the administration of inotropes, mean CVP in hypervolemic group, decreased from 10.867±1.3 to 9.07±1.85 cmH_2O and IVC-CI improved from 11.27±9.71 to 24.30±13.301%, both of which were statistically significant (P<0.001) as depicted in Table 2.



r= -0.913, n=122, p<0.001

Figure 1. Strong negative correlation between CVP and IVC-CI

Table 2. Comparison of Central Venous Pressure and IVC-CI before and after the intervention

		Before intervention	After intervention	P-value
Hypovolemic	CVP	2.318±0.92	5.88±1.79	<0.001
	IVC-CI	62.39±6.00	33.02±12.64	<0.001
Hypervolemic	CVP	10.867±1.3	9.07±1.85	<0.001
	IVC-CI	11.27±4.71	24.30±13.30	<0.001

CVP: Central Venous Pressure,IVC-CI: Inferior vena cava collapsibility index

Table 3. Sensitivity and specificity of IVC-CI in predicting hypovolemia (CVP<5 cmH_2O)

IVC-CI (%)	Sensitivity(%)	Specificity(%)
45	90.1	66.4
55	87.9	82.0
65	47.3	84.3

IVC-CI:Inferior vena cava collapsibility index

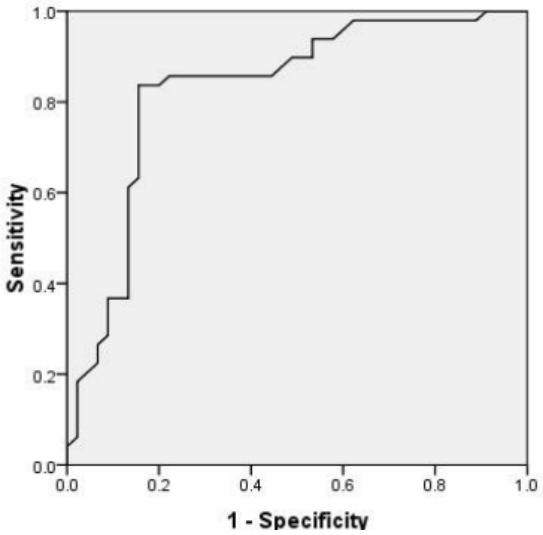


Figure 2. Receiver operating characteristic (ROC) curve analysis of IVC-CI in predicting hypovolemia
Area under curve 0.810. Optimal threshold value of IVC-CI for predicting hypovolemia (CVP<5 cmH_2O) is 55% with 87.9% sensitivity and 82% specificity.

In the hypovolemic group, the IVC-CI cut-off of 55% best predicted CVP <5 cmH2O with the sensitivity of 87.9%, specificity of 82%, positive predictive value of 75.3%, negative predictive value of 58.9% and area under the ROC curve= 0.810 (Table 3; Figure 2). In the hypervolemic group, IVC-CI cut-off of 20% best predicted CVP >8 cmH2O with a sensitivity of 91.1%, specificity of 83.2%,positive predictive value 71.8%, negative predictive value 50.6% and area under the ROC curve= 0.876 (Table 4; Figure 3).

Table 5. Relation of CVP and IVC-CI with volume status

Volume Status	CVP (cmH_2O)	IVC-CI (%)
Hypovolemia	<5	>55
Euvolemia	5-8	20-55
Hypervolemia	>8	<20

Discussion

The present study revealed a strong negative linear correlation between CVP and IVC-CI. IVC-CI cut-off of 55% corroborates with CVP <5 cmH_2O with a sensitivity of 87.9%, specificity of 82%, and area under the ROC curveof 0.810. IVC-CI cut-off of 20% predicted CVP >8 cmH_2O with a sensitivity of 91.1%, specificity of 83.2%, and area under the

Table 4. Sensitivity and specificity of IVC-CI in predicting hypervolemia (CVP>8 cmH_2O)

IVC-CI (%)	Sensitivity(%)	Specificity(%)
10	93.4	62.0
20	91.1	83.2
30	65.1	86.3

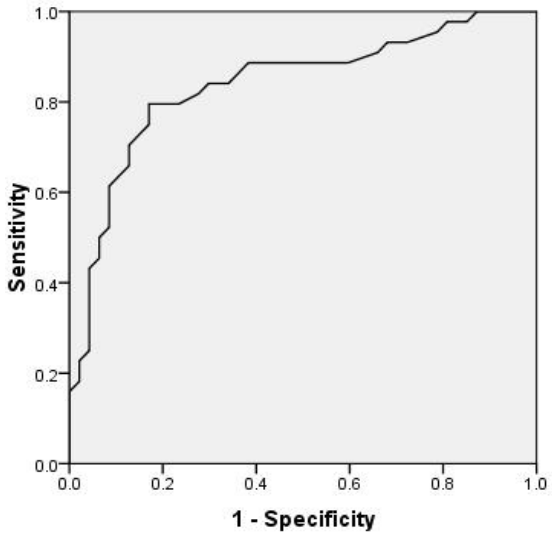


Figure 3. Receiver operating characteristic (ROC) curve analysis of IVC-CI in predicting hypervolemia
The area under the curve is 0.876. The optimal threshold value of IVC-CI for predicting hypervolemia (CVP>8cmH_2O) is 20% with 91.1% sensitivity and 83.2% specificity.

ROC curve of 0.876. These findings among Indian neonates are similar to the observations made among adults in various studies.

Several studies have demonstrated a relatively good correlation between CVP and IVC diameter and/or IVC-CI. In his study, Ilyas et al.found a positive relationship between CVP and minimum/ maximum IVC diameters but an inverse relationship with IVC-CI in a sample of 100 patients with a mean age of 50.4±19.3 years (5). Thanakitcharu et al. studied a group of 70 critically ill patients with a mean age of 63.8±1.9 years and observed a significant correlation between CVP and IVC-CI, CVP and iIVC-CI, and CVP and mean IVC diameter (9). Nagdev et alreported that a 50% collapse of the IVC diameter during a respiratory cycle was strongly associated with a low CVP (10). Iwamoto et al also demonstrated that an IVC-CI of 0.22 predicted elevated CVP in spontaneously breathing pediatric cardiac patients with a sensitivity of 1.0 and specificity of 0.98 (11). Garget alinvestigated 36 patients with septic shock requiring ventilatory support and concluded that CVP and IVC-CI are negatively

correlated (r= -0.626) and both methods can be used for resuscitation and IVC-CI is not inferior to CVP (12). Astudyconducted by Sato et al. on 57 neonates suggested that the ratio of minimum and maximum diameter of IVC strongly correlated with CVP in mechanically ventilated neonates (13).

Nevertheless, there exists little or no information about the usability of IVC parameters for the estimation of CVP in neonates. In the present study, the largest proportion of patients were in hypovolemic states (54.1%) and only a small number of patients (27.9%) were in hypervolemic state. The results of the present study revealed a significant correlation between CVP and IVC-CI. Moreover, the current study also provided important information regarding the behavior of IVC-CI during intravenous fluid boluses or vasopressor administration, especially in the context of simultaneous CVP measurement. Furthermore, it was found that cut-off points of IVC-CI were 55% and 20% at CVP levels of <5 cmH_2O and >8 cmH_2O, respectively.

The determination of body fluid status in critically ill neonates is of utmost importance both for diagnosis and management. CVP should be monitored in cases of shock, circulatory failure, massive infusion or transfusion requirement, as well as in situations where careful fluid resuscitation is a must, such as patients with cardiac problems and acute kidney injury. In normal people, changes in CVP are correlated with changes in left ventricular filling pressure.For this measurement, an invasive procedure is required which is associated with many complications. Therefore, the use of a non-invasive method for hemodynamic monitoring is warranted. It is recognized that IVC diameter exhibits a variation with the respiratory cycle. Initially, studies focused on the comparison of CVP with IVC diameters, and the findings found a positive correlation between mean IVC diameter and CVP. Further studies have compared CVP with ultrasonographic assessment of IVC respirophasicityrather than IVC diameters alone. The knowledge of the changes in IVC diameter and IVC-CI will help in guiding adjustment in fluid and vasopressor therapy in critically-ill neonates.

The results of the present study are similar to the findings of previous studies that revealed aninverse relationship between IVC-CI and CVP. Moreover, measurement of CVP is an invasive procedure and results in several complications, while IVC-CI has the advantageof being a non-invasive procedure. Therefore, IVC-CI can be considered as a very useful and safe procedure for the management of neonatal shock.

Conclusion

The present study shows that ultrasonographic measurement of IVC-CI strongly correlates with CVP and can be used as a tool for guidance of fluid and vasopressor therapy in the management of neonatal shock. Since IVC-CI is a non-invasive method, it has a considerable advantage over CVP in the management of neonatal shock as there is a lesser possibility of complications. Therefore, the present study substantiates that IVC-CI is an effective alternative to CVP in the management of neonatal shock.

Acknowledgments

??

Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of the current article.

Funding source

No funding was secured for this study.

Financial Disclosure

Authors have no financial relationships relevant to this article to disclose.

References

1. Gleason CA, Devaskar SU. Avery's diseases of the newborn. 9th ed. Philadelphia: Elsevier; 2012.
2. Kliegman RM, Behrman RE, Jenson HB, Stanton BM. Nelson textbook of pediatrics e-book. New York: Elsevier Health Sciences; 2016.
3. Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care. Philadelphia: Lippincott Williams & Wilkins; 2012.
4. McIntyre LA, Hebert PC, Fergusson D, Cook DJ, Aziz A. A survey of Canadian intensivists' resuscitation practices in early septic shock. Crit Care. 2007; 11(4): R74
5. Ilyas A, Ishtiaq W, Assad S, Ghazanfar H, Mansoor S, Haris M,et al. Correlation of IVC diameter and collapsibility index with central venous pressure in the assessment of intravascular volume in critically Ill patients. Cureus.2017; 9(2):e1025.
6. Muqloo M M, Malik S, Rubeena A Echocardiographic Inferior Vena Cava Measurement As An Alternative to Central Venous Pressure Measurement in Neonates. Indian J Pediatr. 2017 Oct;84(10):751-756
7. Babaie S, Behzad A, Mohammadpour M, Reisi M. A Comparison between the Bedside Sonographic Measurements of the Inferior Vena Cava Indices and

the Central Venous Pressure While Assessing the Decreased Intravascular Volume in Children. AdvBiomed Res 2018;7:97
8. Lwanga SK, Lemeshow S, World Health Organization. Sample size determination in health studies: a practical manual. Geneva: World Health Organization; 1991
9. Thanakitcharu P, Charoenwut M, Siriwiwatanakul N. Inferior vena cava diameter and collapsibility index: a practical non-invasive evaluation of intravascular fluid volume in critically-ill patients.J Med Assoc Thai.2013;96(Suppl 3):S14-22.
10. Nagdev AD, Merchant RC, Tirado-Gonzalez A, Sisson CA, Murphy MC. Emergency department bedside ultrasonographic measurement of the caval index for noninvasive determination of low central venous pressure.Ann Emerg Med.2010;55(3):290-5.
11. Iwamoto Y, Tamai A, Kohno K, Masutani S, Okada N, Senzaki H. Usefulness of respiratory variation of inferior vena cava diameter for estimation of elevated central venous pressure in children with cardiovascular disease.Circ J.2011;75(5):1209-14.
12. Garg M, Sen J, Goyal S, Chaudhry D. Comparative evaluation of central venous pressure and sonographic inferior vena cava variability in assessing fluid responsiveness in septic shock. Indian J Crit Care Med. 2016;20(12):708-13
13. Sato Y, Kawataki M, Hirakawa A, Toyoshima K, Kato T, Itani Y, et al.The diameter of theinferior vena cava provides a noninvasive way of calculating central venous pressure in neonates. Acta Paediatr. 2013;102(6):e241-6.