Global end-diastolic volume an emerging preload marker vis-a-vis other markers - Have we reached our goal?

Kapoor P. M, Vandana Bhardwaj, Amita Sharma, Usha Kiran
Department of Cardiac Anaesthesia, CTC, AIIMS, New Delhi, India

ABSTRACT

A reliable estimation of cardiac preload is helpful in the management of severe circulatory dysfunction. The estimation of cardiac preload has evolved from nuclear angiography, pulmonary artery catheterization to echocardiography, and transpulmonary thermodilution (TPTD). Global end-diastolic volume (GEDV) is the combined end-diastolic volumes of all the four cardiac chambers. GEDV has been demonstrated to be a reliable preload marker in comparison with traditionally used pulmonary artery catheter-derived pressure preload parameters. Recently, a new TPTD system called EV1000™ has been developed and introduced into the expanding field of advanced hemodynamic monitoring. GEDV has emerged as a better preload marker than its previous conventional counterparts. The advantage of it being measured by minimum invasive methods such as PiCCO™ and newly developed EV1000™ system makes it a promising bedside advanced hemodynamic parameter.

Received: 05-08-16
Accepted: 09-08-16

Key words: EV1000; Global end-diastolic volume; Hemodynamic; PiCCO; Transpulmonary thermodilution

INTRODUCTION

Hemodynamic monitoring is paramount importance for the early identification and management of critical changes in hemodynamic parameters to optimize tissue oxygen delivery.[1] A reliable estimation of cardiac preload is helpful in the management of severe circulatory dysfunction. The assessment of central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), pulmonary capillary wedge pressure (PCWP), and end-diastolic volume (EDV) indices as preload markers has been the mainstream of advanced hemodynamic monitoring for years.[2] The estimation of cardiac preload has evolved from nuclear angiography, pulmonary artery catheterization to echocardiography, and transpulmonary thermodilution (TPTD).[3-17]

TPTD has emerged as a less invasive bedside method to obtain accurate cardiovascular parameters. In addition to cardiac output (CO) measurements, TPTD also provides advance volumetric parameters such as global EDV (GEDV) and extravascular lung water (EVLW).[15-17]

STATIC VERSUS DYNAMIC PARAMETERS

The stroke volume increases with fluid loading till both ventricles are on steep portion of Frank–Starling's Curve. Once the ventricles reach the flat portion of curve, fluid infusion has little effect on CO. Therefore, it is important not only to measure the patient's preload

Access this article online
Website: www.annals.in
DOI: 10.4103/0971-9784.191554
Quick Response Code:

Address for correspondence: Dr. Kapoor P. M, Cardiac Anaesthesia, CTC, AIIMS, New Delhi - 110029, India. E-mail - drpoonamaiims@gmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Cite this article as: Kapoor PM, Bhardwaj V, Sharma A, Kiran U. Global end-diastolic volume an emerging preload marker vis-a-vis other markers - Have we reached our goal?. Ann Card Anaesth 2016;19:699-704.

but also to assess whether the patient will respond to fluid therapy or not. Most of the conventionally used parameters (CVP and PAOP) fail to predict fluid responsiveness of the patient. However, in patients undergoing positive-pressure mechanical ventilation, heart–lung interactions can be used to reliably determine response to fluid infusions using dynamic parameters.[18,19] These parameters can be determined using continuous beat-to-beat CO monitoring devices and echocardiography [Table 1].

CONVENTIONAL PRELOAD MARKERS AND TECHNIQUES

Pulmonary artery catheterization

The introduction of pulmonary artery catheter (PAC) in the 1970s revolutionized the field of hemodynamic monitoring. However, the therapeutic usage of PAC has been questioned based on the studies which failed to demonstrate its beneficial effect.[3] In 1996, Connors *et al*. demonstrated that right heart catheterization may increase mortality in critically ill patients in intensive care.[4] Despite these controversies, PAC-derived parameters such as CVP and PAOP has been used as a pressure estimate of ventricular preload. Nonetheless, these parameters have also been questioned as they failed to correlate with EDV in critically ill and postcardiac surgery patients.[5,6]

As per Frank–Starling Law, the preload is determined by end-diastolic left ventricular fiber length. Hence, instead of these widely used cardiac filling pressures (CVP and PAOP), EDV indices of the left ventricle are better indicators of preload.

Kumar *et al*. demonstrated that neither CVP nor PAOP correlated with EDV index and stroke volume index. Hence, it cannot be used as a predictor of ventricular preload with respect to optimizing cardiac performance.[7]

Pulmonary artery thermodilution

Pulmonary artery thermodilution technique can be used to derive right ventricular EDV index (RVEDVI). In various studies, RVEDVI has shown a better correlation with cardiac performance than cardiac filling pressures.[8-10] A modified version of conventional pulmonary artery thermodilution catheters allows the continuous determination of RVEDVI in form of continuous EDV index (CEDVI).

Wiesenack *et al*. observed that an increased cardiac preload is more reliably reflected by CEDVI than by CVP, PCWP, or left ventricular end-diastolic area (LVEDA) index in cardiac surgery. However, CEDV index failed to be a variable of fluid responsiveness.[11]

Table 1: The dynamic parameters of fluid responsiveness

Dynamic parameter	Description	Method	Remarks
SVV: Change in stroke volume during the respiratory cycle	SVV (%)=$(SV_{max}-SV_{min})/SV_{mean}$	PiCCO, LiDCO, Vigileo	Measured by pulse contour analysis An SVV threshold of 12%, indicates fluid responsiveness
PPV: Changes in peripheral pulse pressure during respiratory cycle	PPV (%)=$(PP_{max}-PP_{min})/PP_{mean}$	LiDCO, Vigileo	Correlates equally well as SVV for volume responsiveness A PPV threshold of 13% differentiates between responders and nonresponders to fluid administration
SPV: Difference between the maximal and minimal values of systolic blood pressure (SBP) over a single respiratory cycle. sum of Δup and Δdown	$\frac{SBP_{max} - SBP_{min}}{SBP_{Mean}}$	LiDCO, Vigileo	Less specific indicator of LV stroke volume and less useful in predicting fluid responsiveness
Aortic blood velocity (ΔV_{peak}): Difference between the maximal and minimal peak velocity of aortic blood flow over a single respiratory cycle divided by the mean of the two values	Expressed in percentage	Doppler echocardiography	Threshold value of 12% discriminates responders and nonresponders
IVC distensibility index: Variation of IVC diameter with respiration (dilates with inspiration)	Maximum diameter at inflation-minimum diameter at expiration/maximum diameter	Transthoracic or transesophageal echocardiography	IVC distensibility index above 18% predicts fluid responsiveness. Major limitation is intra-abdominal pressure
Plethysmographic variability index	Respiratory cycle induced variation in plethysmograph waveform	Modified pulse oximeter (radical 7)	A threshold of 19% suggests fluid responsiveness

SVV: Stroke volume variation, PPV: Pulse pressure variation, SPV: Systolic pressure variation, IVC: Inferior vena cava

Imaging techniques

Radionuclide ventriculography, cardiovascular computed tomography, and magnetic resonance imaging have been used in the past to assess cardiac dimensions; however, these procedures are laborious, noncontinuous, and nonpractical in various clinical settings. Bellenger *et al*. compared the agreement of left ventricular volumes and ejection fraction (EF) by M-mode echocardiography (echo), two-dimensional echo, radionuclide ventriculography, and cardiovascular magnetic resonance in patients with chronic stable heart failure. They found that cardiovascular magnetic resonance imaging is the preferred technique for volume and EF estimation in heart failure patients because of its three-dimensional approach for nonsymmetric ventricles and superior image quality.[12]

Echocardiography

Echocardiography can be done to assess EDV and area as a marker of preload. Cheung *et al*. demonstrated that transesophageal echocardiography was sensitive to detect even 5% of the blood volume change by measurement of LVEDA.[13]

In addition, echocardiographic-derived E/e' has emerged as a surrogate of left ventricular diastolic pressure (LVDP). In a study done by Ommen *et al*., E/e' ratio was found to be the best tissue Doppler imaging parameter to correlate with mean LVDP ($r = 0.64$). The author observed that this correlation was better in patients with EF $<50\%$ ($r = 0.64$) than those with EF $>50\%$ ($r = 0.47$).[14]

However, expertise in performing echocardiography is not widely available among intensive care staff. One of the major drawbacks of echocardiography is that it gives only a snapshot of ventricular functions at a single point of time. It lags behind in continuous monitoring of hemodynamic parameters.

Transpulmonary thermodilution

TPTD is an evolving technique in the field of hemodynamic monitoring which does not require invasive PAC. In addition to intrathoracic blood volume (ITBV), it can also yield pulmonary blood volume and EVLW as a predictor of pulmonary edema.[15-17]

Technique of transpulmonary thermodilution measurements

The technique of thermal dye dilution (indocyanine green [ICG]) to assess ITBV was introduced by a German Company (Pulsion Medical Systems, Munich, Germany). In this method, a cold indicator (ICG dye) is injected into the central vein, and after transpulmonary passage, it is detected by a special thermistor-tipped femoral arterial catheter for computation of TPTD curve.[15] This double-indicator TPTD technique has evolved into a single thermal indicator TPTD technique which has been found to be as accurate as the former.[16] The TPTD technique has been used to derive various hemodynamic parameters such as ITBV, GEDV, a volumetric marker of cardiac preload, and EVLW, a marker of pulmonary edema [Figure 1].[15-17]

Global end-diastolic volume

GEDV is a hypothetical volume that assumes the situation that the four heart chambers are simultaneously in the diastolic phase [Figure 2]. GEDV is the combined EDVs of all the four cardiac chambers. In addition, it also includes volume of central vein and aorta from point of injection of injectate to site of measurement. It is calculated as the difference between the intrathoracic thermal volume (ITTV) and pulmonary thermal volume (PTV).[20-22] It has been found to be a reliable indicator of cardiac preload in critically ill patients.[21]

Mathematical analysis of transpulmonary thermodilution hemodynamic parameters

There are two different systems to assess TPTD hemodynamic parameters. The well-known PiCCO™ system (Pulsion Medical Systems, Munich, Germany) is based on the mathematical analysis described in the 1950s.[20-22] However, recently, a new TPTD system called EV1000™ has been developed and introduced into the expanding field of advanced hemodynamic monitoring.[23,24] It consists of a specific thermistor-tipped arterial catheter, the VolumeView™ catheter, and EV 1000™ monitoring system (Edwards Lifesciences, Irvine, CA, USA). It uses a unique

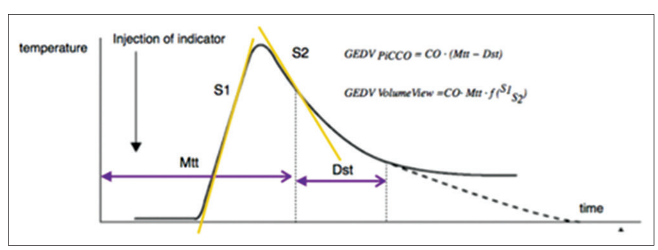

Figure 1: Transpulmonary thermodilution curve analysis. Global end-diastolic volume derived from PiCCO system depends on mean transit time, the time required for half of indicator to pass thermistor in femoral artery catheter and downslope time, time of the temperature decay between two set points of dilution curve. In contrast, global end-diastolic volume from volume view system depends on maximum upslope (S1) and maximum downslope (S2) of dilution curve. GEDV: Global end-diastolic volume, Mtt: Mean transit time, Dst: Downslope time

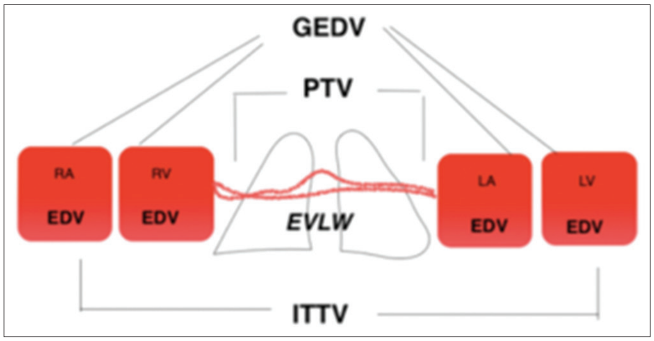

Figure 2: Diagrammatic representation of global end-diastolic volume, pulmonary thermal volume, intrathoracic thermal volume, extravascular lung water, and end-diastolic volume of four cardiac chambers. RA: Right atrium, RV: Right ventricle, LA: Left atrium, LV: Left ventricle, ITTV: Intrathoracic thermal volume, PTV: Pulmonary thermal volume, EVLW: Extravascular lung water, GEDV: Global end-diastolic volume, EDV: End-diastolic volume

algorithm for the mathematical analysis of the thermodilution curve [Figure 1].

The analysis implemented in the PiCCO™ System is based on CO, mean transit time (Mtt), and downslope time (Dst) of TPTD curve [Figure 1]:[20-22]

ITTV = CO. Mtt

PTV = CO. Dst

GEDV = ITTV − PTV

GEDV PiCCO = CO (Mtt − Dst).

In comparison, the EV1000™ system uses a novo algorithm, which is based on maximum up-slope (S_1) and down-slope (S_2) of the TPTD curve [Figure 1]:[23,24]

GEDV EV1000 = CO Mtt f (S_1/S_2)

The algorithm for analysis of EVLW is same for both systems; however, it is based on GEDV which is derived differently by the two systems.

EVLW = CO. Dst (GEDV. 0.25)

Nicholas Kiefer *et al*. compared the volume View EV1000™ measurements to those by PiCCO2™ in 72 critically ill patients. They found that in a mixed Intensive Care Unit (ICU) population, and in a wide range of clinical situations, CO, GEDV, and EVLW values assessed with the new VolumeView™/EV1000 system are interchangeable with the current PiCCO™ method. However, for GEDV, the VolumeView Method has a higher precision.[24]

GEDV and ITBV has been demonstrated to be a reliable preload marker in comparison with traditionally used PAC-derived pressure preload parameters such as CVP and PAOP.[25,26] Godje *et al*. compared these conventional preload markers (CVP and PCWP) with ITBV and GEDV in patients undergoing CABG. The authors demonstrated that changes of CVP, PCWP, and RVEDVI do not correlate with changes of cardiac index and stroke volume index (coefficients ranged from −0.01 to 0.28). In contrast, intrathoracic and GEDV indices with coefficients from 0.76 to 0.87 show a good correlation to cardiac function indices.[25] GEDV has found to be as equivalent reflector of preload as echocardiographic-derived preload indices.[27,28] Hofer *et al*. observed that GEDV index (GEDVI) assessed by the PiCCO system gives a better reflection of echocardiographic changes in left ventricular preload, in response to fluid replacement therapy, than CEDVI measured by a modified PAC.[27]

To compare individual patients, GEDV and EVLW are indexed to body surface area, yielding GEDVI and EVLW index. The numerical values of GEDVI and echocardiographic volume indices show only a moderate correlation.[27,28] The latter can be explained in part by different techniques used for echocardiographic volume calculation.[29] GEDVI has been found to be a helpful parameter in monitoring fluid responsiveness and nonresponsiveness.[30,31]

The reference range for GEDVI as proposed by expert opinion is 680–800 ml/m^2. Wolf *et al*. found that GEDV and ITBV depend on age and gender. The age and sex dependence of GEDV and ITBV was persistent after indexing to body surface area. Therefore, targeting resuscitation by fixed ranges of GEDVI or ITBVI without concern for age and gender is not appropriate.[32] GEDVI has been successfully used in goal-directed therapy. Goepfert *et al*. demonstrated that guiding therapy by an algorithm based on GEDVI leads to a shortened and reduced need for vasopressors, catecholamines, mechanical ventilation, and ICU stay in cardiac surgery patients.[33]

CONCLUSION

GEDV has emerged as a better preload marker than its previous conventional counterparts. The advantage of it being measured by minimum invasive methods such as PiCCO™ and newly developed EV1000™ system makes it a promising bedside advanced hemodynamic parameter. The effective use of GEDV in goal-directed therapy can ease the management of circulatory dysfunction and guide the appropriate use of inotropes and vasopressors.

However, further studies regarding utility of GEDV as preload markers in major cardiac surgeries such as valve repair, CABG, aortic dissections, congenital heart diseases, and noncardiac surgeries are required. Finally, the novel method of GEDV analysis (EV1000™) should further be validated in perioperative field, and research on development of completely noninvasive techniques for preload assessment should be encouraged.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Girbes AR, Groeneveld AB. Circulatory optimization of the patient with or at risk for shock. Clin Intensive Care 2000;11:77-88.
2. Lichtwarck-Aschoff M, Beale R, Pfeiffer UJ. Central venous pressure, pulmonary artery occlusion pressure, intrathoracic blood volume, and right ventricular end-diastolic volume as indicators of cardiac preload. J Crit Care 1996;11:180-8.
3. Sandham JD, Hull RD, Brant RF, Knox L, Pineo GF, Doig CJ, *et al*. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med 2003;348:5-14.
4. Connors AF Jr, Speroff T, Dawson NV, Thomas C, Harrell FE Jr, Wagner D, *et al*. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA 1996;276:889-97.
5. Calvin JE, Driedger AA, Sibbald WJ. Does the pulmonary capillary wedge pressure predict left ventricular preload in critically ill patients? Crit Care Med 1981;9:437-43.
6. Hansen RM, Viquerat CE, Matthay MA, Wiener-Kronish JP, DeMarco T, Bahtia S, *et al*. Poor correlation between pulmonary arterial wedge pressure and left ventricular end-diastolic volume after coronary artery bypass graft surgery. Anesthesiology 1986;64:764-70.
7. Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, *et al*. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit Care Med 2004;32:691-9.
8. Chang MC, Blinman TA, Rutherford EJ, Nelson LD, Morris JA Jr. Preload assessment in trauma patients during large-volume shock resuscitation. Arch Surg 1996;131:728-31.
9. Cheatham ML, Block EF, Nelson LD, Safcsak K. Superior predictor of the hemodynamic response to fluid challenge in critically ill patients. Chest 1998;114:1226-7.
10. Diebel LN, Wilson RF, Tagett MG, Kline RA. End-diastolic volume. A better indicator of preload in the critically ill. Arch Surg 1992;127:817-21.
11. Wiesenack C, Fiegl C, Keyser A, Laule S, Prasser C, Keyl C. Continuously assessed right ventricular end-diastolic volume as a marker of cardiac preload and fluid responsiveness in mechanically ventilated cardiac surgical patients. Crit Care 2005;9:R226-33.
12. Bellenger NG, Burgess MI, Ray SG, Lahiri A, Coats AJ, Cleland JG, *et al*. Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance; are they interchangeable? Eur Heart J 2000;21:1387-96.
13. Cheung AT, Savino JS, Weiss SJ, Aukburg SJ, Berlin JA. Echocardiographic and hemodynamic indexes of left ventricular preload in patients with normal and abnormal ventricular function. Anesthesiology 1994;81:376-87.
14. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, *et al*. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. Circulation 2000;102:1788-94.
15. Godje O, Peyerl M, Seebauer T, Dewald O, Reichart B. Reproducibility of double indicator dilution measurements of intrathoracic blood volume compartments, extravascular lung water, and liver function. Chest 1998;113:1070-7.
16. Costa MG, Pompei L, Rocca GD. Transpulmonary thermodilution technique for cardiac output measurements: Single versus double indicator. Crit Care 2003;7 Suppl 2:192.
17. Sakka SG, Rühl CC, Pfeiffer UJ, Beale R, McLuckie A, Reinhart K, *et al*. Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. Intensive Care Med 2000;26:180-7.
18. Cherpanath TG, Geerts BF, Lagrand WK, Schultz MJ, Groeneveld AB. Basic concepts of fluid responsiveness. Neth Heart J 2013;21:530-6.
19. Mackenzie DC, Noble VK. Assessing volume status and fluid responsiveness in the emergency department. Clin Exp Emerg Med 2014;1:67-77.
20. Reuter DA, Huang C, Edrich T, Shernan SK, Eltzschig HK. Cardiac output monitoring using indicator-dilution techniques: Basics, limits, and perspectives. Anesth Analg 2010;110:799-811.
21. Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL. Global end-diastolic volume as an indicator of cardiac preload in patients with septic shock. Chest 2003;124:1900-8.
22. Newman EV, Merrell M, Genecin A, Monge C, Milnor WR, McKeever WP. The dye dilution method for describing the central circulation. An analysis of factors shaping the time-concentration curves. Circulation 1951;4:735-46.
23. Bendjelid K, Giraud R, Siegenthaler N, Michard F. Validation of a new transpulmonary thermodilution system to assess global end-diastolic volume and extravascular lung water. Crit Care 2010;14:R209.
24. Kiefer N, Hofer CK, Marx G, Geisen M, Giraud R, Siegenthaler N, *et al*. Clinical validation of a new thermodilution system for the assessment of cardiac output and volumetric parameters. Crit Care 2012;16:R98.
25. Godje O, Peyerl M, Seebauer T, Lamm P, Mair H, Reichart B. Central venous pressure, pulmonary capillary wedge pressure and intrathoracic blood volumes as preload indicators in cardiac surgery patients. Eur J Cardiothorac Surg 1998;13:533-40.

26. Wiesenack C, Prasser C, Keyl C, Rödīg G. Assessment of intrathoracic blood volume as an indicator of cardiac preload: Single transpulmonary thermodilution technique versus assessment of pressure preload parameters derived from a pulmonary artery catheter. J Cardiothorac Vasc Anesth 2001;15:584-8.
27. Hofer CK, Furrer L, Matter-Ensner S, Maloigne M, Klaghofer R, Genoni M, *et al*. Volumetric preload measurement by thermodilution: A comparison with transoesophageal echocardiography. Br J Anaesth 2005;94:748-55.
28. Hofer CK, Ganter MT, Matter-Ensner S, Furrer L, Klaghofer R, Genoni M, *et al.* Volumetric assessment of left heart preload by thermodilution: Comparing the PiCCO-VoLEF system with transoesophageal echocardiography. Anaesthesia 2006;61:316-21.
29. Hofer CK, Ganter MT, Rist A, Klaghofer R, Matter-Ensner S, Zollinger A. The accuracy of preload assessment by different transesophageal echocardiographic techniques in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth 2008;22:236-42.
30. Reuter DA, Goepfert MS, Goresch T, Schmoeckel M, Kilger E, Goetz AE. Assessing fluid responsiveness during open chest conditions. Br J Anaesth 2005;94:318-23.
31. Trof RJ, Danad I, Groeneveld AJ. Global end-diastolic volume increases to maintain fluid responsiveness in sepsis-induced systolic dysfunction. BMC Anesthesiol 2013;13:12.
32. Wolf S, Riess A, Landscheidt JF, Lumenta CB, Friederich P, Schürer L. Global end-diastolic volume acquired by transpulmonary thermodilution depends on age and gender in awake and spontaneously breathing patients. Crit Care 2009;13:R202.
33. Goepfert MS, Reuter DA, Akyol D, Lamm P, Kilger E, Goetz AE. Goal-directed fluid management reduces vasopressor and catecholamine use in cardiac surgery patients. Intensive Care Med 2007;33:96-103.