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Article

Influence of Hypovolemia on Cardiac Function Measured by Transpulmonary Thermodilution. A Retrospective Cohort Study

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Abstract: Background and Objectives: Transpulmonary thermodilution has gained interest in recent years. It measures cardiac output (CO), stroke volume (SV), but also calculates global end diastolic indexed volume (GEDVI), and global ejection fraction (GEF). GEDVI is a static variable of cardiac preload. GEF provides information regarding cardiac function. GEF algorithm depends on SV and GEDVI. Therefore, in hypovolemic patients with decreased preload, SV or GEDVI could be decreased, and lead to altered GEF. The aim of our work was to evaluate whether impairment in GEDVI and SV may constitute a limitation for the interpretation of GEF in hypovolemic patients. A secondary objective was to determine factors independently associated with impaired GEF. **Materials and Methods:** A retrospective study was conducted. Statistical analysis was performed by means of Mann Whitney and student *t* test. To determine correlation between GEF with SV, or GEF with GEDVI Pearson's coefficient was used. To determine factors independently associated with the presence of *impaired GEF*, binary logistic regression was performed. **Results:** We included 113 patients with shock. Differences in mortality were detected in GEF (21[16–28] survivors versus 18 in non survivors[11–26]; *p*= 0.01). 38(34%) patients had hypovolemia. 44(39%) of them had depressed GEF values. Hypovolemic patients had lower GEF values than non-hypovolemic patients (16 [12–22] vs 20 [15–27]; *p*=0.01). Both SV and GEDVI had a statistically significant correlation with GEF (SV (Pearson's *r* 0.74; (*p*=0.00)) and GEDVI (Pearson's *r* -0.25; (*p*=0.00)). The only factors independently associated with low GEF were low SV and low GEDVI. **Conclusion:** Hypovolemic patients frequently show low GEF values. We found correlation between SV and GEDVI with GEF. Low SV and low GEDVI were associated with low GEF. This could constitute a limitation in the interpretation of GEF and cardiac pump function. Hypovolemic patients could have low GEF without implying disorders in cardiac contractility.

Keywords: cardiac function; GEF limitation; global ejection fraction; TPTD; transpulmonary thermodilution; hypovolemic shock

1. Introduction

Transpulmonary thermodilution is a technique for hemodynamic monitoring of critically ill patients that has gained great interest in recent years. It measures cardiac output (CO), stroke volume (SV), but also calculates variables related with volume status, cardiac contractility, dynamic predictors of volume response, and extravascular lung water (ELWI) [1–5].

One of the hemodynamic variables that it measures is the global end diastolic indexed volume (GEDVI), which provides the volume of the 4 cardiac chambers and large intrathoracic vessels during diastole. It is a static variable of cardiac preload [5–10].

Another calculated variable is the global ejection fraction (GEF). It provides information regarding cardiac function. GEF reflects the relationship between SV and the volume of the 4 cardiac chambers and large intrathoracic vessels. It assumes that the overall end-diastolic volume

(GEDV) is equal to $GEDV / 4$. This is an approximation since the volume of each of the cardiac chambers is different.

It has been described that impaired GEF values have good correlation with LV ejection fractions below 40 - 30%. Also has been described that GEF adequately track directional changes in ejection fraction when inotropic drugs are being used [11–16,19].

GEF and GEDVI calculations are performed simultaneously from the same CO measurement. The formula that calculates GEDV includes the CO, and the calculation of the GEF includes the SV, therefore there could be a mathematical coupling between both [18].

The aim of our work was to evaluate whether impairment in GEDVI and SV may constitute a limitation for the interpretation of GEF in hypovolemic patients. A secondary objective was to determine factors independently associated with impaired GEF.

2. Materials and Methods

A retrospective study was conducted on a database of patients with shock who received hemodynamic monitoring with transpulmonary thermodilution by means of VolumeView/EV1000™ system (Edwards Lifesciences, Irvine CA, USA) from 2016 to 2023 in a 24-bed medical-surgical intensive care unit (UCI) in Argentina.

The following variables were recorded: sex, age, comorbidities, APACHE II and SOFA scores during the first 24 hours of hospitalization, shock etiology, ICU length of stay, mortality, mean arterial pressure (MAP), heart rate (HR), cardiac index (CI), stroke volume (SV), indexed global end-diastolic volume (GEDVI), indexed systemic vascular resistance (IRVSi) and extravascular lung water (ELWI). Hemodynamic variables were recorded during the first measurement of transpulmonary thermodilution.

Shock was defined as the need of norepinephrine infusion to keep at least TAM of 65 mmHg plus at least 1 sign of tissue hypoperfusion. We defined hypovolemia as SV values less than 60 mL and GEDVI less than 680 mL/m2. Patients were classified according to GEF, GEDVI, and SV values.

To determine correlation between GEF with SV, or GEF with GEDVI Pearson's coefficient was used.

Statistical analysis was performed by means of Mann Whitney test for continuous variables of abnormal distribution and student *t* test for continuous variables of normal distribution. For categorical variables, Pearson's Chi² test was used. To determine factors independently associated with the presence of *impaired GEF*, binary logistic regression was performed. We included all variables with a *p*< value of 0.10 in the univariate analysis and those that were physiologically relevant.

3. Results

We included 113 patients with shock who received hemodynamic monitoring by transpulmonary thermodilution. The most frequent cause of shock that triggered the placement of transpulmonary thermodilution monitoring was sepsis (63%). There were no statistically significant differences in the severity or epidemiological characteristics of the patients. (Table 1).

Table 1. Baseline characteristics.

	All (n=113)	Survivors(n=53)	Non- survivors(n=60)	P
Age (years)	51[60–72]	58 [45–73]	62 [50–70]	0.65
Female (n)	42	18	24	0.28
Apache II	23[17–28]	21[17–25]	23[20–28]	0.15
SOFA	8[5–10]	8[5–9]	8[5–10]	0.05
<u>Comorbidities</u>				

Arterial hypertension (n%)	46 (40)	22 (19)	24 (21)	0.82
	21 (19)	10 ()	11 ()	0.88
Diabetes Melitus II (n%)	13 (11)	6 (5)	7 (6)	0.82
	8 (7.5)	6 (4)	3 (3)	0.26
	9 (8)	3(3)	6 (6)	0.32
COPD (n%)				
Coronary heart disease (n%)	36 (32)	16 (14)	20 (18)	0.96
	18 (16)	11 (10)	6 (5)	0.25
Heart failure (n%)				
Immunosuppression (n%)				
Chronic use of corticosteroids (n%)				
Shock etiology (n%)				
Sepsis	72 (63)	30 (26)	28 (26)	0.12
Hypovolemic	14 (12)	7 (6)	7 (6)	0.97
Cardiogenic	6 (5)	4 (3)	2 (2)	0.67
Perioperative	10 (9)	8 (7)	2 (2)	0.04
ICU Lenght stay (Days)	11[6–17]	12 [7–18]	10 [4–16]	0.26
IMV (Days)	7[3–13]	6[3–12]	8[3–16]	0.20

The haemodynamic characteristics of the first measurement with transpulmonary thermodilution are shown in Table 2a. Statistically significant differences were detected between survivors and non-survivors in GEF (21[16–28] versus 18[11–26]; p= 0.01) and in MAP (79[67–93] mmHg versus 73[62–88] mmHg; (p= 0.00)) 38(34%) patients had hypovolemia. 44(39%) of them had depressed GEF values.

Table 2. a. Hemodynamic variables in transpulmonary thermodilution first measurement.

	All (n=113)	Survivors (n=55)	Non Survivors(n=58)	P
GEDVI(mL/m ²)	636 [543–755]	604 [515–784]	619 [527–710]	0.21
SV (mL)	56 [37–72]	65 [40–73]	56 [40–72]	0.18
ELWI (mL/m ²)	10[8–15]	10 [7.8-15]	10 [8–15]	0.66
IPVP	2,2[1.6-3.1]	2.3 [1.7-3.2]	2.3 [1.6-1.9]	0.61
CI (L/min/m ²)	3,1[2-3.8]	3.3 [2.3-4.1]	2.8 [2-3.6]	0.16
GEF (%)	20[14–27]	21 [17–28]	18 [11–26]	0.00
IRVS(dines-s-m ² /cm ²)	1692[1279–2392]	1543 [1075–2290]	1692 [1279–2392]	0.66
MAP (mmHg)	75[62–85]	79 [67–93]	75 [63–85]	0.00
HR (bpm)	103[82–119]	91 [78–120]	106 [82–116]	0.59

Hypovolemic patients had lower GEF values than non-hypovolemic patients (16 [12–22] vs 20 [15–27]; p=0.01) (Table 2.b) Figura 1.

Table 2. b. Hemodynamic variables in transpulmonary thermodilution first measurement according to volemia.

	All (n=113)	Non Hypovolemia (n=55)	Hypovolemia(n=38)	P
GEDVI(mL/m ²)	619 [527–761]	723 [578–837]	548 [448–620]	0.00
SV (mL)	56 [40–73]	69 [52–83]	40 [30–54]	0.00
ELWI (mL/m ²)	10 [8–15]	10 [8.3-16]	10 [8-12.8]	0.57
IPVP	2,3 [1.7-3]	2.2 [1.6-2.8]	2.4 [2.1-3.3]	0.01

CI (L/min/m ²)	3,1 [2.3-3.9]	3.3 [2.6-4.1]	2.2 [1.8-3.0]	0.00
GEF (%)	20 [14-27]	20 [15-27]	16 [12-22]	0.01
IRVS(dines-s-m ² /cm ²)	1692[1279-2392]	1656 [1209-2288]	2126 [1558-2690]	0.01
MAP (mmHg)	75[62-85]	75 [65-85]	76 [60-87]	0.46
HR (bpm)	103[82-119]	95 [74-114]	115 [83-167]	0.05

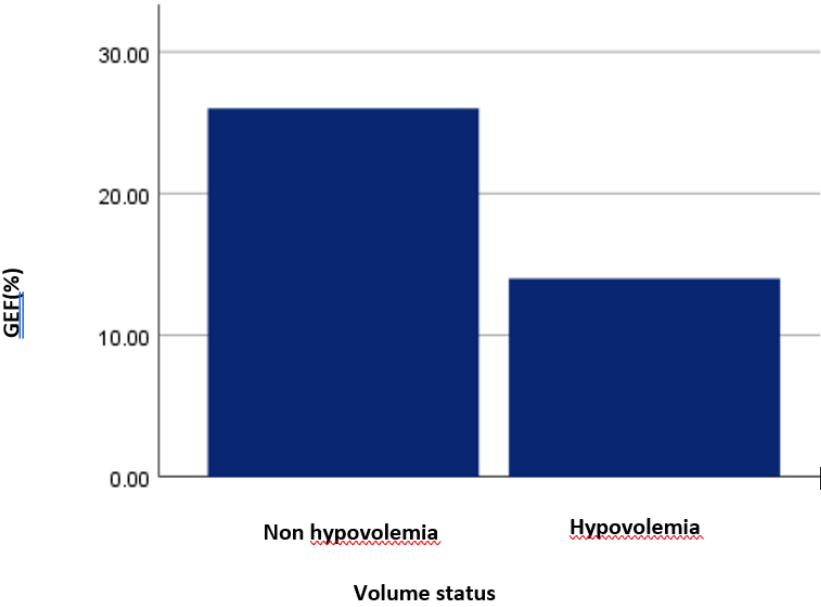


Figure 1. GEF according to blood volume status.

Both SV and GEDVI had a statistically significant correlation with GEF, SV (Pearson's r 0.74; (p=0.00). Figure 2a) and GEDVI (Pearson's r -0.25; (p=0.00). Figure 2b).

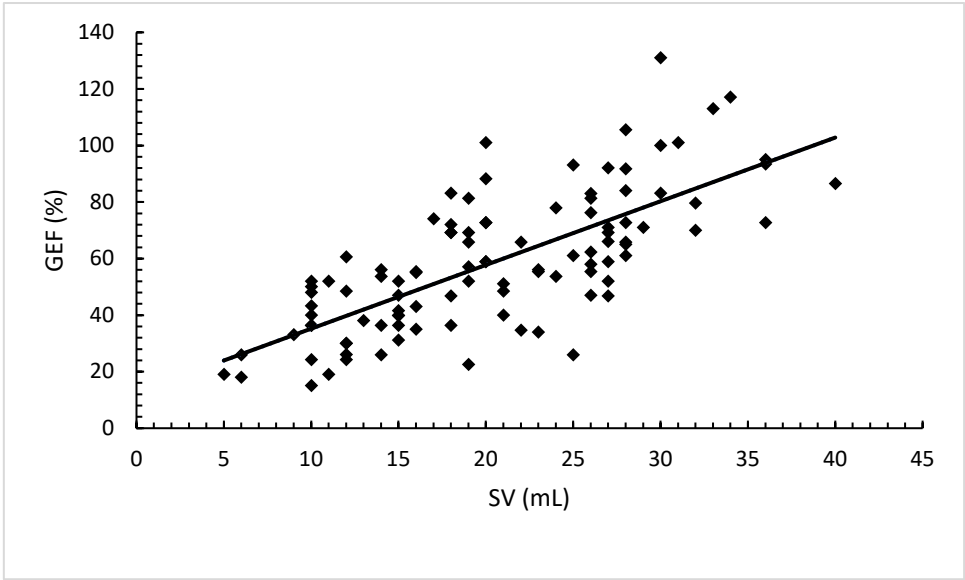


Figure 2. a. Correlation between stroke volume and global ejection fraction.

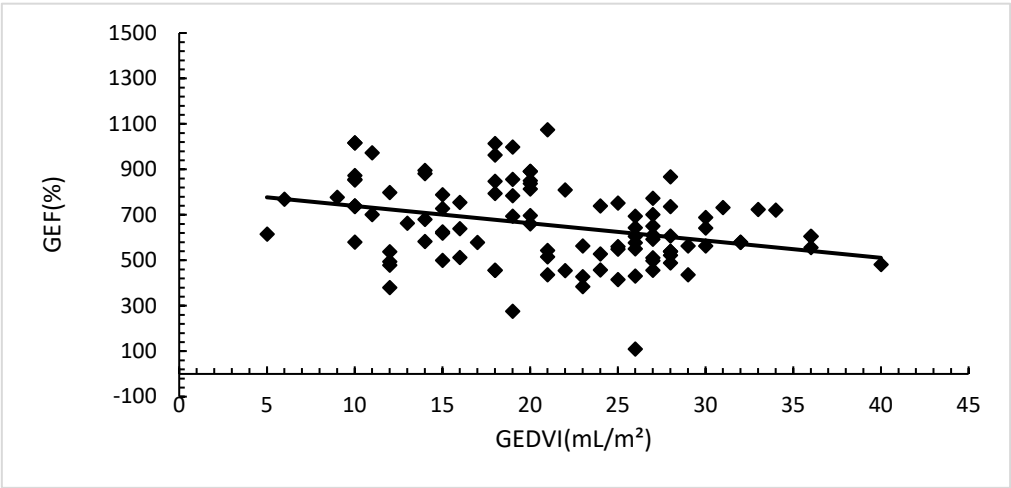


Figure 2. b. Correlation between global end diastolic indexed volume and global ejection fraction.

Transthoracic echocardiogram was performed in 72(64%) patients, 36(31%) of them had depressed GEF values, however in only 19(17%) patients depressed left ventricular ejection fractions by echocardiogram coexist.

The only factors independently associated with the development of low GEF were low SV and low GEDVI. Table 3.

Table 3. Multivariate analysis with low GEF as outcome.

	HR	IC	P
Low GEDVI	6.36	1.95 – 20.75	0.00
Low SV (mL/lat)	20	6.09 - 62.50	0.00

4. Discusión

Our main finding is that in the population of hypovolemic patients, GEF values are lower than in non-hypovolemic patients, therefore; they can’t be interpreted in isolation because it could lead to misinterpretations. Preload conditions determine cardiac ejection fraction, i.e patients with low preload could have low cardiac function and CO. While this statement may not be novel, as it is physiologically known, it has not previously been highlighted as a limitation that underestimates cardiac function measured by TDTP, to the best of our knowledge.

The correlation between SV and GEF was strong, and between GEDVI and GEF was week. It could be due to mathematical coupling in the formulas that are used to make the calculations. GEDV is calculated by the formula $GEDV= CO \times MTt \times f(S1/* S2)$ (MTt: mean transit time. S1 and S2 are respectively the maximum ascending and descending slopes of the transpulmonary thermodilution curve and f is a proprietary function). The calculation of GEF is done using the formula $SV*4 / GEDV$. GEF and GEDVI calculations are performed simultaneously from the same CO measurement, so there is a risk of mathematical coupling [12,18,19].

One way to address this limitation could be to assess, at the same time, fluid response and other preload parameters such as PVC or GEDVI, or to perform echocardiography. It should be borne in mind that GEF is a parameter of overall cardiac function, not cardiac contractility.

The retrospective nature of our study constitutes its main limitation, for this reason we could not establish the volume response of the patients included, since it was impossible for us to determine if the appropriate conditions for the interpretation of VVS were met. We also did not assess whether the GEF was modified after correcting hypovolemia. In addition, we did not perform simultaneous measurements de thermodilution and the echocardiogram, but the latter was performed within 24 hours, and was only performed in part of the patients studied.

5. Conclusions

Hypovolemic patients frequently show low GEF values. We found correlation between SV and GEDVI with GEF. The factors independently associated with low GEF were low SV, low GEDVI. This could constitute a limitation in the interpretation of GEF and cardiac pump function. Hypovolemic patients could have low GEF without implying disorders in cardiac contractility.

Author Contributions: Gonzalez Cecilia contributed to conception and design of the study, performed the main statistical analysis and wrote the first draft of this paper. Rodriguez Louzan Jesica contributed to conception and design of the study, helped collect the data, contributed to the analysis of the data. Traverso Agustin helped collect the data, contributed to the analysis of the data. Giordana Agostina helped collect the data, contributed to the analysis of the data. Papini Emanuele helped collect the data, contributed to the analysis of the data. Latasa Diana helped collect the data, contributed to the analysis of the data. Lovesio Carlos is the study lead and guarantor for this paper. Dubin Arnaldo contributed to conception and design of the study and revised it critically for important intellectual content, proofread and helped write the draft. All authors read and approved the final manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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