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Full Length Research Paper

Flotrac/Vigileo™ validation trials: Are there reliable conclusions?

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We reviewed the comparative trials of the Flotrac/Vigileo™ versus the thermodilution method, published in the last decade. The results about the agreement between the two methods measuring cardiac output are contrasting. We also noticed that almost the whole pertinent literature include studies conducted without a correct statistical design, particularly about the sample size. For this reason, we consider that results of the published studies do not permit any conclusion about the agreement between pulse contour analysis for cardiac output measurement and thermodilution method.

Key words: Pulse contour wave, cardiac output, haemodynamics.

INTRODUCTION

The measurement of blood flow using pulse wave analysis results from the interaction between stroke volume and the vascular system (that is, resistances, compliance and impedance). Modern technology has provided several methods and monitors for hemodynamic assessment, aimed to obtain sufficient precision and low invasiveness. All these methodologies of Cardiac output (CO) measurement have been evaluated and validated with respect to the thermodilution with PAC which is the most widely adopted system. As recently suggested by Pinsky and Payen (2005), we need a continuous functional monitoring as it gives more effective resuscitation in critically ill patients.

It has been established that acceptance of a new method of CO measurement should rely on limit of agreement up to 30% (Critchley and Critchley, 1999). Pulse contour analysis is a new method of CO measurement that has been validated versus thermodilution. Actually, the method cannot replace PAC, because the still contrasting results avoid conclusive matters. It is fundamental that trials about evaluation and comparison of the new method with previous devices have to be planned and performed complying with statistically correct rules. Particularly the sample size computing is too often neglected in a trial. It is clear that it may affect the reliability of observed differences between two methods (the so called power of a study) (Whitley and Ball, 2002). A correct statistical method is necessary to plane a trial which results will be reliable. On the contrary, conclusions may be only speculative.

FloTrac/Vigileo™ is a CO monitor based on the pulse contour analysis, which does not require any calibration: it calculates the stroke volume according the physiological principle of pulse pressure's proportionality to stroke volume itself. Furthermore, the algorithm compensates for the continuously changing effects of vascular tone via analysis of waveform characteristics, directly correlated with vascular tone. Giving the progressive upgrade of the software, the monitor provides more accurate measurements of cardiac output.

We tried to review the reliability of FloTrac/Vigileo™ measurements analyzing the main published trials about its comparison with the reference method of thermodilution.

MATERIALS AND METHODS

As a reliability of a study's results are correlated with the application of correct statistical rules, we tried to review the validation trials of the FloTrac/Vigileo™ (Edwards Lifesciences, Irvine, CA, USA) to establish

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Table 1. Studies included in the analysis.

Study	Authors	Software version	Error (%)	No	Bias (L/min)
1	[3] Sander M	Old version NS	36-54	30	0.6
2	[4] McGee WT	NS	22	84	0.2
3	[5] Button D	1.07	NR	31	0.1-0.6
4	[6] Mayer J	NS	46	40	0.46
5	[7] Manecke GR Jr	New version NS	NR	50	0.55
6	[8] Breuker RM	NS	14-24	20	0.8-1.0
7	[9] Sakka SG	1.07	35	24	0.5
8	[10] Opdam HI	NS	21	6	0.21
9	[11] Cannesson M	NS	38	11	0.26
10	[12] Lorsomradee S	1.07	NR	52	NR
11	[13] Compton FD	1.10	58	25	0.68
12	[14] Metha Y	1.07	29	12	0.26
13	[15] Biasis M	1.07	43	20	0.8
14	[16] Zimmermann A	1.10	20-30	30	0.2
15	[17] Mayer J	1.10	20.7-28.3	40	0.19
16	[18] Senn A	1.07	21.6	25	0.3
17	[19] Biancofiore G	1.10	54	29	1.3
18	[20] Schramm S	1.07	34	20	0.46
19	[21] Hofer CK	1.07	NR	26	0.2

NR = Not reported; No = Number of patients enrolled; NS = Not specified.

Table 2. Age ranges and diseases.

Disease	Age (range)	Mean error (%)	DS of % error	Mean bias (L/min)
CABG and valve replacement	58-72	32.9	10.6	0.35±0.15
Liver transplant	47-51	48.5	7.8	1.0±0.3
Mixed cardiocirculatory disease	24-84	40.0	25.5	0.44±0.34
Septic shock	26-77	35	-	0.5

whether conclusions about the agreement with thermodilution may be realistic or speculative.

Using the keywords Flotrac/Vigileo™, pulse contour analysis and thermodilution-PAC we searched within PubMed database comparative trials published in the last decade and we investigated the studies' design and how they were performed. We analyzed methods adopted to plan each study and the statistical rules applied for the sample size enrollment. We evaluated how data were recorded and computed when it was deduced from the published manuscripts.

RESULTS

We included 19 trials published between 2006 and 2010. Two studies were performed prospectively. Other authors enrolled a sample of patients arbitrarily: they did not expose how they decided to enroll such a number of patients without a preceding statistical elaboration.

The total population included 575 patients, aged 24 to 84 years, 567 were male (98.6%); 442 patients (77.9%) underwent cardiac surgery procedures (Table 1). Error resulted <30% (range 14 to 29%) in six trials; nine studies showed error >30% (range 30 to 58%); four studies did not report the datum. Eighteen studies referred the bias between CO measured by FlowTrac/Vigileo™ and PAC within a range of 0.1 to 1.3 L/min (Table 2).

When we grouped the studies according to the patient's disease and related ranges of age, out of 13 cases only five showed an acceptable agreement between FlowTrac/Vigileo™ and the PAC. Patients of this subgroup can be included in the 6th decade of age; differently, patients aged 24 to 84 years affected by mixed cardiovascular disease showed contrasting agreement.

Patients submitted to liver transplantation (described in two studies) represented the 5th decade of age, and showed a poor agreement between pulse contour analysis and thermodilution (error >30%).

Acute respiratory failure and septic shock were characterized by a wide range of age: 24 to 84 years. In this sub-group of patients a poor agreement between the two methods (error >30%) were found, (Table 2).

Most of cardiac surgery trials excluded patients undergone valve repair procedures. Only two studies

(Button et al., 2007; Hofer et al., 2010) included the surgical replacement of the aortic valve: Button et al. (2007) did not report the percentage error, but they found a bias of 0.1-0.6 L/min. Hofer et al. (2010) measured the CO in two different anatomical sites, that is, radial and femoral arteries. Their results showed comparable values (bias 0.1-0.2 L/min). Comparing CO measured by Flotrac/Vigileo™ with thermodilution measurements, a mean bias of 0.2 L/min was found. Worse agreement resulted when it was analyzed in the postoperative period.

In the subgroup including patients undergone liver transplantation (Biancofiore et al., 2009) a poor agreement resulted between the two methods with bias range 0.8 to 1.3 L/min.

When we analyzed mixed cardiocirculatory cases (McGee et al., 2007; Compton et al., 2008), as expected, we found a wide range of age. McGee et al. (2007) reported a mean error <30% (22%); on the contrary Compton et al. (2008) found a mean error >30% (58%). The former study enrolled mainly patients in the postoperative period (82.1%). In the latter study acute respiratory failure was the disease mostly occurring (76%).

One trial (Sakka et al., 2007) concerned patients suffering from septic shock: authors found a percentage error 35% and the bias resulted in 0.5 L/min.

Only few authors declared the type of study or reported appropriate computing of the sample size, two factors that give the power of a clinical trial (Whitley and Ball, 2002).

Cannesson et al. (2007) enrolled 11 patients: authors did not report the type of study and how they calculate the sample.

The same considerations could be done for McGee et al. (2007), Mayer et al. (2007), Breukers et al. (2007), Sakka et al. (2007), Compton et al. (2008), Metha et al. (2008), Biais et al. (2008), Mayer et al. (2008), Zimmermann et al. (2008), Biancofiore et al. (2009). Furthermore, Opdam et al. (2007) enrolled only 6 patients: it was a very small sample.

Lorsomradee et al. (2007) found a poor agreement between FlowTrac/Vigileo™ and PAC: unfortunately authors did not report both the percentage error and the bias, with the exception of a subgroup of 10 patients with aortic valve regurgitation that showed an error 32%.

The better agreement and precision were noticed in patients that underwent cardiac surgery; in other clinical settings, both percentage error and bias were higher (Table 2).

Giving the lack of complete data and the poor sample enrolling criteria, we did not perform a statistical analysis.

DISCUSSION

It has been ascertained that pulse contour analysis provide helpful hemodynamic monitoring. It is easy to use, objective and provides continuous measurements. As Critchley et al. (2010) stated, a good agreement between two method measuring the same parameter exists whether the percentage error is <30% (Critchley and Critchley, 1999). According to this criterion only few studies matched this result, therefore it might be concluded that FlowTrac/Vigileo™ is not an advisable device to measure CO.

But, as Peyton and Chong (2010) reported, a perchantage error in agreement with thermodilution of + 45% may be more realistic. We retain that this wide variance and poor agreement may depend on several factors. High age variability in the comparative studies might cause differences in the computing of stroke volume by FlowTrac/Vigileo™. In addition, it is indubitable that particular problems due to typology of surgery (core temperature during and after cardio-pulmonary by-pass) or pathologies (septic shock) that notoriously affect vascular bed compliance and resistances play a crucial role in the final results.

We observed the best agreement with PAC in patients submitted to cardiac surgery procedures in the 6th decade of life. Therefore, is FlowTrac/Vigileo™ suitable for monitoring cardiacirculatory function in this specific kind of patients? Current data are not sufficient to answer the question.

The widest disagreement resulted during septic shock monitoring. It may be mainly related with the wide range of patient's age included in this sub-group and to the high cardiac output setting in this particular clinical status. Another issue is whether age is the main factor affecting hemodynamic measurement by FlowTrac/Vigileo™.

We noticed that the most of the studies were not planned and performed according to correct statistical rules. Several authors did not explain how they calculated the sample size or did not declare the type of study they conducted. Both of these issues limit the power to their conclusions. We are aware that the problem about the power of a trial could be debate for all studies regarding other cardiac output monitors: it may be a motivation for further correctly planned trials.

The statistical method of analysis may affect the correct evaluation of the results and then the conclusions of a trial. We agree with Critchley et al. (2010) that a correct evaluation of a CO-measuring device needs to perform three steps: 1) animal study; 2) human/clinical study; 3) clinical utility/outcome study (Critchley et al., 2010). We ignore whether FlowTrac/Vigileo™ passed all these three steps. The benefits of a continuous measurement of CO were introduced in 2005 by Pinsky. The assessment of cardiocirculatory status is difficult as too many variables have to be considered. Flotrac/Vigileo™ provides stroke volume variation (SVV) and vascular resistances. Continuous measurement of SVV is helpful to understand whether a mechanically ventilated and hemodynamically unstable patient will respond to fluid resuscitation.

Vascular reactivity, effective blood volume, myocardial function, blood rheology, core temperature are all

variables that can affect the hemodynamic setting of a patient. In this context the preload responsiveness may be very helpful. Pinsky (2005) MR asserts that SVV alone cannot be considered for clinical decisions making in every hemodynamic picture (Pinsky, 2003).

The last version of the software permit to calculate stroke volume every one minute the upgraded software provides prompt detection of rapid hemodynamic changes and consequently earlier adequate treatments (Pinsky, 2003). A recent meta-analysis showed enhanced agreement of the second-generation software of Vigileo compared with intermittent thermodilution (ITD), although results were limited by the different design of the included trials. Authors concluded that the FloTrach/Vigileo™ may be helpful in preventing severe hemodynamic instability, but when instability occurs, ITD is still the best choice (Mayer et al., 2009).

Unfortunately its precision is lost in patients with atrial fibrillation and/or severe aortic valve regurgitation. Consequently, its employment for hemodynamic monitoring in such patients cannot be recommended. We are strongly convinced that actually the best CO monitoring device does not exist.

We can use several monitors each of them affected by specific limitations that have to be reminded during clinical evaluation of a critically ill patient. We consider that future trials aimed at comparing different methods of hemodynamic monitoring need to be statistically planned to obtain reliable, helpful and comparable results. Our work did not add any concern about FloTrac/Vigileo™ measurements' reliability, but it was not possible as literature does not provide sufficient valid trial about this issue, yet.

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