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P. Estagnasié
K. Djedaini
L. Mier
F. Coste
D. Dreyfuss

Measurement of cardiac output by transesophageal echocardiography in mechanically ventilated patients

Comparison with thermodilution

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P. Estagnasié · K. Djedaini · L. Mier · F. Coste · D. Dreyfuss (✉)
Service de Réanimation Médicine,
Hôpital Louis Mourier,
Faculté Xavier Bichat,
178 rue des Renouillers,
F-92700 Colombes, France
FAX: + 33 (1) 4760 6192

Abstract *Objective*: The determination of basal cardiac output (CO) and of its variations during different therapeutic interventions liable to increase or decrease it in mechanically ventilated patients using transesophageal echocardiography (TEE).
Design: To compare CO measurements simultaneously obtained by transmitral single-plane TEE and thermodilution.
Setting: Medical intensive care unit.
Patients: Twenty-two consecutive mechanically ventilated patients hospitalized for various medical conditions were included.
Interventions: The comparisons between transmitral single-plane TEE and thermodilution measurements were made at baseline and after different therapeutic interventions affecting CO (fluids or dobutamine infusion or positive end-expiratory pressure titration).
Measurements: Seventy-four measurements were obtained. Cardiac output using TEE was the product of the mitral valve area, the time-velocity integral of flow at the same site and the heart rate.
Results: A significant correlation was observed between thermodilution and TEE measurements of CO ($n = 74$, $r = 0.78$, $p < 0.001$) despite wide limits of agreement (mean ± 2SD = –0.3 ± 3.1 l/min). Thermodilution and TEE CO determinations both had significant inverse correlation with the arterial-venous oxygen content difference in ten consecutive patients ($r = 0.77$, $p < 0.01$ and $r = 0.71$, $p < 0.01$, respectively). The correlation between variations of CO greater than 20 % obtained by thermodilution and TEE was significant ($r = 0.89$, $p < 0.001$). The operative characteristics implied the ability of TEE to predict significant variations of thermodilution CO (sensitivity 85 % and negative predictive values 86 %). Moreover, arterial-venous oxygen content difference changes of 5 % or more were better detected using TEE than thermodilution.
Conclusions: These results suggest that although transesophageal CO measurements cannot replace thermodilution ones, the determination of CO variations obtained using TEE may be useful in the management of critically ill mechanically ventilated patients. This technique may make it possible to monitor hemodynamics during initial therapeutic interventions in those patients in whom right heart catheterization cannot be performed immediately.

Key words Cardiac output · Thermodilution · Transesophageal echocardiography · Arterial-venous oxygen content difference

Introduction

The management of critically ill mechanically ventilated patients often requires cardiac output (CO) determination, both for diagnostic and therapeutic purposes. This is usually achieved by the thermodilution method using a catheter inserted in the pulmonary artery [1, 2]. Nevertheless, pulmonary catheter insertion may take time and be hazardous during the initial management of very ill patients, such as those with marked hemodynamic instability or uncontrolled hemostatic disorders. In addition, this procedure can lead to severe complications [3, 4], which may be more likely to occur in the settings of emergency catheter insertion than when this procedure is accomplished under stabilized conditions. For these reasons, this procedure is sometimes delayed while therapeutic modifications, such as volume or catecholamine infusion or titration of positive end-expiratory pressure (PEEP) during mechanical ventilation, are made. In such situations, it might be useful to have a minimally invasive and rapid estimate of the CO value and of its variations during the initial therapeutic interventions. The performance of transesophageal echocardiography (TEE) in mechanically ventilated patients offers the two conditions of speed and a lower risk of severe complications than those associated with emergency pulmonary artery catheterization.

The purpose of this study was to assess whether TEE may give an acceptable estimate of CO and of its variations in critically ill mechanically ventilated patients as compared to the standard thermodilution method.

Patients and methods

Patients

To be included in the study protocol, the patients had to be free of cardiac rhythm disturbances and esophageal disease. In addition, patients in whom TEE showed important mitral annulus calcifications or more than mild mitral regurgitation, as determined by color flow mapping [5], were excluded from the study. Twenty-two consecutive mechanically ventilated patients (13 men, 9 women), whose ages ranged from 33 to 84 years (mean = 61 ± 15) were studied prospectively. Underlying diseases were septic shock and/or acute respiratory distress syndrome in 14 patients, cardiogenic pulmonary edema in 3, acute ventilatory failure secondary to chronic obstructive pulmonary disease in 2, pulmonary embolism in 1 and coma in 2. The simplified acute physiological scores [6] ranged from 8 to 28 (mean = 17 ± 6) . All patients had had a Swan-Ganz catheter inserted in the pulmonary artery for diagnostic or therapeutic purposes before entering the study.

The study protocol consisted of simultaneous determinations of CO using transmitral Doppler examination and thermodilution in all patients. Measurements of the arteriovenous oxygen content difference ($C[a\text{-}v]O_2$) were performed in ten consecutive patients. In each patient, at least two sets of measurements were obtained under baseline conditions and after therapeutic interventions. The latter were the administration of gelatines (250–500 ml) or dobutamine (10–15 mcg/kg per min), which can increase CO, or the introduction of different levels of PEEP (5–15 cm H_2O) during ventilation, which can decrease CO. These interventions were selected on the basis of on the therapeutic requirements of the patients. Heart rate, systolic and diastolic blood pressures and a three-lead electrocardiogram were continuously monitored during the procedure. The protocol was approved by an independent regional committee on human investigations (Comité Consultatif de Protection des Personnes pour la Recherche Biomédicale, Saint-Germain-en-Laye, France). Informed consent was obtained from each patient's nearest relative. Intravenous sedation using hypnotics (midazolam) was given to all patients.

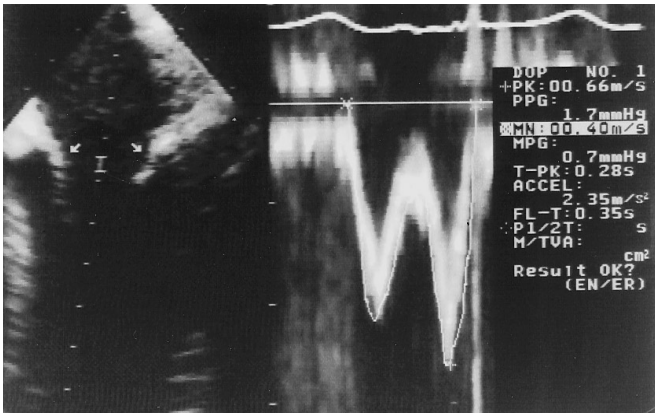


Fig. 1 Caliper measurement of the greatest diastolic mitral diameter (*left panel*) and measurement of the velocity-time integral (*right panel*) at the same level

Transesophageal Doppler echocardiography

Transesophageal two-dimensional and pulsed Doppler echocardiography was performed using an Aloka SSD-870 unit with a 5-MHz single-plane probe (Aloka Co., Tokyo, Japan).

Two-dimensional echocardiographic and pulsed-wave Doppler imaging was performed by an observer blinded to the hemodynamic data. The images and Doppler data were recorded on a VHS videotape (Mitsubitshi, Japan) simultaneously with the measurements of thermodilution CO and blood sampling for $C[a\text{-}v]O_2$ determination in ten consecutive patients. A frontal four-chamber scan of the heart was obtained by advancement and retroflexion of the endoscope in the esophagus. A view allowing for the determination of the largest diameter of the mitral annulus was obtained after appropriate manipulation. Mitral inflow was measured using a pulsed Doppler sample volume (length: 3 mm) at the level of the mitral annulus. Slight adjustments in sample volume position were made to maximize the auditory and graphic quality of the Doppler signal. The volume signal from the respirator (Elema 900 D Servo ventilator, Siemens, Solna, Sweden or Cesar, Compagnie Française des Produits Oxygénés, France) was displayed on the echocardiogram monitor to allow precise identification of the respiratory cycle phase.

All echocardiographic and Doppler measurements were performed off-line and in a random order by a single observer. The maximal mitral diameter (d) was measured and the mitral valve area was calculated as $\pi d^2/4$, assuming a circular shape for the mitral annulus and a constant cross-sectional area throughout diastole (Fig. 1, left panel). The velocity time integral of the left ventricu-

lar inflow was calculated as the product of the mean mitral velocity and Doppler signal duration, determined by a manually tracing shape of flow velocity recorded at a paper speed of 100 mm/s (Fig. 1, right panel). All the data were analyzed at end-expiration and five cardiac cycles were averaged. Cardiac output was calculated off-line as the product of the mitral valve area, the velocity time integral and the heart rate, using the following formula:
CO (ml/min) = mitral valve area (cm^2) × velocity time integral (cm) × heart rate (bpm) × 10^3

Interobserver variabilities of the echographic and Doppler measurements were calculated after the interpretation of all data by a second independent observer. Variability was calculated as the difference between transmitral Doppler echocardiographic measurements obtained by the two observers divided by the mean of the two measurements. Correlation and the absolute value of the differences between the measurements obtained by the two observers were also calculated.

Thermodilution cardiac output

Bedside thermodilution CO measurements were obtained using an 8 Fr balloon-tipped flotation catheter (Abbott, Chicago, Ill.) inserted into the pulmonary artery through the right internal jugular vein, the brachial basilic vein or the femoral vein. Cardiac output measurements were performed at end-expiration by injecting 10 ml of ice-cold 5% dextrose into the right atrium and CO was calculated using a computer (Baxter, Irvine, Calif.) as the mean of five determinations.

Arterial-venous oxygen content difference

In order to obtain an indirect estimate of cardiac index (CI) using an independent method, according to the Fick principle [7], to which both thermodilution and Doppler CI measurements could be compared, radial or femoral arterial and pulmonary mixed-venous blood samples were obtained simultaneously with the echocardiographic and thermodilution measurements in ten consecutive patients. Cardiac index was used in place of CO because C(a-v)O2 reflects oxygen consumption, which depends on body surface area. The blood gas analysis of simultaneously drawn arterial and mixed venous blood specimens was performed using the ABL 30 Acid-Base Analyzer (Radiometer, Copenhagen, Denmark). Hemoglobin levels were determined on a Cobas Argos counter (ABX, Montpellier, France). Oxygen saturations were measured using the GSM3 hemoximeter (Radiometer). Arterial and mixed venous oxygen contents (CaO2 and CvO2 [ml/dl]) were calculated as follows:
(arterial or mixed venous hemoglobin saturation for oxygen X hemoglobin concentration [g/dl] X 1.34) + (arterial or mixed venous pressure for oxygen [mmHg] × 0.003).

Statistical analysis

The data are presented as the means ± SD. Correlations between Doppler and thermodilution CO were evaluated using the least squares method. Agreement between the two methods was assessed according to the procedure described by Bland and Altman [8]. Operating characteristics of the echocardiographic and Doppler techniques for detecting changes of 20% or more in thermodilution CO and changes of 5% or more in C[a-v]O_2 were calculated using standard formulas [9]. A p value of less than 0.05 was considered statistically significant.

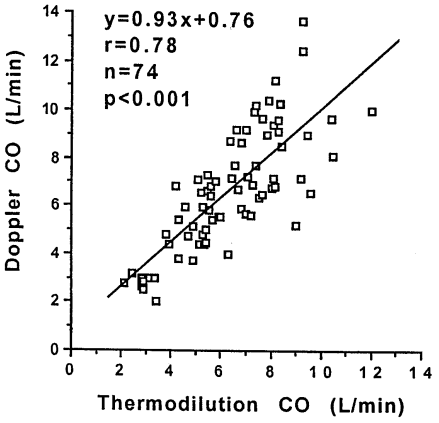


Fig. 2 Correlation between cardiac output (CO) measurements obtained by thermodilution and transesophageal pulsed Doppler echocardiography

Results

A total of 74 CO measurements was obtained in the 22 patients. They consisted of 22 baseline determinations, 23 measurements during treatments aimed at increasing CO, and 29 measurements during PEEP titration involving possible CO decreases. Mitral annulus diameters ranged from 1.8 to 3.3 cm, with a mean of 2.6 ± 0.3 cm, and velocity time integral ranged from 4.19 to 22.65 cm, with a mean of 11.87 ± 3.86 cm. Calculated mitral valve areas ranged from 2.70 to 8.55 cm^2, with a mean of 5.36 ± 1.12 cm^2. Thermodilution and Doppler CO values ranged from 2.1 to 12.0 l/min, with a mean of 6.3 ± 2.1 l/min, and from 2.0 to 13.7 l/min, with a mean of 6.5 ± 2.5 l/min, respectively. The percent of variation of minor and major CO values from the average of the five measurements obtained by TEE, were respectively, 11.5 ± 5.9% and 12.2 ± 6.7%.

Interobserver variabilities for transmitral velocity time integral and annulus diameter measurements were 1 ± 11% and 3 ± 27%, respectively. There was a significant interobserver correlation for Doppler CO determination ($r = 0.86$; $p < 0.001$). The absolute value of the CO difference between the two observers' measurements was 0.2 ± 1.3 l/min.

When all measurements (at baseline and after therapeutic interventions) were pooled, a significant correlation between Doppler and thermodilution measurements was observed ($n = 74$, $r = 0.78$, $p < 0.001$) (Fig. 2). This correlation persisted when only thermodilution CO values of 4.5 l/min or less were considered ($n = 15$, $r = 0.77$, $p < 0.001$) but was no longer present when only CO values of 7.5 l/min or more were considered ($n = 25$, $r = 0.17$, $p = 0.4$). A significant correlation between Doppler and thermodilution measurements performed was present at baseline ($n = 22$, $r = 0.77$, $p < 0.001$), during dobutamine infusion ($n = 13$,

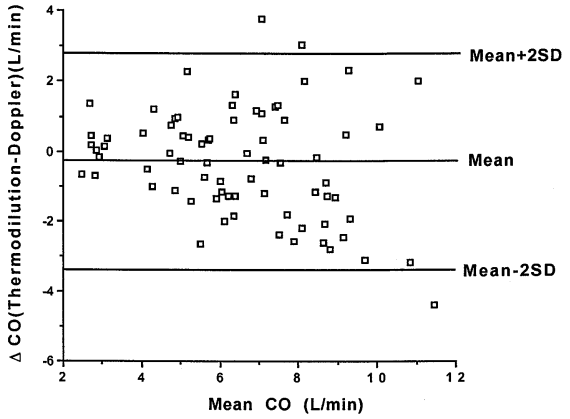


Fig. 3 Agreement between measurements obtained by transesophageal pulsed Doppler echocardiography and thermodilution

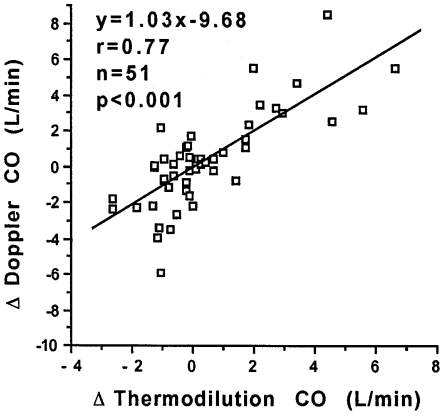
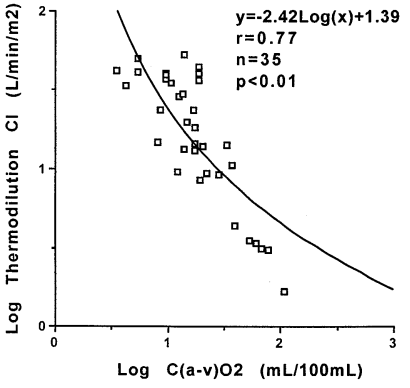


Fig. 4 Correlation between variations (Δ) in cardiac output (CO) measurements obtained by thermodilution and transesophageal pulsed Doppler echocardiography



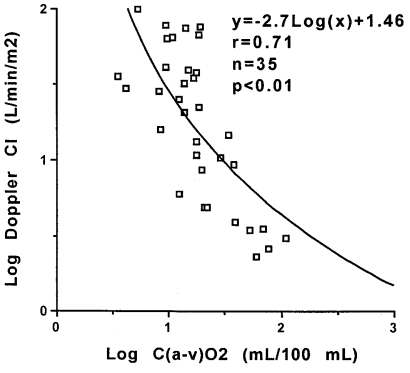


Fig. 5 *Top* Correlation between logarithmic transformation of thermodilution cardiac index (CI) and C[a-v]O2 measurements. *Bottom* Correlation between logarithmic transformation of transesophageal pulsed Doppler CI and C[a-v]O2 measurements ($C[a\text{-}v]O_2$ arterial-venous oxygen content difference)

$r = 0.64$, $p < 0.01$), administration of gelatines ($n = 10$, $r = 0.80$, $p < 0.01$). Similarly, the measurements performed during treatments aimed at increasing CO and during PEEP titration were significantly correlated ($n = 23$, $r = 0.75$, $p < 0.001$ and $n = 29$, $r = 0.84$, $p < 0.001$, respectively). The regression line between Doppler and thermodilution CO measurements was close to the identity line (Fig. 2). The bias, calculated as the mean difference between thermodilution and Doppler measurements [8], was –0.3 l/min (Fig. 3). The difference between thermodilution and Doppler CO values was not significant ($p = 0.10$). The limits of agreement, which are the value of 2 SD of the mean difference [8] were ± 3.1 l/min (Fig. 3). These limits of agreement decreased when CO values of 7.5 l/min or more were deleted (mean ± 2SD = –0.38 ± 2.40 l/min). In order to assess whether the changes induced by therapeutic interventions were similarly detected by both techniques, we studied CO variations after these interventions. Fifty-one different situations were included in this study. We found a significant correlation between variations in Doppler and thermodilution CO measurements ($n = 51$, $r = 0.77$, $p < 0.001$) (Fig. 4). When only changes in Doppler CO of a magnitude equal to or greater than 20 % were taken into account, the correlation with thermodilution CO changes improved ($n = 30$, $r = 0.89$; $p < 0.001$). Under such conditions, the operating characteristics of changes in thermodilution CO greater than 20 %, as detected by Doppler, indicated a sensitivity of 85 % a specificity of 61 %, a positive predictive value of 58 %, and a negative predictive value of 86 %.

We also correlated 35 $C[a\text{-}v]O_2$ values obtained in 10 consecutive patients with Doppler and thermodilution cardiac index (CI) measurements. Using a logarithmic transformation, C[a-v]O2 calculations were significantly correlated with both thermodilution CI data measurements ($n = 35$, $r = 0.77$, $p < 0.01$) (Fig. 5, top) and Dopp-

ler CI data ($n = 35$, $r = 0.71$, $p < 0.01$) (Fig. 5, bottom). Changes in $C[a\text{-}v]O_2$ were inversely correlated with both thermodilution and Doppler CI variations ($n = 25$, $r = 0.74$, $p < 0.01$ and $n = 25$, $r = 0.66$, $p < 0.01$, respectively). The sensitivity of the Doppler technique for detecting changes of 5% or more in $C[a\text{-}v]O_2$ was 68%, specificity was 67%, the positive predictive value was 94% and negative predictive value 22%. The same operating characteristics for the ability of the thermodilution technique to detect changes of 5% or more in $C[a\text{-}v]O_2$ were 50%, 40%, 77% and 16%, respectively.

Discussion

Transthoracic two-dimensional and pulsed Doppler echocardiography is a well-documented alternative method for CO determination [10–14]. However, transthoracic examination is not always feasible in critically ill patients in whom the image quality may be reduced because of the supine position and an increased gaseous interface during mechanically ventilation. This technique has been reported to be inaccurate in the determination of CO in critically ill patients with subarachnoid hemorrhage [15]. Transesophageal echocardiography is a minimally invasive method [16, 17] that relies on high-frequency probes to improve resolution and thus provides high-quality images of cardiovascular structures [18]. This technique has been proposed for measuring CO from transmitral, transaortic and transpulmonary flows, especially during intraoperative cardiac function monitoring with discordant conclusions [19–23].

To our knowledge, no study has assessed the value of transmitral TEE CO determination in critically ill mechanically ventilated patients. A subaortic approach has been proposed in such patients [24]. Nevertheless, the visualization of the outflow tract, which is essential for subaortic CO calculation is not easily obtained and is not described in the TEE technique guidelines [18]. Additionally, the authors did not study variations of CO during different therapeutic interventions in such patients. This patient population may be the more likely to benefit from this minimally invasive technique. Indeed, the insertion of a pulmonary artery catheter is not devoid of risk in very unstable patients [3, 4].

A less invasive technique that would give an acceptable estimate of initial CO level and of its variation with therapeutic intervention (fluid or catecholamine infusion, titration of PEEP level, for instance) might make it possible to postpone emergency pulmonary catheterization until the patient's condition has become stable or even to avoid this procedure in certain instances. Such a technique might improve the initial management of very severely ill patients. We report the results of a prospective study conducted in an intensive care unit to compare CO values calculated from transmitral flow measurements obtained using a transesophageal single-plane probe with thermodilution and $C[a\text{-}v]O_2$ measurements. The purpose of this study was not to assess whether Doppler CO determination can replace thermodilution CO determination, but to evaluate whether a clinically relevant estimate of the latter and of its variations in relation to therapeutic intervention is given by TEE. The therapeutic protocol was guided by the hemodynamic and/or respiratory status of each patient.

The two main findings of this study are, first, that Doppler CO measurement correlates well with thermodilution CO measurement but cannot replace it, second, and more importantly, that clinically significant CO changes are adequately detected by TEE. The good correlation between TEE and thermodilution CO determination is in agreement with previous findings obtained in selected perioperative patients using either transthoracic echocardiography [11] or single-plane transesophageal echocardiography [21, 23]. These results differ dramatically from those reported by Muhiudeen et al. [19], who found no significant correlation between Doppler transmitral and thermodilution CO measurements in the operating room. We found a good correlation between CO values determined with thermodilution and with TEE.

This correlation was observed both with pooled CO values during treatments aimed at increasing or decreasing CO and when examining the effect of each therapeutic intervention (dobutamine, fluids, ventilation with PEEP). This indicates that these results are not influenced by the therapeutic method in itself, but by its effects on CO. However, in this study, left ventricular inflow and mitral valve area were not measured at the same level, as advocated by Dittman et al. [25]. These discrepancies emphasize the importance of measuring mitral inflow at the level of the annulus. All the previous studies, and ours, performed using a single-plane probe assumed the mitral annulus to be circular, although it is well-established that it is elliptical [26]. Closer correlations have been found using the elliptical model with transthoracic echocardiography [27] or two-plane TEE [23].

Despite the significant correlation, there were wide limits of agreement between the echocardiographic measurements and thermodilution data, especially when CO measurements of 7.5 l/min or more were not deleted. However, accurate determination of very high ranges of CO is less important than adequate evaluation of lower CO in critically ill patients. It should be pointed out that most previous studies did not calculate the agreement between the two techniques according to the method described by Bland and Altman [9]; this calculation was performed by Ryan et al. [21], who also found a poor agreement (mean ± 2 SD = –0.86 ± 3.3 l/

min). Inaccuracies in Doppler and thermodilution CO measurements might explain the wide limits of agreement between the two techniques. Another possible explanation is that the mitral annulus area was assumed to be constant throughout diastole. However, Miller [14] demonstrated that this simplified procedure is less reliable in patients with heart rates under 70 beats/min; no such cases were observed in our study.

Although thermodilution is the most commonly used approach to CO measurement in clinical practice, errors can occur even when the technique is faultless. Inaccuracies can occur when the thermistor catheter rests against the arterial pulmonary wall or is surrounded by fibrin, when CO is lower than 2.5 l/min, when the central blood temperature varies rapidly or when there is significant tricuspid or pulmonary regurgitation or left-to-right cardiac shunting [28]. Although Doppler and thermodilution data were gathered simultaneously, another potential cause of discrepancies is hemodynamic instability, particularly after the administration of fluids, vasoactive drugs or changes in mechanical ventilation.

This lack of agreement between the two techniques strongly indicates that Doppler CO determination cannot be used in place of thermodilution measurement. As pointed out above, our purpose was not to make such a proposition. On the contrary, the good correlation between the data obtained using the two techniques indicates that Doppler CO determinations provide reasonable and clinically useful estimates of values that would be measured with a thermodilution catheter. In that sense, this technique may be suitable for the initial assessment of the hemodynamic status of a patient. Moreover, the fact that thermodilution CO variations were adequately detected by Doppler, as demonstrated by the good operating characteristics of the latter, suggests that initial therapeutics may be guided by Doppler CO determination, obviating the need for immediate pulmonary catheterization.

Another indirect argument in favor of the clinical usefulness of this technique derives from its good correlation with $C[a\text{-}v]O_2$. In addition, the good positive predictive value for detecting variations in $C[a\text{-}v]O_2$ of 5% or more further confirms that rapid CO variations induced by different therapeutic procedures may be accurately detected using Doppler.

All echocardiographic and Doppler calculations were analyzed off-line, as the average of five cardiac cycles measured at end-expiration. This procedure is not time-consuming for an experienced observer and can be easily performed on-line at the bedside, as is usually done for various area or regurgitation fraction calculations. In our experience, it takes less than 1 min for a trained physician to determine one transmitral CO value using the procedure described above. This is not fundamentally different from the time taken for thermodilution CO determination. The minimal and maximal variations of transesophageal CO values from the average of the five values taken for each set of measurements were about 10%, which is an acceptable range for CO values. Reproducibility of the transesophageal Doppler measurements was good, with interobserver variabilities less than 5% for both transmitral velocity time integral and annulus diameter. The correlation coefficient between the two observers was greater than 0.85 ($p < 0.001$).

Transesophageal echocardiographic determination of CO derived from the transmitral flow is a reproducible method and correlates satisfactorily with thermodilution data. However, wide limits of agreement between Doppler and thermodilution measurements were observed. Nevertheless, comparisons of changes in $C[a\text{-}v]O_2$ suggested that echocardiography may be as accurate as thermodilution for detecting CO variations after therapeutic interventions. This non-invasive method may be helpful for the initial management of patients receiving mechanical ventilation and/or vasoactive drugs in intensive care units. Cardiac output determination using transesophageal echocardiography may be helpful for diagnosis and initial therapeutic management. Insertion of a Swan-Ganz catheter may be performed secondarily, once the patient's hemodynamic status has improved.

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