Inconsistent Esophageal Doppler Cardiac Output During Acute Blood Loss

Gagan D. Kamal, F.F.A.R.C.S., D.E.A.A.,* Tommy Symreng M.D., Ph.D.,† James Starr, B.S.‡

Application of the Doppler principle can provide relatively non-invasive and continuous measurement of cardiac output. However, it is based on certain assumptions that may introduce error. Esophageal Doppler cardiac output was compared with Fick cardiac output during acute blood loss (35–45% estimated blood volume) in eight anesthetized pigs. Mean Fick cardiac output decreased from 4.8 to 1.9 l/min, mean Doppler cardiac output from 4.9 to 2.9 l/min. This was accompanied by a decrease in mean arterial pressure from 119 to 55 mmHg and increase in heart rate from a mean of 115 to 156 beats/min. There was an inconsistent association between the two methods both within and between individual animals. Cubic polynomial regression equations of cardiac output with time indicated small measurement error in Fick (R^2: mean 0.93, range 0.99–0.75) as opposed to Doppler (R^2: mean 0.67, range 0.93–0.16) cardiac output. In one animal Doppler cardiac output showed an increase with time and in one the Doppler cardiac output measurements were unrelated to time. There was highly variable association comparing Fick *versus* Doppler cardiac output with correlations ranging from −0.76 to 0.98. A sign test for mean differences indicated that Doppler derived cardiac output was higher than Fick cardiac output, and the chance of this occurring if the true difference was zero was less than 1 in 1,000. A test for homogeneity of correlations was also rejected. Inaccuracies in individual assumptions in the computation of esophageal Doppler cardiac output, especially unaccounted changes in aortic diameter, are responsible for the inconsistent and unpredictable values of Doppler cardiac output obtained in this experimental model of hemorrhage. (Key words: Measurement technique: esophageal Doppler; Fick. Monitoring: cardiac output.)

APPLICATION of the Doppler principle in the computation of cardiac output (CO) has the potential of providing relatively noninvasive, on-line or near-continuous quantification of CO, an important parameter in any acute care situation.[1–5] Flow is computed by measuring the velocity of fluid flowing through a cylinder of known cross-sectional area. Calculated velocity is the Doppler frequency shift in an ultrasound beam reflected by the erythrocytes measured over the ejection interval.

The calculation of Doppler derived stroke volume is based on certain assumptions: a flat velocity profile, laminar blood flow, a known angle between the Doppler beam and the blood velocity vectors, and a circular aorta of known cross-sectional area. Although it is recognized that these assumptions may not be accurate, many studies have contended that errors so introduced are minimal, citing good overall correlation and agreement with cardiac output measured by other methods.[6] Despite contradictory results in the literature, it has been suggested that Doppler CO can be legitimately used to quantify relative changes in CO, *i.e.*, as a trending device.[7]

Early techniques of Doppler CO required repeated measurement with a suprasternal probe. The ultrasound crystal has since been incorporated on an esophageal probe,[1] an endotracheal tube,[8,9] and a pulmonary artery catheter.[10] Although this has enabled more practical and continuous CO measurement, it has also added potential inaccuracies and problems unique to each method.

With few exceptions,§ most previously reported studies have compared Doppler CO with intermittent CO techniques. This makes it difficult to critically evaluate a relatively continuous method, especially as a trending device. To examine the usefulness of esophageal Doppler as a measure for absolute CO and as a trending device, we designed a protocol in which esophageal Doppler CO (DCO) was continually measured, simultaneously with Fick CO (FCO), another method of continuous CO measurement. We used anesthetized swine, made acutely hypovolemic by hemorrhage.

Materials and Methods

In a protocol approved by the Institutional Animal Care and Use Committee, eight Yorkshire swine, 35–45 kg, were anesthetized with im ketamine (17 mg/kg). Anesthesia was maintained with an infusion of ketamine (5 mg·kg^{-1}·h^{-1}) and fentanyl (40 μg·kg^{-1}·h^{-1}). Muscle relaxation was obtained with an infusion of succinylcholine (250 mg/h). The animals were supine and their lungs were ventilated *via* a tracheostomy to maintain normocarbia. FI_{O_2} was titrated to keep Sa_{O_2} above 92% without any positive end-expiratory pressure.

Our Fick methodology used oxygen as the indicator for CO calculations (FCO = oxygen consumption/[arterial oxygen content-mixed venous oxygen content]).[11,12] Fiberoptic catheters (Oximetrix, Mountain View, California) were inserted in the carotid and pulmonary arteries for continuous *in vivo* arterial and mixed venous hemo-

§ Siegel LC, Shafer SL, Martinez GM, Ream AK, Scott JC: Simultaneous measurement of cardiac output by thermodilution, esophageal Doppler, and electrical impedance in anesthetized patients. J Cardiothorac Anesth 2:590–595, 1988

globin saturation (Sa_{O_2} and $S\bar{v}_{O_2}$, respectively) and systemic and pulmonary artery blood pressure measurement. Sa_{O_2} and $S\bar{v}_{O_2}$ values along with hemoglobin concentration and oxygen tension (P_{O_2}) were used to calculate arterial and mixed venous oxygen contents. Fiberoptically determined saturations were checked every 10 min against saturations obtained on a co-oximeter (IL 282, Instrumentation Laboratories, Lexington, Massachusetts). The catheters were recalibrated for a difference of $\geq 4\%$. A metabolic gas monitor (MGM II, Utah Medical, Midvale, Utah) was used for continuous measurement of inspired and expired respiratory gas volumes and concentrations for calculation of oxygen consumption ($\dot{V}_{O_2}$). Before each experiment the sensors were calibrated against a standard reference gas, and the flow transducers checked with a calibration syringe. All the data were transmitted into a microcomputer programmed to calculate and display FCO every 20 s. Hemoglobin concentration and arterial CO_2 tension were entered manually.

DCO was measured by an esophageal probe (Accucom, Datascope, Paramus, New Jersey; Software version 3.07) designed to average CO over 12 consecutive heart beats and display the value every 15 s. Gauging signal quality is essentially subjective, based on a combination of sights and sounds. An optimum signal is attained combining Doppler sounds, digital signal level, heart rate, ejection time, and visual transducer positioning. With adequate Doppler signal amplitudes, signal level calculations are synchronized with heart rate.

After stable baselines were established, DCO was calibrated against FCO. At least 5 min were allowed to ensure that the two values continued to be in agreement. After this time exsanguination was begun by withdrawing blood from a femoral arterial catheter at a constant rate (30 ml/min) over 40 min, using a variable speed roller pump (Cole-Parmer, Chicago, Illinois). During exsanguination no attempt was made to recalibrate the DCO or reposition the probe. FCO and DCO were recorded once every minute, disregarding any obviously artifactual values either indicated by advisories on the Accucom, or when the heart rate was greater than 200 beats/min.

Correlations between heart rate, mean arterial blood pressure (MAP), and blood loss *versus* FCO and DCO were calculated. Because of the physiologic ability of the animals to compensate for blood loss, the relationship of cardiac output to time was not linear. This indicated a polynomial regression for analyzing the data. Data analysis carried out separately for each animal indicated that cubic polynomials best described the change of DCO and FCO with time. R^2 of both cardiac outputs with time and simple linear regression of FCO with DCO were obtained. Cubic regression equations for DCO and FCO were plotted and a sign test done on the mean differences between FCO and DCO.

Results

The esophageal Doppler probe was relatively easy to position. Because the animals were anesthetized and paralyzed, there was no subject movement. After induction of anesthesia and insertion of catheters and probes, at least 1 h of hemodynamic stability was ensured before the study was begun and data collected.

Two hundred sixty-eight pairs of simultaneous measurements of FCO and DCO were obtained in the eight pigs. There were nine temporary interruptions in DCO, all of which reverted to the normal monitoring mode without any manipulations or adjustments. The fiberoptic catheters required recalibration a total of four times; at 17 min of bleeding in animal 4, 15 min and 30 min in animal 5, and 37 min in animal 8. Heart rate exceeded 200 in one animal (4) for 6 min.

Total blood loss was 1.2 l (35–45% of estimated total blood volume). Mean FCO decreased from 4.8 (range 2.7–6.8) to 1.9 (1.0–3.6) l/min, and mean DCO decreased from 4.9 (range 2.4–8) to 2.9 (0.8–3.6) l/min (fig. 1). Blood withdrawal was accompanied by a progressive decrease in MAP from a mean of 119 to 55 mmHg and increase in heart rate from 115 to 156 beats/min.

FCO had a strong correlation with changes in MAP ($r = 0.98$), heart rate ($r = -0.88$), and blood loss ($r = -0.96$). Correlations between DCO and MAP ($r = 0.58$), heart rate ($r = -0.61$), and blood loss ($r = -0.57$) were much weaker.

R^2 values for cubic regressions of FCO with time were high (table 1). The regression equations explained at least 90% of the variability in CO in all but two animals and 75% or more in all eight. Using FCO, change in CO with time was statistically predictable.

Similar analysis for DCO showed less consistent results (table 1). R^2 was less than 0.7 for five animals. In one (animal 5) DCO showed an increase with relatively high
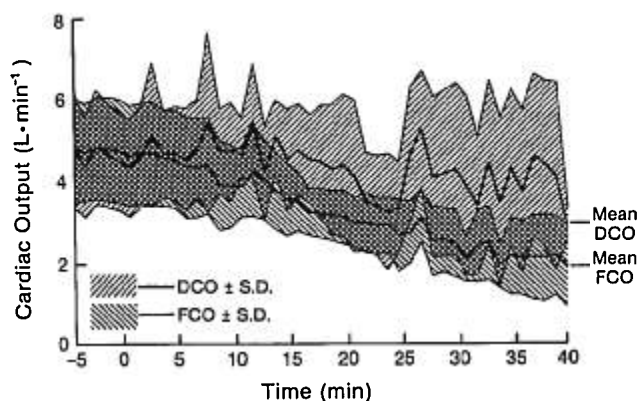

Fig. 1. Cardiac output from 5 min prior to and through hemorrhage (mean ± SD).

TABLE 1. R^2 for Cubic Polynomial Regressions with Time
and Pearson Correlations of FCO with DCO

Animal No.	R^2 FCO	R^2 DCO	Correlation FCO with DCO
1	0.95	0.91	0.93
2	0.96	0.64	0.48
3	0.93	0.68	0.78
4	0.99	0.43	0.46
5	0.87	0.86	−0.76
6	0.98	0.71	0.81
7	0.98	0.93	0.98
8	0.75	0.16	−0.02

predictability (R^2 = 0.86), and in another (animal 8) DCO measurements were unrelated to time (R^2 = 0.16).

There was highly variable association comparing DCO *versus* FCO for each individual animal. Examination of the curves shows that there was no consistent pattern (fig. 2). Simple linear correlations for DCO with FCO ranged from −0.76 to 0.98 (table 1). In animal 5 DCO indicated an increase, and in animal 8 there was no correlation.

Calculating mean differences for each animal, DCO was higher than FCO in all eight animals (table 2). The chances of this occurring if the true difference was zero are less than 1 in 1,000. A test for homogeneity of the correlations, *i.e.*, that the eight correlations represented a random sample of correlations from a population with a single correlation, was also rejected (chi-square = 200.9, $P < 0.0001$).

Discussion

We hypothesized that blood loss would be associated with systematic changes that should be measured with equal accuracy and precision by both FCO and DCO.

R^2 values (table 1) near one indicate a good fit and little deviation between observed and predicted measurements. A good fit suggests consistent changes and small measurement errors. If, as the FCO measurement suggests, there was a systematic decrease in CO with time, DCO measured this change with little precision.

If DCO can be used as a surrogate for FCO, it should closely reflect changes in FCO and the amount of variability in the measurements should be of comparable order. It is not necessary that the two curves overlap, but it is necessary that they have a similar shape and be relatively parallel. In four of the eight animals (fig. 2) this was not the case. The large standard deviations of the mean differences (table 2) indicate that the relationship between FCO and DCO, both between and within individual animals, cannot be described with any accuracy by a single equation. The test for homogeneity of the correlations also implies that the magnitude of the correlations depends on subject, and there is no meaningful
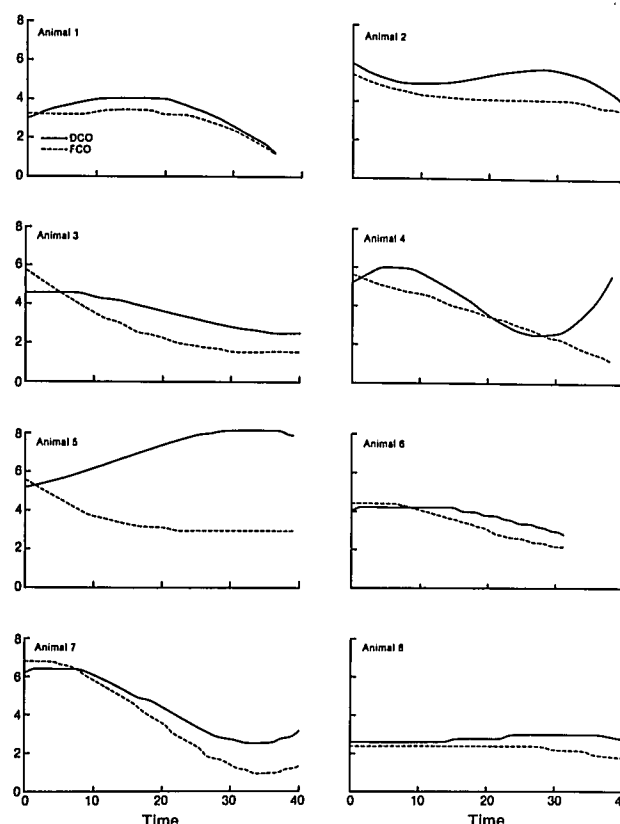

FIG. 2. Cardiac outputs for each animal during hemorrhage. Time (min) on abscissa, cardiac output (l/min) on ordinate.

overall estimate of the underlying correlation between FCO and DCO.

Validity of Doppler derived CO is based on the accuracy of individual assumptions in its computation. Each of these (flat velocity profile, a measurable or small angle of incidence between the Doppler beam and the direction of blood flow, laminar flow at the point of velocity measurement, circular aorta with an accurately measurable diameter) can potentially introduce an error of 5–20%.[6]

TABLE 2. Means and SD (l/min) of Differences*
Between DCO and FCO for Each Animal

Animal No.	Pairs of Measurement (n)	Mean Difference	SD
1	27	0.41	0.36
2	38	0.96	0.51
3	40	0.87	0.85
4	37	0.83	1.73
5	32	3.43	1.93
6	29	0.42	0.49
7	33	0.69	0.81
8	32	0.47	0.57

* Difference (DCO − FCO).

Esophageal placement of the ultrasound crystal for CO measurement has added two further limitations to the reliability and accuracy of the technique: 1) blood velocity is measured in the descending aorta, which assumes a constant ratio of descending aortic to total flow; and 2) aortic diameter is not measured at the point of velocity measurement.

The ratio of ascending to descending aortic flow is described by a constant proportionality factor derived during calibration with CO measured in the ascending aorta.[3] The aorta is asymmetrically curved in three directions and progressively tapers, cross-sectional area decreasing about 50% from the ascending to the descending portion of the aortic arch.[13] Because DCO is measured in the descending aorta, an unaccounted change in this factor will result in error in DCO measured in the descending aorta.

Aortic diameter is probably the most important single determinant of Doppler CO.[14,15] Errors in measurement of aortic diameter are magnified because the square of the diameter is integrated into the calculated CO.[16] Lucas et al.[14] have shown that a 1 mm difference in diameter can result in a 12.4% change in calculated CO. It is well established that aortic diameter changes during the cardiac cycle,[17,18] and with pressure, the relationship being almost linear.[17–20]

The angle between the ultrasound beam and the direction of blood flow can only be estimated. In the vast majority of cases an angle of 20–25° can regularly be achieved producing less than 10% error in calculated cardiac output.[6] Although significant error may be introduced, if this angle is large and uncorrected, this is likely to occur when using the suprasternal notch for velocity measurements.[6] With our experimental design we could not quantify effects due to variations in descending aortic diameter.

The level of operator skill and experience can affect the accuracy of data acquisition.[3] We have used the Accucom monitor extensively in humans and in pigs for 3 years and believe this was not an important variable in this study.

In commercially available esophageal Doppler monitors aortic diameter is not measured. Diameter is derived, or a "known" diameter can be entered. Because there is wide variation in the normal population,[21,22] this might introduce further error in computed DCO. A recently described method, transtracheal Doppler CO,[8,9] measures Doppler frequency shift in the ascending aorta and the ascending aortic diameter. This offers obvious advantages, but its accuracy and trending capability remain to be critically evaluated.

The degree of error introduced by inaccuracies in assumptions in computation of DCO is believed to be small, partly because some negate each other.[6] However, it is entirely conceivable that these inaccuracies may be additive or interact in some other fashion. This is more likely when there are dynamic changes in relevant cardiovascular parameters (changing aortic diameter and profile, tachycardia, turbulent blood flow)[15,16] as in our hemorrhaged pigs. We believe that the large variation of FCO and DCO within as well as between individual animals, and the relatively greater noise and lack of consistency in DCO measurement can be explained by the above. Careful examination of measured variables (heart rate, blood pressure, blood loss) revealed no identifiable association with variations in DCO. This was also true for animals 5 and 8. Decreasing aortic diameter with decreasing pressure would account for DCO being consistently higher than FCO.

The anatomic relationships of the esophagus and descending thoracic aorta of the pig are the same as humans,[23] making it a good model for evaluation of DCO. Compared with older subject humans, relatively compliant aortas in the young animals studied might have greater change in size with changing pressure.[24] Greenfield and Patel, however, found no relation between age and circumferential expansibility of the aorta.[17]

True CO is impossible to measure in any practical way. In the quantification of such a parameter, indirect methods have to be used and a new method is evaluated by comparison with an established one.[25] LaMantia and Barash have suggested the choice of an appropriate "gold standard," appropriate use of the technology, and inappropriate statistical methods as factors that might explain conflicting results in the literature, comparing Doppler derived CO with other methods.¶

The derived value of FCO will be as accurate as are measurements of the individual components of the Fick equation ($\dot{V}_{O_2}$, Sa_{O_2}, $S\bar{v}_{O_2}$, Hgb).[11,12] Increasing FI_{O_2} can produce error in the $\dot{V}_{O_2}$ measurement, but this is not expected in the range used in our experiments (0.21–0.35). Fiberoptically derived saturations have been shown to compare favorably with those measured using bench oximetry.[26,27] Because FCO essentially measures pulmonary blood flow, there is error due to oxygen consumption by the lung, estimated to be 1–4%.[11] A theoretical standard deviation of 0.68 l/min has been predicted for FCO.[12] In our experimental animals, changing hemoglobin might be expected to introduce inaccuracy. However, in any given minute (epoch) of measurement, difference in arterial and mixed venous hemoglobin and oxygen content, is expected to be negligible.[28] Accuracy of FCO increases in low flow states when there is a large arteriovenous oxygen difference.[12]

¶ LaMantia KR, Barash PG: Cardiac output: Measurement of the future or relic of the past? (Editorial). J Cardiothorac Anesth 2:587–589, 1988

Although thermodilution CO is subject to many errors, it is the clinical gold standard. In earlier experiments we had measured thermodilution CO along with FCO and DCO. Injection of saline introduced a qualitative and quantitative artifact in FCO and DCO. Because the triplicate injections resulted in loss of considerable data during the hemorrhage and negated our primary goal of comparing two relatively continuous CO methods, we did not include thermodilution CO in our protocol.

In conclusion, we found DCO to have a highly variable association with FCO in this model of acute blood loss. Compared with FCO there was significant variability within as well as between animals. There was considerable noise in the DCO measurement, often with no apparent relation to expected or predicted CO. These inconsistencies could not be predicted or explained by a calibration error or any single identifiable variable. More disturbing, during hemorrhage the esophageal Doppler often indicated an increase in CO in the face of ongoing blood loss, decreasing blood volume and arterial pressure, and decreasing FCO. In a perioperative or critical care situation, this could result in inappropriate therapeutic decisions to the detriment of the patient.

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