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Cardiac Output Determination Using A Widely Available Direct Continuous Oxygen Consumption Measuring Device: A Practical Way To Get Back To The Gold Standard

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Abstract

Background—Accurate assessment of cardiac output (CO) is essential for the hemodynamic assessment of valvular heart disease. Estimation of oxygen consumption (VO₂) and Thermodilution (TD) is employed in many cardiac catheterization laboratories (CCL) given the historically cumbersome nature of direct continuous VO₂ measurement, the “gold standard” for this technique. A portable facemask device simplifies the direct continuous measurement of VO₂, allowing for relatively rapid and continuous assessment of CO.

Methods and Materials—Thirty consecutive patients undergoing right heart catheterization had simultaneous determination of CO by both direct continuous and assumed VO₂ and TD.

Assessments were only made when a plateau of VO₂ had occurred. All measurements of direct continuous and assumed VO₂, as well as, TD CO were obtained in triplicate.

Results—Direct continuous VO₂ CO and assumed VO₂ CO correlated poorly (R= 0.57; ICC =0.59). Direct continuous VO₂ CO and TD CO also correlated poorly (R= 0.51; ICC=0.60). Repeated direct continuous VO₂ CO measurements were extremely correlated and reproducible [(R=0.93; ICC=0.96) suggesting that this was the most reliable measurement of CO.

Conclusions—CO calculated from direct continuous VO₂ measurement varies substantially from both assumed VO₂ and TD based CO, which are widely used in most CCL. These

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differences may significantly impact the CO measurements. Furthermore, continuous, rather than average, measurement of VO₂ appears to give highly reproducible results.

Keywords

Direct continuous Oxygen Consumption; Assumed Oxygen Consumption; Thermodilution; Cardiac Output

Introduction

Cardiac output (CO) is an important parameter of cardiac performance, an accurate assessment of which is an important function of cardiac catheterization laboratories (CCL). (1) This is especially true in valvular disorders, e.g. in patients with equivocal echo findings where aortic valve area must be calculated for suspected aortic stenosis (AS). (2) A precise measurement of CO and consequently the degree of AS severity is crucial to ensure that only appropriate patients are referred for valve replacement and to prevent both premature or inappropriately delayed aortic valve replacement. (3)

A widely used CO method is the Fick equation, in which the total uptake or release of a substance, such as oxygen, by an organ is the product of the blood flow through the organ and the arteriovenous concentration difference of the substance. (4) When oxygen consumption is directly measured, this is called direct oxygen consumption (Direct, VO₂) and is widely considered the gold standard for CO measurement. Alternatively CO can be calculated using estimated VO₂.

Historically VO₂ was directly measured using a Douglas bag over many minutes, a cumbersome affair. Therefore an estimation of VO₂ is used instead in many CCL, with VO₂ values typically estimated from tables or published predictive equations. (5-8) Reliability and use of predictive equations for CO measurement have been questioned in the CCL setting because of large discrepancies between measured and estimated values, (9-11) which of course have an influence on subsequent hemodynamic and valve area calculations. (12, 13)

Portable devices are available that measure breath-by-breath oxygen and carbon dioxide levels using a facemask and provide direct continuous VO₂ measurements (Figure 1). These devices are well validated to produce very reliable VO₂ assessment similar to those assessed by Douglas bag while being less cumbersome to patients and staff. (14) Importantly, VO₂ can vary during the course of a catheterization. We hypothesized that measuring CO at a time when the VO₂ was not only stable but precisely known (i.e., not an average over time) might give the most reliable calculations of aortic valvular dimensions. We investigated the correlation of the CO based on direct continuous VO₂ measurement by this device to the more commonly used techniques of estimated VO₂ and thermodilution CO. (15, 16).

Methods And Materials

This study was approved by the institutional review board (IRB) of Christiana Care Health System. Thirty patients scheduled for right and left heart catheterization were included in the

study. Catheterization was performed in the usual fashion including measurement of right and left sided pressures. Intravenous midazolam and fentanyl was given to patients as needed. Patients were not placed on supplemental oxygen.

In order to measure VO₂ directly and continuously, patients wore a fitted facemask with an airtight seal over the nose and mouth, which was connected to Ultima Cardio₂ breathing analyzer (Medgraphics, St. Paul, Minnesota) The device allows comparison of inspired and expired air to determine VO₂. To minimize the time of mask use, it was placed only after all catheters were in place for pressure measurements. After a baseline of at least 3 minutes to assure patient comfort and a steady-state VO₂, immediate measurements of femoral artery and pulmonary artery saturations were obtained in triplicate, immediately followed by three thermodilution CO measurements. We could complete these measurements in approximately 90-120 seconds. This process was repeated again after 3 minutes after a new steady-state VO₂ was confirmed in the same manner to get a second set of values. We waited until the continuous VO₂ was relatively stable (Figure 1) before performing the CO determinations in triplicate. If the VO₂ became variable subsequently, we waited for a return of a relatively stable VO₂ before performing the repeat CO determinations (Figure 1). Oxygen consumption was measured continuously for these 2 minutes with the mean VO₂ over that time period used for analysis.

The cardiac output can be assessed in the fick methods utilizing this equation:

$$\text{Cardiac Output} = \frac{\text{Oxygen Consumption}}{\text{A-VO}_2 \text{ Difference}}$$

A-VO₂ difference is the difference in the arterial and venous oxygen blood content. Oxygen blood content can be assessed using this equation:

$$\text{Oxygen blood content} = \text{Oxygen saturation} \times 1.36 \times \text{Hemoglobin (g/dl)}$$

While direct VO₂ was assessed as described above, estimated fick calculation oxygen consumption was assessed using this equation:

$$\text{O}_2 \text{ consumption} = 3\text{ml O}_2 \times \text{weight (Kg)}$$

All patients save one had suitable VO₂ tracings for these measurements. This one patient had unreliable VO₂ tracings due to Cheyne-Stokes respiration. The three values from each cardiac output method were averaged, and those values were compared. Another separate set of direct continuous VO₂, assumed VO₂ and TD CO was then repeated, after steady-state VO₂ was confirmed, to be used as a validation of reproducibility of CO and AVA. The Phillips (XIMS, Phillips Xper Connect, Melbourne, FL) system is in use at our CCL.

Statistics

Correlation of direct continuous VO₂, assumed VO₂ and TD based CO measurements were assessed by linear regression analysis and by variance component analysis. The Pearson

correlation (r) derived from linear regression, assesses the rank ordering of variable values whereas the intra-class correlation (ICC), derived from variance component analysis assesses the degree of agreement between variable values. The ICC is the appropriate statistic for assessing agreement between tests purporting to measure the same thing on the same scale of measurement. The ICC ranges between 0, indicating no agreement, and 1, indicating perfect agreement. Scatter plots of the paired fick and TD based CO variables included the regression line as well as a 45 degree line of equality along which the paired variables would lie if there was perfect agreement between echo-cath measurements (as would the regression line). Bland-Altman plots were also constructed as complementary assessments of different CO measurements.

Results

The baseline characteristics of the 30 patients included in the study patients are displayed in table-1. Direct continuously measured VO₂ CO and estimated VO₂ CO calculations correlated poorly (Figure 2A, $R=0.57$; $ICC=0.59$). Direct continuously measured VO₂ CO and thermodilution CO calculations correlated poorly as well (Figure 2B, $R=0.51$; $ICC=0.60$).

Using a constant assumed VO₂ value led to a large discrepancy in repeated CO measurement during the case (Figure 3A, $R=0.62$; $ICC=0.57$). Repeated TD CO was associated with less discrepancy (Figure 3B, $R=0.78$; $ICC=0.84$). Although direct continuously measured VO₂ changed at times during the course of a procedure, requiring a pause to await a relatively stable value in approximately 1/5 of patients, (although measurements were only made when a steady state was achieved), the resulting repeated CO measurements were closely correlated (Figure 3C, $R=0.93$; $ICC=0.96$) (Table 2).

Discussion

CO calculated by direct continuous VO₂ measurement differs significantly from those based on estimated VO₂ values and thermodilution. The superb reproducibility of CO using this direct continuous VO₂ technique suggests this is the superior CO technique. Although direct VO₂ based CO was felt to be the gold standard historically, cumbersome measurement techniques led to the adoption of the estimated VO₂ determination.⁽⁹⁾ However, many CCL computer systems, including our widely used software program (Phillips Xper, Melbourne FL) make an assumption of a patient's VO₂ based on an equation developed by LaFarge and Miettinen.⁽⁵⁾ This equation was developed with regression analysis using patients aged 3-40 years with congenital heart disease and an average age of 12 years.⁽⁵⁾ The authors themselves recommended against using this equation for patients older than 40 years of age.⁽⁵⁾ Unfortunately using the assumed Fick calculation in patients older than 40 years of age, as were all our patients, can have a significant impact on the validity of the hemodynamic assessment. Even if the estimated VO₂ had a better theoretical underpinning, the variations in direct continuously measured VO₂ occasionally seen during catheterizations would make a single static estimation of VO₂ inaccurate. The large variability in repeated calculated CO using a static value suggests that changes in actual VO₂ during the procedure is a contributing factor. And, of course, any difference in the CO measurement will have a direct

continuous linear effect on the valve area calculation, i.e., a 25% difference in CO measurement will alter the valve area by 25%. At least a 25 % variation in CO was seen in 56% of measurements with both assumed VO₂ and TD when compared to direct continuous VO₂. (11, 13) Similarly Chase et al showed that the rate of 25% error in the equations by LaFarge and Miettinen, Dehmer et al, and Bergstra et al occurred in 11%, 23%, and 45% of patients, respectively. Misclassification of cardiac index derived from each equation for 2 clinically important classifications: cardiogenic shock-21%, 23%, and 32% and hypoperfusion-16%, 16%, and 25%; respectively. (17) Recent studies have showed that the correlation of direct continuous VO₂ and assumed VO₂ derived cardiac output was not impressive even in children. In both of these studies the direct VO₂ was assessed utilizing devices while children underwent general anesthesia, techniques not readily available to adult cardiologists. (18, 19)

Comparisons of CO determination using estimated and direct measured values have previously differed in patients undergoing cardiac catheterization.(9-13, 18-23) In a recent study, Narang et al compared direct VO₂ CO calculated as an average over time using Douglas bags to different formulas of estimated VO₂ CO. The direct and estimated VO₂ CO values differed by >25% in 17% to 25% of patients depending on the formula used. (11) demonstrated Gertz et al, using a facemask device, recently showed that estimates of VO₂ using of the LaFarge formula significantly underestimated CO and hence underestimated AVA, resulting in a high rate of misclassification of AS severity. (3) In their study the difference in calculated valve area in patients with aortic stenosis between using Lafarge table and measured VO₂ was as much as 0.5cm². (3) In our study we found instances where the CO was both under- and over-estimated by the assumed Fick technique.

The other commonly used CO method is thermodilution. TD Technique can show variability in measurement and therefore is not reliable in the setting of many underlying cardiac abnormalities especially tricuspid regurgitation and atrial fibrillation. (24, 25) Despite these limitations, it is still probably more reliable than estimated Fick in those without significant tricuspid regurgitation and/or atrial fibrillation. (3) We found this technique to be reproducible but CO values did not correlate well with direct continuous VO₂.

We used a device that allows an easy reproducible way to measure direct continuous VO₂. The patient wears a full-face mask that is connected via tubing to the actual metabolic cart for collection of data. The patient does not need to be intubated or heavily sedated while undergoing the procedure. VO₂ assessed using metabolic cart has been validated versus those assessed by Douglas bag and was found to give extremely high correlating values (R= 0.99). (14) Both the American Thoracic Society (ATS) and European Respiratory Society (ERS) approve the use of the device, and it is already used routinely during cardiopulmonary testing in many hospitals, as was ours. In our experience, the device is easy to use and the measurements did not cause a significant increase to the procedural time, since the VO₂ measurements may be taken very quickly once all catheters are in place. The fact that all measurements of the CO equation (VO₂ and blood saturations) can be done at exactly the same time may be important, as both of these parameters can change during a procedure (Figure 1B). The accuracy and ease of the use of this device, the availability of this device in most hospitals and the lack of need for general anesthesia and intubation make it practical to

use especially when making decisions about advanced heart failure therapies or valvular surgery.

This study has several limitations. First, it included only a small number of patients. Second; we often used mild sedation, which may affect VO₂ or depress cardiac output. Third, although a reflection of clinical practice, our study included patients with significant tricuspid regurgitation, which may be responsible for underestimation of CO by TD (24, 25). Finally, some patients may be unable to carry out this test if they develop discomfort from wearing the mask or develop anxiety from a sense of claustrophobia, (although all of our patients, were able to tolerate the mask for the duration of the procedure).

Conclusion

Cardiac output calculated from direct continuously measured VO₂ varies substantially from those based on assumed VO₂ values and thermodilution, which are the default methods used in most CCL. Direct continuously measured VO₂-derived CO gives highly reproducible valve area measurements and may be more accurate.

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Figure- 1.

Sample tracings of direct VO2: A- Sample tracings of stable direct VO2, B-Sample tracings of unstable direct VO2, short lines indicate relatively stable times when hemodynamic assessments were done. (VO2 is the upper curve in both tracings. The other curve is VCO2)

Figure-2.

Correlation of CO based on direct continuous VO₂, assumed VO₂ and TD. A-Correlation of direct continuously measured VO₂ CO with assumed VO₂ CO. B-Correlation of direct, continuously measured VO₂ CO With TD CO.

Figure- 3.

Correlation of Repeated CO. A- Repeated Assumed Fick CO. B- Repeated TD CO. C- Repeated direct continuous VO2 CO.

Table-1

Baseline Characteristics of Consecutive Patients:

Characteristics:	N=30
Age (mean)	73 (52-88)
Males	68%
Coronary artery disease.	64%
Hypertension	100%
Diabetes	32%
Cardiomyopathy	55%
Valvular Heart disease	83%
Mild tricuspid regurgitation	65%
Moderate or Severe tricuspid regurgitation	10%
Mild Pulmonary Hypertension	62%
Moderate to severe Pulmonary Hypertension	11%
Atrial fibrillation	50%
Peripheral arterial Disease	14%

Table-2

Cath Lab Measurements of Consecutive Patients:

Patient Number	Mean Direct VO2 CO	Mean Assumed VO2 CO	Mean TD VO2 CO	Mean Pulmonary Artery Saturation	Mean Aortic Artery Saturation	Direct VO2	Assumed VO2
1	5.54	4.84	6.36	57%	91%	315	275
2	6.59	5.72	6.30	56%	92%	345	293
3	6.51	5.84	5.95	62%	92%	350	313
4	7.53	5.62	5.71	66%	93%	420	314
5	3.43	4.88	4.25	67%	94%	202	243
6	4.95	5.41	5.61	59%	85%	240	283
7	3.26	5.61	5.82	57%	87%	170	280
8	3.18	4.89	4.50	63%	91%	170	266
9	3.86	4.37	4.32	54%	86%	216	243
10	3.61	3.99	3.81	52%	88%	220	244
11	2.48	3.16	3.39	41%	89%	170	217
12	4.28	6.35	6.65	59%	89%	165	243
13	2.14	4.0	3.39	60%	95%	120	225
14	1.78	4.2	3.62	62%	94%	100	227
15	4.55	7.30	7.05	67%	93%	190	304
16	3.39	4.19	4.72	65%	93%	160	271
17	1.72	2.64	2.18	50%	98%	158	243
18	1.81	3.25	1.9	44%	88%	135	245
19	5.1	5.85	4.69	46%	85%	269	308
20	5.54	7.10	7.33	74%	94%	190	243
21	3.39	2.96	4.18	42%	94%	335	275
22	4.31	5.2	4.62	70%	93%	217	262
23	5.31	2.57	2.71	63%	93%	255	180
24	7.19	7.83	6.65	64%	97%	279	257
25	3.68	5.31	5.43	63%	94%	190	273
26	2.58	4.80	5.52	66%	93%	142	261
27	4.04	3.36	3.45	40%	88%	240	200
28	5.82	3.56	4.66	68%	96%	280	210
29	5.74	6.23	6.53	51%	89%	260	282
30	6.31	5.82	7.01	65%	91%	310	286