Comparison of Estimations Versus Measured Oxygen Consumption at Rest in Patients With Heart Failure and Reduced Ejection Fraction Who Underwent Right-Sided Heart Catheterization

By: Paul J. Chase,* Paul G. Davis, Laurie Wideman, Joseph W. Starnes, Mark R. Schulz, Daniel R. Bensimhon

Chase, P., Davis, P., Wideman, L., Starnes, J., Schulz, M. R., (2015). "Comparison of Estimations versus Measured Resting Oxygen Consumption in Patients with Heart Failure and Reduced Ejection Fraction Undergoing Right Sided Heart Catheterization". *American Journal of Cardiology*. 116(11), 1724-1730.

Abstract:

Cardiac output during right-sided heart catheterization is an important variable for patient selection of advanced therapies (cardiac transplantation and left ventricular assist device implantation). The Fick method to determine cardiac output is commonly used and typically uses estimated oxygen consumption (VO_2) from 1 of 3 published empirical formulas. However, these estimation equations have not been validated in patients with heart failure and reduced ejection fraction (HFrEF). The objectives of the present study were to determine the accuracy of 3 equations for estimating VO_2 compared with direct measurement of VO_2 and determine the extent clinically significant error occurred in calculating cardiac output of patients with HFrEF. Breath-by-breath measurements of VO_2 from 44 patients who underwent cardiac catheterization (66% men; age, 65 ± 11 years, left ventricular ejection fraction, 22 ± 6%) were compared with the derived estimations of LaFarge and Miettinen, Dehmer et al, and Bergstra et al. Single-sample *t*tests found only the mean difference between the estimation of LaFarge and Miettinen and the measured VO_2 to be nonsignificant (−10.3 ml/min ± 6.2 SE, p = 0.053). Bland-Altman plots demonstrated unacceptably large limits of agreement for all equations. 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. In conclusion, these findings do not support the use of these empiric formulas to estimate the VO_2 at rest in patients with HFrEF who underwent right-sided heart catheterization.

Keywords: cardiac catheterization | heart failure | reduced ejection fraction

Article:

Cardiac output during right-sided heart catheterization is an important variable for patient selection of advanced therapies (cardiac transplantation and left ventricular assist device implantation). The Fick method to determine cardiac output is commonly used and typically uses estimated oxygen consumption (VO_2) from 1 of 3 published empirical formulas. However, these estimation equations have not been validated in patients with heart failure and reduced ejection fraction (HFrEF). The objectives of the present study were to determine the accuracy of 3 equations for estimating VO_2 compared with direct measurement of VO_2 and determine the extent clinically significant error occurred in calculating cardiac output of patients with HFrEF. Breath-by-breath measurements of VO_2 from 44 patients who underwent cardiac catheterization (66% men; age, 65 ± 11 years, left ventricular ejection fraction, 22 ± 6%) were compared with the derived estimations of LaFarge and Miettinen, Dehmer et al, and Bergstra et al. Single-sample *t*tests found only the mean difference between the estimation of LaFarge and Miettinen and the measured VO_2 to be nonsignificant (−10.3 ml/min ± 6.2 SE, p = 0.053). Bland-Altman plots demonstrated unacceptably large limits of agreement for all equations. 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. In conclusion, these findings do not support the use of these empiric formulas to estimate the VO_2 at rest in patients with HFrEF who underwent right-sided heart catheterization.

It is standard practice to use the Fick method to estimate cardiac output in patients with heart failure and reduced ejection fraction (HFrEF).[1 and 2] Using the Fick method requires the input of oxygen consumption (VO_2) at rest but rather than measuring it directly, it is common practice to estimate VO_2 at rest using 1 of 3 equations.[3] All these assume a constant VO_2 at rest based on a set of patient characteristics: body surface area (BSA),[4, 5 and 6] age,[4 and 6] gender,[4 and 6] and heart rate.[4] Despite their wide use in patients with HFrEF, these equations have not been well validated in this patient group. Therefore, the purpose of this study was to measure VO_2 at rest in adult patients with HFrEF during right-sided heart catheterization procedures, investigate the accuracy of 3 widely used equations for the estimation of VO_2 at rest compared with direct breath-by-breath measurement, and determine to what extent clinically significant errors occur when using estimation equations.

METHODS

This study was conducted in conjunction with the Cone Health Advanced Heart Failure Program, the cardiac catheterization laboratory at Moses H. Cone Memorial Hospital and the Department of Kinesiology at the University of North Carolina at Greensboro, Greensboro, North Carolina. All study procedures were concurrently approved by the institutional review boards of Cone Health and the University of North Carolina at Greensboro. All patients provided written informed consent before receiving sedation and any study-related procedures. There was no exclusion based on gender, race, or ethnicity. All patients scheduled for a right-sided heart catheterization with a left ventricular ejection fraction (LVEF) ≤40% within the previous 6 months, with continued signs and symptoms consistent with HFrEF, and having not received

intravenous inotropic therapy ≤7 days of the catheterization were considered for inclusion. Patients were excluded if they (1) were determined to have severe lung disease (diagnosed as such in the patient's medical history or, if spirometry data were available, a forced expiratory volume in 1second ≤1 L and/or a forced expiratory volume in 1 second to forced vital capacity ratio of ≤0.50, or required use of home O_2), (2) were expected to receive >2 mg of midazolam and/or >50 μg of fentanyl, or (3) were expected to need supplemental O_2 after receiving sedation.

Appropriate medical history was obtained to determine the patient's candidacy for participation in the study, which included results of the patient's last LVEF measure and results of the last pulmonary function test (if available). In addition, age, gender, height, weight, and current list of medications were obtained. The results of the catheterization were also obtained after the procedure.

VO_2 at rest was measured using a commercial, open-circuit, breath-by-breath gas analysis system (Ultima-CPX, MGC Diagnostics Corp., St. Paul, Minnesota). System calibration was performed before each study according to the manufacturer's specifications. After the completion of the catheterization procedure, while the patient remained in the catheterization laboratory procedure room (supine on the laboratory table), the patient breathed through a mouthpiece with a noseclip occluding nasal ventilation. After a 5-minute run-in (acclimation) phase, sampling was performed for an additional 5 minutes. The reported value of VO_2 at rest was the average during the 5-minute sampling period.

Estimated VO_2 at rest was calculated according to each of the 3 widely used empirical formulas listed in Table 1. In accordance with these equations, BSA was calculated according to the formula by D. Du Bois and E. Du Bois[7]: BSA (m^2) = 0.007184 × weight (kg)$^{0.425}$ × height (cm)$^{0.725}$.

Table 1
Empirical formulas for estimating oxygen consumption

Authors	Formula
LaFarge & Miettinen (1970) - Male	(138-(11.49*ln (Age))+(0.378*HR))*BSA
LaFarge & Miettinen (1970) - Female	(138-(17.04*ln (Age))+(0.378*HR))*BSA
Demer, Firth & Hillis (1982)	125*BSA
Bergstra, van Dijk, Hillege, et al. (1995)	(157.3*BSA)+(100*Sex[0 for female; 1 for male])-(10.5*ln(Age))+4.8

BSA = body surface area (Du Bois and Du Bois [1916] formula); HR = heart rate; ln(Age) = natural log of age.

All statistical analyses were done with JMP version 10 (SAS Institute Inc., Cary, North Carolina). With the exception of the mean differences, all continuous variables are reported as mean ± SD and categorical variables are reported as the total number (% of total). The mean differences are reported as mean ± SE.

Single-sample *t* tests were performed to compare the mean of differences (estimated − measured) against the hypothetical mean difference of 0 and was considered statistically significantly different when $p \leq 0.05$.

The Bland-Altman method for comparing methods of measuring the same parameter was used to assess the agreement between measured and estimated VO_2.[8] In accordance with this method, % error of the estimation of VO_2 at rest ([estimated − measured]/measured) for each patient was plotted against the corresponding average of the measured + estimated values. The limits of agreement were the mean difference ± 1.96 SD, and poor agreement was considered when the limits of agreement exceeded ± 25% error.

Two different analyses were used to determine if differences between the measured and estimated VO_2 were clinically significant. First, the absolute % error in estimated $VO_2$was calculated by dividing the absolute value of the difference (estimated − measured) by the measured VO_2. An absolute error ≥25% was considered the cut point for clinically significant error to occur.[6, 2 and 9] Second, the actual clinically significant error rate of the sample was calculated based on the cardiac index (cardiac output/BSA). For each equation, data were plotted with the cardiac index derived from the measured VO_2 along the x axis and the cardiac index derived from the estimate on the y axis. Break lines were laid over the plots at values representing the clinically important cutoffs[10, 11 and 12] for cardiogenic shock (< or ≥1.9 ml/min/m^2) and hypoperfusion (< or ≥2.2 ml/min/m^2), resulting in plots with 4 quadrants: 2 representing no clinically significant error (classification by the estimated VO_2 = classification by measured VO_2) and 2 representing clinically significant error (classification by the estimated VO_2 ≠ classification by measured VO_2). For each level, the number of patients falling in the clinically significant error quadrants for cardiac index was summed and divided by the total sample.

RESULTS

Forty-eight patients (75% men; age, 64 ± 11 years; LVEF, 22 ± 6%) were enrolled between August 2013 and August 2014. Four patients were withdrawn from the study before beginning collection of gas exchange: 1 patient received 4 mg of midazolam, 1 patient received 100 μg of fentanyl, 1 patient became hypoxic during the catheterization procedure (requiring O_2), and 1 patient had an LVEF >40% when ventriculogram was performed. All remaining patients completed the 10 minutes of breathing without difficulty or complication.

Demographic data and catheterization and gas exchange results for the 44 patients completing 10 minutes of gas exchange can be found in Tables 2 and 3. All patients with atrial fibrillation had appropriate rate control, which likely had little impact on VO_2 at rest. Arterial and venous oxygen saturation and content from blood gas analysis can also be found in Table 3.

The comparisons of the estimated versus the measured VO_2 for the entire group and for each gender subgroup can be found in Table 4. The mean difference for the equation by LaFarge and Miettinen was found not to be significantly different for the entire group. Mean differences for the equations by Dehmer et al and Bergstra et al were found to be significantly different. Comparison of gender subgroups reveals that females have significant mean differences for both the equations by LaFarge and Miettinen and Dehmer et al.

Figure 1, Figure 2 and Figure 3 are the Bland-Altman plots comparing the agreement between the estimated and measured VO_2. The dotted lines represent the mean error ± 1.96 SD and the dashed lines represent the limits of agreement. All estimation equations have poor agreement with the measured VO_2. The equation by LaFarge and Miettinen does not demonstrate a bias in the estimation. However, equation by Dehmer et al and Bergstra et al appears to have a bias toward overestimation. Although not presented, gender-specific Bland-Altman plots for both genders and for all 3 equations demonstrated large variability outside the limits of agreement. Another feature seen in the Bland-Altman plots (most distinctive in the estimations of Dehmer et al and Bergstra et al) is the systematic error of overestimating low VO_2 and underestimating greater VO_2, centering at ~250 ml/min.

Table 2
Summary of patient demographics and catheterization results (n = 44)

Variable	Variable Summary	Range
Men	29 (66%)	
Age (years)	64.5 ± 10.7	34 - 86
White	29 (66%)	
Body Mass Index (kg/m^2)	28.2 ± 6.4	18.1 - 46.7
Body Surface Area (m^2)	1.96 ± 0.27	1.41 - 2.58
Heart Failure Etiology (Non-Ischemic)	29 (66%)	
Left Ventricular Ejection Fraction (%)	22.0 ± 6.4	10 - 37.5
New York Heart Association Class		
II	9 (20%)	
III	21 (48%)	
IIIb	9 (20%)	
IV	5 (11%)	
Prescribed Beta-Blockers	34 (77%)	
Prescribed ACEI/ARB	36 (82%)	
Prescribed Loop Diuretic	31 (70%)	
Prescribed Aldosterone Antagonist	14 (32%)	
Prescribed Digoxin	7 (16%)	
Prescribed Hydralazine	6 (14%)	
Prescribed Long-Acting Nitrate	7 (16%)	
Atrial Fibrillation During Procedure	7 (16%)	
Systolic Pulmonary Artery Pressure (mm Hg)	45 ± 13	10 - 77
Diastolic Pulmonary Artery Pressure (mm Hg)	20 ± 7	7 - 38
Pulmonary Capillary Wedge Pressure (mm Hg)	19 ± 8	5 - 36
Systolic Right Ventricular Pressure (mm Hg)	46 ± 11	26 - 77
Diastolic Right Ventricular Pressure (mm Hg)	7 ± 3	-1 –16
Systolic Right Atrial Pressure (mm Hg)	12 ± 4	4 - 28
Diastolic Right Atrial Pressure (mm Hg)	11 ± 5	3 - 28

Continuous data presented as mean ± SD. Categorical data presented as number of patients (percentage of total).

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker.

Table 3
Summary of gas exchange results (n = 44)

	Mean ± SD	Range
Oxygen Consumption (ml/min)	229.7 ± 57.5	142 - 382
Oxygen Consumption (ml/kg/min)	2.80 ± 0.61	1.64 - 4.81
Respiratory Exchange Ratio	0.82 ± 0.07	0.64 - 1.07
Heart Rate (beats/min)	73 ± 12	54 - 105
Respiratory Rate (breaths/min)	16 ± 4	9 - 26
Tidal Volume (ml)	532 ± 224	307 -1620
Ventilation (L/min)	8.4 ± 2.9	4.6 - 17.5
Partial Pressure of End-Tidal Carbon Dioxide (mm Hg)	33 ± 5	22 - 45
Ventilatory Equivalent for Carbon Dioxide	44.2 ± 6.6	30.6 - 58.8
Arterial Oxygen Saturation (%)	94 ± 3	89 - 99
Venous Oxygen Saturation (%)	59 ± 7	39 - 70
Arterial Oxygen Content (mL O_2/L)	170.1 ± 21.3	110.1 - 220.8
Venous Oxygen Content (mL O_2/L)	106.0 ± 18.5	59.9 - 152.8

All ventilatory data were derived from breath-by-breath averaged over last 5 minutes of data collection. Heart rate was recorded every 15 seconds and averaged over the last 5 minutes of data collection. Arterial and venous oxygen saturation and content were taken from blood gas analysis performed during the catheterization.

Figure 4 demonstrates the rate at which patients with ≥25% absolute error occurred for each of the equations. Figure 5 demonstrates the process used to determine the clinically significant error rate. Table 5 presents the rates of the clinically significant error in the cardiac index derived from each estimation equation.

Table 4
Overall and gender-specific comparisons of the estimation of oxygen consumption by each empirical formula and the measured oxygen consumption

	Measured VO_2 ±SD (ml/min)	LaFarge & Miettinen		Dehmer et al.		Bergstra et al.	
		VO_2 ±SD (ml/min)	Difference ± SE (ml/min)	VO_2 ±SD (ml/min)	Difference ± SE (ml/min)	VO_2 ±SD (ml/min)	Difference ± SE (ml/min)
Overall group (n=44)	229.7 ± 57.5	219.4 ± 46.0	-10.3 ± 6.2	245.7 ± 34.1	16.0 ± 6.4†	270.3 ± 43.8	40.6 ± 6.4‡
Male (n=29)	249.9 ± 49.1	242.7 ± 30.1	-7.2 ± 8.2	256.3 ± 27.4	6.4 ± 8.2	283.5 ± 35.4	33.6 ± 8.5‡
Female (n=15)	190.6 ± 53.3	174.3 ± 37.2	-16.3 ± 9.2*	225.1 ± 37.2	34.5 ± 8.3‡	244.8 ± 48.1	54.2 ± 8.3‡

Differences were determined by estimated − measured.
*Significant at $p < 0.05$; †significant at $p < 0.01$; ‡significant at $p < 0.001$.

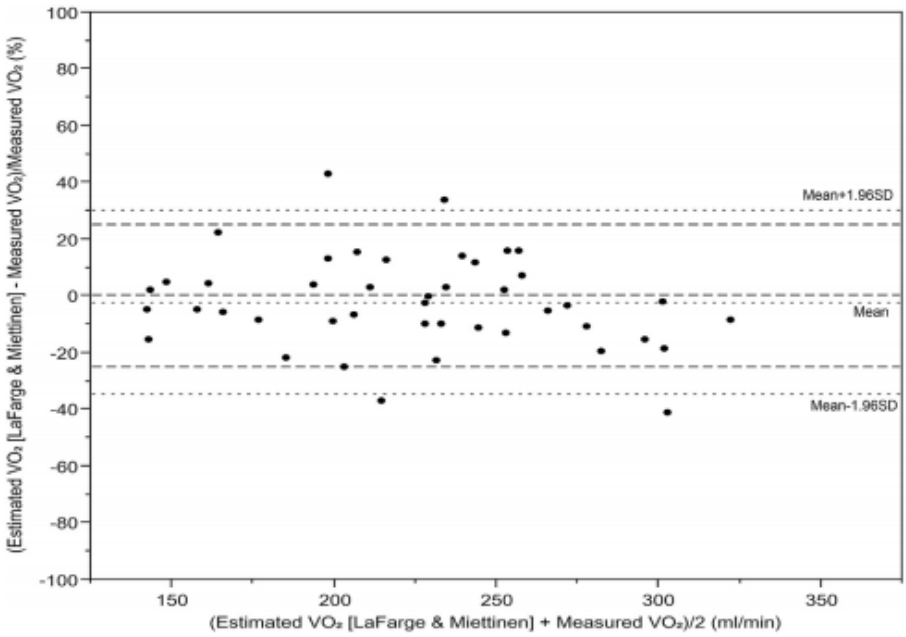

Figure 1. Bland-Altman Plot: percent error of the oxygen consumption at rest estimated by the equation by Lafarge and Miettinen. *Black dashed lines* are 0% error, +25% error, and −25% error; the *dotted lines* are the mean error, +1.96 SD, and −1.96 SD.

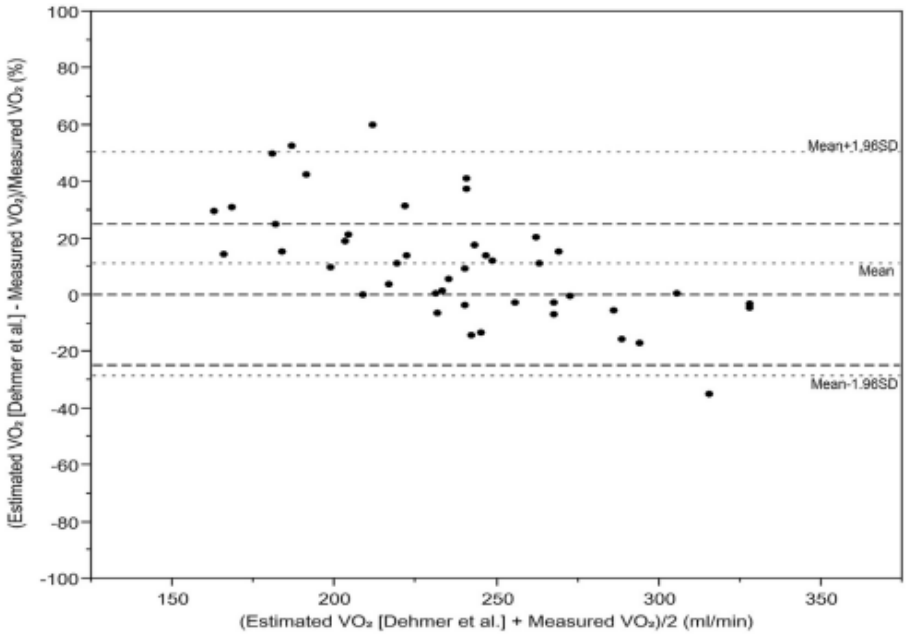

Figure 2. Bland-Altman Plot: percent error of the oxygen consumption at rest estimated by the equation by Dehmer et al. *Black dashed lines* are 0% error, +25% error, and −25% error; the *dotted lines* are the mean error, +1.96 SD, and −1.96 SD.

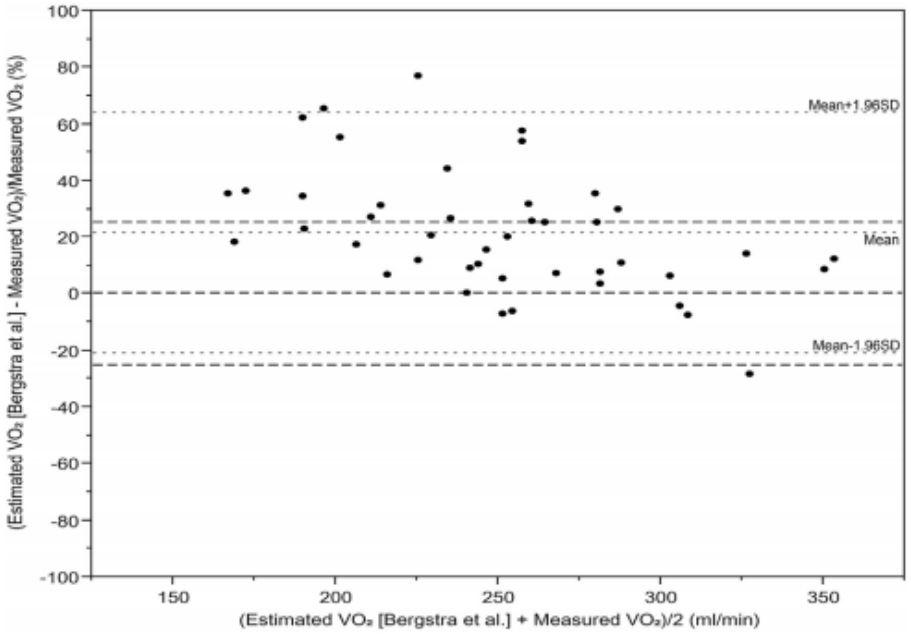

Figure 3. Bland-Altman Plot: percent error of the oxygen consumption at rest estimated by the equation by Bergstra et al. *Black dashed lines* are 0% error, +25% error, and −25% error; the *dotted lines* are the mean error, +1.96 SD, and −1.96 SD.

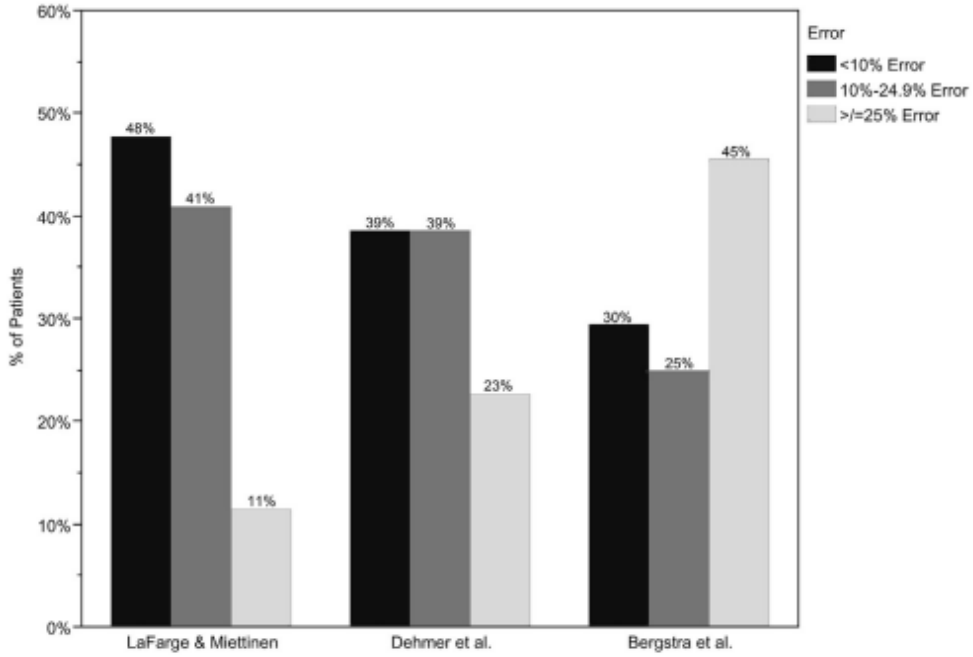

Figure 4. Absolute error rates: percentage of patients with <10%, 10% to 24.9%, and ≥25% absolute error for each of the 3 empirical formulas.

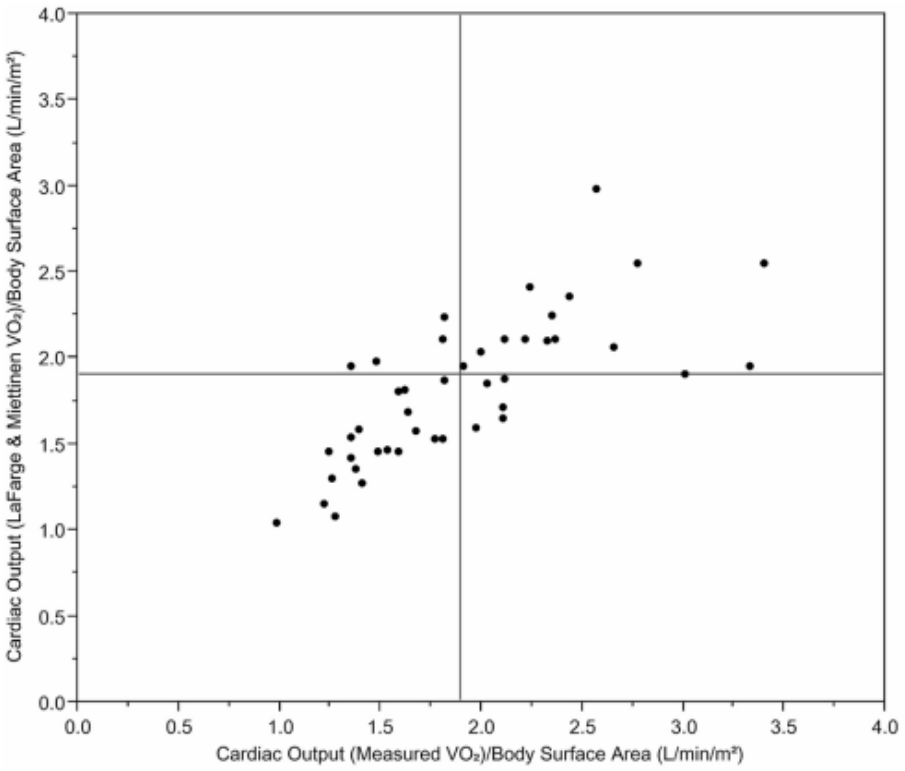

Figure 5. Clinically significant error rate in cardiac index: example of the determination of clinically significant error in cardiac index at the level of cardiogenic shock. Cardiogenic shock considered when cardiac index <1.9 L/min/m^2, indicated by *solid vertical* and *horizontal lines*.

Table 5
Rate of clinically significant error in cardiac index by the empirical formulas for hypoperfusion and cardiogenic shock

	Hypoperfusion (Cardiac Index < 2.2 L/min/m^2)				Cardiogenic Shock (Cardiac Index < 1.9 L/min/m^2)			
	Number with Clinically Significant Error			Clinically Significant Error Rate (%)	Number with Clinically Significant Error			Clinically Significant Error Rate (%)
	Over-Estimation	Under-Estimation	Total Misclassified		Over-Estimation	Under-Estimation	Total Misclassified	
LaFarge & Miettinen	1	6	7	16%	4	5	9	21%
Dehmer et al.	5	2	7	16%	9	1	10	23%
Bergstra et al.	11	0	11	25%	13	1	14	32%

DISCUSSION

This study was designed to accomplish 2 goals. The first was to compare the level of agreement between the measured resting VO_2 and the estimates from 3 commonly used prediction equations. This was accomplished with *t* tests of the differences and Bland-Altman analysis. It was hypothesized that each of the estimations would result in statistically significant differences compared with the measured VO_2. The equations by Dehmer et al and Bergstra et al significantly overestimated VO_2. However, the equations by LaFarge and Miettinen resulted in a nonsignificant underestimation. Importantly, use of a single-sample *t* test provides an objective evaluation of the mean difference, but only partially explains the discrepancy between the measured and estimated VO_2.

Bland-Altman plots reveal information about the mean difference that is not apparent in *t*tests. It was suggested by Bland and Altman that some variability of the difference between 2 measurements should be expected, but the variability should be random (centering on a mean difference of 0), with a small range in the limits of agreement and without an apparent trend in differences across the range of measurements. [8] In the case of this analysis, all 3 estimations resulted in large ranges in the agreement between the measured and estimated VO_2 that exceeded the predetermined acceptable range (±25%). In particular, although the equation by LaFarge and Miettinen did not produce a significantly different VO_2 from measured values, the mean difference is derived from large differences both above and below 0.

There are gender-specific corrections for the equation by LaFarge and Miettinen, and the findings from the mean differences suggest that the female-specific correction lessens the agreement with the measured VO_2. This was also the case for the equation by Dehmer et al (does not have a gender-specific correction), which demonstrated a significant mean difference only for females. There was a similar result found by Narang et al[3] with greater error in obese men than obese women owing the difference to the relatively greater lean mass in men. However, in the much larger analysis of a variety of clinically indicated right-sided heart catheterizations, nonsignificant differences were found between the genders, leading Narang et al to speculate on the need for including an adjustment for gender in the formulas by LaFarge and Miettinen and Bergstra et al.[13]The current analysis does not include a sufficient number of each gender to replicate the findings of Narang et al (2014) in this specific patient group.

In addition, all the estimation equations, especially Dehmer et al and Bergstra et al, trend toward overestimating VO_2 at lower values and underestimating it at greater values (Figure 3, Figure 4 and Figure 5). This trend has been a consistent finding in previous validation studies.[2, 3, 5, 6, 9 and 13]

The second goal of the study was to investigate the rate at which each equation results in a clinically significant error. We hypothesized that each of the equations would result in ≥15% of the patients with ≥25% absolute error. This level was based on what has been suggested in the published studies as being the level at which clinically significant error (in the derived cardiac output) would most likely occur.[2, 6 and 9] These results do not support this hypothesis. Particularly, the estimation by LaFarge and Miettinen resulted in 11.4% of patients falling in this category of absolute error. In the studies that have performed similar analysis, the equation by LaFarge and Miettinen had the lowest rates of patients with ≥25% error.[2, 3, 9 and 13] In this sense, these results are consistent with the published studies. In the present study, estimation using the equation by Bergstra et al resulted in 48% of the patients with ≥25% error, corroborating previous research in HFrEF patients[9] and strongly suggesting that this equation is inappropriate for use in clinical populations,[9 and 13] especially those with HFrEF.

Although the previously mentioned analyses were important in making comparisons with previous studies, further exploration of the true error resulting in a variable derived from the VO_2 (e.g., cardiac index) can provide better insight into the real occurrence of clinically significant error. In the context of HFrEF, cardiac index is used particularly to help guide treatment and determine appropriateness for advanced therapies, such as cardiac transplant or left

ventricular assist device (LVAD).[10, 11, 12 and 14] For example, with patients being considered for LVAD, those who are found to be in cardiogenic shock have a significantly higher rates of major adverse events after LVAD implantation.[11] Despite not currently being listed as an exclusion criteria, there has been a steady decrease in the percentage of patients receiving LVADs with cardiogenic shock since its recognition as a significant risk factor.[15] So misclassifying patients either higher or lower can have significant influence on clinical decision making.

Narang et al performed a similar analysis in a "hypothetical clinical context of aortic valve calculations,"[13] only changing the subject's measured or estimated VO_2.[3 and 13]Specifically, the analyses were performed in patients without heart disease before exercise testing[3] and during clinically indicated right-sided heart catheterizations in 535 patients with a broad range of clinical indications (including 177 patients referred for HF–subanalysis of HF patients was not performed).[13] Therefore, creating a hypothetical scenario homogenized the data for easier analysis. In the current analysis, the patients had HFrEF and the cardiac index was of particular clinical interest. So, understanding the real clinically significant error provides more direct clinical relevance, given that most patients with HFrEF are found to have reduced cardiac index (<2.6 L/min/m^2).[16 and 17] All equations demonstrated >15% of patients with clinically significant error at the level of hypoperfusion and >20% of patients with clinically significant error at the level of cardiogenic shock. Misclassifying patients at these 2 levels can have significant downstream effects in the care and management of patients with moderate-to-severe HFrEF. The findings from the present study do not support the use of these empirical formulas to estimate the VO_2 at rest in patients with HFrEF who underwent right heart catheterization.

This study has limitations. Primarily, patients are generally not accustomed to breathing through a mouthpiece; changing the patient's breathing characteristics.[18] However, this is a common method for measuring VO_2 at rest and was the method used by LaFarge and Miettinen.[4] Furthermore, the proposed sample size was sufficiently powered to compare the measured versus the estimated VO_2 at rest in the whole sample but was too small to evaluate potential confounding factors influencing VO_2 at rest (i.e., gender, race, obesity, pulmonary hypertension, and so forth) in patients with HFrEF.

DISCLOSURES

No author has any relationships with industry or financial associations that might pose a conflict of interest in connection with the submitted study to disclose.

REFERENCES

1. van Grondelle A, Ditchey RV, Groves BM, Wagner WW, Reeves JT. Thermodilution method overestimates low cardiac output in humans. Am J Physiol 1983;245:H690eH692.

2. Kendrick AH, West J, Papouchado M, Rozkovec A. Direct Fick cardiac output: are assumed values of oxygen consumption acceptable? Eur Heart J 1988;9:337e342.

3. Narang N, Gore MO, Snell PG, Ayers CR, Lorenzo S, Carrick-Ranson G, Babb TG, Levine BD, Khera A, de Lemos JA, McGuire DK. Accuracy of estimating resting oxygen uptake and implications for hemodynamic assessment. Am J Cardiol 2012;109:594e598.

4. LaFarge CG, Miettinen OS. The estimation of oxygen consumption. Cardiovasc Res 1970;4:23e30.

5. Dehmer GJ, Firth BG, Hillis LD. Oxygen consumption in adult patients during cardiac catheterization. Clin Cardiol 1982;5:436e440.

6. Bergstra A, van Dijk RB, Hillege HL, Lie KI, Mook GA. Assumed oxygen consumption based on calculation from dye dilution cardiac output: an improved formula. Eur Heart J 1995;16:698e703.

7. Du Bois D, Du Bois E. Clinical Calorimetry. A formula to estimate the approximate surface area if height and weight be known. Arch Intern Med 1916;17:863e871.

8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307e310.

9. Wolf A, Pollman MJ, Trindade PT, Fowler MB, Alderman EL. Use of assumed versus measured oxygen consumption for the determination of cardiac output using the Fick principle. Cathet Cardiovasc Diagn 1998;43:372e380.

10. Ginsberg F, Parrillo JE. Cardiogenic shock: a historical perspective. Crit Care Clin 009;25:103e114; viii.

11. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, Ulisney KL, Baldwin JT, Young JB. Second INTERMACS annual report: more than 1,000 primary left ventricular assist device implants. J Heart Lung Transpl 2010;29:1e10.

12. Slaughter MS, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD, Starling RC, Chen L, Boyle AJ, Chillcott S, Adamson RM, Blood MS, Camacho MT, Idrissi KA, Petty M, Sobieski M, Wright S, Myers TJ, Farrar DJ; HeartMate II Clinical Investigators. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. J Heart Lung Transpl 2010;29:S1eS39.

13. Narang N, Thibodeau JT, Levine BD, Gore MO, Ayers CR, Lange RA, Cigarroa JE, Turer AT, de Lemos JA, McGuire DK. Inaccuracy of estimated resting oxygen uptake in the clinical setting. Circulation 2014;129:203e210.

14. Mehra MR, Kobashigawa J, Starling R, Russell S, Uber PA, Parameshwar J, Mohacsi P, Augustine S, Aaronson K, Barr M. Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidatese2006. J Heart Lung Transpl 2006;25:1024e1042.

15. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Miller MA, Timothy Baldwin J, Young JB. Sixth INTERMACS annual report: a 10,000-patient database. J Heart Lung Transpl 2014;33:555e564.
16. Carlsson M, Andersson R, Bloch KM, Steding-Ehrenborg K, Mosén H, Stahlberg F, Ekmehag B, Arheden H. Cardiac output and cardiac index measured with cardiovascular magnetic resonance in healthy subjects, elite athletes and patients with congestive heart failure. J Cardiovasc Magn Reson 2012;14:51.

17. Cotter G, Moshkovitz Y, Kaluski E, Milo O, Nobikov Y, Schneeweiss A, Krakover R, Vered Z. The role of cardiac power and systemic vascular resistance in the pathophysiology and diagnosis of patients with acute congestive heart failure. Eur J Heart Fail 2003;5:443e451.

18. Perez W, Tobin MJ. Separation of factors responsible for change in breathing pattern induced by instrumentation. J Appl Physiol 1985;59:1515e1520.

* Corresponding author: Tel: 740-593-4653; fax: 740-593-0289. E-mail address: chasep@ohio.edu (P.J. Chase).