Inaccuracy of Estimated Resting Oxygen Uptake in the Clinical Setting

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Background—The Fick principle (cardiac output = oxygen uptake (VO$_2$)/systemic arterio-venous oxygen difference) is used to determine cardiac output in numerous clinical situations. However, estimated rather than measured VO$_2$ is commonly used because of complexities of the measurement, though the accuracy of estimation remains uncertain in contemporary clinical practice.

Methods and Results—From 1996 to 2005, resting VO$_2$ was measured via the Douglas bag technique in adult patients undergoing right heart catheterization. Resting VO$_2$ was estimated by each of 3 published formulae. Agreement between measured and estimated VO$_2$ was assessed overall, and across strata of body mass index, sex, and age. The study included 535 patients, with mean age 55 yrs, mean body mass index 28.4 kg/m$^2$; 53% women; 64% non-white. Mean (±standard deviation) measured VO$_2$ was 241 ± 57 ml/min. Measured VO$_2$ differed significantly from values derived from all 3 formulae, with median (interquartile range) absolute differences of 28.4 (13.1, 50.2) ml/min, 37.7 (19.4, 63.3) ml/min, and 31.7 (14.4, 54.5) ml/min, for the formulae of Dehmer, LaFarge, and Bergstra, respectively (P<0.0001 for each). The measured and estimated values differed by >25% in 17% to 25% of patients depending on the formula used. Median absolute differences were greater in severely obese patients (body mass index > 40 kg/m$^2$), but were not affected by sex or age.

Conclusions—Estimates of resting VO$_2$ derived from conventional formulae are inaccurate, especially in severely obese individuals. When accurate hemodynamic assessment is important for clinical decision-making, VO$_2$ should be directly measured. (Circulation. 2014;129:203-210.)

Key Words: cardiac output ■ catheterization ■ hemodynamics

A

Accurate determination of cardiac output (Qc) is important in the hemodynamic evaluation of valve area, pulmonary and systemic vascular resistance, and severity of heart failure. The Fick method [Qc = oxygen uptake (VO$_2$)/systemic arterio-venous oxygen difference] is the time-honored gold standard for determining Qc and has been used to validate other techniques such as indicator dilution and foreign gas rebreathing. Application of the Fick method requires measurement of VO$_2$. However, direct measurement of VO$_2$ through (1) mass spectrometry analysis of timed Douglas bag collections of exhaled air, or (2) breath-by-breath analysis of exhaled air using indirect calorimetry or metabolic cart analysis is time consuming and involves specific equipment that requires frequent calibration and is expensive to maintain. As a result, resting VO$_2$ is commonly estimated rather than measured using derived formulae available in the peer-reviewed literature. However, the accuracy of the formulae and nomograms most commonly used to estimate resting VO$_2$ is questionable, with most estimating methods derived from limited samples of highly selected, ethnically homogenous populations consisting of similarly aged, lean adults, populations that differ substantially from contemporary adult cardiology practice. Other formulae were derived from clinical populations composed exclusively or primarily of infants and children. Hence, we assessed the accuracy of estimated resting VO$_2$ compared with measured VO$_2$ obtained by the gold-standard analysis of timed collections of exhaled air by the method of Douglas in a large population of consecutive adult patients who underwent right-heart cardiac catheterization for clinical indications at our hospital.

Clinical Perspective on p 210
Methods

We conducted a retrospective study of consecutive patients who underwent right heart catheterization with direct measurement of resting VO₂ at Parkland Memorial Hospital between 1996 and 2005. Charts were reviewed for demographic, anthropometric, and baseline clinical characteristics. This study was approved by the University of Texas Southwestern Medical Center Institutional Review Board.

Calculating Estimated VO₂

Estimated resting VO₂ was calculated by the formula of Dehmer, et al.VO₂ (ml/min) = 125 (ml/min/m²) × body surface area (BSA, m²), with BSA calculated according to the formula of Dubois: BSA (m²) = 0.007184 × Height (kg)0.427 × Height (cm)0.725. For sensitivity analysis, estimation of VO₂ was also calculated using the formula of LaFarge: VO₂ (ml/min) = 138.1 – (X × log age) + (0.378 × Heart Rate) × BSA (Men: X = 11.49; Women: X ≈ 17.04); and the formula of Bergstra: VO₂ (ml/min) = 157.3 × BSA + X – (10.5 × log age) + 4.8 (Men: X = 10; Women = 0).

Direct Measurement of VO₂

Resting VO₂ was measured in all patients using the gold-standard technique of Douglas, with analysis of a 3-minute collection of exhaled air collected through a properly fitted mouth piece with a 3-way valve. Exhaled volume was measured with a Tissot spirometer and concentrations of oxygen, carbon dioxide, and nitrogen were determined by mass spectrometry (Marquette MGA 1100), calibrated before every measurement, and all testing was completed while patients remained in the supine position.

Statistical Analysis

The magnitude of agreement between directly measured and estimated resting VO₂ was assessed by median absolute difference, ordinary least products regression demonstrated significant fixed error (reflected by y intercept >0 (95% confidence interval, 92.4–106.1)) and proportional error (reflected by slope <1.0 (95% CI, 0.53–0.61; Figure 1A). Poor agreement between directly measured and estimated VO₂ was also observed when the LaFarge and Bergstra formulae were used (Figure 2; Figure 1B and 1C). Intraclass correlation coefficients were similar and slightly higher in the LaFarge and Bergstra formulae, when compared with the Dehmer formula, demonstrating slightly more consistency overall in intra-test measurement (Figure 1).

The magnitude of error between measured and estimated VO₂, expressed as a percent error for the overall cohort is shown in Figure 2. For all 3 formulae used to estimate VO₂, the degree of error ranged from 10 to 25% in ≈40% of the overall cohort, and the error was >25% in 17–25% of the cohort, depending on the estimating formula used.

Patient characteristics for the overall cohort and selected strata are shown in Table 1. The overall cohort comprised 535 patients, with mean age 55 years, 53% were women, and the mean BMI was 28.4 kg/m². The mean measured VO₂ for the overall cohort was 241±56.6 ml/min (mean ± standard deviation; Table 2), with a range of 108 to 457 ml/min. Using the Dehmer formula, the mean estimated VO₂ was 235.4 ± 32 ml/min, with a range of 162 to 356 ml/min; it differed significantly from the direct measurement with a median absolute difference of 28.4 (13.1, 50.2) ml/min [median (25th, 75th percentile)] (Table 2 and Figure 1A; P<0.0001).
3 formulae tested. Although statistically significant, the difference in error between sexes was small (<10 ml/min) and varied in direction depending on the estimating formula used.

In analyses stratified by median age, median absolute difference between estimated and measured VO$_2$ comparisons for age groups ≤55 years and >55 years were both large [31.7 (13.5, 55.2) ml/min and 26.5 (12.7, 46.6) ml/min, respectively, P<0.0001 for each] when calculated by the Dehmer formula, though the differences between the 2 groups did not reach statistical significance (P=0.13).

In assessment of both LaFarge and Bergstra formulae, the median absolute difference for both age strata was >30 ml/min, and the differences between age groups similarly did not reach statistical significance (Table 2; P=0.92 and P=0.20, respectively).

We were unable to resolve or improve upon the discordance between measured and estimated resting VO$_2$ using data-derived estimating equations, which we explored using a variety of methods of multivariable linear regression. In all data-derived estimating equations, which we explored using a variety of methods of multivariable linear regression. In all cases of the exploratory models, the mean bias was unacceptably large, and the median percent difference was no less than 15%. Additionally, the predicted $R^2$ based on the PRESS statistic$^{17}$ yielded values no larger than 0.27 (data not shown), demonstrating unacceptably poor model performance.

To demonstrate the clinical importance of error in resting VO$_2$ estimation, we calculated hypothetical Fick-derived Q$_{c}$ based on resting and estimated VO$_2$ from all 3 formulae for each patient in the study. Fick-derived Q$_{c}$ values were used to derive hypothetical AVA by the Hakki equation, as a clinical example to determine the effect of errors in resting VO$_2$ estimation. For this analysis, each patient was assigned an hypothetical mean aortic valve gradient of 40 mmHg and an arteriovenous oxygen difference of 4.5. An AVA of <1.0 cm$^2$ is classified as severe stenosis and warrants consideration for surgical correction. Using AVA <1.0 cm$^2$ derived from directly measured VO$_2$ as the outcome, the Dehmer formula had a sensitivity of 93% (95% CI, 90–95%) with a specificity of 33% (95% CI, 25–40%) and an area under the curve (AUC) of 0.79 (95% CI 0.75–0.84; Table 3). The LaFarge formula had similar sensitivity, specificity, and AUC when compared with the Dehmer formula; the Bergstra formula had the lowest sensitivity of 75% (95% CI, 71–79%) of the formulae tested, but was significantly more specific (77%; 95% CI, 68–86%) with a slightly greater AUC of 0.82 (95% CI, 0.77–0.87) when compared with the other formulae (Figure 3). Similarly, the optimal ROC cut point for the Bergstra formula (0.94 cm$^2$) was the closest of the 3 formulae to the clinically important diagnostic cutoff of 1.0 cm$^2$ (Table 3). Expanded clinical application of

### Table 1. Baseline Descriptive Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=535)</th>
<th>Men (n=252)</th>
<th>Women (n=283)</th>
<th>&lt;25 (n=187)</th>
<th>25–29.9 (n=174)</th>
<th>30–34.9 (n=94)</th>
<th>35–39.9 (n=41)</th>
<th>≥40 (n=39)</th>
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<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>55 (13.5)</td>
<td>55 (13.6)</td>
<td>55 (13.5)</td>
<td>54 (15.4)</td>
<td>57 (12)</td>
<td>54 (13.1)</td>
<td>54 (12.7)</td>
<td>55 (11.2)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>283 (53)</td>
<td>—</td>
<td>—</td>
<td>93 (49.7)</td>
<td>88 (47.1)</td>
<td>51 (54.3)</td>
<td>25 (61)</td>
<td>32 (82.1)</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>192 (36)</td>
<td>101 (40)</td>
<td>91 (32)</td>
<td>65 (34.8)</td>
<td>65 (37.4)</td>
<td>38 (40.4)</td>
<td>11 (26.8)</td>
<td>13 (33.3)</td>
</tr>
<tr>
<td>Black</td>
<td>168 (31)</td>
<td>72 (29)</td>
<td>96 (34)</td>
<td>46 (24.6)</td>
<td>53 (30.4)</td>
<td>32 (34)</td>
<td>19 (46.3)</td>
<td>18 (46.2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>143 (27)</td>
<td>64 (25)</td>
<td>79 (28)</td>
<td>58 (31)</td>
<td>47 (27)</td>
<td>20 (21.3)</td>
<td>10 (24.4)</td>
<td>8 (20.5)</td>
</tr>
<tr>
<td>Other</td>
<td>32 (6)</td>
<td>15 (6)</td>
<td>17 (6)</td>
<td>18 (9.6)</td>
<td>9 (5.2)</td>
<td>4 (4.3)</td>
<td>1 (2.4)</td>
<td>—</td>
</tr>
<tr>
<td>Height, mean (SD), in</td>
<td>66.0 (4.2)</td>
<td>68.9 (3.4)</td>
<td>63.4 (2.9)</td>
<td>66.2 (4.1)</td>
<td>66.2 (4.1)</td>
<td>66.1 (4.5)</td>
<td>65.9 (4)</td>
<td>64.5 (3.9)</td>
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<tr>
<td>Weight, mean (SD), kg</td>
<td>79.9 (21.3)</td>
<td>83.7 (19.7)</td>
<td>76.5 (22.1)</td>
<td>61.9 (10.1)</td>
<td>78 (10)</td>
<td>90.8 (12.7)</td>
<td>104 (13)</td>
<td>123.2 (19.7)</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m$^2$</td>
<td>28.4 (7.1)</td>
<td>27.2 (5.5)</td>
<td>29.4 (8.2)</td>
<td>21.8 (2.1)</td>
<td>27.5 (1.4)</td>
<td>32.1 (1.4)</td>
<td>37.1 (1.3)</td>
<td>45.8 (5.4)</td>
</tr>
<tr>
<td>Pulmonary hypertension, n (%)</td>
<td>166 (31)</td>
<td>68 (27)</td>
<td>100 (35.3)</td>
<td>65 (34.8)</td>
<td>49 (28.2)</td>
<td>26 (27.7)</td>
<td>10 (24.4)</td>
<td>16 (41)</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>143 (27)</td>
<td>90 (35.7)</td>
<td>57 (20.1)</td>
<td>50 (26.7)</td>
<td>52 (29.9)</td>
<td>26 (27.7)</td>
<td>10 (24.4)</td>
<td>9 (22)</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>102 (19)</td>
<td>64 (25.4)</td>
<td>40 (14.1)</td>
<td>33 (16.7)</td>
<td>37 (21.3)</td>
<td>21 (22.3)</td>
<td>5 (12.2)</td>
<td>6 (15.4)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>114 (23.1)</td>
<td>55 (21.8)</td>
<td>59 (20.8)</td>
<td>23 (12.3)</td>
<td>37 (21.3)</td>
<td>27 (28.7)</td>
<td>13 (31.7)</td>
<td>14 (35.9)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>63 (11.8)</td>
<td>32 (12.7)</td>
<td>31 (11)</td>
<td>13 (7)</td>
<td>16 (9.2)</td>
<td>17 (18.1)</td>
<td>6 (14.6)</td>
<td>10 (25.6)</td>
</tr>
<tr>
<td>Primary indication for RHC (%)</td>
<td>292 (54.6)</td>
<td>131 (52)</td>
<td>161 (56.9)</td>
<td>106 (56.7)</td>
<td>100 (57.5)</td>
<td>43 (45.8)</td>
<td>20 (48.8)</td>
<td>23 (59)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>177 (33.1)</td>
<td>97 (38.5)</td>
<td>80 (28.3)</td>
<td>54 (28.9)</td>
<td>59 (33.9)</td>
<td>32 (34)</td>
<td>20 (48.8)</td>
<td>12 (30.8)</td>
</tr>
<tr>
<td>Congential heart disease</td>
<td>46 (8.6)</td>
<td>21 (8.3)</td>
<td>25 (8.8)</td>
<td>22 (11.8)</td>
<td>8 (4.6)</td>
<td>13 (13.8)</td>
<td>3 (7.7)</td>
<td>—</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>20 (3.7)</td>
<td>3 (1.2)</td>
<td>17 (6)</td>
<td>5 (2.7)</td>
<td>7 (4)</td>
<td>6 (6.4)</td>
<td>1 (2.4)</td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; CVD, cardiovascular disease; RHC, right heart catheterization; and SD, standard deviation.
the errors encountered in resting VO$_2$ estimation are shown in Figures 4 and 5 represented by theoretical Fick cardiac output and systemic vascular resistance (hypothetical mean arterial pressure of 75 mm Hg, central venous pressure of 8 mm Hg, arteriovenous oxygen difference of 4.5), where a large majority of data points deviate notably from the line of equality.

Table 2. Comparison of Median Absolute Difference and Typical Error (BMI Only) by Estimating Formulae for Overall Cohort, and Subgroups Stratified by Sex, Age, and Body Mass Index

<table>
<thead>
<tr>
<th>Group</th>
<th>Dehmer Formula†</th>
<th>LaFarge Formula‡</th>
<th>Bergstra Formula§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Measured VO$_2$ (ml/min)</td>
<td>Mean Calc. VO$_2$ (SD, ml/min)</td>
<td>Median* Absolute Difference</td>
</tr>
<tr>
<td>Overall (n=535)</td>
<td>241 (56.6)</td>
<td>235.4 (32)</td>
<td>28.4</td>
</tr>
<tr>
<td>Men (n=252)</td>
<td>260.6 (58.3)</td>
<td>248.1 (29.7)</td>
<td>33.1</td>
</tr>
<tr>
<td>Women (n=283)</td>
<td>224.2 (49.1)</td>
<td>224.1 (29.6)</td>
<td>24</td>
</tr>
<tr>
<td>Age ≤ 55 years (n=255)</td>
<td>250.1 (61.6)</td>
<td>239.9 (34.3)</td>
<td>31.7</td>
</tr>
<tr>
<td>Age &gt; 55 years (n=280)</td>
<td>233.4 (50.3)</td>
<td>234.2 (29.6)</td>
<td>26.5</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>218.6 (48)</td>
<td>212.6 (23.3)</td>
<td>24.6</td>
</tr>
<tr>
<td>25–29.9</td>
<td>242.4 (51.3)</td>
<td>235 (22.8)</td>
<td>26.8</td>
</tr>
<tr>
<td>30–34.9</td>
<td>258.1 (55.5)</td>
<td>250.4 (26.9)</td>
<td>29.3</td>
</tr>
<tr>
<td>35–39.9</td>
<td>265.3 (63.3)</td>
<td>264.6 (25.7)</td>
<td>27</td>
</tr>
<tr>
<td>≥40</td>
<td>280.1 (67.8)</td>
<td>279.5 (29.8)</td>
<td>47</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; Calc, calculated; CV, coefficient of variation; IQR, interquartile range; SD, standard deviation; and VO$_2$, oxygen uptake.

* P<0.005 for median raw difference for overall cohort and subgroups determined by one-sample Wilcoxon signed-ranks test
†Dehmer Formula: VO$_2$ (ml/min) = 125 × Body Surface Area
‡LaFarge Formula: VO$_2$ (ml/min) = 138.1 – (11.49 × logeage) + (0.378 × Heart Rate) × Body Surface Area (Men); VO$_2$ (ml/min) = 138.1 – (17.04 × logeage) + (0.378 × Heart Rate) × Body Surface Area (Women).
§Bergstra Formula: VO$_2$ (ml/min) = 157.3 × Body Surface Area + 10 – (10.5 × logeage) + 4.8 (Men); VO$_2$ (ml/min) = 157.3 × Body Surface Area – (10.5 × logeage) + 4.8 (Women).
Discussion

This study demonstrates that in a large, consecutive sample of adult patients undergoing right-heart cardiac catheterization, estimation of resting VO$_2$ by commonly used formulae is inaccurate compared with the gold-standard analysis of timed collections of exhaled air. Estimated VO$_2$ was most inaccurate in morbidly obese patients with BMI $\geq$ 40 kg/m$^2$. To put the degree of inaccuracy of resting VO$_2$ estimation into clinical context, the observed error and variance in estimated VO$_2$ applied to Fick-calculated Q$_c$ yields up to 38% error within 1 standard deviation (SD) and up to 64% error within 2 SDs. Because Fick-calculated Q$_c$ and resting VO$_2$ are directly proportional, error in estimation of resting VO$_2$ $\geq$25%, a magnitude of error observed in 17% of the present study cohort, can dramatically alter clinical decision-making.

Formulae and nomograms for the estimation of resting VO$_2$, published as early as 1954, were derived from highly selected cohorts of homogeneous ethnicity and age. More recently published estimating formulae presently in broader clinical use, such as that by LaFarge and colleagues, were derived primarily from pediatric patients. Similarly, many of the patients used to derive the Bergstra formula were infants and children with congenital heart disease, possibly confounding the application of these methods in adult patients. Previous studies have demonstrated errors in VO$_2$ estimation using these and other formulae in pediatric and adult populations. However, these analyses have limitations, including small sample size with homogeneity of patient population, lack of sub-group analysis in determining other variables that may influence errors in estimation, and use fewer analytic methods to explain the errors observed. Our study builds on previous analyses by better addressing the above-mentioned limitations, allowing for a comprehensive assessment of errors in resting VO$_2$ estimation not seen to date. In the present study, we observed a substantial fixed and proportional error when VO$_2$ was estimated by each of the 3 formulae compared with analysis of timed collections of exhaled air, with error in excess of 25% in many patients.

We previously demonstrated the inaccuracy of resting VO$_2$ estimation in a smaller cohort of research participants. The present observations confirm and extend these previous findings of exaggerated error in the most obese patients, now in a larger sample of adult patients in a clinical setting where such methods are commonly applied. Several of the contemporary formulae for estimating VO$_2$ incorporate weight or body surface area without taking into account the degree of adiposity, which may impact the accuracy of estimation, because fat has little impact on oxygen uptake. In addition, there is a metabolic requirement for accommodating excess weight, including physical support and respiratory efforts, all of which may materially influence resting VO$_2$. Although predictive formulae for maximal VO$_2$ have adjusted for the metabolic cost associated with excess adiposity to improve accuracy, whether similar adiposity adjustments for the estimation of VO$_2$ at rest could improve accuracy remains to be determined.

In contrast to our previous study where estimation with mean absolute difference was exaggerated in men compared with women, we found no significant difference in observed disagreement between measured and estimated

### Table 3. Diagnostic Performance by Estimating Formula for Calculation of AVA $<1.0$ cm$^2$

<table>
<thead>
<tr>
<th></th>
<th>Dehmer</th>
<th>LaFarge</th>
<th>Bergstra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal ROC cut point (cm$^2$)</td>
<td>0.87</td>
<td>0.78</td>
<td>0.94</td>
</tr>
<tr>
<td>AUC</td>
<td>0.79 (0.75–0.84)</td>
<td>0.79 (0.74–0.84)</td>
<td>0.82 (0.77–0.87)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>93% (90.1–95.3)</td>
<td>96% (93.6–97.5)</td>
<td>75% (71.2–79.2)</td>
</tr>
<tr>
<td>Specificity</td>
<td>33% (25.2–40.2)</td>
<td>30% (20.3–39.5)</td>
<td>77% (68.2–85.9)</td>
</tr>
<tr>
<td>PPV</td>
<td>78% (74.2–81.7)</td>
<td>88% (84.6–90.5)</td>
<td>94% (92–96.8)</td>
</tr>
<tr>
<td>NPV</td>
<td>64% (52.9–74.4)</td>
<td>57% (42.2–70.9)</td>
<td>38% (30.5–44.8)</td>
</tr>
<tr>
<td>Positive LR</td>
<td>1.4 (1.23–1.55)</td>
<td>1.4 (1.19–1.57)</td>
<td>3.3 (2.22–4.83)</td>
</tr>
<tr>
<td>Negative LR</td>
<td>0.2 (0.15–0.34)</td>
<td>0.15 (0.09–0.26)</td>
<td>0.32 (0.26–0.39)</td>
</tr>
</tbody>
</table>

Parentheses indicate 95% confidence interval. AUC indicates area under the curve; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; and ROC, receiver operating characteristic.
We postulate that results from our previous study may be explained by the fact that on average, men have greater absolute and proportional fat-free mass than women, which likely contributed to the sex-based error of the estimating formula. In the present analyses, the error was numerically greater in men compared with women using the Dehmer and Bergstra formulae, whereas with the LaFarge formula the error was numerically greater in women. However, the magnitude of differences was not statistically significant between the groups, and none of the formulae yielded a significant statistical interaction between error and sex, challenging the necessity of inclusion of sex as is done in the LaFarge and Bergstra formulae.

Although early nomograms for estimating VO₂ at rest, some of which were derived from pediatric populations, were stratified by age, we found no age-based error association in this study. No association between the degree of error of the estimating formula and age was present when assessing VO₂ using each of the 3 formulae. Similar results were found in studies of both older adults with mean age 60 years and younger adults with mean age 39 years.

The errors encountered when resting VO₂ is estimated instead of directly measured can potentially impact clinical decision making, including determining the initiation and titration of inotropic support, decision for mechanical ventricular support, determining eligibility and monitoring response of pulmonary vasodilator therapy, and determining candidacy for valve procedures, among others.

Clinical Implications
The clinical relevance of the observed errors in VO₂ estimation as depicted by hypothetical hemodynamic calculations demonstrates the potential impact on critical clinical decision making, including deviations of AVA by all 3 estimating formulae revealed substantial inaccuracies in diagnostic performance. The Dehmer and Large formulae were adequately sensitive in detection of potential severe aortic stenosis but were poorly specific. Using the Dehmer and LaFarge formulae, a significant number of subjects with AVA >1.0 cm² derived from directly measured VO₂ were found to have estimated AVAs <1.0 cm², reflecting the high false positive rate. The Bergstra formula was significantly more specific than the
other formulae tested, but overall had the largest combined proportion of false negative and false positive results, leading to potential clinical misclassification of AVA when estimated to be both greater and less than 1.0 cm². We similarly observed this critical degree of potential clinical error in our previous study, which was composed of research study participants and not actual patients, contrasted with the present study of patients who underwent cardiac catheterization for clinical indications.

From a drug regulatory standpoint, estimation versus measurement of VO₂ is also an important consideration. In 2010, the FDA Cardiovascular and Renal Drugs Advisory Committee convened to discuss the potential role of using pulmonary vascular resistance index (PVRI) and its change in response to therapy as a surrogate for drug efficacy in pediatric patients with pulmonary arterial hypertension (PAH). Therapy in these pediatric patients would consist of drugs and their response to therapy for drug registration studies. Errors in hemodynamic assessment may adversely impact clinical indications.

Conclusions


References


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**CLINICAL PERSPECTIVE**

The Fick method is the gold-standard for determining cardiac output in numerous clinical scenarios. A primary determinant of Fick-derived cardiac output is resting oxygen uptake (VO$_2$), which if inaccurately estimated will proportionally manifest as commensurate error in estimation of cardiac output, a hemodynamic parameter directly influencing critical clinical decision-making. Our study demonstrates the inaccuracies of estimating VO$_2$ with commonly used formulae compared with its direct measurement. It is important to consider these limitations when calculating cardiac output based on estimated VO$_2$, especially in obese and severely obese individuals as commonly encountered in contemporary practice. When accurate hemodynamic assessment is important for clinical decision-making, VO$_2$ should be directly measured.
Inaccuracy of Estimated Resting Oxygen Uptake in the Clinical Setting
Nikhil Narang, Jennifer T. Thibodeau, Benjamin D. Levine, M. Odette Gore, Colby R. Ayers, Richard A. Lange, Joaquin E. Cigarroa, Aslan T. Turer, James A. de Lemos and Darren K. McGuire

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