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Original Article

Body Habitus Considerations During Right Heart Catheterization

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ABSTRACT

Background: Obese and overweight body habitus are common among patients undergoing right heart catheterization for suspected pulmonary hypertension, but previous studies have described only patients with severe obesity. This study examined the effect of body habitus on intracardiac pressures, thermodilution cardiac output (TDCO), indirect Fick (iFick) cardiac output (CO), and pulmonary vascular resistance (PVR) in subjects with normal cardiopulmonary hemodynamics.

Methods: A retrospective analysis was conducted on healthy volunteers and patients referred for right heart catheterization for dyspnea of unknown origin with normal hemodynamics. Of the 65 subjects (53 ± 14 years; 51% female), 31% were normal weight, 49% were overweight, and 20% had obesity, as defined by a body mass index of 30-39.9 kg/m^2. Mixed venous oxygen saturations and intracardiac pressures were compared across body mass index categories. Agreement between iFick CO calculated by 3 formulae, and TDCO and PVR was examined.

Results: No differences in intracardiac pressures were observed, but mixed venous oxygen saturations were lower in the obese group. iFick CO underestimated TDCO, particularly with the LaFarge formula, with a systematic difference of 0.33 L/min for every 1 L/min increase in

RÉSUMÉ

Introduction : Les habitus corporels liés à l'obésité et à l'embonpoint sont fréquents chez les patients qui subissent un cathétérisme du cúur droit en raison d'une suspicion d'hypertension pulmonaire, mais les études antérieures n'ont porté que sur les patients atteints d'une obésité sérieuse. La présente étude portait sur les répercussions des habitus corporels sur les pressions intracardiaques, le débit cardiaque obtenu par thermodilution (DCTD), le débit cardiaque (DC) calculé selon le principe indirect de Fick (iFick) et la résistance vasculaire pulmonaire (RVP) chez les sujets ayant une hémodynamie cardiopulmonaire normale.

Méthodes : Nous avons mené une analyse rétrospective auprès de volontaires en bonne santé et de patients orientés pour un cathétérisme cardiaque droit en raison de dyspnée d'origine inconnue, mais qui avaient une hémodynamie normale. Au sein de 65 sujets (53 ± 14 ans; 51 % de femmes), 31 % avaient un poids normal, 49 % faisaient de l'embonpoint et 20 % souffraient d'obésité d'après l'indice de masse corporelle entre 30-39,9 kg/m2. Nous avons comparé les saturations veineuses mixtes en oxygène et les pressions intracardiaques de toutes les catégories d'indice de masse corporelle. Nous avons examiné la

Right heart catheterization (RHC) remains the gold standard to confirm the diagnosis of pulmonary hypertension (PH). Hemodynamic classification of PH includes the measurement of mean pulmonary artery pressure (mPAP), mean pulmonary artery wedge pressure (mPAWP), and pulmonary vascular resistance (PVR).[1] Recently, thresholds that define PH have been changed, particularly with respect to the mPAP, based on several considerations.[1-3] The new PH definition includes a mPAP > 20 mm Hg instead of ≥ 25 mm Hg at rest. In addition, a PVR ≥ 3 WU is now a requirement for the diagnosis of pre-capillary PH.[1] There is emerging evidence that, for patients with heart failure or with risk factors for PH, prognosis is adversely affected with modest increases in mPAP or PVR.[4] Given narrower margins for disease diagnosis, it is essential to conform to best practices in conducting RHC for reliable and accurate hemodynamic information.

Globally, the rates of overweight and obesity are increasing, a risk factor for the development of heart failure and PH.[5,6] Given this, the prevalence of obesity among patients undergoing RHC is high. Considerations are twofold. First, hemodynamics in individuals who are

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Ethics Statement: All subjects provided written, informed consent, and Mount Sinai Hospital research ethics board (REB no. 11-0190-A and 16-0217-E) had approved this study.

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See page 1115 for disclosure information.

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CO. This difference was largest in the obese group—on average by 23% ± 10%, translating to an overestimation of PVR by 34% ± 16% on average.

Conclusions: In individuals without severe obesity, intracardiac pressures are not different, but mixed venous oxygen saturations are lower. Obesity confounds estimations of CO and PVR by iFick methods, which could result in inappropriate hemodynamic classification. These data can inform best practices in hemodynamic assessment of populations with obesity.

concordance entre le calcul du DC selon le principe iFick au moyen de 3 formules, ainsi que le DCTD et la RVP.

Résultats : Les pressions intracardiaques n'ont montré aucune différence, mais les saturations veineuses mixtes en oxygène étaient plus faibles chez les sujets obèses. Le DC calculé selon le principe iFick a démontré une sous-estimation du DCTD, particulièrement lors du calcul au moyen de la formule LaFarge, qui a révélé une différence systématique de 0,33 L/min à chaque augmentation du DC de 1 L/min. Cette différence qui était plus importante chez les sujets obèses (en moyenne de 23 % ± 10 %, se traduisait en moyenne par une surestimation de la RVP de 34 % ± 16 %).

Conclusions : Chez les individus non atteints d'une obésité sérieuse, les pressions intracardiaques ne sont pas différentes, mais les saturations veineuses mixtes en oxygène sont plus faibles. L'obésité fait remettre en cause les estimations du DC et de la RVP par les méthodes iFick, lesquelles pourraient donner lieu à une classification hémodynamique erronée. Ces données peuvent permettre d'établir des pratiques exemplaires lors de l'évaluation hémodynamique des populations atteintes d'obésité.

overweight or have obesity may indicate adaptation of cardiovascular physiology to changes in body habitus.[7,8] Patients with class III or greater obesity (body mass index [BMI] $\geq$ 40 kg/m^2) have shown increases in cardiac output (CO) and ventricular filling pressures, although less is known about populations with less-extreme ranges of body habitus.[8-10] Second, obesity may confound adjustments that are already made when considering morphometric data[11]; for example, obesity may confound the use of formulae employed to estimate indirect Fick (iFick) CO, which were derived from relatively lean patients.[12-14]

The objective of this study was to understand the effect of body habitus on hemodynamic assessment, particularly the mPAP, mPAWP, CO measured by thermodilution (TDCO) and iFick methods, and derived PVR. In a population with normal resting and exercise hemodynamics, we compared individuals of normal weight, those who were overweight, and those with class I or class II obesity as defined by BMI.[5] As an internal control, we compared men and women, as the effect of sex on body morphometrics and hemodynamics is better understood.[15]

Methods

Study population

Subjects were selected from 2 databases. The first database included healthy volunteers from the community who participated in a physiologic study of RHC during rest and exercise. Hemodynamics from this cohort have been published.[3] Inclusion criteria were age $\geq$ 45 years, normal sinus rhythm, QRS duration of < 110 ms, no prior history of coronary disease, heart failure, diabetes mellitus, hypertension, and not taking medications or hormone replacements.

The second database included patients who underwent RHC at rest and with exercise for the assessment of dyspnea of unknown origin (DUO). Individuals with normal hemodynamics at rest and during exercise were included. DUO patients were excluded if mPAP > 20 mm Hg at rest, or if ΔmPAP/ΔCO > 3 WU and/or if ΔmPAWP/ΔCO > 2 mm Hg/L*min^{-1} during exercise.

BMI categories were defined as follows: normal, 18.5-24.9 kg/m^2; overweight, 25-29.9 kg/m^2; and obese, 30-39.9 kg/m^2.[5] All subjects provided written, informed consent.

Cardiac catheterization standard operating procedures

A balloon-tipped fluid-filled 7F or 7.5F catheter was inserted percutaneously and advanced into the pulmonary artery under fluoroscopic guidance. Pressure transducers were zeroed at the midaxillary level, and simultaneous right atrial, right ventricular, and pulmonary artery pressures were recorded continuously. The balloon was inflated intermittently to record the mPAWP. Mixed venous blood was sampled for oximetry to calculate iFick CO, and TDCO was measured in triplicate with less than 10% variation between measurements. Our procedures for exercise have been published previously.[3,15] Subjects were excluded if they did not have resting data available for both TDCO and iFick CO.

Clinical and hemodynamic data

Demographic variables including age, sex, height, and weight were extracted from databases. In addition to BMI, body surface area (BSA) was calculated by the Dubois formula —0.007184 x Height (cm)$^{0.725}$ x Weight (kg)$^{0.425}$. Hemodynamic variables extracted included resting right atrial and pulmonary artery pressures, end-expiratory mPAWP, heart rate, and TDCO. The arterial, and mixed venous oxygen saturations were recorded, as was hemoglobin concentration. Arterial and mixed venous oxygen content was calculated using

standard formulae, as was the arteriovenous oxygen (a-vO_2) difference.

Estimated resting oxygen consumption (VO_2) was calculated by the Dehmer, Bergstra, and LaFarge formulae defined by the following equations:

$$\text{Dehmer formula}: 125\ (\text{mL/min per m}^2) * \text{BSA};$$

LaFarge formula:

$$138.1 - (X * \ln(\text{age})) + (0.378 * \text{heart rate}) * \text{BSA}\ (\text{men: } X = 11.49;\ \text{women: } X = 17.04);$$

Bergstra formula:

$$157.3 * \text{BSA} + X - (10.5 * 1n(\text{age})) + 4.8(\text{men: } X = 10;\ \text{women: } X = 0).$$

Resting VO_2 was calculated as TDCO * a-vO_2 difference. CO estimated by iFick methods was calculated as VO_2 (mL/min) / a-vO_2 difference and converted to L/min.

Statistical analysis

Statistical analyses were performed using GraphPad Prism v.8.4.2 (La Jolla, CA). Continuous variables are presented as mean ± standard deviation or median (interquartile range), and categorical variables are presented as percentages. Between-group comparisons of BMI categories were conducted using a one-way analysis of variance. Comparisons of variables derived from different methods of CO measurements were conducted using a one-way repeated-measures analysis of variance. Significant main effects were analyzed post hoc using Tukey's multiple comparisons test. Independent-sample Student *t* tests were used to determine statistical significance in subjects stratified by sex. Bland Altman plots assessed the agreement between methods of assessment for VO_2 or CO, and PVR and 95% limits of agreement (LOA) were reported. Linear regression analyses were employed to assess the proportional bias for the overall cohort, and to assess the relationship of the morphometric variables height, weight, BMI, and BSA to TDCO, VO_2, and the a-vO_2 difference. $P < 0.05$ was considered statistically significant.

Three-dimensional plots were constructed using RStudio v1.2.5001 (RStudio, Inc, Boston, MA) assessing TDCO, and a-vO_2 difference relationships with morphometric variables.

Results

Study population and characteristics

A summary of subject selection is presented in Figure 1, and clinical characteristics are shown in Table 1. The database of healthy subjects contained 36 individuals, 8 of whom were excluded due to incomplete data. The median age was 56 years; 50% were female; and the median BMI was 26.3 kg/m^2. The proportions of healthy subjects with a BMI of 18.5-24.9 kg/m^2, 25-29.9 kg/m^2, and 30-39.9 kg/m^2 were 39%, 57%, and 4%, respectively.

The DUO patient database contained 137 participants, of which 37 were eligible for analysis. The median age was 52 years; 51% were female; and the median BMI was 28.1 kg/m^2. The proportions of these patients with a BMI of 18.5-24.9 kg/m^2, 25-29.9 kg/m^2, and 30-39.9 kg/m^2 were 24%, 43%, and 33%, respectively.

By design, DUO patients were hemodynamically normal at rest and with exercise. Eighteen patients (28%) had a risk factor for PH (history of venous thromboembolism or connective tissue disease), and 15 patients (23%) had a

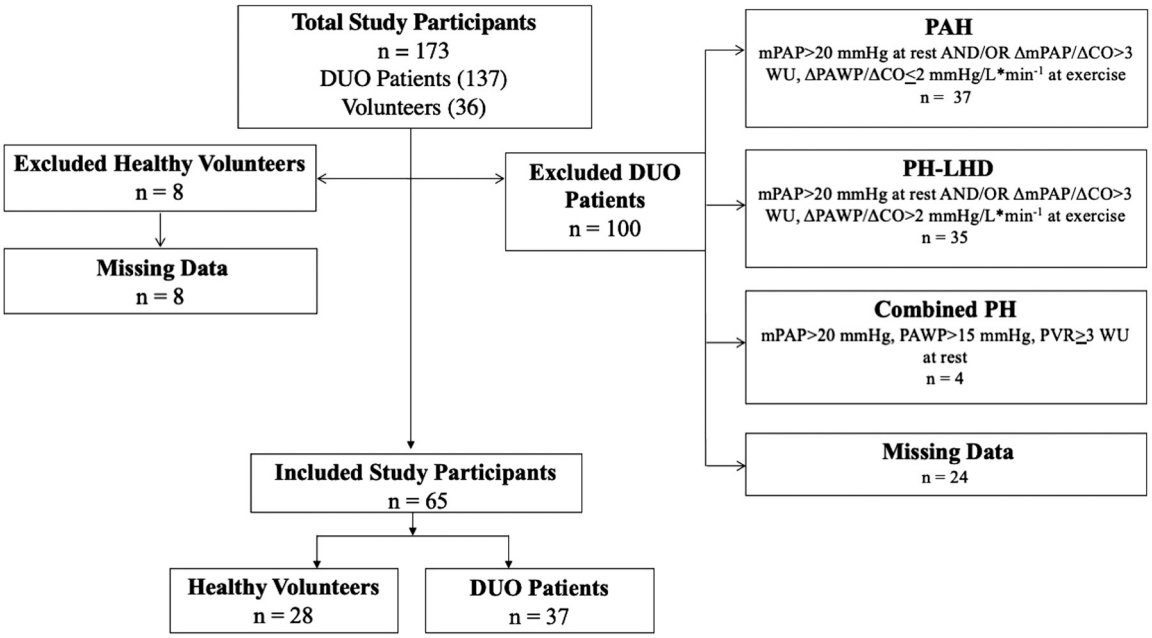

Figure 1. Study flow of participant selection. See text for details. CO, cardiac output; DUO, dyspnea of unknown origin; mPAP, mean pulmonary artery pressure; PAH, pulmonary arterial hypertension; PAWP, pulmonary artery wedge pressure; PH-LHD, pulmonary hypertension due to left heart disease; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

Table 1. Baseline characteristics

	DUO	Healthy volunteers	Total
N	n = 37	n = 28	n = 65
Women, %	51	50	51
Age, y	52 (18)	56 (12)	53 (14)
Height, m	1.70 (0.17)	1.72 (0.14)	1.70 (0.16)
Mass, kg	76.2 (25.5)	75.5 (17.8)	76.0 (21.0)
BSA, m^2	1.88 (0.35)	1.87 (0.32)	1.88 (0.30)
BMI, kg/m^2	28.1 (6.5)	26.3 (3.4)	27.1 (4.5)
18.5−24.9	24%	39%	31%
25−29.9	43%	57%	49%
30−39.9	33%	4%	20%

Data are presented as median (interquartile range) or percentage.

BMI, body mass index; BSA, body surface area; DUO, dyspnea of unknown origin.

cardiovascular risk factor. The final dataset for analysis consisted of 65 subjects (51% female): the proportions with a BMI of 18.5-24.9 kg/m^2, 25-29.9 kg/m^2, and 30-39.9 kg/m^2 were 31%, 49%, and 20%, respectively.

Thermodilution cardiac output: associations with morphometric variables

Hemodynamic characteristics for the overall cohort, men, women, and by BMI categories are given in Table 2. In this study, we assumed that TDCO was the reference standard for assessment of CO. TDCO in the overall cohort was 5.24 L/min. As expected, TDCO and stroke volume were significantly higher in men compared to women, and they correlated as expected with height and weight, as shown in Figure 2A. TDCO also significantly correlated to BSA ($P < 0.001$, $R^2 = 0.21$). We did not observe a significant relationship between TDCO ($P = 0.20$, $R^2 = 0.03$) and stroke volume ($P = 0.13$, $R^2 = 0.04$) with increasing BMI.

Hemoglobin concentration is higher in men than women, and in subjects with a BMI of 30-39.9 kg/m^2. The a-vO_2 difference and calculated VO_2 is also higher in men than women, and in subjects with a BMI of 30-39.9 kg/m^2 compared to the other 2 BMI groups. Figure 2B illustrates the relationship between height, weight, and the a-vO_2 difference. The mixed venous oxygen saturation was not different between men and women. However, in subjects with a BMI between 30-39.9 kg/m^2, compared to the other 2 BMI groups, we observed that the higher a-vO_2 difference was related in part to a significantly lower mixed venous oxygen saturation; consistent with this, we observed a strong correlation between weight and the a-vO_2 difference ($P < 0.0001$, $R^2 = 0.28$).

Contrasting CO and VO_2 derived by thermodilution and iFick methods

iFick calculations for VO_2 and CO are shown in Table 3 alongside TDCO derived VO_2. We observed a positive trend toward increasing VO_2 ($P < 0.0001$) and CO ($P = 0.20$) with BMI by iFick formulae and thermodilution. However, iFick CO and VO_2 from the LaFarge formula significantly underestimated TDCO measurements in the overall cohort and across BMI categories ($P < 0.0001$). The mean percentage difference between VO_2 or CO calculated by the LaFarge formula and TDCO was −18% ± 13%, in individuals with a BMI of 18.5-24.9 kg/m^2, increasing to −23% ± 10% in the BMI 30-39.9 kg/m^2 group. Similarly, the iFick CO and VO_2 from the Dehmer formula significantly underestimated CO compared to TDCO in the overall cohort and across BMI groups. The percentage difference between VO_2 or CO calculated by the Dehmer formula and TDCO was 0% ± 19% in the BMI 18.5-24.9 kg/m^2 group, increasingly significantly to −15% ± 13% in the BMI 30-39.9 kg/m^2 group ($P = 0.04$). Percentage differences were quantitatively smaller with the Dehmer formula compared to the LaFarge formula. Finally, the iFick CO and VO_2 calculated using the Bergstra formula

Table 2. Hemodynamic characteristics, thermodilution cardiac output (TDCO), and derived variables by sex and body mass index (BMI)

		By sex		By BMI (kg/m^2)		
TDCO and hemodynamic variables	Total	Men	Women	18.5−24.9	25−29.9	30−39.9
HR, beats/min	67 ± 11	66 ± 11	67 ± 12	66 ± 11	67 ± 11	67 ± 14
TDCO, L/min	5.24 ± 1.12	5.63 ± 1.07	4.85 ± 1.06*	4.99 ± 1.26	5.15 ± 0.99	5.83 ± 1.09
CI, $L/min/m^2$	2.73 ± 0.52	2.72 ± 0.50	2.73 ± 0.55	2.84 ± 0.58	2.70 ± 0.53	2.63 ± 0.41
SV, mL/beat	80 ± 18	86 ± 18	74 ± 15*	77 ± 18	78 ± 16	89 ± 20
SVI, $mL/beat/m^2$	42 ± 8	42 ± 9	41 ± 8	44 ± 9	41 ± 8	40 ± 8
mRAP, mm Hg	4 ± 3	4 ± 3	4 ± 3	4 ± 4	5 ± 3	4 ± 3
mPAP, mm Hg	16 ± 4	16 ± 4	16 ± 4	15 ± 4	17 ± 4	15 ± 3
mPAWP, mm Hg	9 ± 4	10 ± 4	9 ± 4	8 ± 4	10 ± 4	9 ± 3
TPG, mm Hg	7 ± 3	7 ± 3	7 ± 3	7 ± 2	7 ± 3	6 ± 4
Hb, g/dL	13.8 ± 1.4	14.5 ± 1.2	13.1 ± 1.1*	13.3 ± 1.3	13.7 ± 1.3	14.7 ± 1.3†
SvO_2, %	72 ± 5	72 ± 6	72 ± 4	74 ± 4	72 ± 4	68 ± 6†,‡
SaO_2, %	98 ± 2	98 ± 2	98 ± 2	98 ± 1	98 ± 2	96 ± 3†,‡
CaO_2, mL/L	187 ± 18	196 ± 16	177 ± 15*	182 ± 17	186 ± 17	196 ± 20
CvO_2, mL/L	136 ± 17	143 ± 17	130 ± 15*	136 ± 18	136 ± 16	138 ± 21
a-vO_2 diff, mL/L	50 ± 8	53 ± 9	48 ± 7*	46 ± 5	50 ± 8	58 ± 8†,‡
VO_2, mL/min	262 ± 67	295 ± 65	229 ± 50*	227 ± 52	254 ± 52	335 ± 67†,‡

Data are displayed as mean ± standard deviation.

a-vO_2 diff, arteriovenous oxygen difference; CaO_2, arterial oxygen content; CI, cardiac index; CvO_2, venous oxygen content; Hb, hemoglobin; HR, heart rate; mPAP, mean pulmonary artery pressure; mPAWP, mean pulmonary artery wedge pressure; mRAP, mean right atrial pressure; SaO_2, arterial saturation; SV, stroke volume; SVI, stroke volume index; SvO_2, mixed venous saturation; TPG, transpulmonary gradient. VO_2, oxygen consumption.

*Significant vs men.

†Significant vs BMI 18.5-24.9 kg/m^2.

‡Significant vs BMI 25-29.9 kg/m^2.

Table 3. Comparison of VO_2, CO, and PVR measurements obtained by thermodilution and iFick formulae

		iFick method		
VO_2, mL/min	TD	LaFarge	Bergstra	Dehmer
All	262 ± 67	207 ± 45*	271 ± 40	241 ± 29*
Men	295 ± 65	245 ± 25*	301 ± 33	260 ± 27*
Women	229 ± 50	169 ± 20*	242 ± 21	222 ± 16
BMI, kg/m^2				
18.5–24.9	227 ± 52	184 ± 38*	243 ± 28	219 ± 18
25–29.9	254 ± 52	202 ± 37*	269 ± 30†	240 ± 20†
30–39.9	335 ± 67†	253 ± 39*,†	319 ± 37†	277 ± 28*,†

		iFick method					
CO, L/min	TD	LaFarge	% diff	Bergstra	% diff	Dehmer	% diff
All	5.24 ± 1.12	4.17 ± 0.86*	−19 ± 15	5.48 ± 0.84	7 ± 20	4.88 ± 0.70*	−4 ± 18
Men	5.63 ± 1.07	4.73 ± 0.64*	−14 ± 13	5.80 ± 0.81	5 ± 18	5.02 ± 0.71*	−9 ± 16
Women	4.85 ± 1.06	3.62 ± 0.67*	−24 ± 15	5.17 ± 0.76	10 ± 21	4.74 ± 0.67	1 ± 19
BMI, kg/m^2							
18.5–24.9	4.99 ± 1.26	4.03 ± 0.88*	−18 ± 13	5.35 ± 0.83	10 ± 19	4.82 ± 0.66	0 ± 19
25–29.9	5.15 ± 0.99	4.15 ± 0.86*	−18 ± 17	5.52 ± 0.89	9 ± 21	4.93 ± 0.75	−2 ± 19
30–39.9	5.83 ± 1.09	4.42 ± 0.80*	−23 ± 10	5.58 ± 0.79	−3 ± 14	4.84 ± 0.65*	−15 ± 13†

		iFick method					
PVR, WU	TD	LaFarge	% diff	Bergstra	% diff	Dehmer	% diff
All	1.34 ± 0.63	1.71 ± 0.85*	28 ± 25	1.28 ± 0.60	−4 ± 17	1.42 ± 0.66	8 ± 20
Men	1.17 ± 0.57	1.39 ± 0.71*	20 ± 18	1.15 ± 0.61	−2 ± 17	1.32 ± 0.71*	13 ± 20
Women	1.51 ± 0.65	2.02 ± 0.86*	36 ± 27	1.40 ± 0.56	−5 ± 19	1.52 ± 0.60	3 ± 20
BMI, kg/m^2							
18.5–24.9	1.43 ± 0.60	1.74 ± 0.65*	25 ± 19	1.29 ± 0.45	−7 ± 15	1.42 ± 0.50	3 ± 19
25–29.9	1.40 ± 0.62	1.80 ± 0.90*	28 ± 30	1.33 ± 0.62	−5 ± 19	1.48 ± 0.67	6 ± 21
30–39.9	1.08 ± 0.70	1.44 ± 0.98*	34 ± 16	1.13 ± 0.75	5 ± 14	1.30 ± 0.85*	21 ± 17

Data are presented as mean ± SD, or mean % difference (% diff) ± SD.
BMI, body mass index; CO, cardiac output; iFick, indirect Fick; PVR, pulmonary vascular resistance; VO_2, oxygen consumption.
*Significant vs thermodilution.
†Significant vs BMI 18.5–24.9 kg/m^2.

were not significantly different from TDCO in the overall cohort or across BMI categories.

Figure 3, A-C demonstrates the agreement between the TDCO and iFick estimations of CO. The LaFarge iFick CO underestimates TDCO with an absolute value to the bias of 1.07 L/min (95% LOA −0.64 L/min to 2.78 L/min), with a significant slope (P = 0.0058) such that for every 1 L/min increase in CO, the LaFarge CO underestimated TDCO by 0.33 L/min. Similarly, the Dehmer iFick CO demonstrated a smaller bias in the agreement with TDCO, with an absolute value of 0.36 L/min (95% LOA −1.58 L/min to 2.29 L/min); again, with a significant slope to the bias ($P < 0.0001$) for every 1 L/min increase in CO, the Dehmer CO underestimated TDCO by 0.62 L/min. Finally, the Bergstra iFick CO

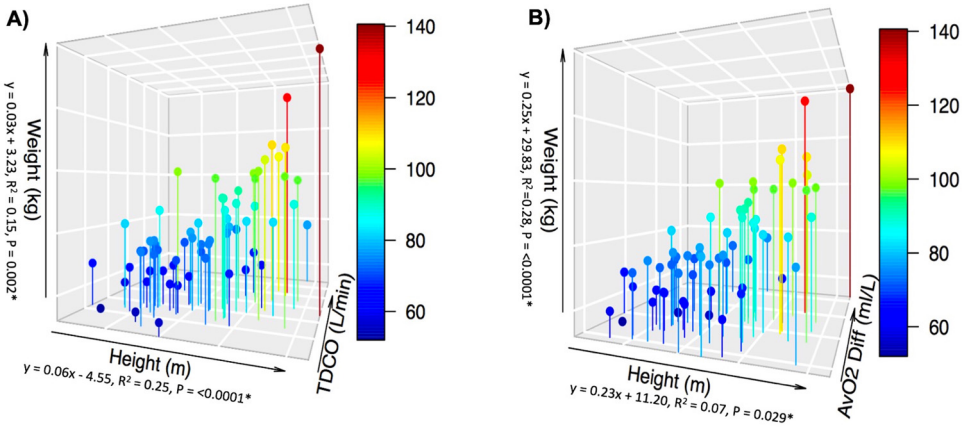

Figure 2. Three-dimensional plots assessing the relationship between (**A**) thermodilution cardiac output (TDCO), (**B**) the arteriovenous oxygen difference (a-vO_2 diff) and height and weight. Linear correlations between TDCO and a-vO_2 diff and morphometric variables are shown below their respective axes. * Statistically significant relationships.

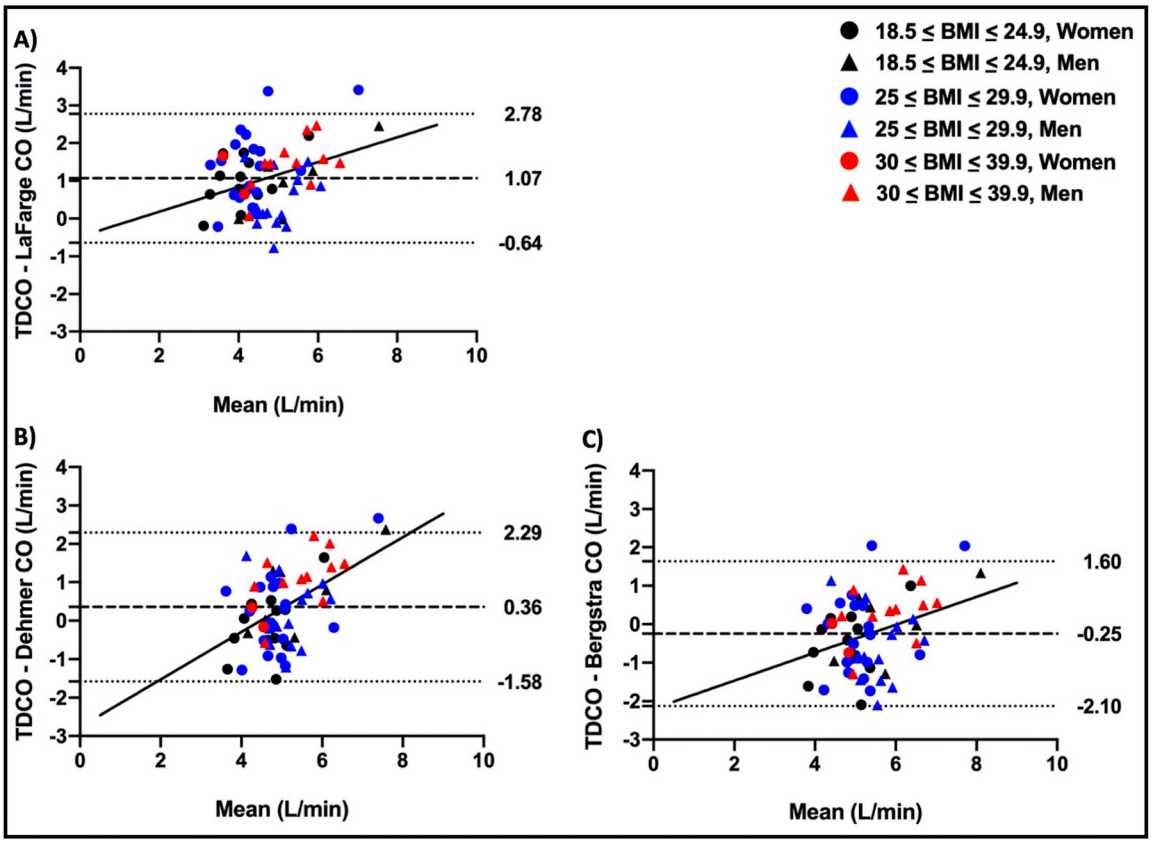

Figure 3. Bland Altman analysis of iFick cardiac output (CO) and thermodilution cardiac output (TDCO). Horizontal lines are displayed at the mean difference and 95% limits of agreement (LOA). The agreement between TDCO and (**A**) the LaFarge CO, (**B**) the Dehmer CO, and (**C**) the Bergstra CO is shown. BMI, body mass index.

overestimated TDCO with an absolute value to the bias of 0.25 L/min (95% LOA −2.10 L/min to 1.60 L/min); again, there is a significant slope to the bias ($P = 0.007$) such that for every 1 L/min increase in CO, the Bergstra CO overestimated TDCO by 0.36 L/min.

Pulmonary vascular hemodynamics: associations with morphometric variables

There were no differences between BMI categories and no significant BMI relationships for mean right atrial pressure, pulmonary artery pressures, and mPAWP (Table 2). TDCO-derived PVR is included in Table 3. There was no significant difference in PVR between men and women or across BMI categories. PVR agreement was examined between values calculated from TDCO and iFick methods and is presented in Figure 4, A-C. The iFick PVR by the LaFarge formula overestimated TDCO-derived PVR with an absolute value to the bias of 0.37 WU (95% LOA −1.15 to 0.42) with a significant slope ($P < 0.0001$) such that for every 1 WU increase, the iFick LaFarge formula overestimates PVR by 0.31 WU. A systematic bias or significant slope to the bias was not observed between TDCO PVR and the Bergstra or Dehmer PVR.

The mean percentage difference between PVR calculated with TDCO vs iFick CO was different among BMI groups, particularly with the LaFarge and Dehmer formulae (Fig. 5). For the Dehmer formula, the mean percentage difference in PVR from the TDCO-derived value was 3% ± 19% in the BMI 18.5-24.9 kg/m^2 group, increasing to 21% ± 17% in the BMI 30-39.9 kg/m^2 group. With respect to the LaFarge formula, the percentage difference in PVR from the TDCO-derived value was overestimated, with a mean percentage difference of 25% ± 19% among the BMI 18.5-24.9 kg/m^2 group, increasing to 34% ± 16% in the BMI 30-39.9 kg/m^2 group. PVR calculated by the LaFarge-derived CO was ≥ 3 WU in 8% of individuals with a BMI of 30-39.9 kg/m^2.

Discussion

We assessed the effect of body morphometrics, classified by BMI, on hemodynamic measurements obtained by RHC in subjects with otherwise normal hemodynamics, at rest and during exercise. Our data reinforce previous recommendations to avoid iFick estimations in favour of TDCO or direct Fick CO methods.

The relationship of body habitus to TDCO and a-vO_2 difference

Prior studies[9,10] examining the associations of body habitus to invasive hemodynamics were primarily focused on subjects with severe obesity, with BMIs ≥ 40 kg/m^2. We aimed to extend our understanding of lessextreme ranges of body habitus, which are more reflective of patients requiring RHC today, by looking at individuals with class I or class II obesity. Although BMI was related to CO in subjects with severe

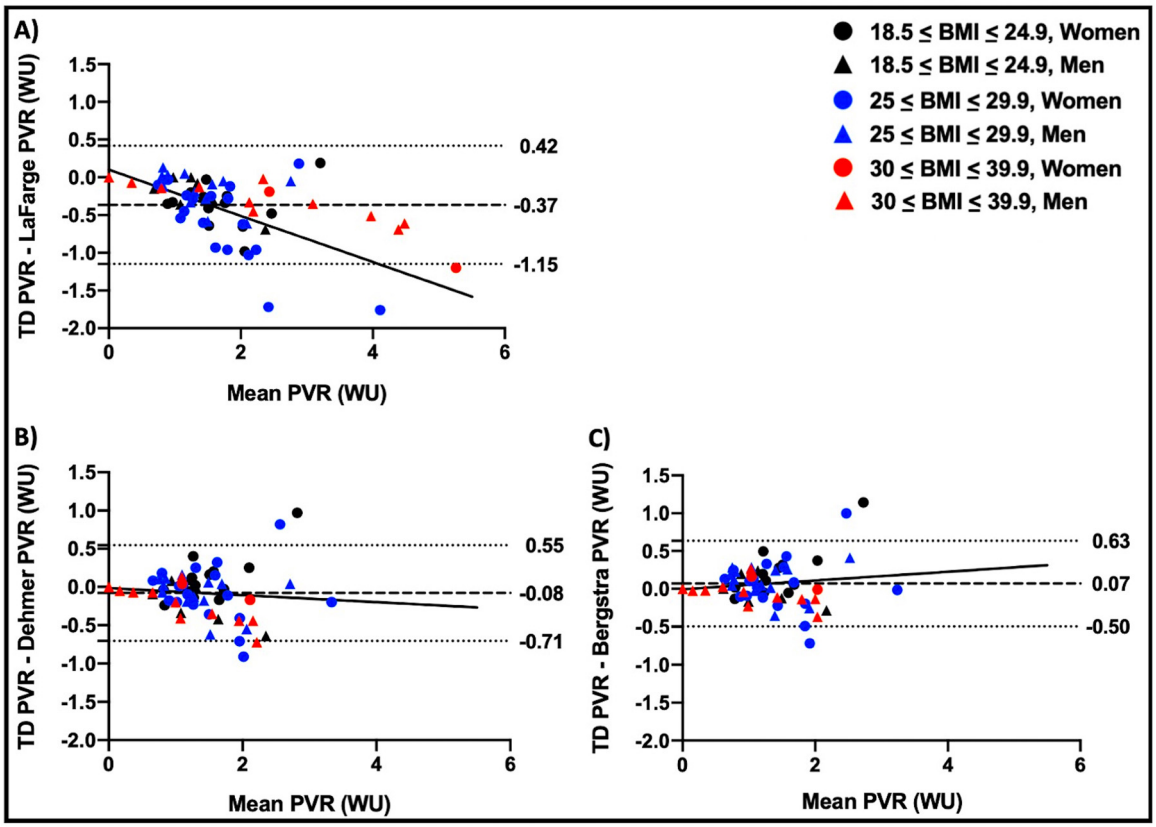

Figure 4. Bland Altman analysis of pulmonary vascular resistance (PVR) calculated by indirect Fick and thermodilution (TD) cardiac output. Horizontal lines are displayed at the mean difference and 95% limits of agreement. The agreement between PVR calculated by TD cardiac output and the (**A**) LaFarge, (**B**) Dehmer, and (**C**) Bergstra formulae is shown. BMI, body mass index.

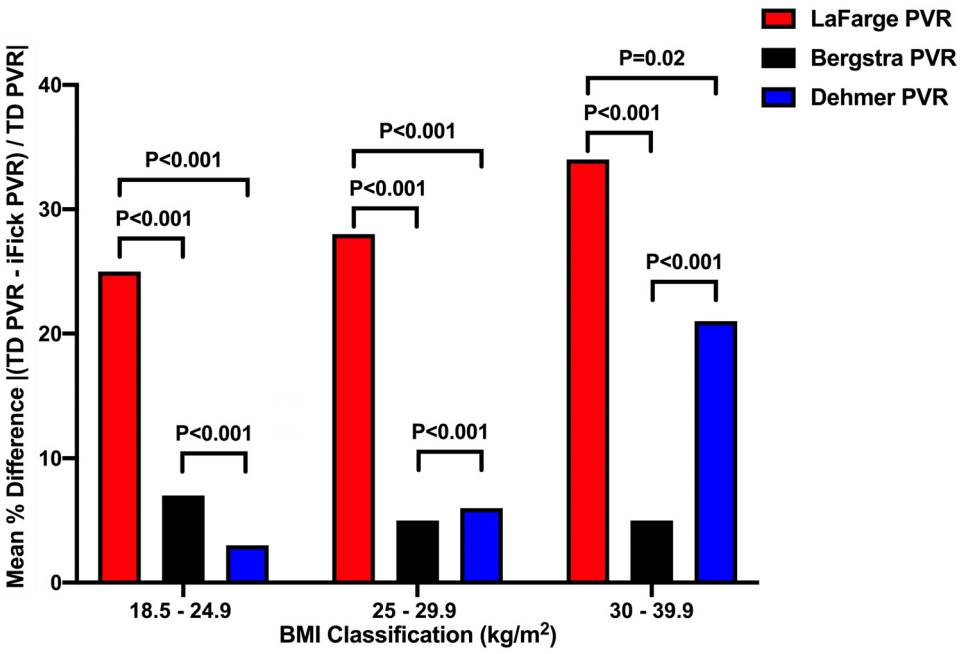

Figure 5. Bar graph depicting the absolute value of the mean percentage difference between thermodilution (TD) cardiac output pulmonary vascular resistance (PVR) and indirect Fick (iFick) PVR, by body mass index (BMI) classification.

obesity, we observed that height and weight were more strongly related to TDCO than BMI across a modest BMI range. Our findings were consistent with previous observations that CO and stroke volume are more closely related to fat-free mass and its determinants, particularly height. As expected, TDCO was larger in men compared to women.[15,16]

We had the opportunity to examine directly measured mixed venous oxygen saturations and a-vO_2 differences across BMI groups. We observed relationships between a-vO_2 differences and body size that stood in contrast to those observed with CO. In this regard, the comparison of men and women was instructive. As expected, commensurate with greater body size and CO, men demonstrated higher hemoglobin concentration, and greater VO_2 and a-vO_2 differences compared to women, but with no differences in mixed venous oxygen saturation. In contrast, individuals with a BMI of 30-39.9 kg/m^2 demonstrated higher VO_2 and a-vO_2 differences, but at the expense of increasing oxygen extraction and a more depressed mixed venous oxygen saturation. We also observed that the a-vO_2 difference was more strongly related to weight than to height. The a-vO_2 difference is a measure of tissue oxygen extraction, and it reflects the oxidative function of metabolically active mass. Our findings may suggest that increased oxygen extraction is an adaptation to sustain a larger body habitus, although the site of extraction is unclear, as adipose tissue has a low metabolic rate.[17] Another interpretation is perhaps that CO in individuals with obesity is insufficient relative to body habitus, thus requiring a greater a-vO_2 difference. Consistent with our findings, Alexander et al.[17] showed that significant weight loss among severely obese subjects was associated with significant reduction in the a-vO_2 difference and CO.

In the population studied, we did not find evidence of any relationships between obese body habitus and pulmonary artery pressures, or right- and left-sided filling pressures. This evidence is in contrast to previous studies that have demonstrated an association between obesity and elevated right atrial pressure and mPAWP.[8,9] These studies, however, predominately included diseased populations and individuals with severe obesity.

Implications for catheterization laboratory practices

It has been demonstrated that there is only modest agreement between iFick methodologies and TDCO, and that TDCO is a better predictor of all-cause mortality.[18,19] iFick formulae were derived from populations across varying age ranges extending to very young subjects, for whom findings are less generalizable to patients requiring RHC today.[13,14,20] Among patients undergoing RHC for suspected PH, iFick generally underestimates CO compared to TDCO.[18-20] The present study extends these findings by demonstrating the effect of body habitus to confound estimates of VO_2, and therefore calculated CO. There was a slope to the bias such that iFick methods demonstrated increasing differences from TDCO as CO increases, and because individuals with a BMI $\geq$ 25 kg/m^2 have a larger CO, these systematic differences will occur more frequently than they do in individuals with a BMI of 18.5-24.9 kg/m^2. We identified several issues, particularly with the LaFarge formula, which underestimated TDCO to a greater degree in women than in men, and further systematically underestimated TDCO across BMI groups, with the greatest differences in the BMI 30-39.9 kg/m^2 group. A similar pattern was identified using the Dehmer formula, which also underestimated CO as BMI increased, particularly in the BMI 30-39.9 kg/m^2 group.[18] If there is no other option but to employ an iFick estimate of CO, our results suggest that the Bergstra formula demonstrated the best agreement with TDCO across BMI categories.

Our study extends previous invasive hemodynamic investigations by inclusion of subjects with a more modest BMI range of overweight and obese body habitus, whereas previous hemodynamic research has focussed on patients with severe obesity.[20] Our findings are relevant to patients undergoing RHC for the evaluation of suspected PH, a condition that exhibits a female predilection, and the proportion of patients with a BMI $\geq$ 30 kg/m^2 is approximately 50%.[21] Obviously, inaccurate estimation of CO will affect the calculation of PVR. In a proportion of our cohort with otherwise normal hemodynamics, use of the LaFarge formula yielded a calculated PVR $\geq$ 3 WU, the current threshold for classification of pre-capillary pulmonary vascular disease. A PVR threshold of 3 WU is also used to differentiate between isolated post-capillary PH and combined pre- and post-capillary PH. Calculation of PVR from iFick methods can result in misdiagnosis of PH and lead to inappropriate and possibly dangerous treatment methods for RHC patients. We showed that overestimation of PVR was more likely in women and individuals with a higher BMI, based on the underestimation of CO by the iFick formulae. Our findings emphasize the importance of best practices for accurate hemodynamic assessment as the prevalence of obesity trends upward in North America.[7]

Limitations

There are limitations to consider in this analysis. We attempted to study the effect of body habitus in subjects with normal resting and exercise hemodynamics, but some individuals had DUO and comorbid medical conditions. The use of BMI to evaluate body habitus also has limitations, and we did not have measures of body composition for the direct assessment of fat-free mass, or other measures of cardiometabolic changes.[16]

Conclusions

This hemodynamic study examined a cohort of subjects who demonstrated a range of body habitus levels. Obesity systematically alters assessment of VO_2, CO, and PVR by the iFick formulae, potentially leading to misclassification of PH patients. Among individuals with a BMI of 30-39.9 kg/m^2, we observed alterations in physiology, including a lowered mixed venous oxygen saturation and a larger a-vO_2 difference. The effect of body habitus on circulatory physiology bears further study.

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Disclosures

The authors have no conflicts of interest to disclose.

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