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RESEARCH ARTICLE

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Impact of body position on hemodynamic measurements during exercise: A tale of two bikes

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Abstract

The addition of exercise testing during right heart catheterization (RHC) is often required to accurately diagnose causes of exercise intolerance like early pulmonary vascular disease, occult left heart disease, and preload insufficiency. We tested the influence of body position (supine vs. seated) on hemodynamic classification both at rest and during exercise. We enrolled patients with exercise intolerance due to dyspnea who were referred for exercise RHC at the Cleveland Clinic. Patients were randomized (1:1) to exercise in seated or supine position to a goal of 60 W followed by maximal exercise in the alternate position. We analyzed 17 patients aged 60.3 ± 10.9 years, including 13 females. At rest in the sitting position, patients had significantly lower right atrial pressure (RAP), mean pulmonary artery pressure (mPAP), pulmonary artery wedge pressure (PAWP) and cardiac index (CI). In every stage of exercise (20, 40, and 60 W), the RAP, mPAP, and PAWP were lower in the sitting position. Exercise in the sitting position allowed the identification of preload insufficiency in nine patients. Exercise in either position increased the identification of postcapillary pulmonary hypertension (PH). Body position significantly influences hemodynamics at rest and with exercise; however, mPAP/CO and PAWP/CO were not positionally affected. Hemodynamic measurements in the seated position allowed the detection of preload insufficiency, a condition that was predominantly identified as no PH during supine exercise.

KEYWORDS
exercise hemodynamics, exercise intolerance, preload insufficiency, pulmonary hypertension, right heart catheterization

INTRODUCTION

Exercise intolerance is a common manifestation of several conditions, including heart failure with preserved ejection fraction (HFpEF),[1,2] preload insufficiency,[1–3] and pulmonary hypertension (PH).[4,5] Differentiating between these conditions is crucial as clinical management is markedly different. Nevertheless, diagnosis can be challenging at rest particularly in early and/or well-compensated disease states. Although noninvasive testing may suggest a specific diagnosis, right heart catheterization (RHC) with exercise remains essential for the diagnosis of occult postcapillary PH, preload insufficiency, and exercise PH.[1–5]

Unfortunately, there is no standardization to guide the implementation of exercise RHC,[5] therefore, exercise tests are performed using diverse procedural practices based on center protocols and/or physician expertise.[6] Body position (i.e., supine or sitting upright) is a crucial factor that may impact the hemodynamic response during exercise.[7–9] Several RHC laboratories continue to use recumbent or semirecumbent bikes since this approach avoids patient repositioning, pressure transducer recalibration, and additional baseline hemodynamic determinations.

Since body position may influence hemodynamic measurements obtained by RHC during exercise, we tested its effect on resting and exercise hemodynamics in a cohort of patients evaluated for exercise intolerance. We hypothesize that body position affects hemodynamic determinations during exercise, predominantly due to the variable effect on ventricular preload. More specifically, we hypothesized that exercise in the supine position increases ventricular preload, enhancing the recognition of HFpEF, whereas exercise in sitting position reduces ventricular preload, increasing the recognition of preload insufficiency.

METHODS

We prospectively enrolled patients referred for exercise RHC at the Cleveland Clinic because of exercise intolerance due to dyspnea between January 2018 and August 2020. The institutional review board of the Cleveland Clinic approved the present study (IRB # 16-872). Informed consent was obtained from all patients. We performed exercise in supine and sitting positions using a crossover design. We randomized patients to start with sitting or supine exercise, in a 1:1 fashion, using blocks of 10 (10 sealed envelopes, half containing cards for supine and half for sitting). After a resting period, we performed a second exercise in the alternate body position.

Baseline right heart catheterization

Baseline RHC was done in a supine position (legs flat) in the outpatient setting under local anesthesia (1% lidocaine) through the right or left internal jugular veins. Pressure transducers were zeroed at the midaxillary line while supine and at the fourth intercostal level while sitting. A 7.5 F pulmonary artery catheter (Biosensor International) was advanced through an 8.5 F introducer to the pulmonary artery. The pulmonary artery catheter position was confirmed by pressure waveform analysis and fluoroscopic imaging. For the hemodynamic determinations, we integrated waveforms from three respiratory cycles for determinations at end-expiration and for a period of 10 s for measurements averaged across the respiratory cycle. The RHC was performed by a single operator (A.R.T.).[6,10]

After pulmonary artery catheter insertion while in the supine position, we recorded right atrial pressure (RAP), systolic, diastolic, and mean PAP (mPAP), and pulmonary artery wedge pressure (PAWP) using established protocols, waveform tracings, and calipers.[11] For RAP, we recorded mean values averaged across the respiratory cycle. For PAP and PAWP, we recorded determinations both at end-expiration and averaged across the respiratory cycle. PAWP was recorded at mid "a" wave (without including the "v" wave). Cardiac output (CO) was measured by the thermodilution method. We calculated the cardiac index (CI: CO/body surface area) and PVR (using end-expiratory determinations).

Exercise protocol

After the aforementioned hemodynamic determinations, we repeated baseline measurements once patients were secured on the exercise equipment. Patients were exercised in randomized order both in the sitting (upright at 90°) and supine (to reach the pedals, the legs were elevated at 30° from the bed) positions. The initial exercise was submaximal to a goal of 60 W.[10] After hemodynamic determinations returned to baseline post-exercise, patients were situated in the alternate body position and completed a maximal exercise testing (Figure 1). Maximal exercise was determined by patient exhaustion. For instance, patients who performed an initial submaximal supine exercise (60 W), then underwent a maximal sitting exercise. Loaded exercise was completed in incremental stages (increasing 20 W every 2 min at a cycling rate of 60 rpm).[10]

Patients included in the analysis completed 60 W protocols in both sitting and supine positions during the

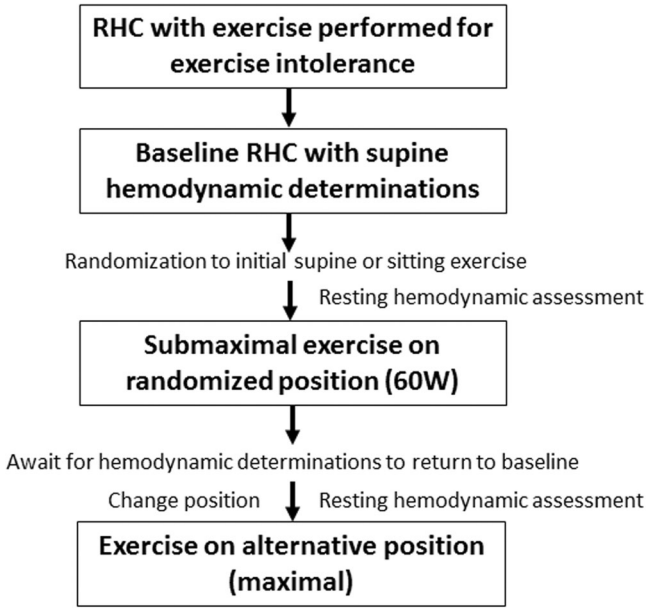

FIGURE 1 Study design. RHC, right heart catheterization.

same session. We excluded patients who could not achieve a workload of 60 W in both exercise position ($n = 2$). All exercise tests were supervised by the same exercise physiologist (D.P.). After the tests, patients were asked to identify which exercise position was easier.

Hemodynamic determinations during exercise

Pressure transducers were zeroed at the 4th intercostal level when sitting and at the midaxillary line when supine. Hemodynamic determinations were obtained at baseline and at every stage of the exercise,[6] including PAP, PAWP, RAP, and CO averaged across the respiratory cycle.[7,10] Before exercise, we measured CO by thermodilution three times at rest on each position, and values with less than 10% difference were averaged. However, given time constraints, we measured CO on one occasion per exercise stage, repeating the determination if it appeared inconsistent. We calculated PVR at every stage and mPAP/CO and PAWP/CO slopes using multipoint assessments of mPAP relative to CO.[12]

Hemodynamic interpretations at baseline and with exercise

We defined hemodynamic phenotypes based on definitions from recent guidelines (precapillary PH: mPAP > 20 mmHg, PAWP ≤ 15 mmHg and PVR > 2 Wood units (WU); postcapillary PH: mPAP > 20 mmHg, PAWP > 15 mmHg and PVR ≤ 2 WU; and combined pre- and postcapillary PH: mPAP > 20 mmHg, PAWP > 15 mmHg and PVR > 2 WU).[4] We defined undifferentiated PH as the hemodynamic profile characterized by mPAP > 20 mmHg, PAWP ≤ 15 mmHg, and PVR ≤ 2 WU.

A standardized approach to interpret hemodynamic changes during exercise is lacking.[5] Both in the sitting and supine positions, we classified patients based on the hemodynamic response observed during exercise, including normal response (mPAP/CO slope ≤ 3 WU and no evidence of preload insufficiency), precapillary PH (mPAP/CO slope > 3 WU and PVR > 2 WU at 60 W), postcapillary PH (mPAP/CO slope > 3 WU and PAWP/CO slope > 2 WU), combined pre and postcapillary PH with exercise (mPAP/CO slope > 3 WU, PAWP/CO slope > 2 WU and PVR > 2 WU) and undifferentiated PH with exercise (mPAP/CO slope > 3 WU, PAWP/CO slope ≤ 2 WU and PVR ≤ 2 WU). Preload insufficiency is a dynamic diagnosis indicative of impaired cardiopulmonary performance due to insufficient cardiac filling that can only be assessed during exercise in the sitting position and has been defined as peak RAP < 6.5 mmHg with a change between baseline and peak exercise <5.5 mmHg, in the absence of the other abnormal hemodynamic profiles.[13]

Statistical analysis

Patient data were summarized as mean ± SD or median (interquartile range: IQR) for continuous variables and as counts and percentages for categorical variables. Normality of the variables was tested using Q-Q plot and by the Kolmogorov–Smirnov test. Hemodynamic determinations in sitting and supine positions in the same patient were compared using paired sample *t*-test or Wilcoxon signed-rank test based on normality. T-test was used to compare independent samples. The level of statistical significance was set at $p < 0.05$ (two-tailed). The statistical analyses were performed using the statistical package IBM SPSS version 22 (IBM).

RESULTS

Patient characteristics

A total of 19 consecutive patients were randomized either to perform the initial exercise in the sitting ($n = 8$) or supine ($n = 11$) position. Two patients initially randomized to supine exercise could not complete the subsequent exercise in upright position due to lower extremity fatigue. Therefore, data from 17 patients were included in

the analysis. RHC was done by cannulation of the right and left internal jugular veins in 14 and 3 patients, respectively.

The mean age was 60.3 ± 10.9 years, with 13 females. Patients were predominantly in WHO functional class II. All patients had normal sinus rhythm and were breathing room air. Only one patient with undifferentiated PH at rest had known risk factors for pulmonary arterial hypertension. Initial resting hemodynamic determinations in the supine position are presented in Table 1. A total of six patients had no PH, one had precapillary PH, two had postcapillary PH, three had combined pre and postcapillary PH, and five had undifferentiated PH.

Hemodynamic determinations in supine and sitting positions at baseline

In the sitting position, we noted a significantly lower RAP, mPAP, PAWP, and CI, with similar PVR (Table 2). When comparing the supine with sitting positions at rest, the average ± SD drop in RAP, mPAP, PAWP, and CI were 10.0 ± 3.7 mmHg, 13.6 ± 5.4 mmHg, 12.9 ± 5.1 mmHg, and 0.9 ± 1.0 L/min/m^2, respectively.

Hemodynamic determinations in supine and sitting positions at different stages of exercise

The median (IQR) time between the two exercise tests was 11 (8–13) min. A total of 15 (88%) patients identified supine as an easier exercise position than sitting. In every stage of exercise (20, 40, and 60 W) we noted that the RAP, mPAP, and PAWP were lower in the sitting compared to the supine position. The PVR was similar in the sitting compared to the supine position at all stages of exercise (Table 2). Between baseline and 60 W, the increase in CI ($p = 0.04$) and PAWP ($p = 0.06$) was more pronounced in the sitting position, which translated to a greater reduction in PVR ($p = 0.01$). Meanwhile, the change in RAP and mPAP between baseline and 60 W was similar in both positions. The slopes of mPAP/CO and PAWP/CO were not significantly different between exercise positions (Table 2). Figure 2 shows the hemodynamic determinations in sitting and supine positions at baseline and during exercise.

During sitting exercise at 60 W, nine patients were classified as having preload insufficiency, six as postcapillary PH, one as combined pre- and postcapillary PH, and one as undifferentiated PH. During supine exercise at 60 W, seven patients were identified as having no PH, seven as postcapillary PH, two combined pre- and postcapillary PH, and one as undifferentiated PH.

TABLE 1 Patient characteristics.

Variables	Mean ± SD or *n* (%)
N	17
Age (years)	60.3 ± 10.9
Gender (female)	13 (77)
BMI (kg/m^2)	28.6 ± 6.8
Systolic blood pressure (mmHg)	158 ± 25
Diastolic blood pressure (mmHg)	83 ± 14
SpO_2 (%)	98 ± 2
WHO functional class	
I	3 (18)
II	10 (59)
III	4 (24)
Diuretics (yes)	4 (24)
Beta-blockers (yes)	2 (12)
RV function	
Normal	15 (88)
Mild dysfunction	2 (12)
LV diastolic function	
Normal	10 (59)
Grade 1	4 (24)
Not reported	3 (18)
NT pro BNP (pg/mL)	153 ± 170
Resting supine hemodynamics	
HR (bpm)	74.1 ± 16.1
Systolic BP (mmHg)	147 ± 21.2
Diastolic BP (mmHg)	76.9 ± 8.5
RA (mmHg)	7.6 ± 3.7
mPAP at end-expiration (mmHg)	25.1 ± 8.4
PAWP at end-expiration (mmHg)	13.9 ± 4.7
TPG (mmHg)	11.1 ± 4.8
CI (L/min/m^2)	3.1 ± 0.7
PVR (Wood units)	1.93 ± 0.56

Abbreviations: BMI, body mass index; BP, blood pressure; CI, cardiac index; HR, heart rate; LV, left ventricle; mPAP, mean pulmonary artery pressure; NT-pro BNP, N-terminal-pro hormone B-type natriuretic peptide; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RA, right atrial pressure; RV, right ventricle; SpO_2, pulse oximetry; TPG, transpulmonary gradient; WHO, World Health Organization.

Figure 3 shows a Sankey diagram with the change in hemodynamic classification from baseline (initial supine determination) compared with exercise in sitting and supine positions. Sitting exercise allowed the identification of preload insufficiency that was otherwise classified

TABLE 2 Hemodynamic determinations supine and sitting positions.

Variables	Sitting mean ± SD, median [IQR 25, 75]	Supine mean ± SD, median [IQR 25, 75]	*p*-Value (paired T-test or Wilcoxon signed ranks test*)
Baseline			
HR (bpm)	81.8 ± 15.5	79.1 ± 19.1	0.36
Systolic BP (mmHg)	151.0 ± 24.2	155.4 ± 15.9	0.32
Diastolic BP (mmHg)	74.4 ± 10.7	78.2 ± 8.9	0.18
RAP (mmHg)	0 (−0.5, 1)	12 (8,14)	<0.001*
mPAP (mmHg)	14.8 ± 6.4	28.4 ± 9.3	<0.001
PAWP (mmHg)	3.6 ± 4.0	16.5 ± 4.7	<0.001
TPG (mmHg)	11.1 ± 5.0	11.9 ± 5.7	0.40
CO (L/min)	5.0 ± 1.5	6.8 ± 3.0	0.002
CI (L/min/m^2)	2.7 ± 0.6	3.6 ± 1.4	0.002
PVR (WU)	2.2 ± 0.9	1.8 ± 0.7	0.13
20 W			
HR (bpm)	94.9 ± 16.8	95.1 ± 16.7	0.94
RAP (mmHg)	1 (0, 4.5)	12 (9.5, 15)	<0.001*
mPAP (mmHg)	20.5 ± 8.1	33.8 ± 10.6	<0.001
PAWP (mmHg)	6.5 ± 4.5	20.0 ± 6.2	<0.001
TPG (mmHg)	14.0 ± 5.3	13.8 ± 5.7	0.88
CI (L/min/m^2)	3.9 ± 1.2	4.3 ± 1.3	0.003
PVR (WU)	2.0 ± 0.6	1.8 ± 0.9	0.46
40 W			
HR (bpm)	107.7 ± 19.4	101.6 ± 17.7	0.005
RAP (mmHg)	1 (0, 5)	12 (10, 17.5)	<0.001*
mPAP (mmHg)	23.4 ± 9.0	37.2 ± 10.7	<0.001
PAWP (mmHg)	9.2 ± 6.3	22.0 ± 6.3	<0.001
TPG (mmHg)	14.2 ± 5.8	15.2 ± 5.6	0.38
CI (L/min/m^2)	4.5 ± 1.4	4.9 ± 1.4	0.07
PVR (WU)	1.7 ± 0.5	1.7 ± 0.8	0.86
60 W			
HR (bpm)	122.2 ± 21.9	107.8 ± 18.3	0.001
RAP (mmHg)	2 (0, 7)	13 (9.5, 17)	<0.001*
mPAP (mmHg)	27.0 ± 9.4	38.8 ± 9.7	<0.001
PAWP (mmHg)	12.3 ± 8.1	22.6 ± 6.3	<0.001
TPG (mmHg)	14.7 ± 5.8	16.2 ± 5.1	0.13
CI (L/min/m^2)	5.2 ± 1.4	5.3 ± 1.4	0.63
PVR (WU)	1.5 ± 0.5	1.7 ± 0.8	0.24
Change at 60 W from baseline			
HR change (bpm)	40.4 ± 15.6	28.7 ± 10.4	0.004

(Continues)

TABLE 2 (Continued)

Variables	Sitting mean ± SD, median [IQR 25, 75]	Supine mean ± SD, median [IQR 25, 75]	*p*-Value (paired T-test or Wilcoxon signed ranks test*)
RAP change (mmHg)	2.3 ± 3.6	2.6 ± 3.6	0.77
mPAP change (mmHg)	12.2 ± 4.9	10.4 ± 3.6	0.17
PAWP change (mmHg)	8.6 ± 5.7	6.1 ± 3.4	0.06
TPG (mmHg)	3.6 ± 2.5	4.3 ± 3.8	0.49
CO change (L/min)	4.6 ± 1.8	3.1 ± 2.0	0.04
CI change (L/min/m^2)	2.5 ± 1.1	1.7 ± 1.2	0.04
PVR change (WU)	−0.7 ± 0.6	−0.2 ± 0.5	0.01
Slope mPAP/CO (WU)	2.7 ± 1.4	3.3 ± 3.1	0.31
Slope PAWP/CO (WU)	2.0 ± 1.4	1.7 ± 3.3	0.70

Note: Baseline determinations in supine position were repeated immediately before the supine exercise and therefore are slightly different than the initial baseline determinations.

Abbreviations: BP, blood pressure; CI, cardiac index; CO cardiac output; HR, heart rate; mPAP, mean pulmonary; RA, right atrial pressure; TPG, transpulmonary gradient; WU, Wood units.

*Wilcoxon signed ranks test.

as no PH or undifferentiated PH at baseline, or predominantly as no PH during supine exercise.

One patient with precapillary PH at baseline had an mPAP of 22 mmHg, PAWP of 11 mmHg, and PVR of 2.2 WU. With exercise in the sitting position, the PVR dropped to < 2 WU, and the RAP remained stable at −3 mmHg, supportive of preload insufficiency. Exercise in the supine position showed a mPAP/CO slope of 3.3 WU but PVR < 2 WU and PAWP/CO slope of 1.6 WU; therefore, labeled as undifferentiated PH with exercise.

Submaximal versus maximal exercises

Five out of 9 patients completed maximal exercise above 60 W in a sitting position. Exercise above 60 W, did not change the diagnosis in four of these patients. Only one patient with initially undifferentiated PH at 60 W, developed precapillary PH at 80 W.

A total of six out of eight patients were able to exercise above 60 W in the supine position. Similarly, supine exercise above 60 W only changed the diagnosis in one patient who was reclassified from no PH at 60 W, to postcapillary PH at 140 W.

Sensitivity analysis based on patients' age

We found no significant differences when we divided patients based on the patients' median age (≥62 years [$n = 8$] vs. < 62 years [$n = 9$]), either in the baseline change in pulmonary hemodynamic determinations between sitting and supine positions, or in the change from baseline to 60 W both in the sitting and supine exercise positions, except for the baseline change in CI in which we noted a drop from supine to sitting positions of 1.4 ± 0.4 versus 0.4 ± 0.5 L/min/m^2 for patients < 62 versus ≥ 62 years ($p = 0.04$); a finding not related to the presence of preload insufficiency since five and four patients were in the group < 62 and ≥ 62 years, respectively.

DISCUSSION

This is the first prospective, randomized, crossover study that compared the hemodynamic response to exercise in two different positions in the same patients being evaluated for exercise intolerance. Hemodynamic determinations during exercise performed in both positions are limited to retrospective evaluations. We showed that resting hemodynamic determinations in the sitting position had lower RAP, mPAP, PAWP, and CI, with similar TPG and PVR. Interestingly, the CI increased more in the sitting than the supine position during exercise, resulting in a more pronounced drop in PVR from baseline to 60 W. Consistent with prior studies, the slopes of mPAP/CO and PAWP/CO, which are currently used to define exercise PH and exercise postcapillary PH, were not significantly different between exercise positions.[5,14] Exercise in the sitting position allowed the identification of several patients with preload insufficiency.

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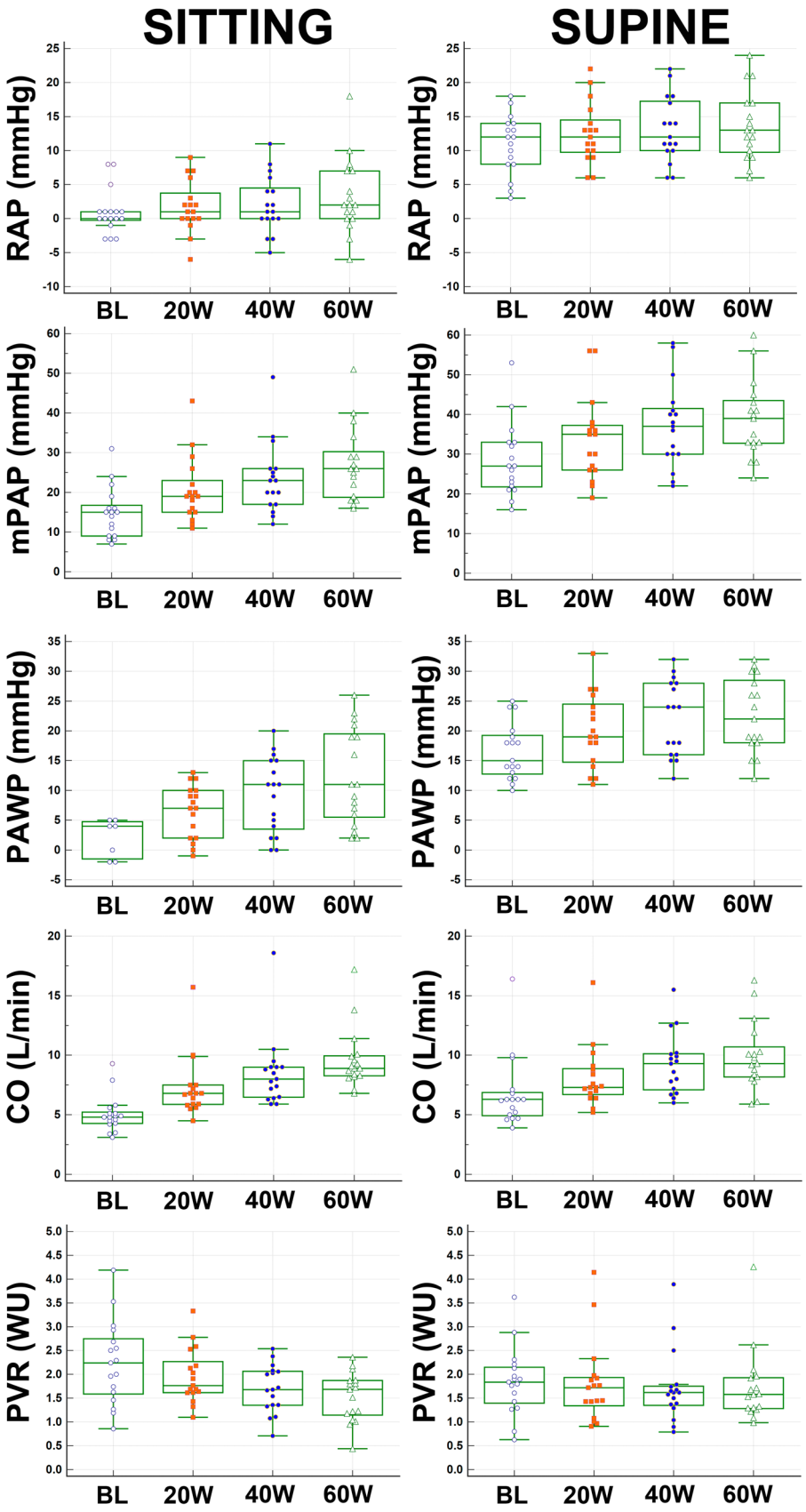

FIGURE 2 Boxplots of hemodynamic determinations during sitting and supine exercises. Hemodynamic determinations include right atrial pressure (RAP), mean pulmonary artery pressure (mPAP), pulmonary artery wedge pressure (PAWP), cardiac output (CO), and pulmonary vascular resistance (PVR). Determinations are shown at baseline (BL), 20, 40, and 60 W for both sitting (left panels) and supine (right panels) exercise positions.

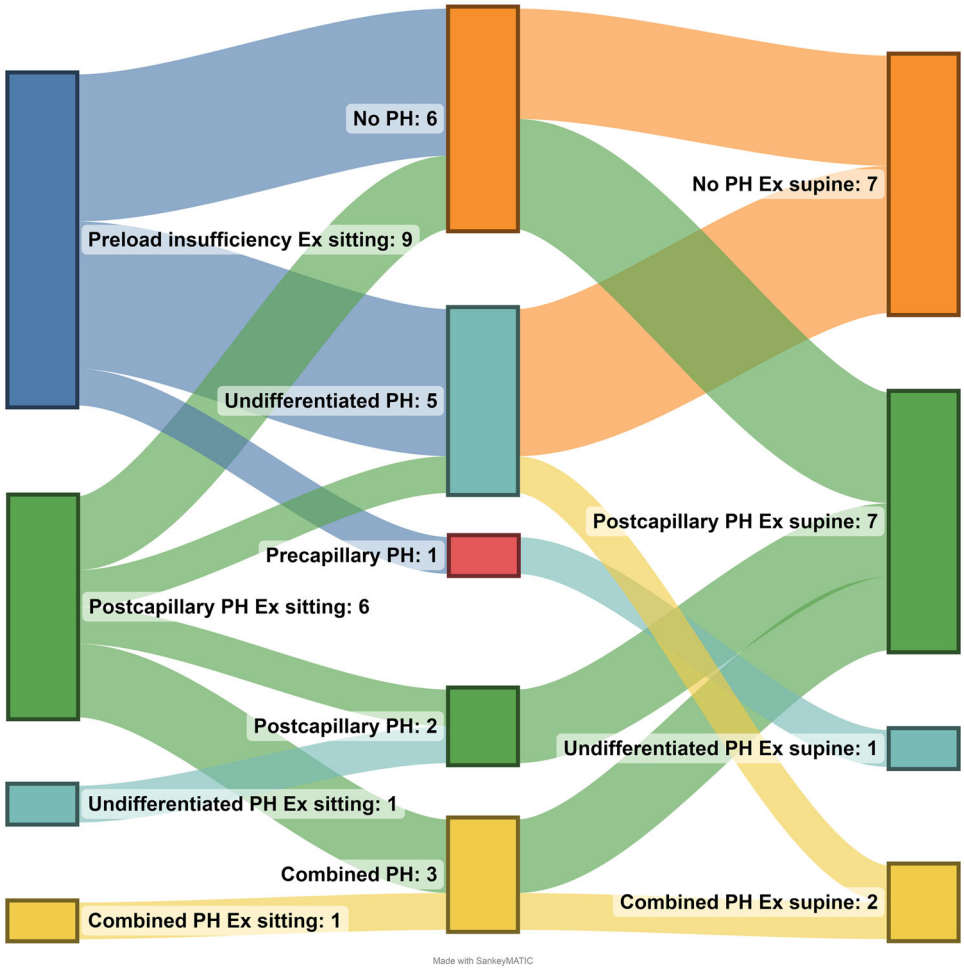

FIGURE 3 Sankey diagram depicting the change in pulmonary hemodynamic classification with exercise in sitting and supine positions compared with baseline determination. The nodes in the center of the figure represent the initial hemodynamic diagnosis at rest in supine position. Nodes on the left and right of the figure represent the hemodynamic diagnosis during sitting and supine exercises, respectively. Links represent the shift in diagnosis after exercise in sitting (left side of the figure) or supine (right side of the figure) positions. For example, six patients had no PH at rest in the supine position. After exercise in the sitting position, four patients were reclassified with preload insufficiency and two with postcapillary PH. When these six patients completed exercise in the supine position, three had no PH, and three had postcapillary PH.

The addition of exercise testing during RHC is useful in detecting causes of exercise intolerance like early pulmonary vascular disease, occult left heart disease and preload insufficiency.[6] Recently published PH guidelines reintroduced exercise PH and defined it by a linearized slope of mPAP/CO > 3 WU in an effort to recognize earlier stages of the disease.[15] Exercise RHC can help identify the predominant hemodynamic phenotype in cases of borderline pulmonary hemodynamics or undifferentiated PH (i.e., mPAP > 20 mmHg, PAWP ≤ 15 mmHg, and PVR ≤ 2 WU) at rest.[16] Nonetheless, there are no specific recommendations on which exercise protocols to use, particularly as it pertains to exercise body position, despite its significant impact on ventricular preload and pulmonary hemodynamics.[7]

When sitting, venous return is reduced due to the gravitational pooling of blood in the lower extremities, diminishing preload (i.e., RAP and PAWP) and ultimately stroke volume (SV).[16–18] When the decrease in SV is not compensated by a proportional increase in heart rate, the CO (CO = SV × HR) is therefore reduced, which also lessens the pulmonary pressures.[15,19] Conversely, the supine position enhances venous return by mobilization of blood from the lower extremities to the core circulation, which increases the ventricular preload, resulting in a higher CO.[8,9] A systematic review of healthy subjects reported that the mPAP (14.8 ± 2.9 mmHg vs. 13.8 ± 3.6 mmHg) and CO (6.6 ± 1.7 vs. 5.5 ± 1.1 L/min) at rest, as well as the mPAP (24.9 ± 7.1 mmHg vs. 22.1 ± 5.0 mmHg) and CO (15.8 ± 3.2 vs. 14.7 ± 2.9 L/min) during submaximal

exercise were slightly lower in the upright than supine position.[15] The reduction in mPAP in the sitting position was more pronounced than expected as we included patients with preload insufficiency and postcapillary PH. Interestingly, patients in our cohort preferred supine positioning as they were able to achieve a higher workload.

Sitting was associated with a drop in CI when compared to the supine resting position; however, the CI increased more during exercise (rest to 60 W) in the sitting than the supine position, hence at 60 W both CI were similar. While the CI was similar at 60 W in both positions, the sitting position demonstrated higher heart rates, emphasizing the role of compensatory tachycardia in maintaining CI.[15] In addition, subjects that exercise in the sitting position have lower left ventricular end-diastolic volumes but they offset this change with a higher left ventricular ejection fraction.[20] PVR was comparable at rest and at all stages of exercise, yet patients in the seated position had a statistically greater absolute reduction in PVR from rest to maximal exercise, likely due to subtle augmentation of pulmonary vascular recruitment and vasodilation.[8,21,22]

Hemodynamic assessment in the sitting position is essential to detect preload insufficiency, an under-recognized etiology of dyspnea characterized by a limited increase in RAP in the context of a lower-than-predicted peak CO with exercise.[3] Inadequate venous return results in low ventricular preload and hence reduced stroke volume that contributes to dyspnea via multiple mechanisms.[3] Exercise in the supine position may mask a preload deficit as exercise is performed with legs elevated on cycle pedals akin to passive leg raising. In our study, we use a low RAP at baseline with limited increase with exercise in a sitting position, in the absence of other hemodynamic conditions responsible for the exercise intolerance. This narrow hemodynamic definition may overdiagnose preload insufficiency, particularly in the absence of the CO peak percentage of predicted, a value that could not be obtained in our study since exercise in one of two positions was submaximal and we did not include an invasive cardiopulmonary exercise test (iCPET).

The higher preload in supine position with legs elevated increases the PAWP at baseline and during exercise; likely increasing the detection of postcapillary PH, particularly when the PAWP is used. In our study, at rest and during all stages of exercise, PAWP remained significantly higher in the supine compared to the sitting position. Interestingly, the PAWP/CO slope was similar between sitting and supine exercise positions, limiting the potential over diagnosis of postcapillary PH based on only PAWP values.[5]

Although the present pilot study is the first to compare hemodynamic measurements during exercise in sitting and supine positions during the same visit in patients with exercise intolerance due to diverse etiologies, there are limitations that must be mentioned. There premature termination and limited recruitment due to the COVID-19 pandemic (the initial target goal was 25 patients). Hemodynamic comparisons were performed during submaximal exercise at 60 W because completion of maximal exercise in two positions during the same visit would be difficult to achieve in our cohort of patients. However, exercise above 60 W in either position did not change hemodynamic classifications in the majority of cases, and previously published studies on the same topic, the average workload achieved was even lower.[8] Lastly, there is no established definition of preload insufficiency, particularly in the absence of complimentary iCPET that could have provided oxygen consumption at different stages (to calculate Fick CO and peak CO percentage of predicted).[3,6]

Body position significantly influences hemodynamics at rest and with exercise; however, the mPAP/CO and PAWP/CO were not positionally affected. Hemodynamic measurements in the sitting position allowed the detection of preload insufficiency in patients being evaluated for exercise intolerance due to dyspnea.

AUTHOR CONTRIBUTIONS

Pradhab Kirupaharan: Participated in the literature review, interpretation of results, drafting, revising, and approving the final manuscript. **James Lane:** Participated in the data collection, interpretation of the results, and critical revision of the manuscript. **Celia Melillo:** Participated in the data collection, interpretation of the results, and critical revision of the manuscript. **Deborah Paul:** Participated in the data collection, interpretation of the results, and critical revision of the manuscript. **Alla Amoushref:** Participated in the data collection, interpretation of the results, and critical revision of the manuscript. **Sami Al Abdi:** Participated in the data collection, interpretation of the results, and critical revision of the manuscript. **Adriano R. Tonelli:** Participated in the design of the study, data collection, statistical analysis, interpretation of the results, writing and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Adriano R. Tonelli takes responsibility for all aspects of the

reliability and freedom from bias of the data presented and their discussed interpretation.

ETHICS STATEMENT

The institutional review board of the Cleveland Clinic approved the present study (IRB # 16-872). Informed consent was obtained from all patients.

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