Accuracy of Echocardiography to Evaluate Pulmonary Vascular and RV Function During Exercise

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ABSTRACT

OBJECTIVES We compared exercise echocardiography and exercise cardiac magnetic resonance imaging with simultaneous invasive pressure registration (ExCMRip) for the assessment of pulmonary vascular and right ventricular (RV) function.

BACKGROUND Exercise echocardiography may enable early diagnosis of pulmonary vascular disease, but its accuracy is untested.

METHODS Exercise imaging was performed in 61 subjects (19 athletes, 9 healthy nonathletes, 8 healthy BMPR2 [bone morphogenetic protein receptor type II] mutation carriers, 5 patients with new or worsening dyspnea after acute pulmonary embolism, and 20 patients with chronic thromboembolic pulmonary hypertension). Echocardiographic variables included mean pulmonary artery pressure (mPAP) and systolic pulmonary artery pressure (sPAP), cardiac output (CO), RV fractional area change, tricuspid annular systolic excursion, and RV end-systolic pressure-area ratio as a surrogate measure of RV contractile reserve. ExCMRip provided measurements of CO, RV ejection fraction, mPAP, sPAP, and RV end-systolic pressure-volume ratio at rest and during exercise. Abnormal pulmonary vascular reserve was defined as mPAP/CO slope >3 mm Hg/l/min by ExCMRip.

RESULTS Echocardiographic determination of mPAP/CO was possible in 53 of 61 subjects (87%). mPAP/CO by echocardiography was higher than that obtained by ExCMRip (±0.9 mm Hg/l/min; 95% limits of agreement, −3.6 to 5.4), but enabled accurate identification of patients with abnormal pulmonary vascular reserve (area under the receiver-operating characteristic curve, 0.88 [95% confidence interval (CI): 0.77 to 1.00, p < 0.0001]). Simplified relationships between sPAP and exercise intensity had similar accuracy in identifying subjects with pulmonary vascular disease (area under the receiver-operating characteristic curve, 0.95 [95% CI: 0.88 to 1.01], p < 0.0001). RV fractional area change by echocardiography correlated strongly with RV ejection fraction by ExCMRip, whereas a moderate correlation was found between tricuspid annular systolic excursion and RV ejection fraction. A moderate correlation was found between ratios of peak exercise to resting RV end-systolic pressure-area ratio and RV end-systolic pressure-volume ratio (r = 0.64, p < 0.0001).

CONCLUSIONS Echocardiographic estimates of RV and pulmonary vascular function are feasible during exercise and identify pathology with reasonable accuracy. They represent valid screening tools for the identification of pulmonary vascular disease in routine clinical practice. (J Am Coll Cardiol Img 2015;8:–) © 2015 by the American College of Cardiology Foundation.
Abbreviations and Acronyms

BMPR2 = bone morphogenetic protein receptor type II
CTEPH = chronic thromboembolic pulmonary hypertension
CMR = cardiac magnetic resonance
CO = cardiac output
EF = ejection fraction
ExCMRip = exercise cardiac magnetic resonance imaging with simultaneous invasive pressure registration
mPAP = mean pulmonary artery pressure
PAP = pulmonary artery pressure
PEA = pulmonary endarterectomy
ROC = receiver-operating characteristic
RV = right ventricular
RVESPV = right ventricular end-systolic pressure-volume ratio
RVESPVR = right ventricular end-systolic pressure-volume ratio
sPAP = systolic pulmonary artery pressure
SV = stroke volume

There is broad agreement that exercise-induced pulmonary hypertension is an important clinical finding with diagnostic and prognostic utility in a broad range of cardiac and pulmonary vascular conditions (1). Echocardiography remains the primary screening tool for pulmonary vascular disease. However, echocardiographic estimation of pulmonary artery pressure (PAP) during exercise is not routine because of concerns regarding the imprecision and lack of standardization of exercise measures (2,3).

Recent studies demonstrated a consistent nearly linear relationship between changes in PAP and cardiac output (CO) (1,4-6) with an expected increase in mean pulmonary artery pressure (mPAP) of ~1 to 2 mm Hg/l/min of CO representing a normal pulmonary vascular response and any value greater than 3 mm Hg/l/min being suggestive of pathology (1). This represents a more physiological appraisal than single peak exercise measures as the flow-dependent characteristics of the circulation are encompassed in the separation of normal from abnormal. Although the advantages of an approach incorporating PAP in relation to CO or exercise intensity are now well accepted, the accuracy and precision of noninvasive estimates of these relationships remain to be proved against gold standard measures.

We sought to validate echocardiographic measures of PAP and CO during intense exercise compared with the reference standards of invasive PAP and exercise cardiac magnetic resonance (CMR), having previously validated this against direct Fick measurements of CO (7). Thus, echocardiographic measures were compared with those from a hybrid invasive CMR technique in healthy subjects and patients with pulmonary vascular pathology. Furthermore, the use of CMR as a gold standard for right ventricular (RV) measures enables us to simultaneously validate echocardiographic measures of RV functional reserve.

Methods

Subjects. Sixty-one subjects underwent evaluation with exercise echocardiography and exercise CMR imaging combined with invasive PAP estimates (subsequently referred to as exercise cardiac magnetic resonance imaging with simultaneous invasive pressure registration [ExCMRip]) within a 24-h timeframe. The study population comprised a range of healthy subjects and patients with pulmonary vascular disease including 19 endurance athletes, 9 healthy nonathletes, 8 asymptomatic carriers of a mutation linked to the development of pulmonary arterial hypertension (BMPR2 [bone morphogenetic protein receptor type II] mutation), 5 subjects with persisting exertional dyspnea after pulmonary embolism, 14 patients with chronic thromboembolic pulmonary hypertension (CTEPH), and 6 patients undergoing routine hemodynamic evaluation 6 months after pulmonary endarterectomy (post-PEA).

Study Design. Cardiopulmonary exercise testing was performed on an upright cycle ergometer to determine maximal exercise power. On the same day, echocardiography was performed with subjects at both rest and during incremental exercise at 25%, 50%, and 66% of maximal upright exercise power, as previously described (7,8).

Within 24 h after exercise echocardiography, all subjects underwent exercise ExCMRip at the same workloads as for the echocardiography protocol. Before exercise, a 7-F pulmonary artery catheter was inserted in the internal jugular vein and guided under fluoroscopy to the proximal right main pulmonary artery. In the CMR suite, these catheters were attached to CMR-compatible pressure transducers that were connected to a PowerLab recording system (AD Instruments, Oxford, United Kingdom). Pressure measurements were continuously recorded during the exercise CMR protocol and analyzed off-line using LabChart v6.1.1 (AD Instruments). All pressure measurements were averaged over 10 consecutive cardiac cycles during unrestricted respiration (1).

Echocardiography. Resting and exercise echocardiography was performed on a semisupine cycle...
ergometer (Easystress, Ecogito Medical sprl, Liege, Belgium). Images were acquired using a Vivid E9 ultrasound system (GE Vingmed Ultrasound AS, Horten, Norway) and analyzed off-line using EchoPAC version 112 (GE Vingmed Ultrasound AS).

Both at rest and during exercise, systolic pulmonary artery pressure (sPAP) was estimated from the maximal transtricuspid regurgitant velocities with colloid contrast enhancement (Figure 1), without the addition of right atrial pressure estimates (4,9), as previous investigations failed to demonstrate reliable accuracy, and no studies have validated estimates during exercise (10). mPAP was estimated from sPAP measurements using the Chemla formula: mPAP = 0.61 / sPAP + 2 (11). CO was derived from the Doppler-estimated stroke volume (SV) using the velocity time integral of flow through the left ventricular outflow tract (5). RV fractional area change (Figure 2A) and tricuspid annular plane systolic excursion were calculated from a single-plane 4-chamber view as described previously (9). The right ventricular end-systolic pressure-area ratio (RVESPAR), a surrogate of RV contractility, was calculated as sPAP divided by RV end-systolic area (9). The ratio of peak exercise RVESPAR divided by resting RVESPAR was calculated as a surrogate of RV contractile reserve.

CMR EQUIPMENT, IMAGE ACQUISITION, AND ANALYSIS. Biventricular volumes were measured during supine cycling exercise using a real-time CMR method that we previously validated against invasive standards (7). In brief, subjects performed supine exercise within the CMR bore using a cycle ergometer with adjustable electronic resistance (Lode, Groningen, the Netherlands). Images were acquired with a Philips Achieva 1.5-T CMR with a 5-element phased-array coil (Philips Medical Systems, Best, the Netherlands).

Using an in-house-developed software program (RightVol, Leuven, Belgium), left ventricular and RV end-diastolic volume, end-systolic volume, and SV were calculated by a summation of disks (Figure 2B). CO was measured as the product of SV and heart rate, whereas ejection fraction (EF) was calculated as SV/ end-diastolic volume. Similar to RVESPAR, the ExCMRip-derived RVESPVR was calculated as sPAP/ RV end-systolic volume, whereas the ratio of peak exercise to resting RVESPVR was used to estimate RV contractile reserve.

STATISTICAL ANALYSIS. Data were analyzed using SPSS version 22 software (IBM, Chicago, Illinois). Gaussian distribution of all continuous variables was tested using a Kolmogorov-Smirnov test. Descriptive data for continuous variables are presented as mean ± SD or as median (25% and 75% percentiles) where appropriate. Categorical data were compared using the Fisher exact test.

The relationships between individual PAP, CO, and workload were determined using linear regression analysis (8). A Bland-Altman analysis was used to assess the accuracy and precision of echocardiography-derived hemodynamics compared with ExCMRip (12). The bias, SD, and 95% limits of agreement were reported. Receiver-operating characteristic (ROC) curves were constructed to determine the diagnostic accuracy of echocardiography-derived pulmonary vascular pressure/workload relationships to detect an abnormal pulmonary vascular reserve, defined as an mPAP-CO slope >3 mm Hg/l/min by ExCMRip. Similarly, ROC curves were constructed to assess the diagnostic
accuracy of RVESPAR to identify CTEPH and post-PEA patients in whom RV contractile reserve during exercise is impaired (8). Diagnostic accuracy was quantified by the area under the ROC curve.

The impact of exercise on the sPAP-mPAP relationship was evaluated by a linear mixed model that included sPAP, condition (rest vs. peak exercise), and their interaction as fixed effects. To account for the repeated nature of the data, an unstructured variance-covariance matrix was included in the model. A p value < 0.05 was considered statistically significant.

RESULTS

The clinical characteristics of the 61 subjects are summarized in Table 1.

ASSESSMENT OF PAP BY ECHOCARDIOGRAPHY VERSUS INVASIVE MEASURES. At rest, echocardiographic measures of sPAP were possible in 57 of 61 subjects (93%). The number of subjects in whom a Doppler echocardiographic estimate of sPAP could be obtained decreased to 46 (75%), 49 (80%), and 42 (69%) for low-, moderate- and peak-intensity exercise, respectively.

At rest, an excellent correlation was found between echocardiographic and invasive measures, for both sPAP and mPAP (Figure 3A). No significant bias was observed for echocardiographic estimation relative to invasive sPAP, whereas mPAP calculated from echocardiography-derived sPAP using the Chemla formula were higher than invasively measured mPAP (Table 2). The difference in sPAP was < 10 mm Hg in 41 of 57 subjects (72%) and > 20 mm Hg in 5 subjects (9%). Similarly, for mPAP, the difference was < 10 mm Hg in 47 subjects (83%) and > 20 mm Hg in 1 subject (2%).

At peak exercise, echocardiography-derived sPAP and mPAP correlated strongly with invasive measures (Figure 3A). There was no significant bias between invasive and echocardiographic measures of sPAP at peak exercise, whereas echocardiography overestimated mPAP (Table 2). The difference in peak exercise invasive and echocardiography-derived sPAP was < 10 mm Hg in 20 of 42 subjects (48%) and > 20 mm Hg in 4 subjects (10%).
Considering all workloads, echocardiographic estimates of mPAP were higher than those measured invasively (+5.1 ± 6.9 mm Hg; p < 0.0001), whereas the bias in sPAP was not statistically significant (mean bias +1.6 ± 11.6 mm Hg; p = 0.055). The bias in mPAP remained significant when CTEPH and post-PEA patients were excluded (mean bias +4.9 ± 6.7 mm Hg; p < 0.0001). Analysis of the relationship between invasive sPAP and mPAP revealed an excellent linear correlation (mPAP = 0.54 × sPAP + 1.9, R² = 0.96; p < 0.0001). When the values at each exercise intensity were considered separately, the relationship between invasive sPAP and mPAP was very similar (Online Table 1), indicating consistency of the relationship throughout exercise. Using the regression equation derived from our data (mPAP = 0.54 × sPAP + 1.9) in preference to the Chemla formula, there was only minimal bias between echocardiography and ExCMR ip measures of mPAP (+1.3 ± 6.7 mm Hg; p = 0.008) with 95% limits of agreement of −11.8 to 14.4 mm Hg. Estimation of sPAP by echocardiography did not include addition of right atrial pressure such that sPAP measurements by echocardiography equaled invasively derived sPAP minus right atrial pressure. When this formula was used to compare echocardiographic and invasive measurements, a small but consistent bias was seen (Online Figure 1), demonstrating that some of the inaccuracy between echocardiography and invasive measurements was due to exercise-induced increases in right atrial pressure in the pulmonary hypertension patients.

**Assessment of Pulmonary Vascular Reserve.**

At rest, CO measured by echocardiography was significantly lower than values using ExCMR ip due to underestimation of SV (Table 2, Figure 3B). The difference in SV remained similar from rest to peak exercise, whereas the difference in CO increased because peak exercise heart rate was lower during exercise echocardiography (141 ± 24 beats/min vs. 124 ± 19 beats/min; p < 0.0001).

One healthy subject (4%), 1 BMPR2 carrier (13%), 3 post-pulmonary embolism patients (60%), 12 CTEPH patients (86%), and 6 post-PE patients (10%) had abnormal pulmonary vascular reserve as defined by the mPAP/CO cutoff of >3.2 mm Hg/l/min by ExCMR ip (Online Figure 2). Multipoint PAP/CO slope determination by echocardiography was possible in 53 of 61 subjects (87%), whereas the success rate in obtaining peak exercise PAP measurements alone was 69% (p = 0.028). As depicted in Figure 4, echocardiography had good accuracy and precision for the assessment of individual mPAP/CO slopes. For the detection of the presence of abnormal pulmonary vascular reserve, the area under the ROC curve was 0.88 (95% confidence interval [CI]: 0.77 to 1.00; p < 0.0001), and mPAP/CO by echocardiography of 3.2 mm Hg/l/min was identified as the most favorable threshold, with 88% sensitivity and 81% specificity.

We also evaluated the use of simplified relationships by plotting sPAP against CO and exercise intensity in Watts. As shown by Online Figure 3, we found a consistent linear relationship between CO and exercise intensity with limited interindividual variability (CO = 0.07 × power [in Watts] + 6.8). ExCMR ip-derived mPAP/CO slopes correlated strongly with echocardiography-derived sPAP/W and sPAP/CO slopes (Figure 4). ROC analysis showed that cutoff values of >0.47 mm Hg/W for sPAP/W and >5.2 mm Hg/l/min for sPAP/CO slopes had a sensitivity of 86% and 88% and a specificity of 94% and 81% to depict abnormal pulmonary vascular reserve (area under the curve, 0.95 [95% CI: 0.88 to 1.01] and 0.88 [95% CI: 0.77 to 1.0], respectively; p < 0.0001).

**Evaluation of RV Contractile Reserve.**

The number of patients in whom tricuspid annular plane systolic excursion and RV fractional area change could be obtained decreased from 60 (98%) and 57 (93%) at rest to 53 (87%) and 50 (82%) at peak exercise, respectively.

At both rest and peak exercise, the correlation between RVEF and RV fractional area change was higher than that between RVEF and tricuspid annular plane systolic excursion (Figure 5). An example of exercise echocardiography and ExCMR ip for the assessment of RV functional reserve in a CTEPH patient is provided in Figure 2 and Online Video 1.

The association between RV ESPAR and RV ESPSVPR was strong at rest and moderate at peak exercise (Figure 5). Overall, an excellent correlation was found when either sPAP or mPAP was used to calculate

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**Table 1 Clinical Characteristics**

| Age, yrs | 46 (32, 57) |
| Male | 46 (75) |
| Height, cm | 175 ± 12 |
| Weight, kg | 79 ± 14 |
| BMI, kg/m² | 26.1 ± 4.8 |
| Subjects | |
| Endurance athletes | 19 |
| Healthy nonathletes | 9 |
| BMPR2 mutation carriers | 8 |
| Post-PE patients | 5 |
| CTEPH patients | 14 |
| Post-PEA patients | 6 |

Values are median (25th, 75th percentile), n (%), or mean ± SD.

BMI = body mass index; BMPR2 = bone morphogenetic protein receptor type II; CTEPH = chronic thromboembolic pulmonary hypertension; PE = pulmonary embolism; PEA = pulmonary endarterectomy.
RVESPVR ($R^2 = 0.86; p < 0.0001$). The correlation remained excellent when only CTEPH and post-PEA patients were considered ($R^2 = 0.89$). The ratio of peak exercise to resting RVESPVR correlated moderately with the ratio of peak exercise to resting RVESPVR (Figure 5). At rest, CTEPH and post-PEA patients had higher RVESPVR and RVESPAR compared with the other groups (0.73 ± 0.24 mm Hg/ml vs. 0.32 ± 0.23 mm Hg/ml and 3.56 ± 1.05 mm Hg/cm² vs. 2.31 ± 1.27 mm Hg/cm²; $p < 0.01$). However, the ratios of peak exercise to resting RVESPVR and RVESPAR were significantly reduced in CTEPH and post-PEA patients (1.45 ± 0.30 vs. 3.30 ± 1.09 and 1.45 ± 0.38 vs. 2.84 ± 1.24; both $p < 0.01$), indicating that the exercise-induced increase in RV contractility was impaired. The RVESPVR ratio of 2.01 from rest to peak exercise had a sensitivity and specificity of 1.64 had a respective sensitivity and specificity of 82% and 96% (AUC 0.94 [95% CI: 0.87 to 1.02]) (Figure 6).

**DISCUSSION**

We demonstrate that measures obtained during exercise echocardiography can provide a sufficiently robust estimate of PAP changes during exercise and CO to justify inclusion in daily clinical practice as a means of identifying abnormalities in pulmonary vascular function. Determination of PAP/CO slopes by echocardiography was feasible in the majority of subjects and had good accuracy for identifying abnormal vascular reserve. Furthermore, simplified relationships between sPAP and exercise intensity measured in Watts can also be used to identify pathology and may represent a simpler clinical tool by avoiding the need for CO quantification. Finally, this is the first study to validate echocardiographic
whereas the invasive measurement of sPAP was the highest tricuspid regurgitant velocity signals, the fact that sPAP was generally estimated from the different regression equation in our study is explained by the use of colloid-agitated contrast enhancement (13,14). Moreover, the use of multipoint exercise measurements enabled PAP/CO slope determination in 87% of subjects, even when PAP could not be determined at peak intensity exercise. This technique has significant advantages over the more commonly used method of comparing rest values with a single “peak exercise” value obtained when imaging constraints are greatest.

The use of agitated contrast enhancement may also explain the higher precision of sPAP estimates compared with some previous studies (2,15), although there was a tendency to overestimate sPAP, which may also be a consequence of contrast enhancement due to broadening of the spectral Doppler signal (14). Some of this “overestimation” may also be due to the fact that sPAP was generally estimated from the highest tricuspid regurgitant velocity signals, whereas the invasive measurement of sPAP was recorded as the average of maximal values. This averaging can lead to significantly lower values, especially during exercise when the respiratory variation in sPAP is considerable.

Interestingly, although there was no significant bias between invasive sPAP and echocardiographic estimates, invasive mPAP values were significantly lower than echocardiographic estimates. mPAP is not measured directly using echocardiography, and, thus, accuracy is dependent on extrapolation from sPAP conversions. When we used the regression equation from our own invasive data, we found that much of the overestimation of echocardiography-derived mPAP was in fact due to a slightly different regression equation in our cohort compared with the Chemla formula. We cannot exclude that the different regression equation in our study is explained by the use of fluid-filled catheters as opposed to high-fidelity micromanometers in the study by Chemla et al. (11). Also, the inclusion of CTEPH patients (with and without PEA) may have influenced the relationship between sPAP and mPAP (16), even though exclusion of these patients did not alter our results.

**PULMONARY VASCULAR PRESSURE/FLOW AND PRESSURE/WORKLOAD RELATIONSHIPS.** When differentiating a normal from an abnormal pulmonary vascular response to exercise, it is important to interpret changes in PAP against CO or workload (4). Noninvasive and invasive studies have suggested that

### TABLE 2

<table>
<thead>
<tr>
<th>Measure</th>
<th>ExCMR&lt;sub&gt;i&lt;/sub&gt;</th>
<th>Echocardiography</th>
<th>Bias</th>
<th>p Value of Bias</th>
<th>SD of Difference</th>
<th>Limits of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>sPAP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>36.1 ± 25.9</td>
<td>37.7 ± 22.9</td>
<td>1.7</td>
<td>0.21</td>
<td>10.0</td>
<td>−17.9 to 21.2</td>
</tr>
<tr>
<td>Peak exercise</td>
<td>61.9 ± 31.4</td>
<td>64.8 ± 25.1</td>
<td>2.9</td>
<td>0.17</td>
<td>13.6</td>
<td>−23.7 to 29.6</td>
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<tr>
<td>mPAP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>21.0 ± 14.2</td>
<td>25.0 ± 14.0</td>
<td>4.1</td>
<td>&lt;0.0001</td>
<td>6.1</td>
<td>−7.9 to 16.0</td>
</tr>
<tr>
<td>Peak exercise</td>
<td>34.2 ± 17.2</td>
<td>41.5 ± 15.3</td>
<td>7.3</td>
<td>&lt;0.0001</td>
<td>7.4</td>
<td>−7.1 to 21.7</td>
</tr>
<tr>
<td>CO, l/min</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Rest</td>
<td>6.5 ± 1.8</td>
<td>5.5 ± 1.5</td>
<td>−1.0</td>
<td>&lt;0.0001</td>
<td>1.6</td>
<td>−4.0 to 2.1</td>
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<tr>
<td>Peak exercise</td>
<td>16.6 ± 7.2</td>
<td>12.4 ± 4.3</td>
<td>−4.2</td>
<td>&lt;0.0001</td>
<td>4.0</td>
<td>−12.0 to 3.7</td>
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<td>SV, ml</td>
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<td></td>
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<td></td>
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<tr>
<td>Rest</td>
<td>98.0 ± 32.7</td>
<td>80.4 ± 24.5</td>
<td>−17.6</td>
<td>&lt;0.0001</td>
<td>20.6</td>
<td>−58.1 to 23.0</td>
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<tr>
<td>Peak exercise</td>
<td>114.9 ± 38.7</td>
<td>100.0 ± 28.0</td>
<td>−15.0</td>
<td>&lt;0.0001</td>
<td>21.5</td>
<td>−57.2 to 27.2</td>
</tr>
<tr>
<td>mPAP/CO, mm Hg/l/min</td>
<td>3.3 ± 3.6</td>
<td>4.1 ± 3.8</td>
<td>0.90</td>
<td>0.007</td>
<td>2.3</td>
<td>−3.6 to 5.4</td>
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<tr>
<td>sPAP/CO, mm Hg/l/min</td>
<td>5.9 ± 6.4</td>
<td>6.8 ± 6.2</td>
<td>−0.85</td>
<td>0.18</td>
<td>4.6</td>
<td>−8.1 to 9.8</td>
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<tr>
<td>sPAP/W, mm Hg</td>
<td>0.42 ± 0.40</td>
<td>0.42 ± 0.37</td>
<td>0.001</td>
<td>0.99</td>
<td>0.24</td>
<td>−0.47 to 0.47</td>
</tr>
</tbody>
</table>

**Values are mean ± SD.**

CMR = cardiac magnetic resonance; CO = cardiac output; ExCMR<sub>i</sub> = exercise cardiac magnetic resonance imaging combined with invasive pulmonary artery pressure estimates; mPAP = mean pulmonary artery pressure; mPAP/CO = mean pulmonary artery to cardiac output slope; sPAP = systolic pulmonary artery pressure; sPAP/CO = systolic pulmonary artery pressure to cardiac output slope; sPAP/W = systolic pulmonary artery pressure to workload (in Watts) slope; SV = stroke volume.
the slope of mPAP/CO ranges should not exceed 3.0 mm Hg/l/min in healthy subjects (1). We found that mPAP/CO slopes obtained with echocardiography were consistently higher than those obtained with ExCMR<sub>ip</sub>. This resulted from both overestimation of mPAP, on the one hand, and underestimation of CO, on the other, particularly at peak exercise intensity. Nevertheless, the echocardiography-derived mPAP/CO

FIGURE 4 Comparison of Pulmonary Vascular Pressure/Flow and Pressure/Workload Relationships by Echocardiography and ExCMR<sub>ip</sub>

Correlation coefficients with 95% confidence intervals (A through C) and Bland-Altman plots (B through F) of the slopes of mean PAP to CO (mPAP/CO slopes) (A), of systolic pulmonary artery pressure to cardiac output (sPAP/CO slopes) (B), and sPAP to workload in Watts (sPAP/W slopes) (C). CO = cardiac output; other abbreviations as in Figures 2 and 3.
slope predicted an abnormal pulmonary vascular response in the majority of subjects in whom ExCMRip values were abnormal. Even better accuracy was found for the slopes of sPAP to exercise intensity in Watts rather than CO. In general, determination of PAP to CO is preferred over workload because the main determinant of PAP is flow (1). However, despite the marked interindividual variability of CO at any given workload, our data demonstrate that the increase in CO relative to the increase in workload is in fact very similar among all study subjects. Moreover, we demonstrate that the sPAP-to-workload relationship can be used to identify pathology. This may be a simpler and more pragmatic approach to include evaluation of pulmonary vascular reserve in clinical practice by avoiding the need for CO quantification.

**RV FUNCTIONAL RESERVE.** Although some studies have analyzed pulmonary vascular responses to exercise, there are very few data assessing changes in RV function during exercise. Exercise CMR has

![Correlations between RVEF and right ventricular fractional area change (RVFAC) (A) and tricuspid annular plane systolic excursion (TAPSE) (B), respectively, at both rest (solid lines) and peak exercise (dashed lines). (C) Relationship between resting (solid line) and peak exercise (dashed line) right ventricular end-systolic pressure/volume ratio (RVESPVR) by ExCMRip and right ventricular end-systolic pressure/area ratio (RVESPAR) by echocardiography. (D) Correlation, with 95% confidence intervals, of the ratios of peak exercise with resting RVESPVR and RVESPAR. Abbreviations as in Figures 2 and 3.](image-url)
emerged as a promising technique enabling accurate and reproducible quantification of biventricular volumes during strenuous exercise (7). However, although exercise CMR offers superb insights into the mechanics and quantification of impaired cardiac reserve, simpler tests are needed for clinical practice.

In this study, we found a good correlation between echocardiographic measurement of exercise-induced RV dimensional changes, such as RV fractional area change and tricuspid annular plane systolic excursion, and RVEF obtained by ExCMRip. However, due to the influence of load on these measures, they tend to reflect right ventricular-arterial coupling rather than measures of RV contractility per se (9). To distinguish between RV dysfunction and/or pathological increases in pulmonary vascular load, we combined sPAP and RV end-systolic area using echocardiography to calculate RVESPAR as a surrogate of RV contractility (9). Our current results show that exercise-induced increases in RVESPAR correlate strongly with increases in RVESPVR obtained by ExCMRip. Recent data from our group indicated that CTEPH and post-PEA patients have higher RV contractility at rest compared with healthy subjects to compensate for increases in RV afterload (8). However, the right ventricle’s ability to further increase contractility with exercise is diminished in these patients, resulting in an uncoupling of RV contractility and pulmonary arterial load (8). Resting RVESPVR and RVESPAR are higher in CTEPH patients, whereas the ratios of peak exercise to resting RVESPVR and RVESPAR are significantly reduced. Therefore, the ratio of peak exercise to resting RVESPAR may be a promising noninvasive index of RV contractile reserve. It has been shown for the left ventricle that the end-systolic pressure-volume ratio response to exercise using echocardiography predicts clinical outcome and provides additional information beyond ejection fraction (17,18). The same approach, however, remains to be tested for the right ventricle.

**STUDY LIMITATIONS.** There are several potential limitations to our study. First, the subject population consisted of a mixture of various diagnostic groups that may not reflect the population in a clinical setting and may have artificially improved correlations among measures. Second, the exercise ExCMRip and exercise echocardiography tests cannot be performed simultaneously because of technical considerations. Furthermore, because the study protocol consisted of several exercise tests, we thought that performing all the measurements on 1 day was not feasible. However, all subjects underwent the
Echocardiography for Pulmonary Vascular and RV Function

**CONCLUSIONS**

Echocardiography is a feasible and accurate tool for the evaluation of pulmonary vascular and RV functional reserve during exercise in clinical practice. Simplified relationships between sPAP and exercise intensity in Watts can be used to identify pathology and may represent a simpler clinical tool by avoiding the need for CO quantification. Further studies are needed to determine the clinical relevance of these novel exercise parameters for identifying pulmonary vascular disease and RV dysfunction at an early stage.

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**KEY WORDS** cardiac magnetic resonance imaging, echocardiography, exercise, pulmonary artery pressure, pulmonary hypertension, right ventricular function

**APPENDIX** For the supplemental video and legends, and online table and figures, please see the online version of this article.