Title: Differential Blood Pressure and Heart Rate Response to 6-minute Walk Testing in Patients with Group 1 Vs. Group 2 Pulmonary Hypertension

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Abstract:

Background/Objective: Reduced heart rate recovery (HRR) after exercise has been associated with poor prognosis in pulmonary hypertension (PH) and heart failure. We sought to compare the blood pressure and heart rate response/recovery after six-minute walk test (6MWT) between patients with pulmonary arterial hypertension (PAH) and left heart disease-associated PH (LHD-PH) to investigate their phenotypic differences.

Methods: This retrospective study included outpatients in a single comprehensive PH center evaluated from August 2016 to December 2022. Blood pressure and heart rate (HR) were measured at rest, immediately after 6MWT, and 5 minutes later. Change in systolic blood pressure (sBP) was calculated as [sBP(immediately post)-sBP(pre)]/sBP(pre). Heart rate recovery at 5 minutes (HRR5) was defined as HR(immediately post)-HR(5 minutes post-exercise). Comparisons were made between PAH and LHD-PH patients using t-test or Mann-Whitney U. Correlations to sBP change were conducted in LHD-PH patients using a Spearman test.

Results: Compared to PAH patients (n=82), LDH-PH patients (n=43) had a higher BMI (36.9±11.6 vs 28.5±7.1kg/m^2, p<0.0001), higher rate of blood pressure medication use (81% vs 62%, p=0.04), higher E/e' (13.4±8.2 vs 8.9±5.9, p = 0.005), with a lower rate of echocardiographic right ventricular dysfunction (14% vs 49%, p<0.0001) and enlargement (37% vs 68%, p = 0.002). At rest, systolic blood pressure (sBP, 133±16 vs 120±18, p = 0.0002) and diastolic blood pressure (77±15 vs 72±12, p = 0.04) were higher in LHD-PH than PAH patients. There was a no significant difference in sBP change after exercise in LHD-PH compared to PAH patients (Table). In the LHD-PH patients, sBP change correlated to lower HR at rest (r=-0.40), higher pulmonary artery wedge pressure (r=0.34), and longer 6-minute walk distance (6MWD, r=0.30). HR at rest was similar between PAH and LHD-PH, but LHD-PH patients showed less increase in HR after exercise than PAH patients, even after adjusting for 6MWD and BP medication use. HRR5 was significantly lower in LDH-PH compared to PAH patients (Table).

Conclusion: Unlike sBP change, HR response to exercise during 6MWT was significantly lower in LHD-PH patients compared to those with PAH. Additionally, heart rate recovery was impaired in LHD-PH. These findings may be due to chronotropic incompetence and/or autonomic dysfunction in LHD-PH. Further studies are needed to determine the physiological mechanisms and clinical significance of impaired HR response in LHD-PH.

Table 1. Blood pressure and heart rate during 6-minute walk test

Variable	PAH (n=82)	LHD-PH (n=43)	p value
sBP change (%)	7.7% (3.5, 14)	12.7% (0.7, 22.0)	0.30
HR at rest (bpm)	80 ± 14	80 ± 15	0.94
HR change (bpm)	27 (18, 38)	21 (11, 33)	0.04
HRR5 (bpm)	-26 ± 13	-20 ± 12	0.01

PAH=pulmonary arterial hypertension; LHD-PH=left heart disease-associated pulmonary hypertension; sBP=systolic blood pressure; HR=heart rate; bpm=beats per minute; HRR5=heart rate recovery at 5 minutes