

**Title:** Blood Pressure Change During Six-minute Walk Test is an Independent Predictor of Clinical Worsening in Patients with Pulmonary Hypertension

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**Abstract:**

**Background/Objective:** Risk stratification has emerged as standard of care in treating patients with pulmonary hypertension (PH), but further refinements may improve patient care. Six-minute walk tests (6MWT) are routinely used to monitor patients, but there are parameters beyond walking distance that may be informative. We aimed to investigate blood pressure response to exercise during a 6MWT in PH patients and whether this is associated with clinical outcomes.

**Methods:** This retrospective study included outpatients in a single comprehensive PH center evaluated from August 2016 to December 2022. Patients had a 6MWT performed at that facility within 6 months of their initial visit. Pre-exercise and immediate post-exercise systolic blood pressures (sBP) were recorded, with sBP change calculated as sBP(post)-sBP(pre). We compared sBP change in patients with and without right ventricular (RV) dysfunction or enlargement using Mann Whitney U, and sBP change was correlated to TAPSE using Spearman correlation. Receiver operating characteristics curve analysis determined the optimal cutoff of sBP change for clinical worsening events, defined as the first occurrence of death, lung transplant, PH-related hospitalization, or worsened functional class leading to PH medication escalation. Cox regression models were used to assess the relationship between change in sBP and time to clinical worsening (TTCW), adjusted for REVEAL lite 2 risk score.

**Results:** One hundred two patients with PH were studied (80% Group 1, 13% Group 4, age  $54 \pm 15$  years, pulmonary vascular resistance  $7.5 \pm 4.5$  Wood units). Median sBP change post-exercise was 9mmHg (interquartile range 4, 16). sBP change did not significantly correlate with TAPSE ( $r=0.14$ ,  $p=0.22$ ). While sBP change was similar in those with or without RV dysfunction ( $p=0.18$ ), those with RV enlargement showed a smaller increase in sBP ( $p=0.02$ ). Fifty-six percent of patients had a worsening event. Patients unable to generate a sBP change  $>6$  mmHg during 6MWT had approximately a 2-fold increased risk of clinical worsening (hazard ratio 1.92, 95% confidence interval [CI], 1.15 to 3.13,  $p=0.01$ , Figure). When adjusting for REVEAL lite 2, there remained a significant association of sBP change with TTCW (hazard ratio, 1.82; 95% CI, 1.07-3.03,  $p=0.03$ ).

**Conclusion:** While BP response during a 6MWT in PH patients are variable and does not strongly correlate with RV dysfunction, insufficient sBP change in response to exercise independently predicted time to clinical worsening in PH patients. If externally validated, this easily obtained parameter may be useful for risk stratification.

