Physiologic and prognostic implications of the negative diastolic pulmonary pressure gradient in patients with left heart disease

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Background: The diastolic pressure gradient (DPG) has been introduced as a reliable metric for defining combined pre-capillary pulmonary hypertension (Cpc-PH) in left heart disease (LHD). The hemodynamic advantage of DPG against the traditionally used trans pulmonary gradient and pulmonary vascular resistance was initially supported by the superiority of DPG as a prognostic marker. However, more recent studies have challenged the prognostic power of the DPG, evoking a need for a better understanding of the optimal use and limitations of this measure. In particular, the clinical relevance of negative DPG (DPGNEG) measurements remains to be clarified.
Objectives: We hypothesized that large V-waves in the pulmonary artery wedge (PAWP) curve that cause an asymmetric pressure transmission, conceivably influencing the DPG calculation are responsible for the frequently occurring phenomenon of DPGNEG values. This prospective study was undertaken in order to clarify the physiological meaning of DPGNEG measurements and to investigate their prognostic implication.
Methods: Right heart catheterization and echocardiography was performed in 316 patients with left heart disease (LHD) due to primary myocardial dysfunction or valvular disease (rheumatic mitral stenosis - MS). Simultaneous PAWP and direct left atrial pressure (LAP) measurements were performed in 51 patients.
Results: 256 patients had PH-LHD (MS 37%) of whom 48% had DPGNEG. The V-wave was inversely associated with DPG ($r= -0.45$, $p<0.001$) in patients with low pulmonary vascular resistance (PVR<3 WU), but not in those with elevated PVR ($p>0.05$). Patients with large V-wave had lower DPG as compared to those without augmented V-wave ($p<0.001$) despite similar PVR ($p>0.05$). Simultaneous PAWP and direct LAP measurement yielded similar DPGNEG incidence. Positive but normal DPG (0–6 mmHg) was associated with worse 2-year prognosis for death and heart transplantation compared to DPGNEG (adjusted hazard ratio: 2.97; $p<0.05$).
Conclusion: Our results advocate against the current notion of DPGNEG constituting a measurement bias. Instead, we propose that DPGNEG can be partly ascribed to large V-waves and carries a better prognosis as compared to DPG within the normal positive range.