In the hands of Ohm
Hemodynamic Aspects of Pulmonary Hypertension

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Sal C, 9 trappor, Tandläkarhuset onsdagen den 5 juni, kl. 13:00.
Avhandlingen kommer att försvaras på svenska.

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Title
In the hands of ohm. Hemodynamic aspects of pulmonary hypertension.

Abstract
The majority of patients with Congestive heart failure (CHF) do not experience any discomfort at rest and may demonstrate normal findings when assessed. Small increases in systemic blood pressure and or venous return, caused by activity may result in severe elevation of filling pressures if left ventricular compliance is decreased. This highlights the need to perform cardiac investigations during stress to provoke symptoms. Increased pulmonary vascular resistance (PVR), commonly found in pre-capillary PH, is a condition that shares many symptoms with CHF, and is also associated with poor prognosis. It is highly important but a challenging task to differentiate pre- and post-capillary PH.

Methods
All included patients were in sinus rhythm, had dyspnea and were admitted for right heart catheterization (RHC). Echocardiographic(TTE) examinations were performed simultaneously with RHC, except in the third study, wherein echocardiography were performed within 3 days to the RHC. TTE derived pulmonary artery acceleration time (PAcT) was tested as a screening method for identification and differentiation of pre and post-capillary PH (study 1). The ability to calculate PVR by TTE, was assessed by replacing the invasive pressure and flow components with most related TTE derived measures. PVR_{echo} = mPAP_{chem} - Left atrial strain rate during atrial systole (LASRa) / Cardiac Output_{echo} (study 2).

Invasively measured PCWP response to passive leg lifting, and its ability to predict pathological increase in PCWP during supine bicycling, was tested in a population of 85 patients with normal left ventricular ejection fraction and suspicion of CHF based on NT-proBNP levels (Study 3). Finally, evaluation of standard and novel TTE parameters, potentially useful in identifying patients who may develop increased PCWP during passive leg lifting (PLL), was carried out (study 4).

Results
Study 1: PAcT of <90 ms had a sensitivity of 84% and a specificity of 85% in identifying patients with PVR ≥ 3.0 WU. Regardless of normal or elevated left sided filling pressures, PAcT differed significantly in patients with normal, compared to those with elevated levels of, PVR (p < 0.01). A significant difference was also found on comparison of the PAcT/PASP ratio (p < 0.01), with a lower ratio among patients with PVR ≥ 3.0 WU. Study 2: Left atrial strain rate during atrial systole (LASRa) had the highest significant positive correlation with PCWP (r² = 0.65, P < 0.001). By adopting a linear line of best-fit, LASRa may therefore be substituted for PCWP. Subsequently, LASRa was substituted into the PVR equation. PVR calculation by echo is significantly correlated with RHC generated PVR values (r² = 0.69, P < 0.001).

Study 3: Only 11 out of 55 patients with elevated NT-proBNP had PCWP above normal at rest. However, in response to PLL, 47% of patients developed elevated PCWP and the likelihood of developing high PCWP during supine cycling exercise could be determined by PLL, with a sensitivity and specificity of 90%.

Study 4: At rest, left atrial volume indexed (LAVI) and mitral deceleration time were independently related to PCWP during PLL. However, during PLL univariate regression analysis revealed LASRa (β = −0.77, P < 0.001) and E/LVSR (β = 0.47, P < 0.021) as most related to elevated PCWP_{PLL}. Multiple regression analysis fortified LASRa and E/LVSR as relevant PCWP_{PLL} related independent parameters.

Conclusion
A PAcT < 90ms is strongly suggestive of increased PVR (>3.0 WU). Based on study 1, there is clear evidence that suggests these findings apply irrespective of PCWP. LASRa used as a surrogate measure of PCWP enables non-invasive PVR estimation with high precision. Insufficient LV compliance results in the inability to cope with increased cardiac preload and NT-proBNP levels are oftenly elevated. Nearly half of the study population with elevated NT-proBNP showed increased PCWP during PLL, which is indicative of underlying ventricular stiffness. LAVI at rest, LASRa and E/LVSR during PLL, proved independently related to PCWP during PLL.

Keywords
Pulmonary hypertension, PVR, PCWP

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