Stress echocardiography allows reasonable estimation of RV contractile reserve compared to gold standard exercise magnetic resonance imaging

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Rationale/Background: Accurate estimation of contractility is important because it enables the clinician to identify the onset of right ventricular (RV) failure at an early stage independent of the confounding influence of raised afterload in patients with pulmonary hypertension (PH).

We sought to compare different echocardiographic measures of RV contractile reserve against a gold standard cardiac magnetic resonance (CMR) and invasive pressure-volume measure.

Methods/Materials: Twenty-nine participants (nine controls and 20 patients with chronic thromboembolic pulmonary hypertension [CTEPH]) underwent echocardiography and CMR both at rest and during incremental exercise. Three echocardiographic measures of RV contractile reserve (exercise-to-rest ratio of the RV pressure area relationship [RVESPAR], exercise-to-rest difference in peak longitudinal strain [ΔRV-LS], and exercise-to-rest difference in peak strain rate [ΔRV-SRs]) were compared with the exercise-to-rest ratio of the RV pressure volume relationship (RVESPVR) obtained from gold standard CMR volumes and direct invasive pressure measurements.

Results: ΔRV-LS ($R2 = 0.46$, $P = 0.001$) and ΔRV-SRs ($R2 = 0.45$, $P = 0.001$) correlated with RVESPVR to a similar extent (Fig. 1), perhaps surprisingly given the claim that SRs is less load-dependent than LS. RVESPAR ($R2 = 0.69$, $P < 0.001$) tended to have the strongest correlation with RVESPVR, although the incremental improvement over RV-LS and RV-SRs was not significant ($P = 0.245$ and $P = 0.243$, respectively).

Summary/Conclusions: The strong correlation between RVESPAR and gold-standard estimates of RV contractility during exercise suggest that this is a good non-invasive surrogate measure. RVESPAR is the most promising echocardiographic measure for identifying early RV dysfunction in patients with increased RV afterload.

Effects of sildenafil on right ventricular function at rest and during exercise in chronic thromboembolic disease: an exercise cardiac magnetic resonance study

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Rationale/Background: It is unclear whether the beneficial effects of pulmonary vasodilator therapy in chronic thromboembolic pulmonary hypertension (CTEPH) also extend to patients with chronic thromboembolic disease without pulmonary hypertension (CTED). We compared the effects of sildenafil on exercise hemodynamics in patients with chronic thromboembolic pulmonary vascular disease with or without PH at rest.

Methods/Materials: Thirty participants (11 CTED and 19 CTEPH patients) underwent exercise cardiac magnetic resonance imaging with simultaneous registration of invasive pulmonary and systemic arterial pressures both before and after administration of a single dose of 50 mg sildenafil. As right ventricular (RV) function, expressed by RV ejection fraction (RVEF), is dependent on both afterload and RV contractility, the effects of sildenafil on the relationship between mean pulmonary artery pressure and cardiac output (mPAP/CO slope) as a measure of afterload and the ratio of peak-exercise to resting RV end-systolic pressure/volume relationship (RVESPVR) as measure of contractility were assessed.

Results: Sildenafil increased RVEF in both CTEPH (35.8% before vs. 40.4% after at peak exercise, $P < 0.001$) and CTED patients (65.6% before vs. 67% after at peak exercise, $P = 0.035$) although the increase was greater in CTEPH ($P < 0.001$ for the interaction sildenafil* group). This increase was explained by a significant decrease in the mPAP/CO slope in CTEPH patients (8.8 ± 4.0 before vs. 6.4 ± 3.4 after, $P = 0.025$), while only a trend towards reduction was noted in CTED patients (3.1 ± 1.7 before vs. 2.6 ± 1.7 after, $P = 0.135$, Fig. 2). RV contractility was not influenced by sildenafil in either CTEPH (1.36 before vs. 1.44 after, $P = 0.118$) or CTED patients (2.25 before vs. 2.13 after, $P = 0.339$, Fig. 3).

Summary/Conclusions: Sildenafil significantly increases RV performance mainly due to a decrease in RV afterload and not by increased contractility. Although still significant, the observed benefits were less pronounced in CTED patients, potentially reflecting less small vessel vasculopathy.

Pulmonary arterial hypertension-related morbidity is prognostic for survival: insights from the SERAPHIN and GRIPHON studies

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Rationale/Background: Clinical and registry data suggest that pulmonary arterial hypertension (PAH) progression is indicative of poor prognosis.

Methods/Materials: The prognostic relevance of PAH-related morbidity was evaluated based on observations from randomized controlled trials SERAPHIN (n = 742) and GRIPHON (n = 1156). Both studies were double-blind, long-term, event-driven Phase III trials. In both, the primary endpoint was a composite of morbidity/mortality, prospectively defined and independently adjudicated. At three landmark time points—months 3, 6, and 12—the risk of all-cause death until end of study was assessed according to whether patients had experienced a primary endpoint morbidity event up to the landmark.

Results: At month 3, 720 SERAPHIN patients were at risk of death. Of those, 38 had experienced a morbidity event up to month 3. Within the median follow-up period of 27 months, patients had a more than threefold increased risk of death compared with the 682 patients who had not experienced a morbidity event up to month 3 (hazard ratio [HR] = 3.39, 95% confidence interval [CI] = 1.94–5.92). Similar observations were made in the GRIPHON population: 1127 patients were at risk of death at month 3; 62 patients had experienced a morbidity event up to month 3 and had a more than fourfold increased risk of death within the next 20 months (median follow-up) compared with the 1065 patients who had not (HR = 4.48, 95% CI = 2.98–6.73). In both studies, analyses at months 6 and 12 yielded similar findings.

Summary/Conclusions: These results confirm the prognostic relevance of PAH-related morbidity and the importance of its prevention in patients with PAH.

Pulmonary hypertension due to left heart disease: a predictive model using the National Echo Database of Australia (NEDA)

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Rationale/Background: Pulmonary hypertension due to left heart disease (PH-LHD) is common, but may be difficult to diagnose by echo in the absence of sufficient tricuspid regurgitation (TR). Once PH has progressed to moderate or severe disease, prognosis is poor.

Our objective is to create a predictive model using diastolic echo markers to diagnose PH, even in the absence of a measurable TR velocity.

Methods/Materials: A total of 302,746 echos (174,229 patients) were analyzed. Univariate analysis was used to establish significant diastolic markers of PH in 99,025 patients with sufficient TR (79,268 with PH vs. 19,767 with no PH). The whole cohort (including no measurable TR velocity) was randomized to two groups: Group A (151,373 echos) to perform multivariate regression analysis on the diastolic markers and to create a predictive model; and Group B to validate the predictive model (151,373 echos).

Results: Age, E', E/e', E:A, and indexed left atrial volume (LAVI) were identified in group A as markers of PH-LHD. A constant ($-6.649 + [0.035 \times \text{age}] + [0.072 \times E'] + [0.077 \times E/e'] + [0.509 \times E/A] + [0.03 \times \text{LAVI}]$) was developed and applied in group A to predict PH-LHD, with an area under the curve (AUC) of 0.746 (95% confidence interval [CI] = 0.729–0.762). We then validated this model on group B, with an AUC of 0.757 (95% CI = 0.741–0.773). TR is not measurable in 40% of echos. We have developed a new model that can predict PH-LHD with 75% accuracy, regardless of measurable TRV, using Age, E', E/e', E:A, and LAVI. Our model may be useful in echo software to automatically calculate a probability of PH-LHD.

Summary/Conclusions: TR is not measurable in 40% of echos. We have developed a new model that can predict PH-LHD with 75% accuracy, regardless of measurable TRV, using Age, E', E/e', E:A, and LAVI. Our model may be useful in echo software to automatically calculate a probability of PH-LHD.