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Additive prognostic value of coronary flow and heart rate reserve during vasodilator stress echocardiography in hypertrophic cardiomyopathy

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Background: Coronary flow velocity reserve (CFVR) and heart rate reserve (HRR) during vasodilator stress echocardiography (SE) assess coronary microvascular function and cardiac sympathetic reserve respectively. Both CFVR and HRR can be impaired in hypertrophic cardiomyopathy (HCM).

Objectives: To evaluate the prognostic value of CFVR and HRR during vasodilator SE in HCM.

Methods: We enrolled 244 HCM patients (age=51±15 years, 116 men) studied with vasodilator SE from 1999 to 2019 in 5 certified centers. Stress modality was either adenosine (Ado, 0.14 mg/kg/min in 2', n=171) or dipyridamole (Dip, 0.84 mg/kg in 6', n=73). Left ventricular outflow tract obstruction was present at rest in 80 patients (33%). We assessed CFVR in left anterior descending coronary artery (by TTE in 225, and TEE in 19 patients) and HRR (peak/rest heart rate). Abnormal values of HRR were based on receiver operating characteristics for Ado and Dip separately calculated. All patients completed the follow-up.

Results: CFVR was 2.17±0.46 for Dip and 2.13±0.43 for Ado (p=ns); HRR was 1.36±0.19 for Dip and 1.10±0.16 for Ado (p<0.001). An abnormal CFVR (<2.0 for both Ado and Dip) was present in 28 patients for Dip and 73 for Ado (38% vs 43%, p=ns). An abnormal HRR ($\leq$1.34 for Dip and $\leq$1.03 for Ado) was present in 39 patients for Dip and in 70 patients for Ado (53% vs 41%, p=ns). During a median follow-up of 67 months (interquartile range: 29–103 months), 97 spontaneous events occurred in 71 patients: 29 all-cause deaths, 32 new hospital admission for acute heart failure, 3 sustained ventricular tachycardias, 32 atrial fibrillations and 1 heart transplantation. Event rate was 2.5%/year in patients with normal CFVR and HRR, 4.7%/year in patients with only one abnormal criterion and 10.9%/year in patients with abnormal responses of both criteria (see figure). At multivariate analysis, abnormality of both CFVR and HRR (Hazard ratio 4.033, 95% CI 1.863–8.729, p<0.001) was independent predictor of events.

Conclusions: A reduced CFVR and blunted HRR during vasodilator SE identify distinct phenotypes and show independent value in predicting outcome in HCM patients.
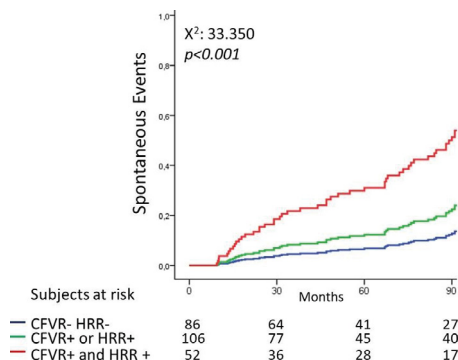
Figure 1. Kaplan-Meier spontaneous event-free survival curves based on HRR and CFVR. Kaplan-Meier survival curves (considering spontaneous events) in patients stratified with the abnormal HRR and/or CFVR. Number of patients at risk per year is shown.