Prognostic value of reduced heart rate reserve during exercise stress-echocardiography in hypertrophic cardiomyopathy

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Background: Heart rate reserve (HRR) during exercise evaluates chronotropic incompetence and is a prognostically important marker of cardiac autonomic dysfunction, additive to regional wall motion abnormalities (RWMA) in patients with coronary artery disease.

Objectives: To assess determinants and prognostic value of HRR in patients with hypertrophic cardiomyopathy (HCM).

Methods: From 1998 to 2019, we enrolled 774 HCM patients (age = 48.8±15.9 years, 410 men) with exercise stress echocardiography (ESE) in 10 certified centres of the international stress echo network. During ESE we assessed: left ventricular outflow tract obstruction (LVOTO, significant when >50 mmHg); RWMA; HRR (peak/ rest heart rate), 344 in betablockers therapy (44.4%). Patients were followed for a median 49 months (IQ range, 25–78 months). The study end-point was all-cause mortality. **Results:** During ESE, we observed stress-induced RWMA in 42 (5.4%) and LVOTO in 248 (33%); HRR was 1.92.±0.41. There were no differ-

ence in patients with normal and abnormal HRR with and without beta-blockers therapy (147, 41.1% vs 211, 58.9%, p=0.079). During follow-up, 43 deaths occurred. Beta blockers therapy in univariate analysis did not have prognostic role (HR 1.105, 95% Cl 0.602–2.028, p=0.768). The lowest HRR quartile (≤ 1.62) had a 10-fold higher 6-year death rate (10.9%) than the highest quartile (>2.16, 1.04%): see figure. At multivariable analysis, lowest HRR quartile (HR 2.074, 95% Cl 1.082–6.773, p=0.034), age (HR 1.045, 95% Cl 1.014–1.077, p=0.004), maximal wall thickness (HR 1.137, 95% Cl 1.054–1.226, p=0.001), stress-induced RWMA s(HR 4.289, 95% Cl 1.733–10.615, p=0.002) and \geq moderate mitral regurgitation at rest (HR 3.127, 95% Cl 1.507–6.488, p=0.002) predicted death.

Conclusions: A blunted HRR during ESE predicts adverse outcome independent of inducible RWMA in HCM patients. Autonomic dysfunction deserves consideration as a potential therapeutic target in this disease.

