

## Chest pain of unknown coronary origin: can exercise ECG testing contribute to long-term risk prediction on top of vasodilator stress cardiac magnetic resonance?

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**Funding Acknowledgement:** Type of funding source: Public grant(s) – National budget only. Main funding source(s): This study was funded by “Instituto de Salud Carlos III” and “Fondos Europeos de Desarrollo Regional FEDER” (PIE15/00013, PI17/01836, and CIBERCV16/11/00486 grants) and by Generalitat Valenciana (GV/2018/116).

**Background:** The prognostic value of both exercise ECG testing (Ex-ECG) and vasodilator stress cardiac magnetic resonance (VS-CMR) is well-known in patients with chest pain of unknown coronary origin. However, it is unknown whether performing both techniques can improve the risk stratification of these patients.

**Purpose:** We aim to confirm the additive prognostic value of ExECG and VS-CMR in a real-world cohort of patients with chest pain of unknown coronary origin.

**Methods:** We retrospectively included 288 patients in which ExECG and VS-CMR had been subsequently performed within one year. Clinical, Ex-ECG and VS-CMR variables were registered. We performed univariate and multivariate analysis to check for the association of variables with the risk of MACE, defined as a combined endpoint of acute coronary syndrome (ACS), admission for heart failure (aHF) or all-cause death.

**Results:** During a mean follow-up of 4.2±2.15 years, we registered 27 MACE (15 ACS, 8 aHF and 8 all-cause deaths). The history of hypertension, previous coronary artery disease and/or coronary artery bypass grafting, lower maximal heart rate during ExECG (maxHR) and more extensive ischemic burden (segments with perfusion defects -PD- on stress first-pass perfusion) and myocardial necrosis (number of segments with

necrosis at late gadolinium enhancement imaging) associated with the MACE endpoint. However, the only independent predictors of MACE were maxHR during ExECG (HR 0.98 [0.96–0.99], p=0.01) and more extensive segments with PD in the VS-CMR (HR 1.2 [1.07–1.34], p=0.002). We identified the best cut-off using the Youden index derived from receiver operating characteristics (ROC) analysis to predict MACE - it was ≤130bpm for maxHR during ExECG and ≥2 segments with PD on VS-CMR. These categories allowed us to stratify the annualized rate of MACE, which was very low (0.97%/year) in patients with normal maxHR and no PD on VS-CMR, intermediate in patients with only abnormal maxHR (1.98%/year) or PD on VS-CMR (3.24%/year) and high in patients with both abnormal maxHR and segments with PD (6.26%/year). Adding maxHR to the multivariable model including stress-induced PD by VS-CMR significantly improved the predictive power of MACE as derived from the continuous reclassification improvement index (0.47 [0.10–0.81], p<0.05).

**Conclusions:** ExECG and VS-CMR can have an additive prognostic value to predict the long-term risk of MACE in patients with chest pain of unknown coronary origin. Patients with maxHR during ExECG ≤130bpm and ≥2 segments with PD on VS-CMR are at the highest risk of MACE.

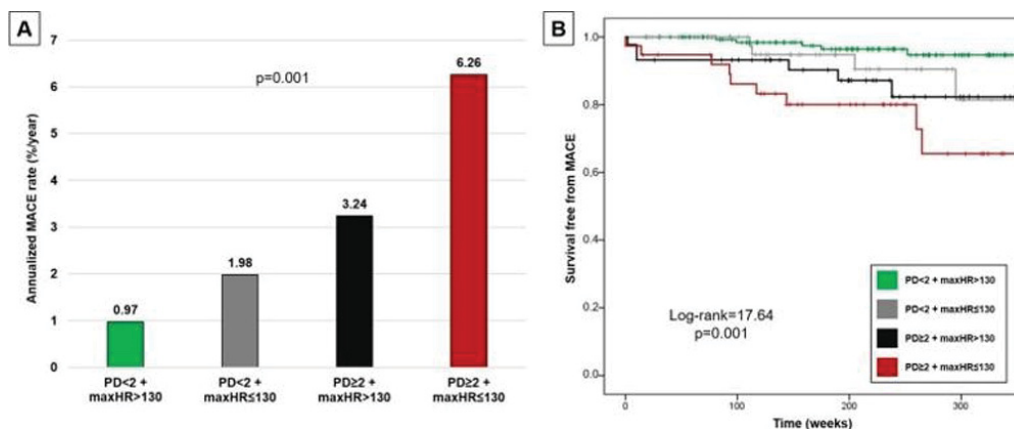


Figure 1. MACE risk stratification.