Disproportionate functional mitral regurgitation: clinical validation of a new conceptual framework

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Background: Disproportionate functional mitral regurgitation (FMR) is a novel concept that tries to identify hemodynamically significant FMR by readjusting the effective regurgitant orifice area (EROA) and regurgitant volume (RegVol) cut-offs according to left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF). However, this theoretical concept lacks clinical validation. The aim of this study was to assess the clinical significance of disproportionate FMR.

Methods: Patients with at least mild FMR and reduced LVEF (<50%) who underwent transthoracic echocardiography between 2010 and 2014 were retrospectively identified in our laboratory database. Optimal medical therapy (including cardiac resynchronization when indicated) for ≥3 months was a prerequisite for inclusion. Hemodynamically significant FMR was defined as regurgitant fraction >50% and the patient-specific theoretical RegVol cut-off was calculated according to the formula presented in Fig. 1a. The difference between the estimated RegVol by the PISA method and the theoretical RegVol cut-off was considered to represent the haemodynamic burden of MR. The primary endpoint was all-cause death. Patients were censured if mitral intervention or heart transplant was undertaken. Survival analysis was used to assess the effect of disproportionate FMR on mortality in 2 subgroups (LVEF <30% and 30–49%).

Results: A total of 289 patients (median age 69 years [IQR 60–77], 75% male, 53% of ischemic aetiology) were included. More than 90% were on beta-blockers and renin-angiotensin inhibitors, 44% on aldosterone receptor antagonists, and 73% had implanted devices. The median LVEF and LVEDV were 34% (IQR 27–41) and 170mL (IQR 128–220), respectively. Median EROA was 10mm^2 (IQR 3–21) and RegVol was 15 mL (IQR 4–30). RegVol distribution across the cohort was: <10mL: 41%; 10–20mL: 18%; 20–30mL: 15% and >30mL: 26%. Disproportionate FMR was present in 83 patients (29%). These patients had significantly higher SPAP values (41mmHg [IQR 33–50] vs. 33mmHg [IQR 29–40]; p<0.001).

During a median follow-up of 44 months (IQR 19–73), 106 patients died. In the LVEF <30% subgroup, age (HR 1.05 per year [1.02–1.08]; p<0.001), LVEF (HR 0.94 per 1% [0.89–0.99]; p=0.042) and TAPSE (HR 0.92 per mm [0.86–0.99]; p=0.030) were independent predictors of mortality. In the LVEF 30–49% subgroup, age (HR 1.05 per year [1.02–1.08]; p=0.003), LVEF (HR 0.94 per 1% [0.89–0.99]; p=0.020) and disproportionate FMR (HR 1.02 per mL [1.01–1.03]; p=0.01) were independently associated with increased mortality.

Conclusions: Disproportionate FMR proved to be an important independent predictor of mortality in patients with LVEF between 30–49%. These findings were not replicated in those with LVEF<30%, where the degree of biventricular dysfunction seems to outweigh all other echocardiographic parameters, leaving FMR as a bystander.

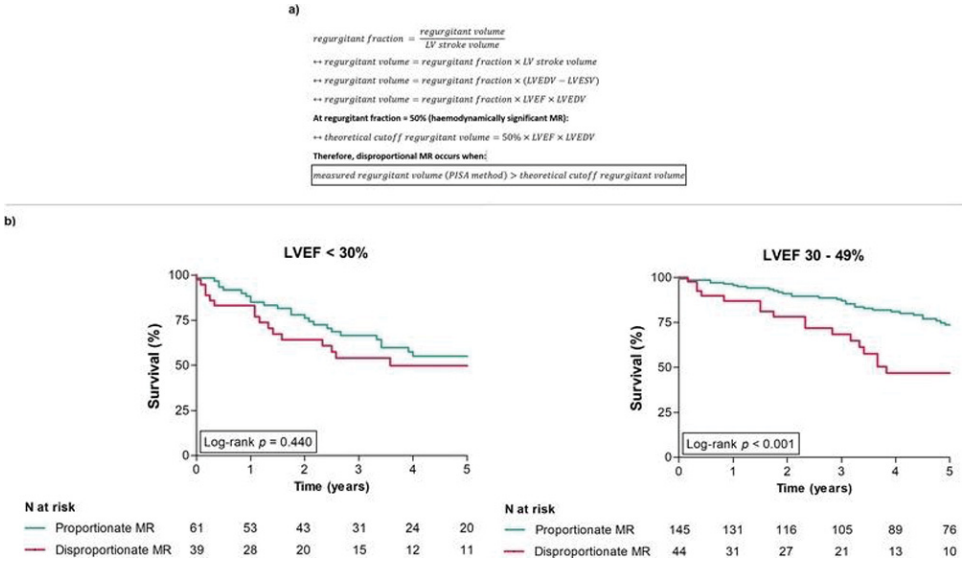

Figure 1