Principal morphomic components of secondary mitral regurgitation

Heitzinger G.[1]; Bartko PE.[1]; Spinka G.[1]; Pavo N.[1]; Prausmueller S.[1]; Arfsten H.[1]; Gebhard C.[1]; Mascherbauer J.[1]; Hengstenberg C.[1]; Strunk G.[2]; Huelsmann M.[1]; Goliasch G.[1]

[1]Medical University of Vienna, Vienna, Austria
[2]FH Campus Vienna and Complexity Research, Vienna, Austria

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Background: Secondary mitral regurgitation in patients with heart failure and reduced ejection fraction (sMR) results from distortion of the physiologic cardiac architecture. Underlying morphological components might account for the clinical impact of sMR but have not yet been assessed systematically or related to outcome.

Objectives: To investigate the morphologic features of sMR and their prognostic impact on outcome.

Methods: This study used morphomic network profiling in patients with stable heart failure under guideline directed medical therapy. Principal component analysis was applied and three factors extracted, of which Factor 1 and 2 were strongly related to sMR and outcome. Based on the factors, four morphologically distinct clusters were derived.

Results: Morphomic data from 383 patients were profiled. Factor 1 consists of high loadings of left atrial morphological information, factor 2 high loadings of left ventricular morphology. Cluster analysis revealed four morphologically distinct phenotypes. sMR was most prominent in cluster 3 and 4. The morphological difference was left ventricular size (enddiastolic volume 188ml (160-224) versus 315ml (264-408), P < 0.001). Clusters were associated with mortality (P < 0.001), however, sMR remained independently associated with mortality after adjusting for the clusters (adj.HR 1.42, 95% CI 1.14–1.77; P < 0.01) (Figure 1/ Panel B). The detrimental association of sMR with mortality was mainly driven by cluster 3 (HR 2.18, 95% CI 1.32-3.60; P = 0.002), the "small LV cavity" phenotype (Figure 1/ Panel A).

Conclusions: These results challenge the current perception of sMR resulting exclusively from global or local LV remodeling and, supported by previous concepts, emphasize the role of the atrial component as a pathophysiologic mechanism. The association of sMR with mortality cannot be purely attributed to cardiac morphology alone. Additionally, other key aspects such as balance of closing and tethering forces contribute to mitral valve closure. The association of sMR with mortality mainly driven by the small LV cavity phenotype refines the prognostic impact of sMR in relation to the underlying anatomic variability.

Abstract Figure. Survival for clusters and adj. sMR