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RESPONSE TO LETTER TO THE EDITOR

Response by Essayagh et al to Letter Regarding Article, "The MIDA-Q Mortality Risk Score: A Quantitative Prognostic Tool for the Mitral Valve Prolapse Spectrum"

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In Response:

We appreciate the interest of Figliosi and colleagues in the results of the MIDA-Q registry (Mitral Regurgitation International Database Quantitative). We are gratified that our research consortium gathered the largest current cohort of patients with isolated mitral valve prolapse (MVP), in which the addition of counts related to the quantification of degenerative mitral regurgitation to those of the classic MIDA score provided mortality prediction with incremental prognostic power, and with wide outcome separation.[1] In this international registry, all measures were obtained in routine practice, allowing applicability of MIDA-Q-score to the whole MVP spectrum, wide geographical range, and routine clinical practice. Hence, integrating MIDA-Q in clinical practice quantifies risks incurred by patients with MVP receiving medical management and is essential to reduce degenerative mitral regurgitation undertreatment.

Figliosi and colleagues also mention MVP arrhythmic complications that may result in sudden cardiac death (SCD). SCD is (fortunately) rare and thus a problematic end point, but MVP arrhythmic risk has not escaped our attention. Although the systematic review cited suggests an association between MVP and SCD, it suffers from biases of the individual reports gathered. Indeed. a later autopsy study by the same authors found a low percentage of MVP among SCD,[2] raising the question of whether SCD occurs with MVP or because of MVP? As a group, MVP carriers with no/mild degenerative mitral regurgitation enjoy a normal life expectancy identical to the general population. Circumscribing the obligatory small MVP subset with arrhythmic risk requires demonstrating a common phenotype that involves syncope, ECG repolarization abnormalities, severe myxomatous mitral degeneration with mitral annular disjunction,[3] and perimitral fibrosis.[4] In assessing the small MVP subset with arrhythmic risk, arrhythmia severity defines vital risks, whereas phenotype defines frequency/duration of rhythm monitoring but not therapy, thereby avoiding undue worrying of patient subsets with MVP who enjoy a generally benign outcome. This crucial point was summarized by a consensus document[4] widely adopted, providing an actionable plan for detection/treatment of ventricular arrhythmias associated with MVP.

Figliosi and colleagues also mention left ventricular (LV) fibrosis in patients with MVP. Myocardial fibrosis is the end result of all types of cardiac diseases. In the MVP context, seminal data suggest that LV fibrosis is associated with ventricular arrhythmias.[5] Although we agree that these proof-of-concept data are potentially important, for those to become part of widely applicable risk scores requires that the use of magnetic resonance imaging becomes routine practice in large proportions of patients with MVP in multiple centers. This implies that all results are reported at diagnosis and included in registries as they were provided to the clinicians in routine practice, similarly to degenerative mitral regurgitation quantitation in the MIDA-Q registry. Subsequently, it will be possible to conduct multicenter studies demonstrating that addition of LV fibrosis severity/location(?) to the integrated measures of known predictors of outcome, provides incremental prognostic power in defining risks incurred by patients affected by MVP. We believe that risk scores are clinically useful by being living instruments that include characteristics that fulfill these conditions and look forward to enriching the MIDA-Q score by defining and studying those characteristics, possibly LV fibrosis, that follow the rigorous process of demonstrating their worth in routine clinical practice.

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REFERENCES

1. Essayagh B, Benfari G, Antoine C, Grigioni F, Le Tourneau T, Roussel J-C, Bax JJ, Delgado V, Ajmone Marsan N, van Wijngaarden A, et al. The MIDA-Q mortality risk score: a quantitative prognostic tool for the mitral valve prolapse spectrum. *Circulation*. 2023;147:798–811. doi: 10.1161/CIRCULATIONAHA.122.062612
2. Han HC, Parsons SA, Teh AW, Sanders P, Neil C, Leong T, Koshy AN, Vohra JK, Kalman JM, Smith K, et al. Characteristic histopathological findings and cardiac arrest rhythm in isolated mitral valve prolapse and sudden cardiac death. *J Am Heart Assoc*. 2020;9:e015587. doi: 10.1161/JAHA.119.015587
3. Essayagh B, Sabbag A, Antoine C, Benfari G, Yang L-T, Maalouf J, Asirvatham S, Michelena H, Enriquez-Sarano M. Presentation and outcome of arrhythmic mitral valve prolapse. *J Am Coll Cardiol*. 2020;76:637–649. doi: 10.1016/j.jacc.2020.06.029
4. Sabbag A, Essayagh B, Barrera JDR, Basso C, Berni A, Cosyns B, Deharo J-C, Deneke T, Di Biase L, Enriquez-Sarano M, et al. EHRA expert consensus statement on arrhythmic mitral valve prolapse and mitral annular disjunction complex in collaboration with the ESC Council on valvular heart disease and the European Association of Cardiovascular Imaging endorsed by the Heart Rhythm Society, by the Asia Pacific Heart Rhythm Society, and by the Latin American Heart Rhythm Society. *Europace*. 2022;24:1981–2003. doi: 10.1093/europace/euac125
5. Constant Dit Beaufils AL, Huttin O, Jobbe-Duval A, Senage T, Filippetti L, Piriou N, Cueff C, Venner C, Mandry D, Sellal J-M, et al. Replacement myocardial fibrosis in patients with mitral valve prolapse: relation to mitral regurgitation, ventricular remodeling, and arrhythmia. *Circulation*. 2021;143:1763–1774. doi: 10.1161/CIRCULATIONAHA.120.050214