LETTERS TO THE EDITOR

Flail Mitral Valve and Sudden Cardiac Death

The recent report by Grigioni et al. (1) of an increased risk of sudden death in mitral regurgitation due to a flail leaflet was of interest to us, and we are sure, to many other cardiologists. Certainly, the Mayo Clinic group has been instrumental in advancing our understanding of the natural history of patients with mitral regurgitation. Specifically, Grigioni et al. (1) presented data suggesting that patients with a flail mitral leaflet, even in the absence of severe symptoms and left ventricular dysfunction, incur an enhanced risk of sudden unexpected death due to their valvular abnormality. As suggested in the accompanying editorial by Carabello (2), the potentially important role of associated atherosclerotic coronary disease in causing these sudden deaths could not be excluded, particularly given the rather advanced ages of those patients who died (mean age 71 years). Of the 25 sudden deaths, coronary artery disease was excluded in only four, and seven other patients were said to have a history consistent with this condition. We wonder: if such patients, who are likely to have ischemic heart disease (an alternative cause for sudden death at an advanced age), had been segregated in the authors’ sophisticated statistical analysis, would their results and conclusions have been as definitive? Perhaps under these circumstances, the authors should have been more conservative in their conclusions: “Sudden death is relatively common in patients with mitral regurgitation–flail leaflet who are conservatively managed,” as well as in the attractive title of the paper: “Sudden Death in Mitral Regurgitation Due to Flail Leaflet,” rather than potentially over-estimating the consequences of the flail mitral valve to clinicians.

A second area of concern involves issues related to mitral valve anatomy. Although we assume that the etiology of the flail leaflets and mitral regurgitation in most of the patients of Grigioni et al. (1) is mitral valve prolapse (i.e., myxomatous degeneration) with chordal disruption, this is not explicitly stated. Flail leaflets demonstrate a broad morphologic and functional spectrum, and there appears to be some uncertainty as to whether relatively mild or moderate degrees of flail (due to localized chordal disruption) were included among the authors’ study group of 348 patients, who have been characterized in the report as being at increased risk for sudden death. Should patients with relatively mild or segmental flail leaflets also be regarded to be at increased risk? Are the authors suggesting that all patients with flail segments represent a distinct subgroup within the mitral valve prolapse spectrum, as asposed to other patients with prolapse with moderate to severe mitral regurgitation, such as those with elongated chordae? Perhaps a clarification of these points would help clinicians better appreciate the potential consequences of the flail mitral valve.

Kevin M. Harris, MD, FACC
Barry J. Maron, MD, FACC
Director, Cardiovascular Research
Minneapolis Heart Institute
920 E. 28th Street
Suite 300
Minneapolis, Minnesota 55407

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REPLY

We appreciate the interest of Drs. Harris and Maron regarding our recent article in JACC (1). In their comments, Drs. Harris and Maron raised the question of an “increased” or “enhanced” risk of sudden death in mitral regurgitation due to a flail leaflet. We did not use such terms, because there is no available method to compare the rates of sudden death between patients and the general population. Therefore, it is impossible to determine whether rates of sudden death are statistically in excess of those observed in the population. This is an important limitation of all studies on sudden death. Age-stratified rates of sudden death were reported in the Framingham Study (2). An informal comparison of those rates suggests that at similar ages, rates of sudden death in mitral regurgitation due to a flail leaflet (without risk factors for sudden death) are approximately twice those observed in the general population (0.8% vs. 0.37%). Hence, the terms “relatively common” or “notable” seem more appropriate to describe the rates of sudden death observed in mitral regurgitation due to a flail leaflet.

The issue raised regarding coronary artery disease (CAD) is an important one. The age of patients with a flail leaflet is also an age at which there is a relatively high prevalence of CAD. However, as in our study, practicing cardiologists usually assess the risk of sudden death without the information provided by coronary angiography, a test usually performed only preoperatively. If we examine, as suggested by Drs. Harris and Maron, patients without a history of possible CAD, the 10-year rate of sudden death is 17.2 ± 4.7%. In patients in functional class I or II, with an ejection fraction ≥60%, no atrial fibrillation and no history of possible CAD, the linearized sudden death rate is 0.86% per year. Therefore, accounting for a history of clinically overt coronary disease would not have modified the conclusion of our study. Both the notable rate of sudden death in patients with mitral regurgitation due to a flail leaflet and the decreased rate of sudden death observed after mitral regurgitation surgery suggest a link between mitral regurgitation and this dreadful event.

The other question raised by Drs. Harris and Maron is about the concept of mitral valve prolapse and flail leaflets. Contrary to the statement of Drs. Harris and Maron, the criteria for a diagnosis of a flail leaflet (page 2079, Methods) and the cause of a flail leaflet (page 2079, Results) are explicitly mentioned. We are not aware of criteria supporting the description of mild, moderate or severe degrees of flail leaflets mentioned by Drs. Harris and Maron. In contrast, the degree of mitral regurgitation can be assessed and is mentioned in the Results section. Among the 317 patients in whom the degree of mitral regurgitation was graded, 82% had grade III or IV mitral regurgitation. Nevertheless, the comments of Drs. Harris and Maron raise an important question that will need to be addressed in future studies. The respective risks of sudden death attached to the degree of mitral regurgitation, left
ventricular volume overload or left atrial volume overload, and to the morphologic characteristics of the mitral valve (i.e., simple mitral valve prolapse vs. flail leaflet or the presence of severe myxomatous infiltration), cannot yet be analyzed. Recently, it has been suggested that mitral valve prolapse is uniformly a good prognosis (3). It is unclear how these various components of the clinical presentation of patients with mitral valve diseases contribute to the outcome, in particular to the risk of sudden death. We agree that further studies are needed on the outcome of various types of mitral valve disease. Such studies will require analysis of large population-based groups of patients with mitral valve disease. At this point, our study allows us to define the notable risk of sudden death incurred under conservative management by patients with flail leaflets, who represent a large group of candidates for surgical correction of mitral regurgitation.

Maurice Enriquez-Sarano, MD, FACC
Cardiovascular Diseases and Internal Medicine
Mayo Clinic
200 First Street SW
Rochester, Minnesota 55905

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U-Wave Alterations: Singular Noninvasive Electrocardiographic Diagnostic Markers

The recent absorbing report by Miwa et al. (1) is, secondarily, a reaffirmation of the considerable utility of the 12-lead electrocardiogram (ECG) and why it continues to be the most frequently used cardiovascular laboratory procedure. It was refreshing to learn that exercise-induced prominent U waves implicated significant left circumflex or right coronary artery disease and that patients with good collateral vessels could be identified by the finding of exercise-induced U-wave alterations. Furthermore, these alterations predicted the development of acute myocardial infarction or hemodynamic instability for low-risk patients upon abrupt closure of a stenotic coronary artery during coronary angioplasty.

There are three practical tenets regarding the at-rest negative U wave on the ECG. There are diverse cardiovascular etiologies, and only with knowledge of the history and physical findings will the full cognitive base residing in the experienced electrocardiographer’s repertoire be mobilized. It is an extremely important wave, as it may be the earliest and only marker of an evolving myocardial infarction (2), and it is an important clue in identifying the congenital long QT syndromes, such as the Jervell and Lange-Nielsen and the Romano-Ward syndromes, which harbor a malignant arrhythmogenic potential (3). Negative U waves may also be recorded in the presence of left ventricular enlargement; left anterior descending coronary artery disease (4); valvular heart disease such as aortic stenosis, mitral regurgitation and aortic insufficiency; and hypertension and variant angina (5). Second, transient U-wave inversion may be seen with both hypertension and variant angina; it can be differentiated on the ECG by initial or terminal negative deflections within the TP segment—the latter as related to myocardial ischemia (5). Finally, Miwa et al. (1) found a lower ejection fraction in patients with severe angina, exercise-induced U-wave alterations and good collateral vessels. Interestingly, in this vein, some 20 years ago, Gerson and McHenry (4) reported that at-rest U-wave inversion was an indicator of stenosis of the left anterior descending coronary artery, and they also found that U-wave negativity was a significant predictor of left ventricular dysfunction, usually segmental anteroapical akinesia or dyskinesia. Miwa et al. (1) and Gerson and McHenry (4) are applauded.

John A. M. Morphet, MD, FRCP(C), FACC, FESC
R.R. #1
225 Breisacher Road
Huntsville, Ontario
Canada P1H 2J2

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