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iVIEW

EDITOR'S PAGE

Redrawing the Borders

Considering Guideline Revision in Functional Mitral Regurgitation

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The development and updating of guidelines is a vital step in ensuring quality. Indeed, care conflicting with guidelines has traditionally been perceived as reflective of poor quality (1). In the past 2 years, 2 important guidelines were released by the European Society of Cardiology and the European Association for Echocardiography concerning functional secondary mitral regurgitation (MR). The ESC valvular disease guidelines (2) state, "In secondary mitral regurgitation, because of their prognostic value, lower thresholds of severity, using quantitative methods, have been proposed [20 mm^2 for effective regurgitant orifice area (EROA) and 30 ml for regurgitant volume]." The European Association for Echocardiography valvular regurgitation guidelines (3) state, "In functional ischemic MR, an EROA $\geq$20 mm^2 or an RVol $\geq$30 ml identifies a subset of patients at an increased risk of cardiovascular events." In this issue of *iJACC*, an opinion piece by Beigel and Siegel (4) questions this emphasis, which is distinct from the European valvular heart disease guidelines for severe primary MR, as well as from quantification of all MR, irrespective of etiology, in the American College of Cardiology/American Heart Association and American Society of Echocardiography guidelines (5,6), which identify severe MR in the presence an EROA >40 mm^2. This is a controversial step, and it brings with it a range of considerations that are worthy of attention from physicians contributing to and using guidelines.

The rationale for adjusting the severity threshold for functional MR is that the risk of these patients is high, especially in the ischemic population (7). At first sight, this change seems to erode the process of quantification: we might consider that MR severity and risk are 2 separate phenomena. But disease severity is an arbitrary construct, and using risk to guide the classification of severity is as good as, or better than, any other determinant. However, the step poses several other problems.

First, if we are to consider that MR severity should be quantified on the basis of risk, we should be sure that the risk is purely attributable to MR severity. This is likely untrue in functional MR, for which risk is influenced by age, underlying heart disease, left ventricular status, and comorbidities, among other factors (8). In fact, this situation is a typical challenge of causal inference (Fig. 1), as these other variables also influence the severity of MR. Although the association of MR is an independent predictor of outcomes, it is difficult to alter the threshold for intervention on this basis without knowing the contributions of other factors.

Second, an association with risk does not confirm that risk as being treatable. In this particular case, the merits of valvular intervention are contested (9). Moreover, arguments based on the balance of mortality from surgery and the natural history ignore the impact of major morbid events such as stroke and renal failure. In the absence of a randomized controlled trial, statistical simulations that include these risks have shown that an aggressive surgical approach is not justified in kindred situations such as asymptomatic aortic stenosis (10).

Third, the quantification of functional MR is inexact. A variety of quantitative approaches have been described, and as discussed by Beigel and Siegel (4), these have technical limitations as well as variability between observers. Furthermore, the data on severity and its clinical outcome are scant. The assessment of MR severity remains multiparametric

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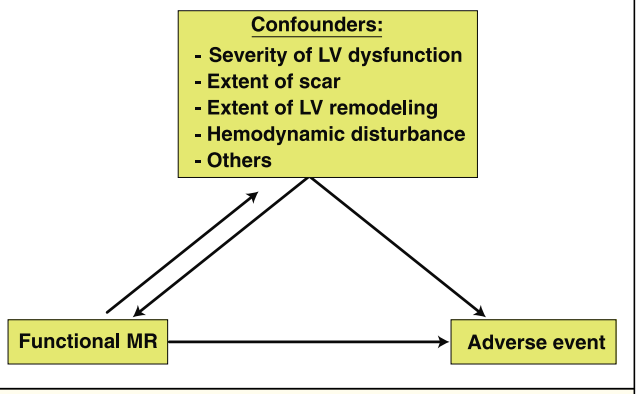

Figure 1. Directed Acyclic Graph to Represent Confounders in the Causal Pathway Between Functional MR and Adverse Events

If the association of functional mitral regurgitation (MR) with events is influenced by these other parameters, it seems unlikely that alteration of the interventional threshold of MR quantification is likely to alter outcomes.

(6), of which jet measurements remain but one component. Compared with primary MR, quantitation of functional MR is particularly challenging because of a frequent low-flow state pushing the limits of quantitative techniques and because the regurgitant orifice is usually crescent shaped, along the coaptation line of the valve leaflets. The latter results in underestimation of EROA and vena contracta derived with conventional, single-plane, 2-dimensional color Doppler (11,12); this may be a major reason behind the proposed lower EROA cutoff (2,3). Although 3-dimensional color Doppler would provide a more accurate measurement of vena contracta and derivation of EROA, it has not yet gained wide clinical use. The challenge to us as imaging specialists is to produce more accurate and reproducible methods to quantify MR. To this end, we published a review document on new techniques for this purpose (13), and we remain keen to see evidence based on these.

Despite all the effort that has been put into randomized controlled trials, it remains an inconvenient truth that guidelines are heavily dependent on expert opinion (14). This is especially true in guidelines relating to imaging and valvular disease and less true related to coronary disease intervention, for which industry involvement propelled the accumulation of high-level evidence. Unfortunately, surgical trials are difficult to do.

The U.S. and European guidelines are discordant on the management implications of moderate functional MR. It is troubling that, 25 years after Eddy and Billings (15) linked quality of evidence and quality of care, we still lack high-quality evidence to guide the management of this important clinical entity. In this context, we welcome ongoing debate regarding the optimal strategy.

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