

Knowledge and application of European Society of Cardiology (ESC) Guidelines in the management of mitral regurgitation: this is not bad but we can do much better

Philippe Pibarot^{1*} and Patrizio Lancellotti^{2,3}

¹Québec Heart & Lung Institute, Laval University, Department of Medicine, Québec, Canada; ²University of Liège Hospital, GIGA Cardiovascular Sciences, Departments of Cardiology, Heart Valve Clinic, CHU Sart Tilman, Liège, Belgium; and ³Gruppo Villa Maria Care and Research, Anthea Hospital, Bari, Italy

This editorial refers to ‘Educational needs and application of guidelines in the management of patients with mitral regurgitation. A European mixed-methods study’[†], by B. lung et al., on page 1295.

Mitral regurgitation (MR) is one of the most challenging valvular heart diseases (VHDs) to diagnose and manage. It is thus extremely important and useful for the medical community to have high-quality and well-disseminated guidelines.^{1,2} However, this exercise may become futile if we do not know whether the physicians are aware of these guidelines and apply them in real-life clinical practice. In this issue of the journal, lung et al. reported the results of an elegant study in which they performed a mixed-methods educational needs assessment.³ An online survey was undertaken using three case scenarios (asymptomatic severe primary MR, symptomatic severe primary MR in the elderly, and severe secondary MR) with 115 primary care physicians (PCPs) and 439 cardiologists or cardiac surgeons from seven European countries. The important good news of this survey was that ESC guidelines are widely used by European cardiologists. However, it also revealed some bad news and need for improvement.

Underuse of systematic auscultation by the PCPs

Although systematic auscultation is probably the best way to screen for VHD, it was performed by only 54% of PCPs in asymptomatic patients. The decline in the utilization and training of cardiac auscultation is an unfortunate but most probably irreversible trend. Within

the past four decades, the role of the stethoscope has indeed evolved from the primary screening and diagnostic tool in medicine to more an ostentatious sign of the healthcare professional. Not only is the stethoscope used less and less by PCPs and cardiologists, but their ability to detect and interpret heart sounds adequately has also deteriorated over time. This loss of expertise in cardiac auscultation is of particular concern for the PCPs because the stethoscope remains for them the best screening tool for VHD.

Assessment of MR severity was good for primary MR but not for secondary MR

More than 75% of cardiologists appropriately interpreted the mechanism and severity of primary MR cases and concluded that the MR was due to mitral valve prolapse and was severe. On the other hand, only 44% recognized that the case with secondary MR was severe. Are the cardiologists the only ones to blame for their relatively poor performance in interpreting the echocardiographic severity parameters in secondary MR? Certainly not, and the inconsistencies and discordances in the literature and between the different guidelines may also have contributed to this situation.

In the 2012 and 2017 ESC-EACTS guidelines,^{1,2} severe MR is defined as an effective regurgitant orifice area (EROA) >40 mm² and a regurgitant volume (RV) >60 mL in the case of primary MR, but >20 mm² and 30 mL, respectively, in the case of secondary MR. First, having different sets of MR severity cut-off points depending on the MR aetiology may be misleading for the cardiologists and could certainly have contributed to the underestimation of the MR severity in

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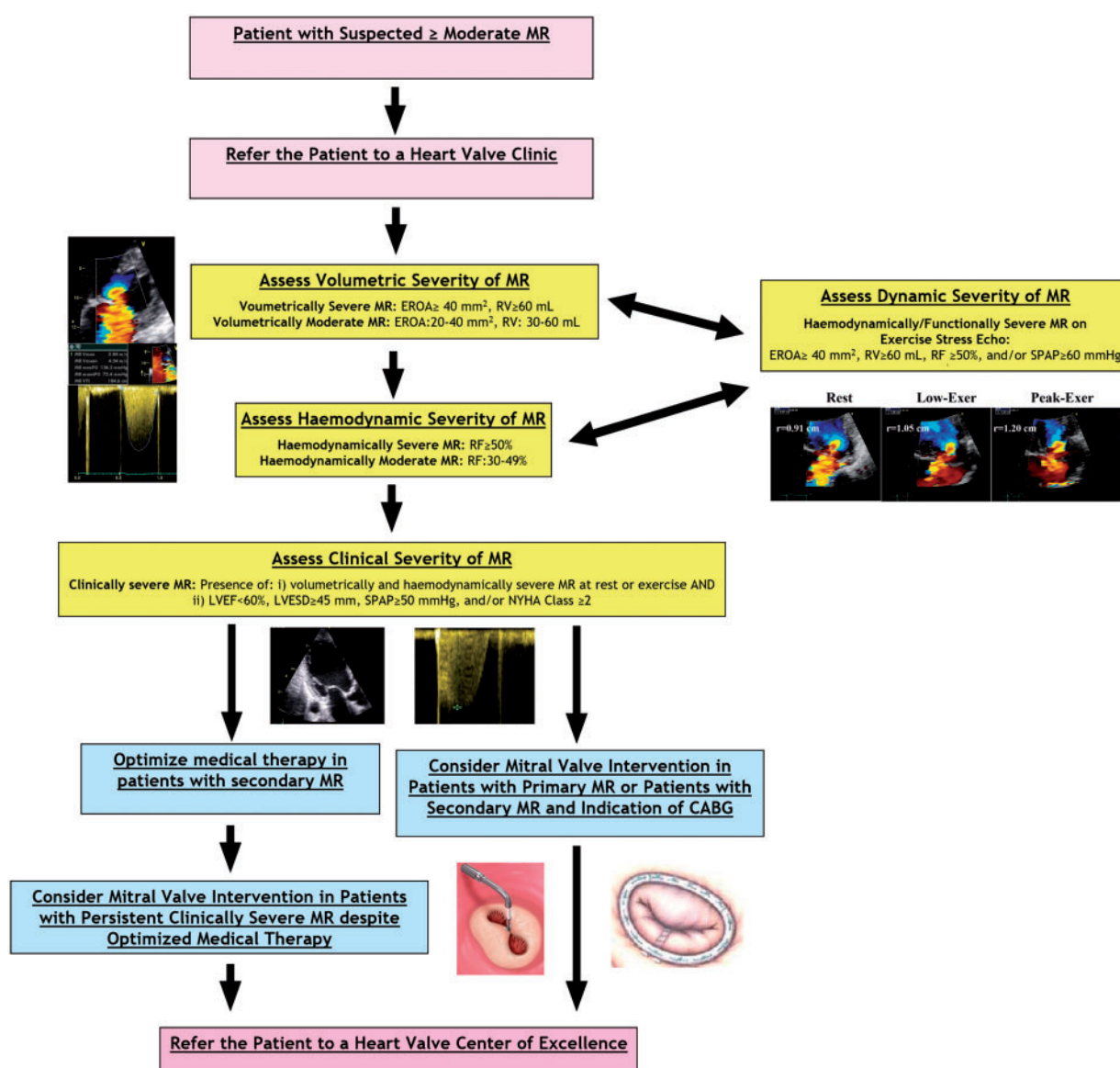
* Corresponding author. Institut universitaire de cardiologie et de pneumologie de Québec–Université Laval, 2725, Chemin Sainte-Foy, Québec City, Québec, Canada G1V 4G5. Tel: +1 418 656 8711 (ext. 5938), Fax: +1 418 656 4602, Email: philippe.pibarot@med.ulaval.ca

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the case of secondary MR.³ The major difference in the MR severity cut-off points proposed in the ESC guidelines^{1,2} between primary and secondary MR is based on the rationale that patients with secondary MR generally have depressed left ventricular (LV) function and are thus more vulnerable to the effect of concomitant MR. Although this rationale is quite logical, the adjustment of the severity cut-off points for secondary MR (i.e. two-fold lower than those for primary MR) is based on very limited published evidence.⁴ On the other hand, the 2014 and 2017 ACC-AHA guidelines^{5,6} have used the same severity cut-off points (EROA >40 mm² and RV >60 mL) in primary and secondary MR, and they also included a regurgitant fraction (RF) $>50\%$ as an additional cut-off point for severe MR.

For the sake of clarity and simplification, it is probably preferable to use the same set of EROA (>40 mm²) and RV (>60 mL) cut-off

points to define haemodynamically severe MR in secondary vs. primary MR. This approach has the advantage of being applicable in all types of MR, regardless of the aetiology, i.e. primary, secondary, or mixed (as is often the case in the elderly population), and of being more straightforward to apply for the cardiologist. However, it is also important to distinguish the haemodynamic severity vs. the functional severity vs. the clinical severity of MR (*Take home figure*). Although these three categories of severity are generally (but not always) well aligned in the context of primary MR, they often diverge in secondary MR. Hence, a secondary MR (e.g. EROA, 25 mm²; RV, 35 mL) may be 'volumetrically' moderate (when using the same cut-off points as primary MR) but nonetheless 'haemodynamically' severe on the basis of the RF ($>50\%$) if the patient has a low LV ejection fraction (EF) and low LV output (*Take home figure*). Hence, when assessing the severity



Take home figure Proposed strategies for the optimization of management of mitral regurgitation (MR). EROA, effective regurgitant orifice area; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association Class; RF, regurgitant fraction; RV, regurgitant volume; SPAP, systolic pulmonary arterial pressure.

of MR in patients with depressed LVEF and secondary MR, more emphasis should be put on the RF rather than on EROA and RV. If the RF is >50%, the MR should be considered severe and managed as such, even if the EROA and RV are moderate or even mild.

Furthermore, the fact that a secondary MR is volumetrically and haemodynamically moderate does not necessarily imply that it has no impact on clinical outcomes (*Take home figure*). A moderate MR by all quantitative parameters (e.g. EROA, 25 mm²; RV, 35 mL; RF, 45%) may actually be very well tolerated by a left ventricle with preserved LVEF but poorly tolerated by a depressed left ventricle. Hence, a volumetrically moderate MR may be clinically severe and potentially require intervention.

The randomized trials of the Cardiothoracic Surgical Network are certainly the studies that provided the most robust evidence for the management of secondary ischaemic MR.^{7,8} In these trials, severe MR was defined as an EROA >40 mm² and moderate MR as an EROA between 20 and 40 mm², which is in line with the severity criteria used in primary MR but larger than those proposed by the ESC guidelines for secondary MR. In the trial of patients with severe MR,⁷ mitral valve replacement provided a more durable correction of MR compared with mitral valve repair, but there was no difference in LV remodelling or clinical outcomes between groups. In the trial of moderate MR,⁸ the addition of mitral valve repair to coronary artery bypass grafting provided a more durable correction of MR, but did not lead to significant differences in terms of LV remodelling or survival at 1 year. These studies were published in 2014, so after the 2012 ESC-EACTS guidelines and their methods (MR severity cut-off points), and the results could have influenced the cardiologists' assessment and interpretation of MR severity. These findings further emphasize the importance of having the capability to update the guidelines rapidly when important new studies are published.

Mitral regurgitation, and especially secondary MR, is not static but highly dynamic (*Take home figure*). Indeed the severity of MR may increase drastically during exercise and this may negatively impact on outcomes. This phenomenon may explain why a moderate secondary MR (that becomes severe on exercise) may be associated with poor prognosis and require intervention. In addition, a large proportion of patients with MR (primary or secondary) and normal pulmonary arterial pressures at rest actually develop hypertension during exercise, and these patients with exercise-induced pulmonary hypertension exhibit worse outcomes.^{9,10} The only way to assess the dynamic component of MR is to perform exercise stress echocardiography. The role of this diagnostic modality should certainly be expanded in the guidelines and in clinical practice (*Take home figure*).¹¹ Surprisingly, and despite substantial evidence, the role and utility of exercise stress echocardiography have been downplayed in the 2017 edition of the ESC-EACTS guidelines.²

Medical therapy is overused in primary MR but underused in secondary MR

In asymptomatic severe primary MR with an indication for surgery, the authors reported that 27% of PCPs did not refer the patient to a cardiologist and medical therapy was over-used by 19% of

cardiologists.³ The term 'over-used' is probably too strong because, in such a situation, the recommendation for mitral valve surgery is a class IIa with a level of evidence C.^{1,2} Hence, although it is reasonable to consider mitral valve surgery in this case, conservative management with close follow-up also remains an acceptable option. What is more concerning in these findings about this primary MR case is that about one-third of PCPs did not refer this patient with severe MR to a cardiologist.³ The main reason for this choice of the PCPs was probably the fact that the patient was asymptomatic. This further emphasizes the important need for education of PCPs. Obviously, PCPs do not, and reasonably cannot, know in detail the content of all guidelines on all diseases including VHDs.

In severe symptomatic secondary MR, optimization of medical therapy was recommended by only 51% of PCPs and 33% of cardiologists, and surgery was considered in 30% of cases (transcatheter edge-to-edge repair in 64%). The case scenario proposed in this survey was complex, and the guidelines for this disease entity are also complex and differ depending on the medical societies. As mentioned above, the important discrepancies in the MR severity cut-off points for secondary MR in the different guidelines and randomized trials^{1,2,5-8} may have created some uncertainty and confusion with regard to the quantitation and management of secondary MR by the cardiologists. Furthermore, and in contrast to ACC-AHA guidelines,^{5,6} the ESC-EACTS guidelines^{1,2} also included other criteria such as LVEF (< or >30%) and presence/absence of myocardial viability to decide between medical therapy and surgical management. Given the limited evidence on the management of secondary MR, a simplification of the criteria and algorithms presented in the ESC-EACTS guidelines could be considered.

MitraClip is frequently proposed in high-risk patients with primary MR or secondary MR

This finding is not necessarily surprising because MitraClip allows elimination or reduction of MR in a less invasive manner compared with surgery, which is a significant advantage in patients with high surgical risk. Furthermore, several studies on MitraClip experience were published after the 2012 ESC-EACTS guidelines. These studies may have encouraged the cardiologists and cardiac surgeons to consider this procedure more often as an alternative to surgery, although there was no specific recommendation in the guidelines. Nonetheless, the MitraClip procedure is not a panacea and may not be able to achieve complete and durable correction of MR in all patients. Specific and precise recommendations should be included in the guidelines regarding the utility and limits of this procedure, and these recommendations should be rapidly updated when new studies are published.

Referral to specialized centres is mentioned by most cardiologists

This is one of the most important pieces of good news from this survey.³ The patients with scenarios like those presented in this study should ideally be referred and followed by specialized heart valve

clinics, and, when intervention is contemplated, the patients should be referred to a heart valve center of excellence or a comprehensive heart valve centre. The Heart Valve Clinics (*Take home figure*).^{12,13} These structures would probably improve the adherence of cardiologists to the current guidelines. On the other hand, they will not necessarily solve the issue of underdetection and under-referral of patients with MR to these specialized structures.

Conclusion

According to the survey of lung *et al.*, the knowledge and application of the ESC guidelines for the management of MR are overall adequate for primary MR but often inappropriate for secondary MR. There is obviously an important need to develop educational programmes not only for cardiologists but also, and importantly, for PCPs in order to better disseminate and apply the recommendations contained in the guidelines. With regards to the ESC guidelines *per se*, there is also a need to: (i) minimize and reconcile the discrepancies with the guidelines of other medical societies such as, for example, those of the ACC-AHA; (ii) simplify, as much as possible, the algorithms and criteria for the management of MR, and especially secondary MR; (iii) give more emphasis to the role of heart valve clinics and heart valve centres of excellence; and (iv) develop a mechanism to update rapidly, at least in part, the guidelines when important new information is published.

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