

Transcatheter therapies for mitral regurgitation: how will recent guidelines shape the field?

“...treatment of mitral valve disease is undergoing profound changes ... some of these changes have already been incorporated in current international guidelines.”

Keywords: guidelines • Heart Team • MitraClip • mitral regurgitation • transcatheter mitral valve repair

Recently, updates of both the European Society of Cardiology (ESC), as well as the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines on the management of patients with valvular heart disease (VHD) have been released [1,2]. Several important revisions were incorporated, which have the potential to fundamentally alter treatment for many patients. The most important of these changes relate directly to the advent and increasing clinical application of novel transcatheter-based treatment modalities for VHD, more specifically transcatheter aortic valve implantation for aortic stenosis and percutaneous edge-to-edge repair using the MitraClip system (Abbott Vascular, CA, USA) for mitral regurgitation (MR). While historically, relevant VHD has been the domain of surgical valve repair or replacement, it has meanwhile been well recognized that only a fraction of patients with a formal indication for surgery are actually referred for such [3,4]. Commonly, this is explained by an elevated surgical risk profile due to comorbidities, advanced age and/or impaired left ventricular function [5]. It is for these patients that less invasive transcatheter therapies have been evaluated in clinical trials and were subsequently introduced to rapidly become clinical routine at specialized centers in many European countries.

This article will focus on the implications of recent international guidelines on current clinical practice and future trends in the treatment of patients with severe chronic primary and secondary MR.

What are the most important changes within the new guidelines?

Owing to different regulatory restraints in North America and in Europe, the extent to which the respective guidelines were revised differs substantially. Nonetheless, there are also a few common issues inherent in the revisions of both documents.

The Heart Team & specialized centers

Not only were the revised guidelines developed as a collaborative effort of the respective European (ESC and European Association for Cardio-Thoracic Surgery) and North American (ACC/AHA and American Association for Thoracic Surgery/Society of Thoracic Surgeons) societies for cardiology and cardiac surgery. In addition, the importance of an interdisciplinary Heart Team consisting minimally of a cardiologist and a cardiac surgeon has now been formally recognized. If needed, this dedicated team can involve further medical specialities particularly when managing high-risk patients considered for transcatheter therapies. In many instances, allocation to the optimal therapeutic modality and treatment of these complex cases are best performed at specialized centers offering all available options. Referral of patients to such a center is now recommended as reasonable according to both European and North American guidelines.

Transcatheter therapies for MR

Among many devices evaluated for percutaneous correction of relevant MR, the only one currently in widespread clinical use is the



Lenard Conradi

Author for correspondence:
University Heart Center
Hamburg, Department of
Cardiovascular Surgery,
University Medical Center
Hamburg-Eppendorf,
Martinistr. 52, D-20246,
Hamburg, Germany
Tel.: +49 40 7410 53440
Fax: +49 40 7410 54931
lconradi@uke.de

Hendrik Treede

University Heart Center
Hamburg, Department of
Cardiovascular Surgery,
University Medical Center
Hamburg-Eppendorf,
Martinistr. 52, D-20246,
Hamburg, Germany

Hermann Reichenspurner

University Heart Center
Hamburg, Department of
Cardiovascular Surgery,
University Medical Center
Hamburg-Eppendorf,
Martinistr. 52, D-20246,
Hamburg, Germany

MitraClip system allowing for percutaneous edge-to-edge repair. Following the North American EVEREST trials [6], as well as experience from European registries [7,8], recommendations regarding use of this technique were included in both guideline documents. While approval of the MitraClip device by the US FDA for the North American market was granted early in 2014 only, it has been commercially available in Europe since receiving a CE mark in 2008. Correspondingly, recommendations are more restrictive according to the ACC/AHA compared with the ESC guidelines. While both documents recommend indication of percutaneous treatment in high-risk or inoperable patients following Heart Team approval, use of percutaneous edge-to-edge repair is permitted for primary MR only in North America. This is a direct consequence of the landmark EVEREST trial, which enrolled patients according to strict echocardiographic and morphologic eligibility criteria and thus included mostly patients with primary degenerative MR.

“...feasibility of mitral valve-in-valve procedures following bioprosthetic failure has been demonstrated using devices originally designed for treatment of native aortic stenosis.”

By contrast, the vast majority of patients treated in Europe presents with secondary MR, frequently in the wake of congestive heart failure. Indeed, MitraClip treatment is increasingly considered to be evolving towards a heart failure treatment and as an adjunctive rather than competitive option to mitral valve surgery [9]. Thus, percutaneous edge-to-edge therapy is recommended regardless of etiology (i.e., primary or secondary MR) as long as it remains restricted to use in patients unfit for surgery due to comorbidities. Finally, both ACC/AHA and ESC guidelines state that percutaneous mitral valve repair should only be performed in patients with a reasonable life expectancy. For the majority of elective patients with severe MR and regardless of etiology, mitral valve surgery remains the standard of care.

Future trends in the management of MR

With accumulating scientific data, further changes in the treatment of relevant MR can be anticipated for the future. In addition, ongoing preclinical evaluation of novel transcatheter-based devices will possibly lead to a broader armamentarium of nonsurgical options. There is some indication that many of these novel devices may aim at transcatheter mitral valve replacement rather than valve repair and there are several issues supporting this notion. For one, as known from mitral valve surgery, reconstruction of regurgitant mitral valves is the technically more demanding procedure, frequently requiring intervention on more than one of the different

components of the mitral valve (e.g., leaflets, chordae and annulus). Combining such a complex procedure in just one percutaneous device seems challenging if not technically impossible. Combining two or more types of devices on the other hand may lead to a both costly and time-consuming stepwise procedure, which may not be well suited for routine clinical use.

Furthermore, there is mounting scientific evidence that in patients with secondary MR and chronic heart failure, chordae-sparing prosthetic mitral valve replacement may not be as disadvantageous as proven in primary degenerative MR. Mainly, this is due to relevant rates of recurrent MR after initially successful valve repair, which naturally is not an issue after valve replacement [10].

Finally, another possible future scenario arises from the newly available technique of transcatheter aortic valve implantation. Recently, feasibility of mitral valve-in-valve procedures following bioprosthetic failure has been demonstrated using devices originally designed for treatment of native aortic stenosis [11]. Indeed, in the ESC guidelines, the option of valve-in-valve procedures in patients at prohibitive risk for conventional reoperation is already stated. For the future, the availability of this technique may influence the choice of valve type (i.e., biological vs mechanical prostheses) at the time of surgical valve replacement. Eventually, this development may lead to a more liberal indication of surgical biological valve replacement even below the current guideline driven threshold of 60–65 years of age.

Conclusion

At present, treatment of mitral valve disease is undergoing profound changes regarding available therapeutic approaches. Some of these changes have already been incorporated in current international guidelines. The European guidelines were altered earlier and more extensively compared with the North American guidelines due to different regulatory conditions. Most importantly, a collaborative approach to VHD has been formally recommended, especially in the light of increasing availability of transcatheter therapies. For the future, increasing importance of such transcatheter therapies can be anticipated further emphasizing the need for a Heart Team approach for indication and the procedure itself.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

- 1 Vahanian A, Alfieri O, Andreotti F *et al.*; ESC Committee for Practice Guidelines (CPG); Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC); European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur. J. Cardiothorac. Surg.* 42, S1–S44 (2012).
- 2 Nishimura RA, Otto CM, Bonow RO *et al.* 2014 AHA/ACC Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J. Am. Coll. Cardiol.* 63(22), e57–e185 (2014).
- 3 Iung B, Baron G, Butchart EG *et al.* A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. *Eur. Heart J.* 24, 1231–1243 (2003).
- 4 Iung B, Cachier A, Baron G *et al.* Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur. Heart J.* 26, 2714–2720 (2005).
- 5 Mirabel M, Iung B, Baron G *et al.* What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur. Heart J.* 28, 1358–1365 (2007).
- 6 Feldman T, Foster E, Glower DD *et al.* Percutaneous repair or surgery for mitral regurgitation. *N. Engl. J. Med.* 364, 1395–1406 (2011).
- 7 Maisano F, Franzen O, Baldus S *et al.* Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. *J. Am. Coll. Cardiol.* 62, 1052–1061 (2013).
- 8 Baldus S, Schillinger W, Franzen O *et al.*; German Transcatheter Mitral Valve Interventions (TRAMI) investigators. MitraClip therapy in daily clinical practice: initial results from the German transcatheter mitral valve interventions (TRAMI) registry. *Eur. J. Heart Fail.* 14, 1550–1055 (2012).
- 9 Conradi L, Seiffert M, Treede H *et al.* Towards an integrated approach to mitral valve disease: implementation of an interventional mitral valve programme and its impact on surgical activity. *Eur. J. Cardiothorac. Surg.* 44, 324–328 (2013).
- 10 Acker MA, Parides MK, Perrault LP *et al.* CTSN. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. *N. Engl. J. Med.* 370, 23–32 (2014).
- 11 Seiffert M, Conradi L, Baldus S *et al.* Transcatheter mitral valve-in-valve implantation in patients with degenerated bioprostheses. *JACC Cardiovasc. Interv.* 5, 341–349 (2012).