

## Current management of aortic and mitral valve disease

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### Summary

New guidelines provide recommendations for the treatment of aortic, mitral and tricuspid valve disease. For aortic stenosis and mitral valve regurgitation especially, catheter-based therapies are increasingly used or have almost become the standard therapy. Transcatheter aortic valve implantation (TAVI) is currently recommended for patients at intermediate risk, as recent literature has shown good results for TAVI. Newer literature might pave the way to expanding the indication for TAVI to low-risk patients. The evidence for mitral regurgitation is not quite as extensive. The only transcatheter therapy that is recommended is the Mitraclip for high-risk surgical patients. It is also clearly recommended that treatments unlikely to improve quality of life and survival must be avoided by means of a strict evaluation of the patients and discussion among the heart team, which ranks high in the guidelines. We are facing rapid developments in the field of structural heart disease. Surgeons have to be actively involved in transcatheter therapies and not only stand by during procedures to comply with legal requirements.

**Keywords:** guidelines, aortic valve, mitral valve, cardiac surgery

### EACTS/ESC guidelines for the treatment of valvular heart disease

The common guidelines of the European Society for Cardiology (ESC) and the European Association for Cardiothoracic Surgery (EACTS) for the diagnosis and treatment of heart valve disease were presented at the 2017 ESC annual meeting and were published concurrently [1]. An update was necessary because of an accumulation of new study results, especially in the field of interventional treatment options, risk assessment and timing of interventions, as well as new anticoagulant treatment options. Additionally, the guidelines were optimised for better usability in routine clinical practice. The chapters were harmonised with the corresponding chapter in the ESC Textbook of Cardiovascular Medicine [2], which is available free of charge as an online version “ESC CardioMed”.

The guidelines provide recommendations on the diagnostic workup and therapy options for acquired diseases of the aortic, mitral and tricuspid valves, but not for endocarditis and congenital heart disease for which there are separate guidelines. The central role of the heart team and the development of heart valve centres is particularly relevant in this context. The importance of noninvasive imaging techniques is specifically identified. For example, the use of computed tomography in the evaluation of patients who are being considered for transcatheter aortic valve interventions is highlighted. Techniques such as magnetic resonance tomography for grading mitral valve disease receive special consideration, as these techniques are of utmost importance before and during transcatheter procedures, as well as for the planning of minimally invasive cardiac surgical procedures. This article focuses mainly on aortic and mitral valve disease because of their high relevance and the controversy surrounding their management in daily clinical practice.

### Aortic valve disease

Surgical therapy remains the gold standard for the treatment of aortic valve regurgitation (AR). Transcatheter aortic valve implantation (TAVI) plays merely a minor role because no TAVI prosthesis has, in fact, been approved for this indication. Only the JenaValve (JenaValve Technology GmbH, Munich, Germany) as a dedicated prosthesis for pure AR is available as an investigational device [3]. Other prostheses are used off label [4]. Because more evidence has become available, there is a new IIa B instead of a IIa C recommendation for asymptomatic patients with severe AR, preserved left ventricular ejection fraction and severe left ventricular dilatation. There is a new I C recommendation for discussion by the heart team of patients for whom aortic valve repair appears feasible. A referral to a heart valve centre with extensive expertise in surgical aortic valve repair is expedient, because very good long-term results with a better quality of life can be achieved [5].

With regard to the choice of type of prosthesis, standards used in aortic stenosis are not simply transferable. The degree of oversizing in particular has to be calculated differ-

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ently because of the lack of calcification of the valve. Results have improved with newer-generation TAVI devices, but are still inferior to surgery. Nevertheless, TAVI might be an option for patients with severe AR and a high surgical risk.

The most relevant changes are in the recommendations for the diagnosis and treatment of aortic valve stenosis (AS). The definitions of the entities “low-gradient AS” and “high-gradient AS” have been refined, which facilitates the assessment of severity, especially of low-flow, low-gradient AS. Clearly defined thresholds of biomarkers and pulmonary hypertension are considered, which reflects the current literature. More emphasis is put on computed tomography, especially for assessing the degree of calcification of the aortic valve and for planning therapy, as well as for TAVI and surgical aortic valve replacement (planning of minimally invasive surgical access such as hemisternotomy and right anterolateral thoracotomy). For asymptomatic patients with an indication for aortic valve replacement, surgical replacement is still the gold standard, because no data are available for this patient cohort with regard to TAVI treatment.

For patients with severe, symptomatic AS, there is a clear recommendation for therapy. There are new graduated recommendations regarding low-flow, low-gradient aortic valve stenosis in symptomatic patients. The precise evaluation within the heart team of the pathology and anatomy, as well as the evaluation of the patient, are emphasised.

Clear recommendations are made with regard to the choice of procedure in symptomatic AS. For patients at high surgical risk, TAVI is recommended. Surgical replacement is recommended for patients with a low perioperative risk, which is defined as a Society of Thoracic Surgeons (STS) score or EuroSCORE II <4% or a logEuroSCORE <10%. For patients with an intermediate surgical risk, defined as an STS score >4%, studies showed similar results in terms of intermediate-term mortality for both strategies. Additional criteria for decision making within the heart team are defined. These include anatomical and functional parameters, as well as factors that are not assessed in conventional risk assessment scores, such as frailty. These recommendations are made on the basis of results of prospective, randomised studies and large registries [6, 7].

It is also highly recommended to take into account the morphology of the device landing zone and the resulting individual risks for TAVI procedures. For example, surgical valve replacement is recommended for bicuspid aortic valves despite good early outcomes with TAVI [8]. The same holds true for a severely calcified prosthesis landing zone in the left ventricular outflow tract. For patients with small annuli, with the risk of prosthesis-patient mismatch, TAVI is recommended.

Besides the recommendations in the guidelines, very recent results from two large prospective randomised studies including patients with a low perioperative risk for mortality (the mean STS score in both trials was 1.9%) have been published [9, 10]. Patients were randomised to TAVI with a balloon-expandable valve or to surgical aortic valve replacement in the PARTNER 3 trial, and to TAVI with a self-expandable prosthesis or surgery in the Medtronic Evolut low-risk trial. Briefly, in these landmark trials TAVI was noninferior with regard to mortality, stroke and addi-

tional endpoints in both studies. Based on the guidelines and current evidence, an expansion of the indication for TAVI to patients with an intermediate and low perioperative risk, which would also include younger patients, can be expected. In this context, it is very important to discuss with the patient the fact that, for example, only biological prostheses with a shorter long-term durability than mechanical prostheses can be implanted via catheter-based procedures. For younger patients especially, this limitation is often counteracted by the introduction of valve-in-valve therapies. This approach has to be considered critically because there are only limited data available; in particular, there are no long-term data. Some results have been published only for TAVI in degenerated surgical prostheses [11, 12]. Although these results are promising, they are not yet very meaningful owing to the low numbers of patients and short follow-up periods. In this context, relevant studies have been published that showed a reduction of complications following the use of oral anticoagulants through INR self-monitoring [13]. This is a relevant argument against the preference for biological valves, that is, for a TAVI prosthesis over mechanical aortic valve prosthesis.

The heart team is of key significance in this context. It is still recommended to perform TAVI procedures in hospitals in which a cardiac surgery department and a cardiology department collaborate with one another in one institution under one roof, working side by side in the treatment of AS. The guidelines give only level C recommendations in this context because randomised trials are naturally not available. Case studies describing the outcome of patients who had to undergo emergency surgery during a TAVI procedure as a result of severe complications such as coronary obstruction or annulus rupture have been published. Recently, the rate of these complications has decreased markedly (1–2%), but immediate treatment can be life-saving [14].

The highest mortality rate is seen in patients who develop complications during a TAVI procedure in a catheter laboratory. Transportation to a surgical operating room is the limiting factor in these cases [15]. It is evident from these results that it is necessary to have a cardiac surgical department available in hospitals that perform TAVI procedures and that the procedures must be in a hybrid operating room to avoid endangering patients. Therefore, the current guidelines recommend not only that TAVI procedures be performed in a heart team, but that heart valve centres be developed to increase the case load and the experience of individual centres in order to improve the outcomes of interventions [16].

Another very important point is to discourage physicians from performing an intervention if an improvement in the quality of life and survival cannot be expected.

### Mitral valve disease

Today, the incidence of mitral valve stenosis in western industrialised nations is low. The current recommendations have not changed significantly.

In the treatment of mitral valve regurgitation (MR), surgical therapy remains the gold standard for both primary and secondary pathologies. There is only one relevant in-

terventional therapy concept available today, namely edge-to-edge reconstruction with the Mitraclip (Abbott, Menlo Park, CA, USA).

For primary (degenerative) MR, surgical reconstruction has excellent long-term outcomes, which have been described in several studies, and it is therefore recommended as the gold standard in current guidelines. However, it is recommended that the surgery be performed in specialised centres with documented high reconstruction rates. In this situation, Mitraclip therapy plays only a minor role. It is only recommended for patients who meet anatomical criteria and are judged as inoperable by the heart team (IIB C recommendation). This is because intermediate- and long-term results are worse than those of surgical therapies, especially in patients with preserved left ventricular ejection fraction [17].

The evidence is much scarcer with regard to the grading of, and indications for, surgical or interventional procedures for secondary MR. Because secondary MR results mainly from a dysfunctional left ventricle, only a symptomatic but not a prognostic improvement has been shown for reconstruction or replacement of the mitral valve. Perioperative mortality is higher for secondary than for primary MR. Additionally, evidence on replacement versus reconstruction is controversial. Current studies showed similar survival rates but much higher rates of recurrent regurgitation after reconstruction with annuloplasty [18].

For percutaneous edge-to-edge mitral valve repair, for the first time a recommendation has been issued for patients with functional or secondary MR without an indication for revascularisation, at an increased risk for mortality and with a left ventricular ejection fraction >30% that remains symptomatic despite optimal medical therapy (IIB C). If the left ventricular ejection fraction is <30%, a detailed evaluation should be carried out prior to the intervention, including stratification for mechanical circulatory support and heart transplantation.

A prognostic benefit after percutaneous mitral valve interventions has not been shown, especially for patients with a poor left ventricular ejection fraction. Two large trials that have been published recently had contradictory results. Obadia et al. showed in the MitraFR study that the Mitraclip therapy has no benefit in patients with severe heart failure and MR as compared with patients who had optimal medical treatment only [19]. In contrast, the COAPT study, with a slightly different patient cohort (earlier stage of heart failure and definitely severe MR) showed completely different results, with a clear benefit of the Mitraclip therapy [20].

For Mitraclip therapy, there is no recommendation regarding the necessity of an on-site cardiac surgery department. Discussion within the heart team is strongly recommended. Despite this, treatment of these patients in heart valve centres with expertise in surgical mitral valve treatment appears to be useful. This should be discussed again in the near future, especially in view of the increasing development of catheter-based mitral valve replacement (TMVI) and annuloplasty systems. These therapies are, in fact, still in the very early stages of development. For most mitral valve prostheses, transapical access is necessary for the time being. This means that a surgeon has to be involved in any case.

But also for percutaneous treatment modalities, the procedures should be performed in a heart team with the involvement of an interventional cardiologist and a cardiac surgeon, because these procedures are highly complex and have a strong potential for complications such as pericardial effusion with tamponade and rupture of chordae tendineae or parts of mitral valve leaflets.

Cost factors could be limiting, because these new therapies, especially shortly after their introduction, will be very expensive. Besides new guidelines, new legal requirements will be necessary.

## Conclusions

In the treatment of structural heart disease, transcatheter therapies play a very important role in modern medicine. This is reflected in current guidelines. For TAVI and Mitraclip therapies, there are recommendations for specific patient populations. The field of interventional treatment modalities for structural heart disease is growing. Only teams that are able to perform all treatment options for all heart valve pathologies unbiased will be able to choose the best possible therapy for an individual patient from the wide range of available techniques. Additionally, these teams should also be able to treat possible complications resulting from the procedures themselves, including interventional, surgical and hybrid modalities. In doing so, and by including precise preprocedural planning mainly through multimodality imaging, the periprocedural mortality and morbidity can be reduced to a minimum. Cardiac surgical competence as an equivalent, core component within the heart team is decisive. Surgeons should not merely be a passive back-up bystanders, but must be active members of the heart team during the implantation and should perform procedures themselves on both the aortic and the mitral valve.

## Take-home messages

- **Heart team and heart valve centres:** The heart team plays a decisive role in decision making. Additionally, it is advisable to develop and establish heart valve centres with personnel and structural standards in order to create an optimal environment for the treatment of patients with valvular heart disease.
- **Aortic valve stenosis:** There are clear criteria for decision-making in regards of transcatheter aortic valve implantation (TAVI) or surgical valve intervention in current European guidelines. In these, TAVI is also recommended for patients with an intermediate surgical risk. Current literature also supports TAVI implantation in patients with a low surgical risk.
- **Mitral valve regurgitation:** Following the latest European guidelines, surgical reconstruction remains the gold standard for the treatment of primary and secondary mitral valve regurgitation. For secondary mitral valve regurgitation, catheter-based treatment options are steadily increasing.

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