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THE PRESENT AND FUTURE

JACC GUIDELINE COMPARISON

ACC/AHA and ESC/EACTS Guidelines for the Management of Valvular Heart Diseases

JACC Guideline Comparison

Augustin Coisne, MD, PhD,[a,b] Patrizio Lancellotti, MD, PhD,[c,d] Gilbert Habib, MD, PhD,[e] Madalina Garbi, MD,[f] Jordi Sanchez Dahl, MD, PhD,[g] Marco Barbanti, MD,[h] Mani A. Vannan, MD,[i] Vassilios S. Vassiliou, MD,[j] Dariusz Dudek, MD,[k] Ovidiu Chioncel, MD,[l,m] Johannes L. Waltenberger, MD, PhD,[n,o] Victoria L. Johnson, MD,[p] Ruggero De Paulis, MD,[q] Rodolfo Citro, MD, PhD,[r,s] Philippe Pibarot, DVM, PhD,[t]
on behalf of the EuroValve Consortium

ABSTRACT

Valvular heart disease (VHD) is common and poses important challenges from the standpoints of diagnosis and therapeutic management. Clinical practice guidelines have been developed to help health care professionals to overcome these challenges and provide optimal management to patients with VHD. The American College of Cardiology, in collaboration with the American Heart Association, and the European Society of Cardiology, in collaboration with the European Association for Cardio-Thoracic Surgery, recently updated their guidelines on the management of VHD. Although these 2 sets of guidelines are generally concordant, there are some substantial differences between these guidelines, which may have significant implications for clinical practice. This review prepared on behalf of the EuroValve Consortium describes the consistencies and discrepancies between the guidelines and highlights the gaps in these guidelines and the future research perspectives to fill these gaps. (J Am Coll Cardiol 2023;82:721-734) © 2023 by the American College of Cardiology Foundation.

From the [a]University Lille, Inserm, CHU Lille, Institut Pasteur de Lille, Lille, France; [b]Cardiovascular Research Foundation, New York, New York, USA; [c]University of Liège Hospital, GIGA Cardiovascular Sciences, Departments of Cardiology, Heart Valve Clinic, CHU Sart Tilman, Liège, Belgium; [d]Gruppo Villa Maria Care and Research, Maria Cecilia Hospital, Cotignola, and Anthea Hospital, Bari, Italy; [e]APHM, La Timone Hospital, Cardiology Department, Aix Marseille University, Marseille, France; [f]Royal Papworth Hospital, Cambridge University Health Partners, Cambridge Biomedical Campus, Cambridge, United Kingdom; [g]Department of Cardiology, Odense University Hospital, Odense, Denmark; [h]Università degli Studi di Enna "Kore," Enna, Italy; [i]Marcus Heart Valve Center, Piedmont Heart Institute, Atlanta, Georgia, USA; [j]Department of Cardiology, Norwich Medical School, University of East Anglia and Norfolk and Norwich University Hospital, Norwich, United Kingdom; [k]Institute of Cardiology, Jagiellonian University, Krakow, Poland; [l]Emergency Institute for Cardiovascular Diseases 'Prof. C.C. Iliescu,' Bucharest, Romania; [m]University of Medicine Carol Davila, Bucharest, Romania; [n]University of Muenster, Medical Faculty, Muenster, Germany; [o]Hirslanden Clinic in Park, Zurich, Switzerland; [p]Department of Cardiology, University Hospital Giessen, Giessen, Germany; [q]Department of Cardiac Surgery, European Hospital, Rome, Italy; [r]Cardio-Thoracic-Vascular Department, University Hospital "San Giovanni di Dio e Ruggi d'Aragona," Salerno, Italy; [s]Department of Vascular Physiopathology, IRCCS Neuromed, Pozzilli, Italy; and the [t]Quebec Heart and Lung Institute, Laval University, Québec City, Quebec, Canada.

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ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

AHA = American Heart Association

AR = aortic regurgitation

AS = aortic stenosis

AVR = aortic valve replacement

EACTS = European Association for Cardio-Thoracic Surgery

ESC = European Society of Cardiology

MR = mitral regurgitation

MV = mitral valve

PMR = primary mitral regurgitation

SMR = secondary mitral regurgitation

TAVR = transcatheter aortic valve replacement

TR = tricuspid regurgitation

TV = tricuspid valve

The American (American College of Cardiology [ACC]/American Heart Association [AHA])[1] and European (European Society of Cardiology [ESC]/European Association for Cardio-Thoracic Surgery [EACTS])[2] guidelines on the management of valvular heart disease were updated recently. Although most of the recommendations are consistent in both guidelines, there are notable differences and discrepancies between these guidelines for some recommendations. The objective of this review written by representatives of the EuroValve Consortium is to present a comparison between the 2020 American and 2021 European guidelines for the management of valvular heart disease. The specific aims of this review article are as follows: 1) to describe the recommendations that are consistent between the 2 guidelines; 2) to highlight the recommendations that are different or discrepant between the 2 guidelines, and to describe the potential reasons for these differences/discrepancies as well as their clinical implications; and 3) to identify the gaps in these guidelines to provide a roadmap for future position statements or future research.

HIGHLIGHTS

- Both the American and European guidelines on management of VHD were recently updated.
- Although generally concordant, some differences have potentially important implications for clinical practice.
- Recommendations based on disease staging or phenotyping should be considered in the management of individual patients.

TABLE 1 Selected Recommendations on Management of Aortic Stenosis

Recommendation	American	European
Symptoms and:		
High-gradient	I-A	I-B
LFLG, LVEF <50% and flow reserve	I-B	I-B
LFLG, LVEF <50% and no flow reserve	I-B	IIa-C
LFLG, LVEF ≥50%	I-B	IIa-C
No symptoms and:		
LVEF <50%	I-B	I-B
LVEF <55%		IIa-B
LVEF <60%	IIb-B (3 serial imaging)	
Symptoms on exercise test	I-B	I-B
Fall in SBP on exercise test	IIa-B (10 mm Hg)	IIa-B (20 mm Hg)
Very severe AS (Vmax ≥5 m/s) and low risk	IIa-B	IIa-B
Vmax progression ≥0.3 m/s per y	IIa-B (high gradient)	IIa-B (severe calcification and low risk)
3-fold increase in BNP/N-terminal proBNP	IIa-B (low risk)	IIa-B (only BNP)
Severe AS undergoing other cardiac surgery	I-C	I-B
Moderate AS undergoing other cardiac surgery	IIb-C	IIa-C
Percutaneous BAV in severe AS		
In bridge to SAVR/TAVR	IIb-C	IIb-C
Before noncardiac surgery		IIb-C
Severe comorbidities with survival <1 y		III-C

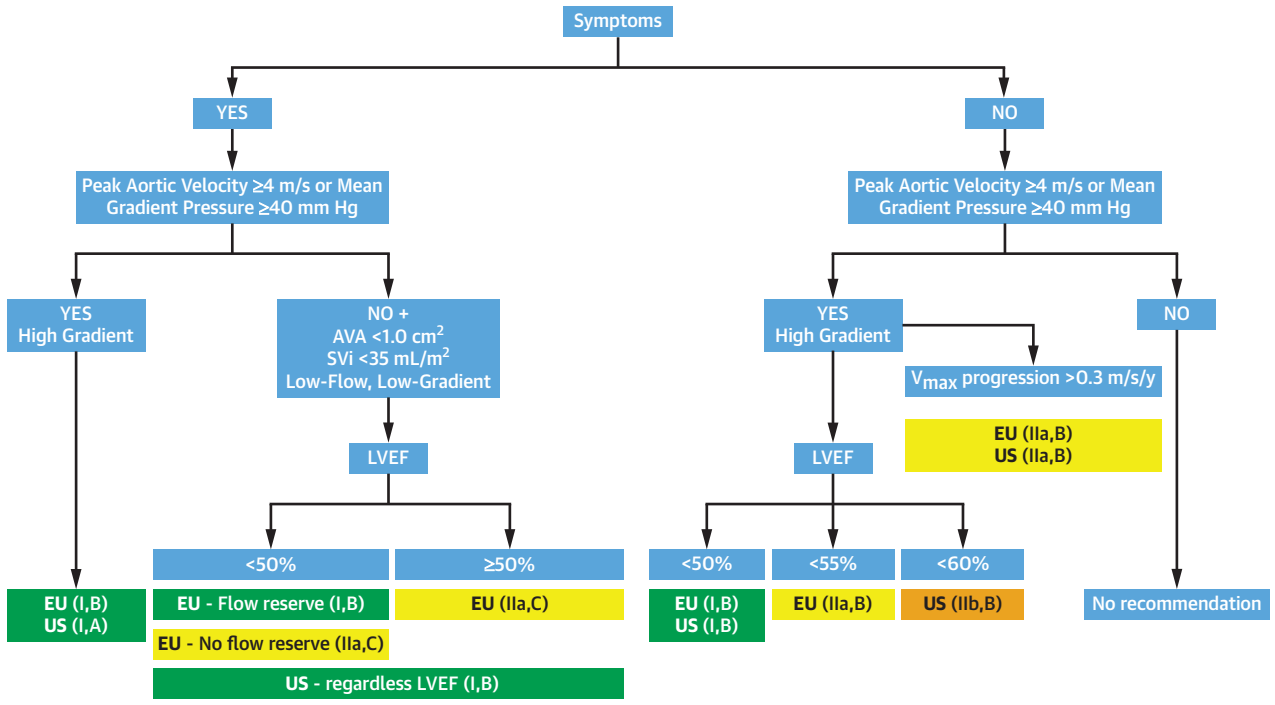
AS = aortic stenosis; BAV = balloon aortic valvuloplasty; BNP = brain natriuretic peptide; LFLG = low flow low gradient; LVEF = left ventricular ejection fraction; SAVR = surgical aortic valve replacement; SBP = systolic blood pressure; TAVR = transcatheter aortic valve replacement.

AORTIC STENOSIS

CONSISTENCIES BETWEEN GUIDELINES. Overall, the definition of severe aortic stenosis (AS) is consistent among the guidelines (Table 1). There is agreement that besides the classic high-gradient AS (peak aortic jet velocity ≥4 m/s), AS may also be severe when peak velocity or mean gradient are low (<4 m/s or <40 mm Hg). In patients with low-gradient AS presenting with reduced left ventricular ejection fraction (LVEF) ≤50% (classical low-flow low-gradient AS), the use of dobutamine stress echocardiography and/or noncontrast computed tomography (CT) aortic valve calcium scoring is recommended, and the latter is also recommended when LVEF is >50% if aortic valve area is <1.0 cm^2 and stroke volume index is reduced (<35 mL/m^2) (paradoxical low-flow low-gradient AS). According to both American and European guidelines, the severity of paradoxical low-flow low-gradient AS should be assessed using an integrative approach including echocardiographic, CT aortic valve calcium score, and clinical variables.

Furthermore, there is an ample concordance between American and European guidelines in the timing of aortic valve replacement (AVR) (Table 1). Both guidelines recommend intervention in the presence of symptoms documented by history or exercise stress test, very severe AS (peak aortic jet velocity ≥5 m/s), reduced left ventricular (LV) function, or elevated brain natriuretic peptides. In addition, American and European guidelines both recommend AVR in asymptomatic patients if undergoing other cardiac surgery when AS is severe (Class I)

FIGURE 1 **Management of Patients With Severe Aortic Stenosis**



Management of patients with severe aortic stenosis based on symptoms and echocardiography according to American (US) and European (EU) guidelines. AVA = aortic valve area; LVEF = left ventricular ejection fraction; SVi = stroke volume index.

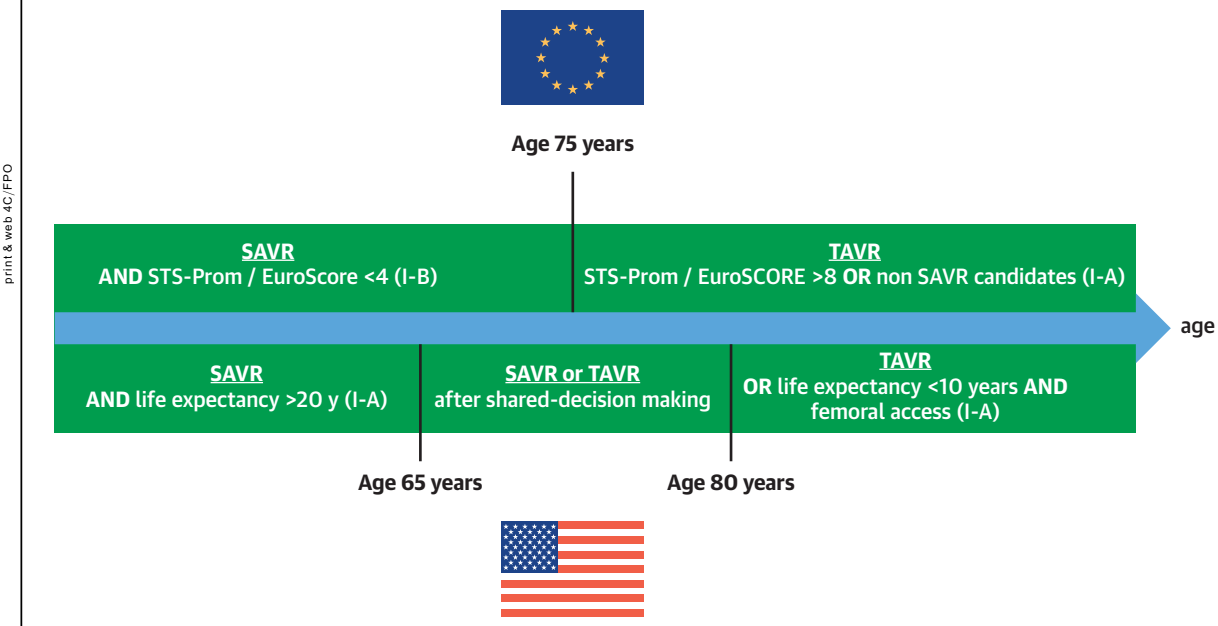
or moderate (Class IIa), or if AS is rapidly progressing defined as a progression rate exceeding 0.3 m/s/y. Finally, the American and European guidelines recommend surgery (Class IIa) if natriuretic peptides are increased by 3-fold vs age- and sex-predicted upper normal limit.

DISCREPANCIES BETWEEN GUIDELINES. Although the guidelines agree on recommending intervention in asymptomatic patients with severe AS surgery based on exercise test findings, brain natriuretic peptide (BNP) levels, and/or decline in LV function, different thresholds have been proposed (Table 1). The European guidelines recommend surgery (Class IIa) when systolic blood pressure falls by more than 20 mm Hg during exercise, whereas the American guidelines recommend AVR when it falls by more than 10 mm Hg.

The use of natriuretic peptides also differs between guidelines, as American guidelines propose the use of both BNP and N-terminal proBNP, whereas the European only recommend the use of BNP. Although both the American and European guidelines concur that LVEF <50% is a Class I indication for intervention, the novel recommendation of intervening based on "subclinical LV dysfunction" is different between guidelines (Figure 1). The European guidelines propose a Class IIa indication for intervention when LVEF is <55%, whereas the American guidelines propose this indication when LVEF is <60%.

For patients with paradoxical (preserved LVEF) low-flow, low-gradient severe AS, both guidelines recommend AVR but as Class I in the American guidelines vs Class IIa in the European guidelines (Table 1). The most notable differences are in the recommendations for transcatheter aortic valve replacement (TAVR) in patients with AS. Both American and European guidelines recommend stratifying patients into 3 groups: one suitable for TAVR, a second suitable for surgical aortic valve replacement (SAVR), and a third group in between where the choice between TAVR and SAVR should be based on shared decision-making using an individualized approach (Figure 2). However, the American guidelines consider only patients <65 years of age with life expectancy exceeding 20 years to be strict SAVR candidates, in contrast to the European guidelines,

FIGURE 2 **Mode of Intervention When Aortic Valve Replacement Is Indicated for Aortic Stenosis**



Mode of intervention for aortic stenosis according to American and European guidelines. SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

which recommend SAVR for patients <75 years of age with an STS-PROM/EuroSCORE <4 or operable patients if femoral TAVR was not possible. Candidates for TAVR should be those older than 75 years or with high-risk (STS-Prom/EuroSCORE >8) in the European guidelines, or those older than 80 years or with life expectancy <10 years in the American guidelines. Finally, the American guidelines clearly underline that the choice of prosthetic valve should be based on a shared decision-making process (Class I) and give a Class IIb indication for the treatment with renin-angiotensin-aldosterone system blockade in patients undergoing TAVR.

KNOWLEDGE GAPS AND FUTURE PERSPECTIVES. The most important knowledge gaps and future perspectives relate to the management and the recommendations for AVR in asymptomatic severe AS, as well as in moderate AS with heart failure (HF). Several randomized clinical trials are indeed ongoing to assess the timing of AVR in asymptomatic severe AS and in symptomatic moderate AS. The results of these trials may determine a further paradigm shift in the treatment of patients with AS. Additionally, the guidelines should consider the role of global LV longitudinal strain measured by speckle tracking, the presence and extent of LV myocardial fibrosis measured by cardiac magnetic resonance, and the recently proposed multiparameter cardiac damage staging to identify the asymptomatic patients with severe AS who may benefit from an early intervention.[3] The role of blood biomarkers in assessing the severity of VHD and related cardiac damage or predicting the risk of progression and the occurrence of adverse events in patients with VHD before and after AVR should be explored. Machine learning-based identification of phenotypes, based on clinical and imaging variables, is also an emerging tool that may aid in risk-stratification, optimization of the timing of intervention, and even in prediction of futility of AVR.[4,5] Finally, more data and recommendations for the selection of TAVR vs SAVR in patients with bicuspid aortic valve disease are needed.

CHRONIC AORTIC REGURGITATION

CONSISTENCIES BETWEEN GUIDELINES. There is good agreement between guidelines in recommending surgery for symptomatic patients with severe aortic regurgitation (AR) and for asymptomatic patients with severe AR with signs of LV overload, or in patients requiring cardiac surgery for another condition (Table 2). There is an agreement for left ventricular end-systolic diameter (LVESD) >50 mm in both guidelines, and for indexed LVESD of >25 mm/m^2 in American and European guidelines. In addition, the

European guidelines suggest that surgery may be considered in asymptomatic patients with an indexed LVESD >20 mm/m^2 if surgery is at low risk.

DISCREPANCIES BETWEEN GUIDELINES. Minor differences exist in the recommendations for the management of asymptomatic patients with severe AR (Table 2). Although both guidelines agree that patients with LVEF <50% should be referred for surgery (Class I), the American guidelines extend this indication to patients with LVEF between 50% and 55%. In contrast, the European guidelines propose that surgery only may be considered in this subgroup (Class IIb).

For patients with moderate AR undergoing cardiac surgery for another reason, American guidelines recommend surgery (Class IIa), whereas European guidelines recommend heart team discussion (Table 2). American guidelines recommend surgery (Class IIb) for asymptomatic patients with severe AR who demonstrate a progressive decline in LVEF in 3 serial echocardiograms studies. This is not considered in European guidelines.

Finally, the European guidelines discuss whether aortic valve repair should be offered, limiting the indication to selected patients in experienced centers. This aspect is not addressed in the American guidelines. American guidelines do not recommend (Class III) TAVR in patients with isolated AR who are at low surgical risk.

KNOWLEDGE GAPS AND FUTURE PERSPECTIVES. The role of advanced echocardiographic modalities (3-dimensional, speckle tracking, and cardiac magnetic resonance)[6] for assessing myocardial remodeling and for risk stratification of patients with AR is poorly described in the guidelines as well as the place of exercise testing. The role and indication of surgical aortic valve repair or TAVR vs surgical aortic valve replacement needs to be better documented. There is also a growing momentum toward assessment of LV volumes in this VHD, especially using cardiac magnetic resonance imaging. The latter is also of interest for accurately assessing regurgitant volume, regurgitant fraction, as well as interstitial myocardial content and fibrosis, and should therefore be increasingly used in the future for the evaluation of patients with AR, which combines an increase in preload and afterload.

MITRAL STENOSIS

CONSISTENCIES BETWEEN GUIDELINES. Both guidelines agree in recommending percutaneous mitral commissurotomy (PMC) in patients with symptomatic severe mitral stenosis (MS) and favorable anatomy with high level of evidence. Additionally, the guidelines suggest considering PMC in asymptomatic patients with favorable anatomy and elevated pulmonary pressures (systolic pulmonary artery pressure >50 mm Hg at rest) (Class IIa). Likewise, there is consensus with strong evidence to perform mitral valve surgery in severe MS if PMC is not suitable for anatomical reasons. Regarding medical therapy, the American and European guidelines recommend a beta-blocker or Ivabradine to achieve reduced heart rate in patients with sinus rhythm.

TABLE 2 Selected Recommendations on Management of Aortic Regurgitation

Recommendation	American	European
Symptoms	I-B	I-B
No symptoms and		
LVEF ≤55%	I-B	IIb-C
LVEF ≤50%	I-B	I-B
Progressive decline in LVEF to 55%-60% on 3 serial studies	IIb-B	
LVESD >50 mm or >25 mm/m^2	IIa-B	I-B
LVESD >20 mm/m^2 if low risk		IIb-B
Severe AR undergoing other cardiac surgery	I-C	I-C
Moderate AR undergoing other cardiac surgery	IIa-C	
Aortic valve repair in selected patients at experienced centers when durable results are expected		IIb-C

AR = aortic regurgitation; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter.

DISCREPANCIES BETWEEN GUIDELINES. Although European guidelines emphasize the need for regular follow-up, only the American guidelines recommend PMC being performed in a comprehensive valve center depending on functional status with Class IIa/IIb recommendation.

Only the American guidelines recommend PMC being performed in a comprehensive valve center. Furthermore, minor differences exist in the assessment of MS severity. Only American guidelines highlight invasive hemodynamic assessment during cardiac catheterization if there is discrepancy between the symptoms and the severity of MS assessed by transthoracic echocardiography.

KNOWLEDGE GAPS AND FUTURE PERSPECTIVES. There is a gap in the guidelines regarding the applicability of direct oral anticoagulants in patients with severe mitral stenosis. The recent results of the INVICTUS VKA (INVestIgation of rheumatiC AF Treatment Using Vitamin K Antagonists, Rivaroxaban or Aspirin Studies, Non-Inferiority) trial, showing that treatment with vitamin K antagonists (VKAs) resulted in a lower rate of composite cardiovascular events or death compared with treatment with rivaroxaban, may help fill this gap.[7] Finally, there is a gap in both guidelines regarding MS related to mitral annulus

TABLE 3 Selected Recommendations on Management of Chronic Mitral Regurgitation

Recommendation	American	European
Primary MR		
Symptoms	I-B	I-B
No symptoms and		
LVEF ≤60% and/or LVESD ≥40 mm	I-B	I-B
AF secondary to MR		IIa-B
SPAP at rest >50 mm Hg		IIa-B
LA dilatation (LAVi ≥60 mL/m^2 or LAD ≥55 mm)		IIa-B
High likelihood of durable repair (>95%) and expected mortality rate <1%	IIa-B	
MV surgery if progressive increase in LV size or decrease in EF on >3 serial imaging studies	IIb-B	
TEER if favorable MV anatomy, severe symptoms (NYHA functional class III or IV), high or prohibitive surgical risk, and no futility	IIa-B	IIb-B
Secondary MR		
GDMT and management by a collaborative heart team first	I-C	I-B
MV surgery in patient undergoing CABG		
In patient undergoing CABG	IIa-B	I-B (and other cardiac surgery)
For ventricular SMR if symptoms despite GDMT	IIb-B	IIb-C (and appropriate for surgery)
For atrial SMR and preserved LVEF if symptoms despite GDMT	IIb-B	
TEER		
Symptoms despite optimal GDMT and not eligible for surgery and criteria suggesting an increased chance of responding to TEER		IIa-B
Symptoms despite optimal GDMT and LVEF 20%-50%, LVESD ≤70 mm, SPAP ≤70 mm Hg and appropriate anatomy	IIa-B	
TEER or other transcatheter therapy in high-risk symptomatic patients not eligible for surgery and no criteria suggesting an increased chance of responding to TEER, after careful evaluation for ventricular assist device or heart transplant.		IIb-C

AF = atrial fibrillation; CABG = coronary artery bypass graft; EF = ejection fraction; GDMT = guideline-directed medical therapy; LA = left atrium; LAD = left atrium diameter; LAVi = left atrial volume index; LV = left ventricle; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; MV = mitral valve; SMR = secondary mitral regurgitation; SPAP = systolic pulmonary artery pressure; TEER = transcatheter edge-to-edge-repair.

calcification, and future studies should explore the utility of multimodality imaging in assessing MS etiology and severity, stratifying the risk as well as considering new therapeutic options, particularly percutaneous, for this frail population with high surgical risk.

CHRONIC MITRAL REGURGITATION

CONSISTENCIES BETWEEN GUIDELINES. Primary mitral regurgitation. The American and European guidelines consider the same threshold to define LV dysfunction (LVEF <60% and/or LVESD >40 mm) in patients with primary mitral regurgitation (PMR). There is substantial agreement between guidelines for mitral valve (MV) surgery in symptomatic patients with severe PMR irrespective of LV function (Class I recommendation in the American and European guidelines). In asymptomatic patients with LV dysfunction, defined as described previously, both guidelines recommend surgery (Class I recommendation in the American and European guidelines) (Table 3). The preference for MV repair over MV replacement is clearly stated in both guidelines. Although with the same level of evidence, but with different class of recommendation, the European and American guidelines indicate that transcatheter edge-to-edge repair (TEER) may be considered as an alternative to MV surgery only in patients with symptomatic severe PMR and LV dysfunction and considered to be at high/prohibitive risk for surgery by the heart team (Table 3).

Secondary mitral regurgitation. Both guidelines agree that the best therapy for chronic secondary mitral regurgitation (SMR) is not clear because mitral regurgitation (MR) is only 1 component of the disease, because restoration of MV competence is not curative, and because of limited evidence that MV interventions improve survival in patients with severe SMR (Table 4). All therapeutic decisions should be taken by the heart team. MV surgery/intervention is recommended only in patients with severe SMR who remain symptomatic despite guideline-directed medical therapy (GDMT) (including cardiac resynchronization therapy, if indicated, Class I-C in American guidelines and Class I-B in European guidelines).

TABLE 4 Selected Recommendations on Management of TR

Recommendation	American	European
TV surgery in patients undergoing left-sided valve surgery		
Severe TR	I-B	I-B (secondary TR) or I-C (primary TR)
Moderate primary TR		IIa-C
Secondary TR and TA >40 mm or prior signs of right-sided HF	IIa-B (progressive TR)	IIa-B (mild or moderate TR)
TV surgery in severe primary TR		
No or mild symptoms and RV dilatation (appropriate for surgery)		IIa-C
Symptoms and signs of right-sided HF	IIa-B	I-C (without severe RV dysfunction)
Progressive RV dilation or systolic dysfunction	IIb-C	
TV surgery in severe secondary TR		
Symptoms and RV dilatation and no severe RV or LV dysfunction or severe PH	IIb-B	IIa-C
Symptoms and signs of right-sided HF and no PH or left-sided disease or response to medical therapy	IIa-B	
Transcatheter treatment of symptomatic secondary severe TR in inoperable patients at a heart valve center with dedicated expertise		IIb-C

HF = heart failure; LV = left ventricle; PH = pulmonary hypertension; RV = right ventricle; TA = tricuspid annulus; TR = tricuspid regurgitation; TV = tricuspid valve.

The 2 guidelines propose that MV surgery may be considered in patients with severe SMR regardless of the level of LV dysfunction or mechanism of SMR (ie, ventricular or annular dilation) if still symptomatic after GDMT and at low risk for surgery (Class IIb), whereas TEER should be considered in severe SMR patients with appropriate anatomy and fulfilling COAPT criteria who are still symptomatic after GDMT (Class IIa-b in the American and European guidelines) (Table 4).

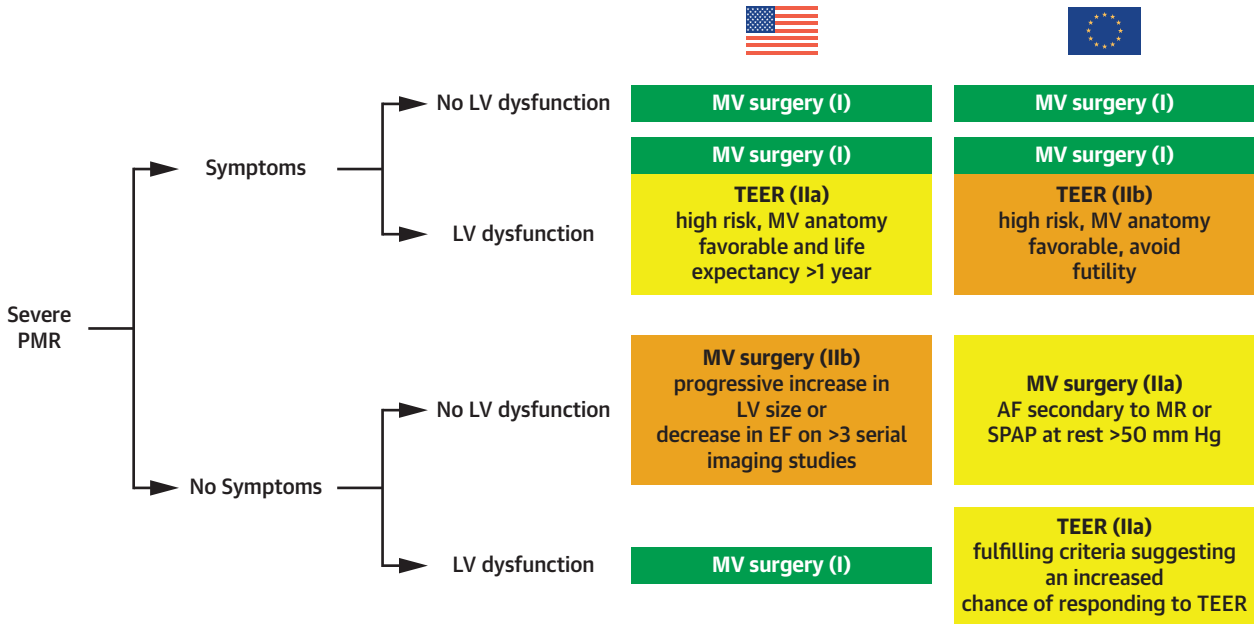
DISCREPANCIES BETWEEN GUIDELINES. Primary MR. Distinct from the European guidelines, the American guidelines provide specific recommendation for the type of MV surgery: MV repair is recommended in preference to MV replacement in degenerative disease if a successful and durable repair is possible (Class I-B), whereas MV replacement should not be considered unless MV repair has been primarily attempted (Class III-B) (Table 3). A successful and durable MV repair is defined only in the American guidelines. MV repair may also be considered in rheumatic etiology when the procedure is performed by an experienced surgical team in a valve center (Class IIb-B).

Although both American and European guidelines agree that symptoms do not always coincide with LV dysfunction, other associated triggers for intervention or imaging follow-up are necessary to plan surgery before severe LV dysfunction occurrence (Table 3). For asymptomatic patients with severe primary MR without LV dysfunction, the 2 guidelines have different thresholds for surgery, with slightly different classes of recommendations (Figure 3). For the American guidelines, mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1%, when it can be performed at a primary or comprehensive valve center (Class IIa-B), or in case of progressive increase in LV size or decrease in LVEF on >3 serial follow-up studies (Class IIb-C), whereas for the European guidelines, watchful waiting is a safe strategy except in the presence of atrial fibrillation or systolic pulmonary arterial pressure >50 mm Hg at rest (Class IIa-B).

Secondary MR. In patients with severe symptomatic SMR, MV surgery is recommended, albeit at different classes, in the American and the European guidelines (Class IIa-B in the American guidelines and Class I/B in the European guidelines) at the time of CABG for the treatment of myocardial ischemia (Table 3, Figure 4). For patients with coronary artery disease and LV dysfunction, the American guidelines recommend chordal-sparing MV replacement over MV repair (Class IIb-B). Only the European guidelines mention that MV repair restores valve competency, improves symptoms, and results in reverse LV remodeling while MV replacement avoids recurrence of MR, without expressing any specific recommendation over the preference between repair and replacement.

Regarding TEER, there are several differences between the guidelines (Table 3). The European guidelines recommend TEER only in patients who are not eligible/appropriate for MV surgery (either for isolated SMR [Class IIa-B] or when TEER is planned in addition of percutaneous coronary intervention or

FIGURE 3 Management of Patients With Severe PMR



Management of patients with severe primary mitral regurgitation (PMR) according to the existence of symptoms and/or left ventricular (LV) dysfunction. EF = ejection fraction; MV = mitral valve; SPAP = systolic pulmonary artery pressure; TEER = transcatheter edge-to-edge repair.

TAVR [Class IIa-C]), whereas the American guidelines recommend TEER exclusively on the basis of an appropriate anatomy and the COAPT criteria, not taking into consideration eligibility for surgery. Furthermore, the European guidelines consider TEER or other transcatheter mitral valve intervention as part of the heart team decision process for advanced HF therapies, even in patients not fulfilling the COAPT criteria (Class IIb-C).

Finally, the associated risk of intervention and futility are precisely defined in the American guidelines, while no grading is provided by the European guidelines (Table 4). The latter recommends consideration of surgery based on multiple criteria, including LVEF (<15%: any intervention is futile), predicted surgical risk, amount of myocardial viability, coronary anatomy/target vessels, type of concomitant procedure needed, TEER eligibility, likelihood of durable surgical repair, need of surgical mitral replacement, and local expertise.

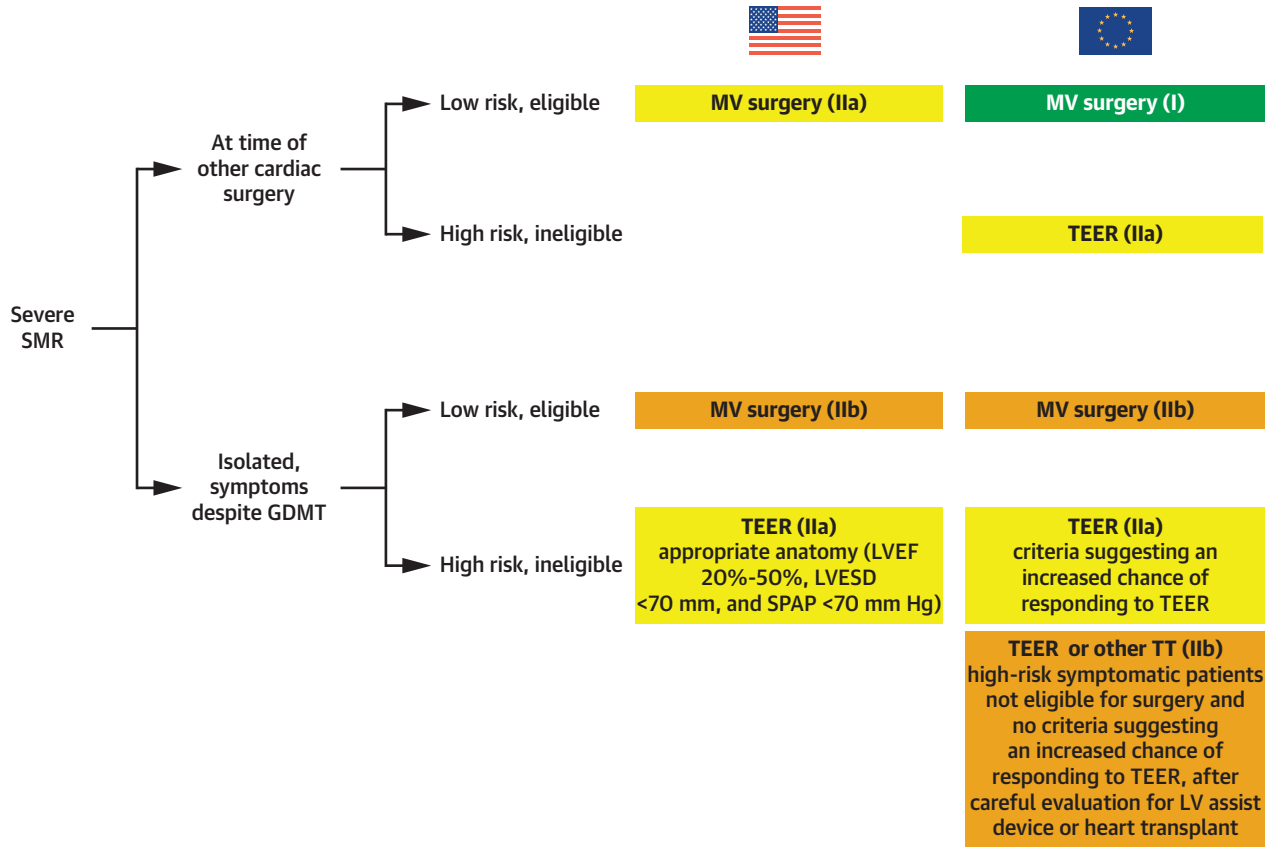
KNOWLEDGE GAPS AND FUTURE PERSPECTIVES. The role of advanced echocardiographic modalities (3-dimensional, speckle tracking, and cardiac magnetic resonance) in the management of both primary and secondary MR is poorly described, and therapeutic decisions are still based on planar measurements (LV dimensions rather than volumes) or estimation of pulmonary pressure. One major limitation in all of the guidelines is the absence of any data about management of severe MR in the setting of acute HF and what is the optimal timing of intervention for severe MR after an episode of decompensation. There are not sufficient data to guide the procedure related risk, for both MV surgery and TEER, and simply adapting the model from AS in a population with MR may lead to errors.

For asymptomatic patients with severe PMR without LV dysfunction, the timing of intervention remains unclear and debatable. Also, the timing and indication for surgery in patients with moderate to severe PMR who are candidates for other major cardiac surgery are not uniformly described.

Although the quantitative criteria for defining severe MR are the same for PMR and SMR in the guidelines, lower thresholds should be explored to identify patients with clinically significant SMR who may require intervention.

The potential impact of TEER on LV reverse remodeling and long-term outcomes should be better documented. The role of newer transcatheter treatment options, such as transcatheter mitral valve replacement, are not considered in the current

FIGURE 4 Management of Patients With Severe SMR



Management of patients with severe secondary regurgitation according to the need for other cardiac surgery, the existence of symptoms and the surgical risk. GDMT = guideline-directed medical therapy; SMR = severe secondary regurgitation; TT = transcatheter therapy; other abbreviations as in Figure 3.

guidelines. Last, disease staging and phenotype clustering approached for PMR and SMR are novel approaches that may further refine clinical decision-making.[8,9]

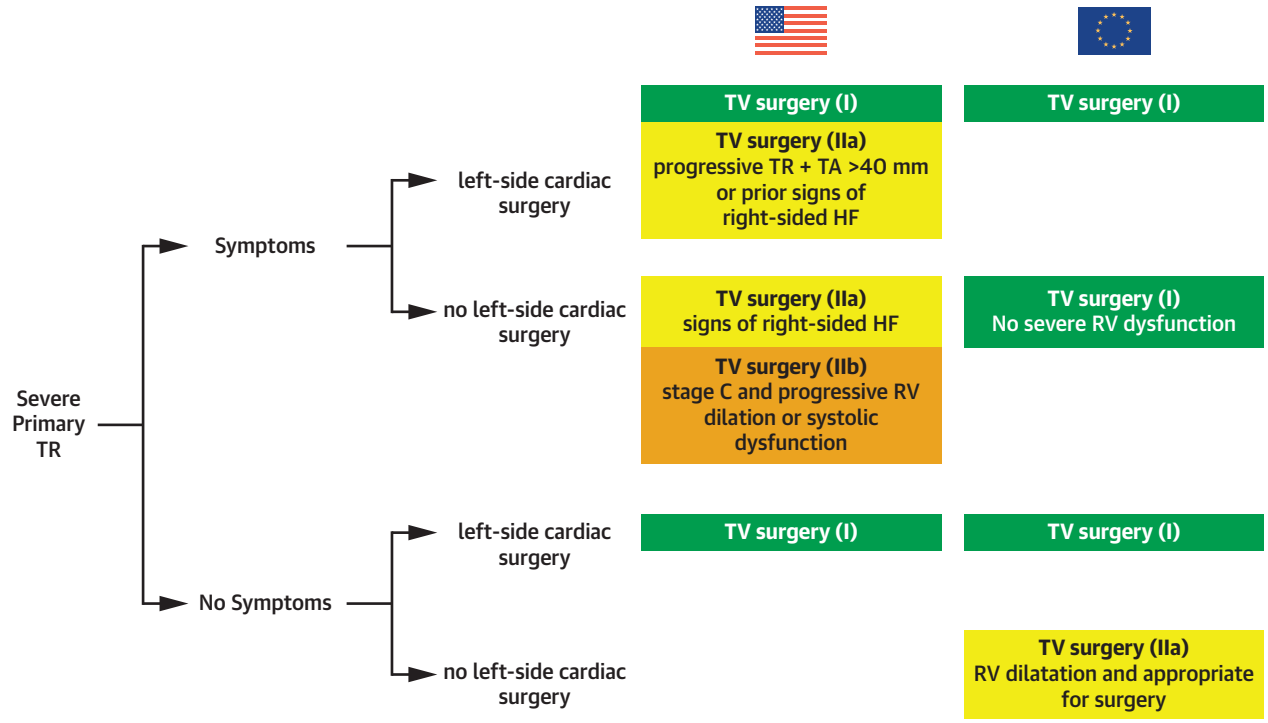
Further studies should also explore the characteristics, clinical significance, and potential therapeutic options of atrial SMR.

TRICUSPID REGURGITATION

CONSISTENCIES BETWEEN GUIDELINES. In patients with significant tricuspid regurgitation (TR), appropriate timing for intervention is important to prevent right ventricular (RV) dilatation and dysfunction with subsequent worsening and increased mortality.[10,11] Although with different levels of evidence (B-NR for both primary and secondary TR [ACC/AHA], C for primary TR and B for secondary TR [ESC/EACTS]), both the American and European guidelines recommend surgery in patients with severe TR undergoing left-sided valve surgery (Class I) (Figures 5 and 6). American as well as European guidelines recommend (B-NR for ACC/AHA guidelines; and Class IIa, Level of Evidence: B for ESC/EACTS guidelines) tricuspid valve (TV) surgery even in patients with only mild-to-moderate secondary TR undergoing left-sided valve surgery in the presence of tricuspid annular dilatation or prior signs and symptoms of right-sided HF (Table 4).

DISCREPANCIES BETWEEN GUIDELINES. With regard to assessment of severity of TR, the European guidelines include a central jet area of TR that is >50% of right atrium, presence of a flail leaflet or abnormal TV morphology, a very large central jet or eccentric wall impinging jet, PISA radius >9 mm, and an E-wave dominant (≥1 m/s) tricuspid inflow as additional markers of severe TR (Table 4). The

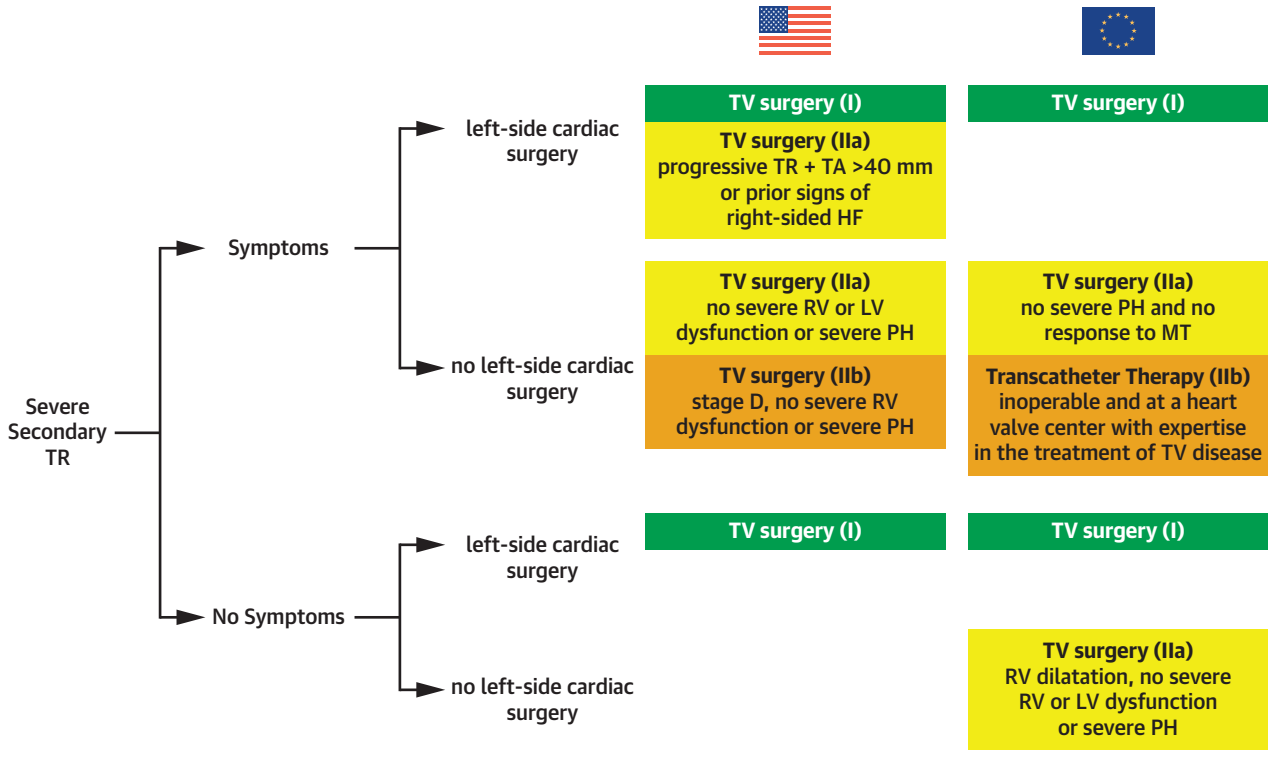
FIGURE 5 Management of Patients With Severe Primary TR



Management of patients with severe primary tricuspid regurgitation (TR) according to the need for other left-side cardiac surgery and the existence of symptoms. HF = heart failure; RV = right ventricular; TA = tricuspid annulus; TV = tricuspid valve.

American guidelines do not recommend the use of these parameters in the assessment of the degree of TR. In the European guidelines, the etiology of TV disease is specified as primary or secondary. In the American guidelines, such differentiation is not emphasized; instead, they propose staging TR as asymptomatic, progressive, and symptomatic disease. The class of recommendation regarding surgery in patients with isolated severe symptomatic primary TR is lower in the American guidelines compared with the European guidelines (Class IIa vs Class I). Likewise, in asymptomatic patients with severe primary TR and progressive RV dilatation or systolic dysfunction, isolated TV surgery is recommended by both the European and the American guidelines but with different Class of Recommendation (Class IIa vs Class IIb, respectively). The American guidelines weakly recommend (Class IIb) isolated TV surgery in patients with symptomatic severe TR who have already undergone left-sided valve surgery in the absence of severe pulmonary hypertension or severe RV systolic dysfunction. On the other hand, according to European guidelines, TV surgery should be considered (Class IIa, Level of Evidence: B) regardless of the history of left-sided valve surgery in patients with severe secondary TR who are symptomatic or have RV dilatation, in the absence of severe RV or LV dysfunction and severe pulmonary hypertension. The American guidelines specifically mention atrial functional TR in the setting of patients with permanent atrial fibrillation and recommend (Class IIa) isolated TV surgery in patients with signs and symptoms of right-sided HF refractory to medical therapy. Similarly, severe isolated secondary TR caused by annular dilation in the absence of pulmonary hypertension or left-sided disease is also a Class IIa indication for TV surgery. There is no such specific recommendation in the European guidelines (Table 4). The European guidelines recommend (Class IIb) transcatheter treatment of symptomatic secondary severe TR in anatomically eligible patients not amenable for surgery in whom improvement of quality of life or survival can be expected, especially at a heart valve center with expertise in such treatment. Noteworthy, the American guidelines do not include transcatheter therapy for TR.

FIGURE 6 Management of Patients With Severe Secondary TR



Management of patients with severe secondary TR according to the need for other left-side cardiac surgery and the existence of symptoms. LV = left ventricular; other abbreviations as in Figure 5.

KNOWLEDGE GAPS AND FUTURE PERSPECTIVES. Several uncertainties and controversies persist in the American and European guidelines concerning grading severity of TR and the optimal management of TR.[12,13] The optimal modalities and timing for TV surgery have yet to be fully clarified because severe RV dysfunction and/or dilatation may result in futile intervention. However, no specific values of echocardiographic parameters indicating severe impairment of RV function and dimension have been established to date, thus leading to medical therapy or transcatheter interventions as preferable treatments. Furthermore, optimal medical treatment has not yet been uniquely defined for right-sided HF. Although early studies and registries have demonstrated feasibility, safety, and efficacy of transcatheter tricuspid valve intervention with multiple devices in patients with symptomatic secondary severe TR ineligible for surgery, data from randomized controlled trials are still lacking.[14-16] In addition, the characteristics of the patient who could best benefit from these procedures have not yet been clarified. There is also a need to investigate the usefulness of cardiac magnetic resonance imaging in assessing TR severity, defining RV dysfunction, and supporting a decision-making process for the selection of the most suitable therapy: medical, surgical, or transcatheter intervention. These persistent knowledge gaps make transcatheter tricuspid valve interventions still poorly recommended in European guidelines and not present in American guidelines. Like AS and MR, various proposals for risk scores, staging, and machine learning-based phenogrouping of patients with TR are emerging, and these may yet improve the evidence-base for timely intervention for chronic TR.[17-20]

PROSTHETIC VALVES

The introduction of valve replacement surgery in the early 1960s has radically improved the outcome of patients with valvular heart disease.[21] Throughout all of these years, prosthetic heart valves underwent remarkable improvements in their design and

CENTRAL ILLUSTRATION **Comparison Between Guidelines in the Management of Valvular Heart Disease**

Aortic Stenosis		Aortic Regurgitation		Mitral Stenosis	
AVR if symptoms and high gradient (I) – AVR if asymptomatic and LV dysfunction or other cardiac surgery (I) – AVR if asymptomatic and Vmax >5 m/s or >0.3 m/s/y, exercise intolerance (IIa)	AVR in AG (I) vs AVR in EG (IIa) for preserved EF low-flow, low-gradient severe AS – TAVR considered vs SAVR in patient >65 y of age (AG) vs >75 y of age (EG)	AVR if symptoms (I) – AVR if asymptomatic and LV dysfunction or other cardiac surgery (I)	LV dysfunction = LVESD >50 mm or LVESD >25 mm/m^2 or LVEF ≤50% in EG vs LVEF ≤55% in AG – – AVR if moderate AR and other cardiac surgery (IIa) in AG vs no recommendation in EG	PMC if symptoms and favorable anatomy (I) – Surgery if PMC is not suitable (I)	PMC at a Comprehensive Valve Center (I) in AG vs no recommendation in EG

Primary Mitral Regurgitation		Secondary Mitral Regurgitation		Tricuspid Regurgitation	
MV surgery if symptoms (I) – MV repair if asymptomatic and LV dysfunction (I) – Repair > Replacement	TEER for high-risk patients IIa for AG vs IIb for EG – MV surgery if asymptomatic and high probability of successful and durable repair in AG (IIa) vs watchful waiting except if AF or SPAP >50 mm Hg in EG (IIa)	MV intervention if symptoms after GDMT (I) – MV surgery if symptoms and low-risk after GDMT (IIb)	MV surgery if symptoms at time of CABG I for EG vs IIa for AG – TEER if symptoms and ineligible for surgery in EG (IIa) vs no surgical consideration (only anatomy and COAPT criteria) in AG (IIb)	TV surgery in TR undergoing left-sided valve surgery if severe (I) or if mild-to-moderate and TA dilatation or prior signs and symptoms of right-sided HF	TV surgery if symptoms and severe primary TR (I in EG vs IIa in AG) – TTVI if symptoms, anatomically eligible and not amenable for surgery in EG (IIb) vs no recommendation in AG

Consistencies between guidelines	Discrepancies between guidelines

Coisne A, et al. J Am Coll Cardiol. 2023;82(8):721–734.

Consistencies and discrepancies between American and European guidelines. AG = American guidelines; AR = aortic regurgitation; AS = aortic stenosis; AVR = aortic valve replacement; CABG = coronary artery bypass graft; EG = European guidelines; GDMT = guideline-directed medical therapy; HF = heart failure; LV = left ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; MR = mitral regurgitation; MV = mitral valve; PMC = percutaneous mitral commissurotomy; SPAP = systolic pulmonary artery pressure; TA = tricuspid annulus; TAVR = transcatheter aortic valve replacement; TEER = transcatheter edge-to-edge repair; TR = tricuspid regurgitation; TTVI = transcatheter tricuspid valve intervention; TV = tricuspid valve.

implantation techniques, which had positive effects in patients' outcomes. Today there is a wide range of prostheses types available, each of them with its strengths and limitations. As a consequence, there are many factors that play a role in valve selection, including the patient's life expectancy, lifestyle, and environmental factors; bleeding and thromboembolic risks related to anticoagulation; potential for surgical or transcatheter reintervention; and patient preference. Both the last European and American guidelines for the management of VHD incorporated specific paragraphs[1,2] that help physicians to handle prosthetic valve-related issues.

CONSISTENCIES BETWEEN EUROPEAN AND AMERICAN GUIDELINES. There are many consistencies between the 2 documents, mainly in their fundamentals. First, both guidelines recommend that the choice of prosthetic valve should be based on a shared decision-making process that accounts for the patient's preferences and includes discussion of the indications for and risks of anticoagulant therapy (Class I-C) (Supplemental Figure 1). Second, the patient's age and life expectancy, the presence of risk factors associated with accelerated valve deterioration, and the type of diseased valve (mitral vs aortic) play an important role in choosing the type of prosthesis (mechanical vs biological). Third, both guidelines indicate the importance that all patients with prosthetic valves require lifelong follow-up to detect deterioration in prosthetic function. Finally, European and American guidelines devoted large space to the management of prosthetic valve degeneration, providing comprehensive flow algorithms for its recognition, characterization, and treatment.

DISCREPANCIES BETWEEN EUROPEAN AND AMERICAN GUIDELINES. Minor differences exist between European and the American guidelines. Different cutoffs for mechanical vs biological prostheses are

present in the 2 documents: On the one hand, European guidelines recommend that a mechanical prosthesis should be considered in patients aged <60 years for prostheses in the aortic position and aged <65 years for prostheses in the mitral position (Class IIa-B); on the other hand, the American guidelines cutoff for mechanical prosthesis is 65 years for both aortic and mitral valves (Class IIa-B). In addition, in patients <50 years of age who prefer a bioprosthetic AVR and have appropriate anatomy, the American guidelines consider the replacement of the aortic valve by a pulmonic autograft (the Ross procedure) (Class IIb-B).

Regarding antithrombotic therapy after bioprosthesis implantation in patients with no baseline indications for oral anticoagulation, the European guidelines recommend VKA for the first 3 months in those who had a bioprosthesis implanted in the mitral or tricuspid position (Class IIa-B), VKA or single antiplatelet therapy (SAPT) for the first 3 months in those who had a bioprosthesis implanted in the aortic position (Class IIa-B), and SAPT lifelong after TAVR (Class I-A). The American guidelines do not differentiate between aortic or mitral/tricuspid bioprostheses and recommend VKA for the first 3 to 6 months after surgical bioprosthesis implantation (Class IIa-B) followed by ASA 75 to 100 mg daily lifelong (Class IIa-B). In TAVR recipients, it is recommended ASA 75 to 100 mg daily lifelong (Class IIa-B), with the possibility to prescribe dual antiplatelet therapy with ASA 75 to 100 mg daily and clopidogrel 75 mg daily for 3 to 6 months, in patients at low bleeding risk (Class IIb-B).

In case of symptomatic left-sided mechanical valve thrombosis requiring urgent treatment, in the American guidelines, surgery and systemic fibrinolysis had the same class of recommendation (Class I-B), individualizing the management based on multiple clinical factors and local experience and expertise; in the European guidelines, urgent surgery is preferred (Class I-B) over fibrinolysis (Class IIa-B), which should be reserved in inoperable patients.

GAPS IN EUROPEAN VS AMERICAN GUIDELINES. Despite the detailed guidelines, gaps in evidence exist. The rapid technological advancements of both surgical and transcatheter devices do not allow for a definite recommendation regarding what type of bioprosthesis should be implanted. In fact, it is known that particular subsets of patients may benefit more from certain prosthetic valves to reduce the risk of patient-prosthesis mismatch and optimize potential valve-in-valve procedures in case of prosthetic degeneration.

CONCLUSIONS AND NEXT STEPS

The American and European guidelines are consistent for most recommendations but present some differences that are generally minor (**Central Illustration**). These differences commonly occur in areas where the evidence is insufficient or conflicting, further underlining the need for randomized controlled trials in these areas. Some of these differences and discrepancies between guidelines may translate into differences in the clinical management of patients. Another consideration for the future is to transition from (or at least include) recommendations rooted primarily on the severity of the valve lesion to staging or phenotyping the disease in a given patient. Given that the diagnostic and therapeutic modalities and evidence for intervention are evolving rapidly, an update of the guidelines every 5 or 6 years is suboptimal. Thus, it may be important to implement mechanisms that facilitate timely updates of the guidelines to maximize the benefit to patients with valvular heart disease.

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ADDRESS FOR CORRESPONDENCE: Dr Augustin Coisne, Heart and Lung Institute, Lille University Hospital, Bd Pr Jules Leclercq, 59000, Lille, France. E-mail: augustin.coisne@chu-lille.fr OR acoisne@crf.org.

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APPENDIX For a supplemental figure, please see the online version of this paper.