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2017 Focused Update for Management of Patients With Valvular Heart Disease: Summary of New Recommendations

Richard Matiasz, MD; Vera H. Rigolin, MD

Valvular heart disease (VHD) is present in ≈2.5% of the general US population, with prevalence increasing to 11.7% to 13.3% in those aged >75 years.[1] Valve-disease–related deaths account for 1.9% of total US mortality. Of these, aortic and mitral valvular disease represent 99% of identified pathology and mortality. Valve surgeries account for 120 000 procedures per year in the United States.[2] The number of surgeries continues to increase, particularly in the elderly population.[2]

In 2014, the joint American College of Cardiology and American Heart Association (ACC/AHA) guidelines for the management of VHD underwent a thorough overhaul. Important changes included identifying stages of disease and stressing the importance of the specific mechanisms of valvular disorders.[3] Since that iteration, extensive new data from recent trials have been published that have dramatically changed the way we treat valve disease. The ACC/AHA valve guidelines were updated in 2017.[4] In this review, we aim to highlight the new recommendations in the updated guidelines and discuss the evidence supporting the changes. This summary will highlight the class (strength) of each recommendation as well as the level (quality) of supporting evidence (Table 1) and how these have been modified in the 2017 updated guidelines.

Endocarditis Prophylaxis

Endocarditis remains a serious problem for patients with VHD. In the updated 2017 valve guidelines, the patients recommended to receive antibiotic prophylaxis preceding dental procedures remain in alignment with the AHA guidelines published in 2007,[5] in which prophylaxis is limited to only the highest-risk individuals (Table 2). Infective endocarditis (IE) is a rare but devastating condition, with mortality rates of 16% at 30 days and 40% at 1 year.[6,7] Antibiotic prophylaxis is reliant on the idea that certain healthcare–related procedures have increased rates of transient bacteremia, and patients with certain conditions or prosthetic materials are at increased risk of infection.

Evidence for the effectiveness of antibiotic prophylaxis is conflicting. A 2013 Cochrane study that included studies between 1946 and 2013 evaluated the effect on outcomes of antibiotic prophylaxis preceding dental procedures. This analysis was inconclusive about the effectiveness of antibiotic prophylaxis preceding dental procedures for the prevention of IE.[8] Incidence of IE has steadily increased in the United States since 2000,[9] but data are conflicting on whether this trend is related to the more-restricted recommendation from the 2007 AHA/ACC guideline revisions.[10,11] The updated 2017 ACC/AHA valve guideline recommendations still include antibiotic prophylaxis for high-risk groups, but with a weakened level of evidence (B to CL-D). However, maintenance of the best oral hygiene to minimize seeding is emphasized. Also new in the updated guidelines is the emerging evidence that patients with prosthetic material after cardiac repair, such as annuloplasty rings and chords, have higher rates of infection than those with repairs without foreign material and have higher mortality.[12,13] In addition, patients who undergo transcatheter aortic valve replacement (TAVR) are at equal or higher risk of IE compared with those that undergo surgical aortic valve replacement (SAVR).[14] As a result, such individuals are included in the list of patients eligible for antibiotic prophylaxis preceding dental procedures.

Anticoagulation for Atrial Fibrillation With VHD

In the 2014 ACC/AHA valve guidelines, the recommendation for anticoagulation for stroke prophylaxis in patients with atrial fibrillation (AF) was limited to those with mitral stenosis. Recommendations for patients with other valve disorders were not addressed. The 2017 updated guidelines now

From the Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, Chicago, IL.

Correspondence to: Vera H. Rigolin, MD, Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, 675 N. St Clair St–Suite 19-100, Chicago, IL 60611. E-mail: vrigolin@nm.org

J Am Heart Assoc. 2018;7:e007596 DOI: 10.1161/JAHA.117.007596.

Table 1. Class (Strength) of Recommendation[4]

Class I (strong)	Benefit ⋙ Risk
Class IIa (moderate)	Benefit ≫ Risk
Class IIb (weak)	Benefit > Risk
Class III (no benefit) (moderate)	Benefit = Risk
Class III (harm) (strong)	Risk > Benefit
Level (quality) of evidence	
Level A	1. High-quality evidence from more than 1 RCT 2. Meta-analysis of high-quality RCTs 3. One or more RCTs corroborated by high-quality registry studies
Level B-R	1. Moderate-quality evidence from 1 or more RCTs 2. Meta-analyses of moderate-quality RCTs
Level B-NR	1. Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
Level C-LD	1. Randomized or nonrandomized observational or registry studies with limitations of design or execution 2. Meta-analyses of such studies 3. Physiological or mechanistic studies in human subjects
Level C-EO	Consensus of expert opinion based on clinical experience

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include anticoagulation recommendations for a broader spectrum of valvular disorders (Table 3).

Data from multiple new randomized control trials (RCTs) evaluating the effectiveness of the direct oral anticoagulants (DOACs) for stroke prophylaxis in AF are now available.[15–17] These new agents have broadened the anticoagulation options for a large number of patients. However, recommendations for the use of these agents in patients with VHD were previously not addressed. Subgroup analysis of the patients with VHD in the major DOAC trials all noted a similar or increased risk for thromboembolism in this population.[15–17] Additionally, efficacy and safety of DOACs was similar to that of warfarin in this population. Notably, valvular exclusion criteria differed between trials, but significant mitral stenosis, valve disease requiring intervention, and mechanical heart valves were generally excluded.

Table 2. Recommendations for IE Prophylaxis[4]

COR	LOE	Recommendation
IIa	C-LD	Prophylaxis against IE is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with the following: 1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts. 2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords. 3. Previous IE. 4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of, or adjacent to the site of, a prosthetic patch or prosthetic device. 5. Cardiac transplant with valve regurgitation attributed to a structurally abnormal valve.

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The CHA_2DS_2-VASc score was also incorporated in the 2017 updated guidelines, in alignment with modern AF management.[18] A retrospective cohort analysis of 73 538 patients assessed risk factors associated with thromboembolism and found that the use of CHA_2DS_2-VASc improved identification of low- and high-risk populations.[19] For those with a score of 2 or greater, anticoagulation is recommended. Those with bioprosthetic valves and valve repair are considered increased risk and should be anticoagulated regardless of score.

The 2017 updated guidelines recommend the use of a DOAC as an alternative to vitamin K antagonists (VKAs) in patients with AF and native aortic valve disease, tricuspid valve disease, and mitral regurgitation (MR) and a CHA_2DS_2-VASc score of 2 or greater (Class IIa, C-LD).

In rheumatic mitral stenosis with AF, the 2017 updated guidelines continue to recommend VKAs as the agents of choice,[20] given that this population has been excluded from the RCTs with DOACs. Although not recommended for therapy, a retrospective analysis of patients with rheumatic and nonrheumatic mitral stenosis showed similar rates of stroke and bleeding in DOAC and VKA patients.[21]

Aortic Stenosis

In the 2104 AHA/ACC valve guidelines, there was recognition for the role of percutaneous interventions for treatment of severe, symptomatic aortic stenosis (AS) in

Table 3. Recommendations for Anticoagulation for AF in Patients With VHD[4]

COR	LOE	Recommendations
I	B-NR	Anticoagulation with a VKA is indicated for patients with rheumatic MS and AF
I	C-LD	Anticoagulation is indicated in patients with AF and a CHA_2DS_2-VASc score of 2 or greater with native aortic valve disease, tricuspid valve disease, or MR
IIa	C-LD	It is reasonable to use a DOAC as an alternative to a VKA in patients with AF and native aortic valve disease, tricuspid valve disease, or MR and a CHA_2DS_2-VASc score of 2 or greater

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AF indicates atrial fibrillation; COR, Class of Recommendation; DOAC, direct oral anticoagulant, LD, limited data; LOE, level of evidence; MR, mitral regurgitation; MS, mitral stenosis; VHD, valvular heart disease; VKA, vitamin K antagonist.

patients who carried significant surgical risks. TAVR was recommended for patients with severe AS who met the indication for aortic valve replacement (AVR) who had prohibitive surgical risk (Class I, level of evidence [LOE] B) and as an alternative to surgery for those with high surgical risk (Class IIa, LOE B). In the updated 2017 guidelines, the recommendation for TAVR in both high- and prohibitive-risk patients is now a Class 1, LOE A (Table 4). This change is supported by multiple high-quality RCTs with multiyear follow-up that showed nonsignificant differences in mortality between the TAVR and SAVR in these groups.[22,23] Since the 2014 guidelines, 2 recent randomized trials using TAVR have also shown noninferiority end points in intermediate-risk patients. In the PARTNER (Placement of Aortic Transcatheter Valves) IIA trial, 2032 patients with symptomatic severe AS and intermediate risk (Society of Thoracic Surgeons Predicted Risk of Mortality score average, 5.8%) were randomized to TAVR or SAVR.[24] At 2 years, no significant difference was found for death (TAVR 19.3% versus SAVR 21.1%; P=0.33), neurological events (12.7% versus 11%; P=0.25), or pacemaker implantation (11.8% versus 10.3%; P=0.22). Major bleeding (17.3% versus 47%; P<0.001) and new AF (11.3% versus 27.3%; P<0.001) were both lower in TAVR when compared with SAVR.[24] In a prospective observational study, 1077 patients at intermediate surgical risk (Society of Thoracic Surgeons score 5.2) were compared with 1021 patients in the surgical arm of PARTNER 2A (Society of Thoracic Surgeons score 5.4). At 1 year, TAVR was superior to SAVR for the composite primary end point (all-cause mortality, stroke, or moderate-to-severe aortic regurgitation at 1 year). Evidence for discussion about TAVR versus SAVR options for those at intermediate surgical risk has changed the patient discussion. As a result, TAVR is now a reasonable alternative to

Table 4. Recommendations for Choice of Intervention for AS[4]

COR	LOE	Recommendations
I	C	For patients in whom TAVR or high-risk surgical AVR is being considered, a heart valve team consisting of an integrated, multidisciplinary group of healthcare professionals with expertise in VHD, cardiac imaging, interventional cardiology, cardiac anesthesia, and cardiac surgery should collaborate to provide optimal patient care.
I	B-NR	Surgical AVR is recommended for symptomatic patients with severe AS (Stage D) and asymptomatic patients with severe AS (Stage C) who meet an indication for AVR when surgical risk is low or intermediate.
I	A	Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences.
I	A	TAVR is recommended for symptomatic patients with severe AS (Stage D) and a prohibitive risk for surgical AVR who have a predicted post-TAVR survival greater than 12 months.
IIa	B-R	TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences.
IIb	C	Percutaneous aortic balloon dilation may be considered as a bridge to surgical AVR or TAVR for symptomatic patients with severe AS.
III: no benefit	B	TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AS indicates aortic stenosis; AVR, aortic valve replacement; COR, class of recommendation; LD, limited data; LOE, level of evidence, NR, nonrandomized; R, randomized; TAVR, transcatheter aortic valve replacement; VHD, valvular heart disease.

SAVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences (Class II1, LOE B-R).

Studies evaluating TAVR in the low-risk population are currently ongoing.[25,26] There were insufficient data at the time of publication to include this population in the 2017 updates guidelines.

Of note, bicuspid, unicuspid, and noncalcified valves continue to be excluded from general recommendations for TAVR because they have been excluded from earlier trials, though there is ongoing interest in examining the role for percutaneous intervention.[27,28]

Mitral Regurgitation

The 2014 AHA/ACC valve guidelines stressed the importance of identifying the mechanism of MR given that management and outcomes differ between chronic primary and secondary MR (Figures 1 and 2). Additionally, in recognition of the increased risk of adverse outcomes with smaller effective regurgitant orifice[29] in secondary MR, the 2014 guidelines defined severe MR using a lower quantification threshold for secondary MR. This led to a great deal of confusion in the imaging community in how to precisely grade MR. As a result, in the updated 2017 guidelines, quantification of MR severity was modified so that both primary and secondary MR are graded similarly. Specifically, for both primary and secondary MR, severe MR is defined as the effective regurgitant orifice ≥0.4 cm^2 and regurgitant volume to ≥60 mL. However, careful recognition of the adverse outcomes observed with lower effective regurgitant orifice in secondary MR remains important.[30] Focused measurement of MR is suggested for accurate diagnosis and staging.[31,32] The unified grading scheme is in alignment with the recent quantification of valvular regurgitation guidelines from the American Society of Echocardiography.[31]

Primary MR

In the updated 2017 valve guidelines, the majority of the recommendations for surgical or percutaneous intervention for patients with chronic, severe primary MR remain similar (Table 5). The exception is the new recommendation that mitral valve (MV) surgery is reasonable for asymptomatic patients (stage C1) and preserved left ventricular (LV) size and function (LV ejection fraction >60% and LV end systolic dimension <40 mm) with a progressive increase in LV size or decrease in LV ejection fraction on serial imaging studies (Class IIa, LOE C-LD). This change is attributed to the realization that patients with severe MR who reach an ejection fraction ≤60% or LV end systolic dimension >40 mm have already developed LV systolic dysfunction. Watchful waiting has increasing come under scrutiny.[33] The increased volume load associated with MR can lead to a vicious cycle of LV dilation and deformation of the mitral apparatus, and microscopic fibrosis. A number of studies questioned the idea of waiting for typical surgical triggers.[34] Prospective analysis of 840 degenerative MV repair patients found that survival was near normal postoperative except in those with LV systolic dysfunction or New York Heart Association (NYHA) class IV symptoms.[35] A retrospective analysis of 4253 patients with

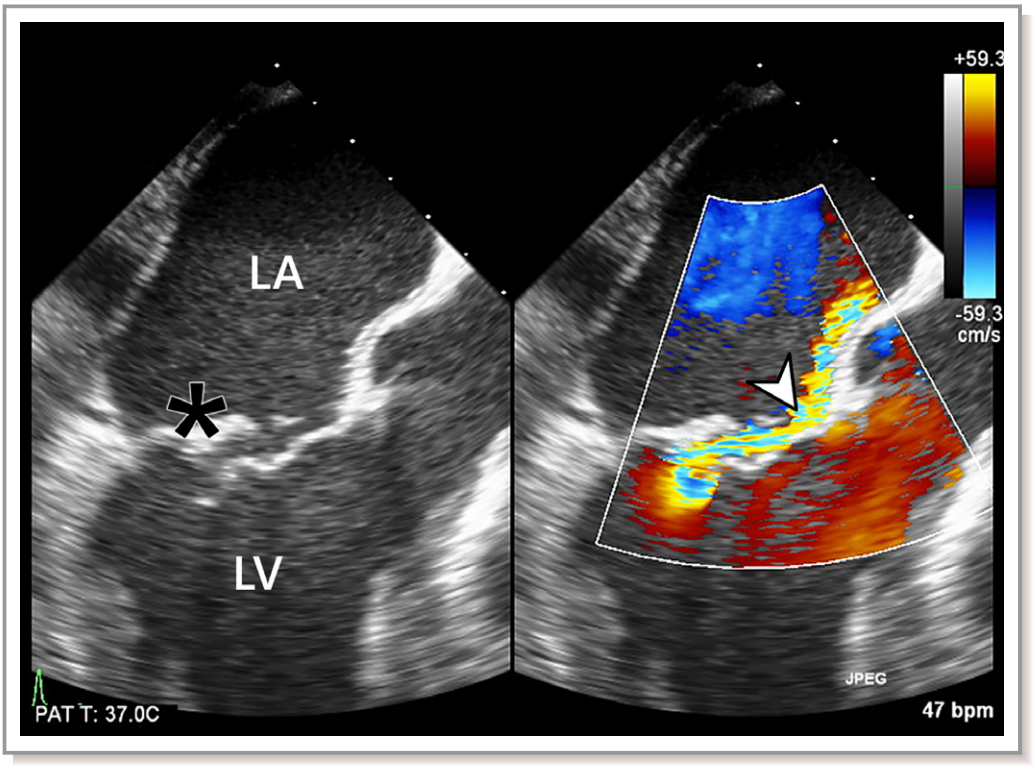

Figure 1. Echocardiographic image of a patient with primary, myxomatous mitral valve disease. Note the large jet of mitral regurgitation (arrowhead) attributed to a flail leaflet (asterisk). LA indicates left atrium; LV, left ventricle.

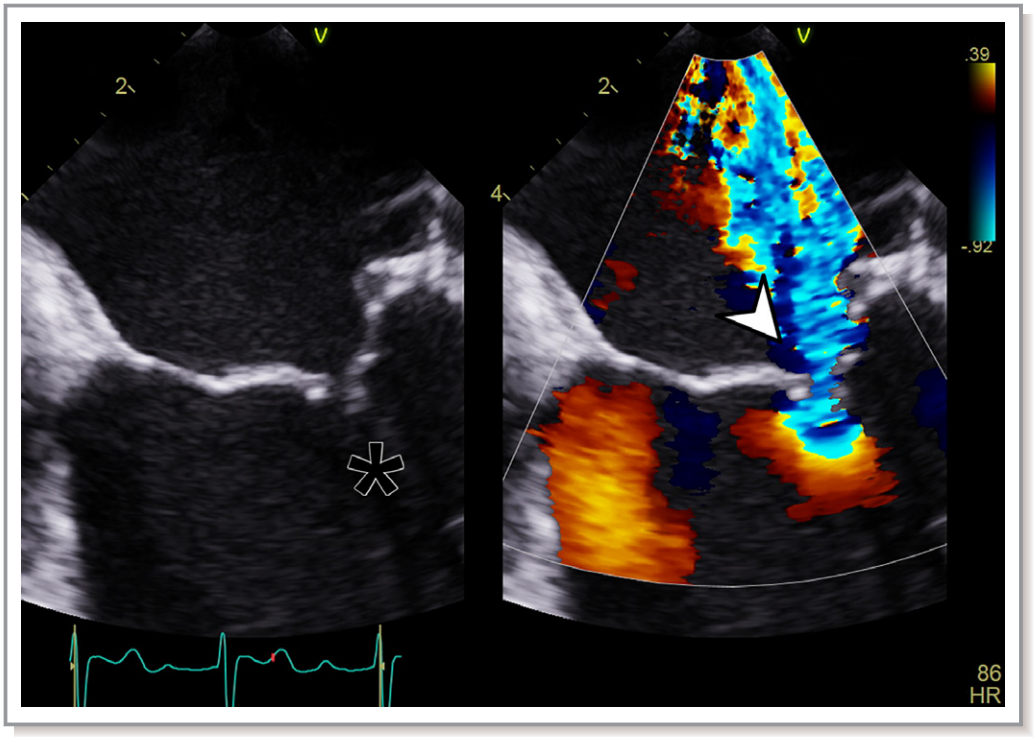

Figure 2. Echocardiographic image of a patient with secondary, functional mitral regurgitation. Note large jet of mitral regurgitation (arrowhead) attributed to leaflet tethering (asterisk) as a result of left ventricular remodeling. LA indicates left atrium; LV, left ventricle.

primary degenerative MR associated any symptoms beyond NYHA class I with lower rates of survival.[36] When assessing registry data on 2097 patients with flail mitral leaflet and severe MR, early surgery was associated with reduced mortality and heart failure at 10 years compared with a match cohort.[37] Additionally, if patients presented with pulmonary hypertension or LV dilation before surgery, postoperative mortality was increased.[34] This increasing level of evidence has prompted the consideration for earlier intervention in the appropriate patients.

Secondary MR

The 2014 guidelines recognized that for secondary MR, the focus of treatment was to correct the underlying cause of the MR whenever possible. If this is attributed to LV dysfunction, goal-directed medical therapy and cardiac resynchronization therapy are class I indications. Management in secondary MR is challenging, given that the valve is structurally normal, and the underlying LV dysfunction is worsened by volume load from MR. Correcting the MR only alters 1 part of the disease and has shown limited effectiveness. The role of surgical intervention of secondary MR was restricted to those with NYHA class III/IV symptoms that persisted despite medical therapy (class IIb indication).

The 2017 updated guidelines have added a class IIa recommendation to choose chordal-sparing MV replacement over annuloplasty with repair, but with the caveat that this should be limited to those with chronic severe MR that persists despite goal-directed medical therapy (Table 6). This is heavily influenced by an RCT involving 251 patients with severe secondary MR who were randomized to MV repair versus replacement.[30,38] Favorable reverse remodeling rates (normalization of LV size and function) did not differ significantly between repair and replacement groups, with similar mortality rates (hazard ratio, 0.79; 95% confidence interval [CI], 0.46–1.35; P=0.39). Recurrent moderate-to-severe MR was significantly higher in the repair versus the replacement group (58.8% versus 3.8%; P<0.001), as was a higher rate of complications from heart failure and repeat cardiac hospitalizations.

A RCT involving patients with moderate ischemic mitral regurgitation undergoing surgical revascularization randomized 301 patients to coronary artery bypass grafting and MV repair or coronary artery bypass grafting alone.[39,40] Patients with MV repair had significantly less MR at 2 years (11.2% versus 32.3%; P<0.001), but did not have improved reverse remodeling (z score, 0.38; P=0.71), or improved survival (hazard ratio, 0.90; 95% CI, 0.45–1.83; P=0.78), with an increase in early neurological events (P=0.03).

Table 5. Recommendations for Primary MR Intervention[4]

COR	LOE	Recommendations
I	B	Mitral valve surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF greater than 30%.
I	B	Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30–60% and/or left ventricular end-systolic diameter [LVESD] ≥40 mm, stage C2).
I	B	Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet.
I	B	Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished.
I	B	Concomitant mitral valve repair or MVR is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications.
IIa	B	Mitral valve repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence.
IIa	C-LD	Mitral valve surgery is reasonable for asymptomatic patients with chronic severe primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) with a progressive increase in LV size or decrease in EF on serial imaging studies.
IIa	B	Mitral valve repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) in whom there is a high likelihood of a successful and durable repair with (1) new onset of AF or (2) resting pulmonary hypertension (pulmonary artery systolic arterial pressure >50 mm Hg).
IIa	C	Concomitant mitral valve repair is reasonable in patients with chronic moderate primary MR (stage B) when undergoing cardiac surgery for other indications.
IIb	C	Mitral valve surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF less than or equal to 30% (stage D).
IIb	B	Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for HF.
III: harm	B	MVR should not be performed for the treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless mitral valve repair has been attempted and was unsuccessful.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AF indicates atrial fibrillation; COR, class of recommendation; EF, ejection fraction; ESD, end systolic diameter; GDMT, goal-directed medical therapy; HF, heart failure; LD, limited data; LOE, level of evidence; LV, left ventricle; MR, mitral regurgitation; MVR, mitral valve repair; NYHA, New York Heart Association; NR, nonrandomized; R, randomized; TAVR, transcatheter aortic valve replacement; VHD, valvular heart disease.

The updated 2017 guidelines reflect the lack of clear benefit for repairing moderate MR in patients undergoing coronary artery bypass grafting (Table 6).

Prosthetic Valve Choice

Recognition of the strengths and limitations of different prosthetic valves, and the need to include patients on the

Table 6. Recommendations for Secondary MR Intervention[4]

COR	LOE	Recommendations
IIa	C	Mitral valve surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR.
IIa	B-R	It is reasonable to choose chordal-sparing MVR over downsized annuloplasty repair if operation is considered for severely symptomatic patients (NYHA class III to IV) with chronic severe ischemic MR (stage D) and persistent symptoms despite GDMT for HF.
IIb	B	Mitral valve repair or replacement may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe secondary MR (stage D) who have persistent symptoms despite optimal GDMT for HF.
IIb	B-R	In patients with chronic, moderate, ischemic MR (stage B) undergoing CABG, the usefulness of mitral valve repair is uncertain.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AVR indicates aortic valve replacement; CABG, coronary artery bypass grafting; COR, class of recommendation; GDMT, goal-directed medical therapy; HF, heart failure; LOE, level of evidence; MR, mitral regurgitation; MVR, mitral valve repair; NYHA, New York Heart Association; R, randomized.

Table 7. Recommendations for Intervention of Prosthetic Valves[4]

COR	LOE	Recommendations
I	C-LD	The choice of type of prosthetic heart valve should be a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for, and risks of, anticoagulant therapy and the potential need for, and risk associated with, reintervention.
I	C	A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired.
IIa	B-NR	An aortic or mitral mechanical prosthesis is reasonable for patients aged <50 years who do not have a contraindication to anticoagulation.
IIa	B-NR	For patients aged between 50 and 70 years, it is reasonable to individualize the choice of either a mechanical or bioprosthetic valve prosthesis on the basis of individual patient factors and preferences, after full discussion of the trade-offs involved.
IIa	B	A bioprosthesis is reasonable for patients aged >70 years.
IIb	C	Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered for young patients when VKA anticoagulation is contraindicated or undesirable.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. COR, class of recommendation; LD, limited data; LOE, level of evidence; NR, nonrandomized; VKA, vitamin K antagonists.

discussion regarding the risks and benefits of each valve type, remains highly emphasized in the 2017 updated guidelines. A careful discussion with the patient on the benefits of a bioprosthetic heart valve (BHV) versus a mechanical heart valve (MHV) remains a class I indication. However, longer-term follow-up on patients with prosthetic valves and new management options have been reflected in the 2017 updated guidelines (Table 7).

A strong influencing factor when choosing the type of valve prosthesis is patient age. For those under 50, the 2017 updated guidelines provide a IIa recommendation for MHV in order to reduce the need for reoperation. For the very young, a pulmonary autograft could be considered (Class IIb). For those over 70, BHV are recommended (Class IIa). For those between the ages of 50 and 70, either mechanical or BHV could be

Table 8. Recommendations for Antithrombotic Therapy for Patients With Prosthetic Heart Valves[4]

COR	LOE	Recommendations
I	A	Anticoagulation with a VKA and INR monitoring is recommended in patients with a mechanical prosthetic valve.
I	B	Anticoagulation with a VKA to achieve an INR of 2.5 is recommended for patients with a mechanical bileaflet or current-generation single-tilting disc AVR and no risk factors for thromboembolism.
I	B	Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical AVR and additional risk factors for thromboembolic events (AF, previous thromboembolism, LV dysfunction, or hypercoagulable conditions) or an older-generation mechanical AVR (such as ball-in-cage).
I	B	Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical MVR.
I	A	Aspirin 75 mg to 100 mg daily is recommended in addition to anticoagulation with a VKA in patients with a mechanical valve prosthesis.
IIa	B	Aspirin 75 mg to 100 mg per day is reasonable in all patients with a bioprosthetic aortic or mitral valve.
IIa	B-NR	Anticoagulation with a VKA to achieve an INR of 2.5 is reasonable for at least 3 months and for as long as 6 months after surgical bioprosthetic MVR or AVR in patients at low risk of bleeding.
IIb	B-R	A lower target INR of 1.5 to 2.0 may be reasonable in patients with mechanical On-X AVR and no thromboembolic risk factors.
IIb	B-NR	Anticoagulation with a VKA to achieve an INR of 2.5 may be reasonable for at least 3 months after TAVR in patients at low risk of bleeding.
IIb	C	Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to lifelong aspirin 75 mg to 100 mg daily.
III: harm	B	Anticoagulant therapy with oral direct thrombin inhibitors or anti-Xa agents should not be used in patients with mechanical valve prostheses.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AF indicates atrial fibrillation; AVR, aortic valve replacement; COR, class of recommendation; INR, international normalized ratio; LD, limited data; LOE, level of evidence; LV, left ventricle; MVR, mitral valve replacement; NR, nonrandomized; R, randomized; TAVR, transcatheter aortic valve replacement; VKA, vitamin K antagonist.

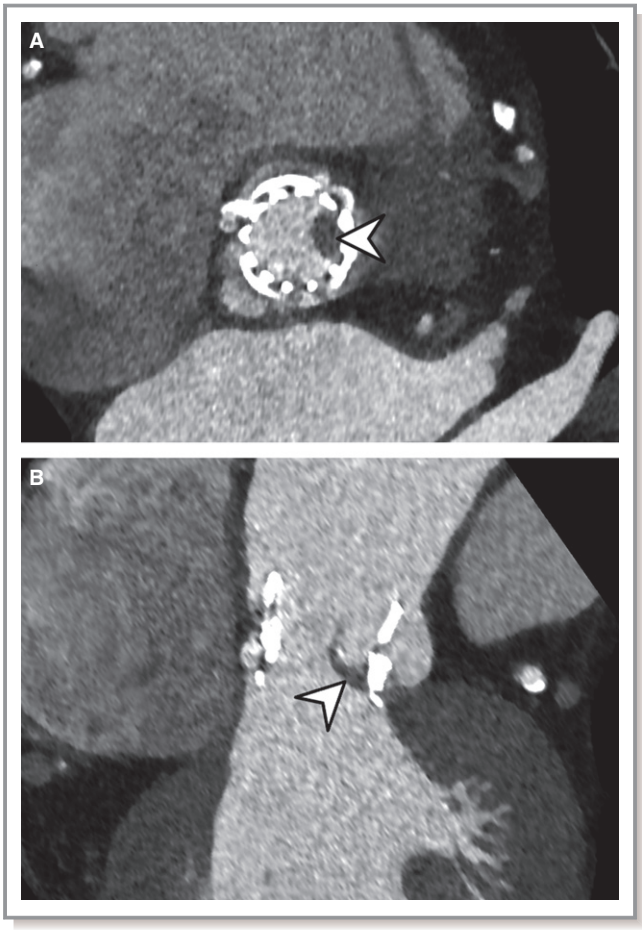

Figure 3. A, Short-axis view of an MRI of a Sapien 3 TAVR valve with thrombus noted on left leaflet of the prosthesis (arrow). B, Long-axis view of an MRI of a Sapien 3 TAVR valve with thrombus noted on left leaflet of the prosthesis (arrow). MRI indicates magnetic resonance imaging; TAVR, transcutaneous aortic valve replacement.

considered with patient preference or risk factors (need for anticoagulation, bleeding risk) weighing in the discussion (Class IIa).

Multiple randomized trials and observational studies have been published on valve selection. Consistently, BHV carry a higher risk of reoperation, primarily attributed to valve failure, most prominently beyond the 10- to 12-year mark.[41,42] When comparing a 15-year outcomes, survival and stroke risk were relatively similar regardless of valve choice. However, BHV was associated with a higher rate of reoperation (12.1%; CI 6.2–11 versus 6.9; CI, 4.2–9.6), but lower major bleeding (6.6%; CI 4.8–8.4 versus 13.0; CI, 9.9–16.1).[43] A prospective cohort followed 310 patients randomized to BHV versus MHV out to 108±28 months and showed no difference in mortality, bleeding, or valve thrombosis, but with significant increases in valve failure (P=0.0001) and need for reoperation (P=0.0003).[44] A RCT including veterans showed increased mortality in aortic BHV over MHV, primarily attributed to valve failure.[41]

Added to the modern discussion of valve choice is the potential for transcatheter valve-in-valve (VIV) procedures. Though the published data are limited in this group so far, the Valve-In-Valve International Database registry has published on 459 patients undergoing VIV procedures for bioprosthetic valve failure. Success rates are reasonable, with 93% survival at 30 days and significant improvement in functional class (to class I/II).[45,46] One-year survival rates were 83%, and factors that were associated with mortality included a small surgical prosthesis (21 mm) and prosthetic stenosis as the primary indication for intervention (rather than regurgitation).[45] These new data allow for additional topics of discussion when deciding on type of prosthesis with patients who need valve surgery aged between 50 and 70 years.

Prosthetic Valve Antithrombotic Therapy

Recommendations for anticoagulation strategies for prosthetic heart valves remains similar between the 2014 valve guidelines and the 2017 updated guidelines with a few

Table 9. Recommendations for Bridging Therapy for Prosthetic Valves[4]

COR	LOE	Recommendations
I	C	Continuation of VKA anticoagulation with a therapeutic INR is recommended in patients with mechanical heart valves undergoing minor procedures (such as dental extractions or cataract removal) where bleeding is easily controlled.
I	C	Temporary interruption of VKA anticoagulation, without bridging agents while the INR is subtherapeutic, is recommended in patients with a bileaflet mechanical AVR and no other risk factors for thrombosis who are undergoing invasive or surgical procedures.
IIa	C-LD	Bridging anticoagulation therapy during the time interval when the INR is subtherapeutic preoperatively is reasonable on an individualized basis, with the risks of bleeding weighed against the benefits of thromboembolism prevention, for patients who are undergoing invasive or surgical procedures with a (1) mechanical AVR and any thromboembolic risk factor, (2) older-generation mechanical AVR, or (3) mechanical MVR.
IIa	C	Administration of fresh frozen plasma or prothrombin complex concentrate is reasonable in patients with mechanical valves receiving VKA therapy who require emergency noncardiac surgery or invasive procedures.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. AVR indicates aortic valve replacement; COR, class of recommendation; INR, international normalized ratio; LD, limited data; LOE, level of evidence; LV, left ventricle; MR, mitral regurgitation; MVR, mitral valve replacement; VKA, vitamin K antagonist.

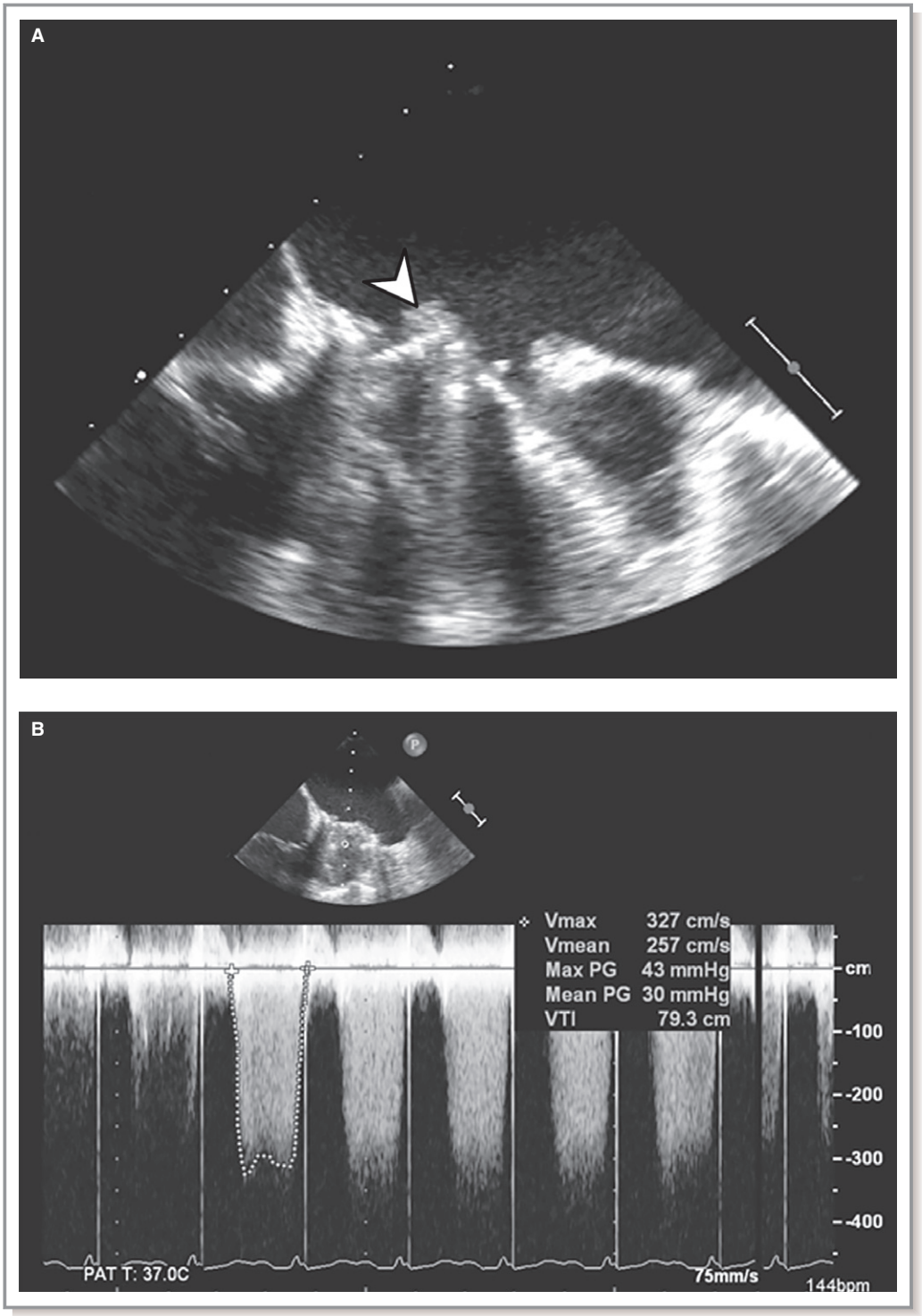

Figure 4. A, Transesophageal echo demonstrating a thrombosed mechanical heart valve in a patient that was noncompliant with warfarin therapy. Note the thrombus on the atrial side of the valve (arrowhead). B, Doppler interrogation of the thrombosed mechanical valve demonstrating severe mitral stenosis. PG indicates pressure gradient; VTI, velocity time integral.

exceptions (Table 8). Anticoagulation in patients with a mechanical heart is based on the monitored use of VKA with international normalized ratio (INR) ranges targeted based on factors that affect thrombogenic potential. For bileaflet tilting disc valves in the aortic position, the target INR is 2.5 (with a range of plus or minus 0.5). For valves in the mitral position, older mechanical aortic prosthesis, or mechanical AVR with additional risk factors for thromboembolism, the target INR is

Table 10. Fibrinolysis Versus Surgery for Prosthetic Valve Thrombosis[4]

Favor Surgery	Favor Fibrinolysis
Readily available surgical expertise	No surgical expertise available
Low surgical risk	High surgical risk
Contraindication to fibrinolysis	No contraindication to fibrinolysis
Recurrent valve thrombosis	First-time episode of valve thrombosis
NYHA class IV	NYHA class I to III
Large clot (>0.8 cm^2)	Small clot (≤0.8 cm^2)
Left atrial thrombus	No left atrial thrombus
Concomitant CAD in need of revascularization	No or mild CAD
Other valve disease	No other valve disease
Possible pannus	Thrombus visualized
Patient choice	Patient choice

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3.0. Use of low-dose aspirin is also recommended because it has found to reduce the residual risk of stroke for a small increase in bleeding risk. Additionally, acetylsalicylic acid continues to be reasonable for BHV for lifelong thromboembolic prophylaxis (Class IIa). Anticoagulation with a VKA to achieve an INR of 2.5 for at least 3 months and for as long as 6 months after surgical bioprosthetic MV replacement and AVR in patients with a low risk of bleeding remains a class IIa recommendation, but the level of evidence has been upgraded from C to B-NR. This change is supported by the increased rate of thromboembolism, presumed to be related to implanted material until endothelialization occurs. TAVR valves are managed differently, because the early trials had used dual antiplatelet agents with acetylsalicylic acid and clopidogrel 75 mg for 6 months postinsertion. Finally, there is now a Class III recommendation for DOACs in mechanical valves because increased rates of mechanical valve thrombosis were noted with these agents.

As TAVR use expanded and new data became available, increased recognition of clinical and subclinical leaflet thrombus was detected (Figure 3A and 3B). With imaging data from TAVR trials, reduced leaflet motion was observed in 7% to 40% of TAVR patients,[47–50] though clinically evident effects were rare (1%).[50] VKA usage was found to effectively treat thrombosis.[48–50] Additionally, those who were on VKAs for other reasons had significantly lower rates of valve thrombosis (10.7% versus 1.8%; relative risk, 6.09; 95% CI, 1.86–19.84).[48,50] Because of these data, VKA is considered reasonable for at least 3 months post-TAVR in low-bleeding-risk patients.

A new, lower targeted INR was included for a specific mechanical AVR, the On-X valve. A single randomized trial with 375 patients compared a regimen of acetylsalicylic acid for all, INR 2.0 to 3.0 for 3 months, and then either targeting an INR of 1.5 to 2.0 or 2.0 to 3.0. There was an increased rate of major bleeding in the standard INR group (3.26% versus 1.48%; P=0.047), with no significant difference in thrombotic events (relative risk, 1.6; 95% CI, 0.81–3.17; P=0.178) observed early on in this small trial.[51]

Bridging Therapy for Prosthetic Valves

For patients with MHV who had scheduled procedures, the 2014 valve guidelines recommendations were based on opinions and limited retrospective data. These recommendations included continuing anticoagulation for minor procedures, temporary interruption for bileaflet mechanical aortic valves without other risk factors, and bridging with heparinoids for others with mechanical prosthesis.

Although the BRIDGE (Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for Elective Invasive Procedure or Surgery) trial excluded MHV,

Table 11. Recommendation for Mechanical Prosthetic Valve Thrombosis Intervention[4]

COR	LOE	Recommendation
I	B-NR	Urgent initial treatment with either slow-infusion low-dose fibrinolytic therapy or emergency surgery is recommended for patients with a thrombosed left-sided mechanical prosthetic heart valve presenting with symptoms of valve obstruction.
Recommendation for Mechanical Prosthetic Valve Thrombosis Diagnosis and Follow-up[4]		
COR	LOE	Recommendation
I	B-NR	Urgent evaluation with multimodality imaging is indicated in patients with suspected mechanical prosthetic valve thrombosis to assess valvular function, leaflet motion, and the presence and extent of thrombus.

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Table 12. Recommendations for Prosthetic Valve Stenosis and Regurgitation[4]

COR	LOE	Recommendations
I	C	Repeat valve replacement is indicated for severe symptomatic prosthetic valve stenosis.
I	B	Surgery is recommended for operable patients with mechanical heart valves with intractable hemolysis or HF attributed to severe prosthetic or paraprosthetic regurgitation
IIa	C-LD	In patients with suspected or confirmed bioprosthetic valve thrombosis who are hemodynamically stable and have no contraindications to anticoagulation, initial treatment with a VKA is reasonable.
IIa	C-LD	Surgery is reasonable for asymptomatic patients with severe bioprosthetic regurgitation if operative risk is acceptable.
IIa	B	Percutaneous repair of paravalvular regurgitation is reasonable in patients with prosthetic heart valves and intractable hemolysis or NYHA class III/IV HF who are at high risk for surgery and have anatomical features suitable for catheter-based therapy when performed in centers with expertise in the procedure.
IIa	B-NR	For severely symptomatic patients with bioprosthetic aortic valve stenosis judged by the heart team to be at high or prohibitive risk of reoperation, and in whom improvement in hemodynamics is anticipated, a transcatheter valve-in-valve procedure is reasonable.
IIa	B-NR	For severely symptomatic patients with bioprosthetic aortic valve regurgitation judged by the heart team to be at high or prohibitive risk for surgical therapy, in whom improvement in hemodynamics is anticipated, a transcatheter valve-in-valve procedure is reasonable.

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this randomized trial assigned patients on chronic anticoagulation to receive low-molecular-weight heparin versus placebo for bridging before elective surgery and found no significant difference in arterial thromboembolism, but a significant increase in major bleeding (relative risk, 0.41; CI, 0.20–0.78). This study raised concerns that by bridging with overlapping anticoagulation agents can increase bleeding risk without reducing risk of thromboembolism. In light of this evidence, the recommendation for bridging has been altered from I, LOE C, to a level IIa, LOE C-LD (Table 9).

Prosthetic Valve Thrombosis

Obstruction of MHV and BHV can occur from either pannus growth or thrombus formation, or both. The 2014 guidelines recognized challenges in diagnosis. Transthoracic echo was a class I indication for assessment of severity and monitoring for resolution of thrombosis, with transesophageal echo for assessing valve motion and thrombus size (Class Ia; Figure 4A and 4B) and computed tomography or fluoroscopy used for adjunctive assessment (Class IIa).

Valve obstruction can be difficult to classify by transthoracic echo alone. The 2017 updated guidelines suggest urgent multimodality imaging for thorough assessment of valve function, leaflet motion, and to assess for the presence and size of thrombus (Class I; Table 10). Increasingly, the recognition for each modality's strengths and weaknesses should be taken into account for a complete assessment. Transthoracic echo provides prompt availability and excellent hemodynamic assessment, but the views of valve motion are often limited.[52] Transesophageal echo can better assess valve motion, and thrombus or pannus formation and differentiation.[53,54] Additionally, prosthetic shadowing on transesophageal echo can limit assessment of aortic valves.[55] Computed tomography can differentiate thrombus from pannus as well as assess thrombus size and valve motion.[56,57] Cinefluoroscopy has excellent ability to visualize valve motion for both diagnosis and treatment.[52,58]

In the 2014 guidelines, medical management of valve thrombus was limited to recent onset (<14 days), NYHA class I to II, and small thrombus (<0.8 cm^2) or for right-sided thrombosis. Surgery was often the first and only option. Increasingly, thrombolytic therapy has been incorporated into clinical practice. Various regimens from ultrarapid to low-dose continuous infusion have been attempted.[59–65] Ozkan showed efficacy and increased safety with an echo-guided, no-bolus, low-dose, slow-infusion regimen,[60] and analysis of 114 patients treated with 1 or more sessions showed a high rate of success (90%) and low rate of complications (embolism 1.7%, major bleed 1.7%, and minor bleed 1.7%).[59]

The decision on management of this condition is complex. The 2017 updated guidelines provide a Class I recommendation for urgent therapy with either slow-infusion, low-dose fibrinolytics or emergency surgery diagnosis and consideration of patient- and site-specific factors (Table 11).

Prosthetic Valve Stenosis and Regurgitation

Before modern percutaneously implantable valves, options for management of prosthetic valve stenosis and regurgitation were limited. In valvular stenosis, surgical replacement was essentially the exclusive intervention. These patients were not only higher risk because of increased age and

Table 13. Recommendations for IE Intervention[4]

COR	LOE	Recommendations
I	B	Decisions about timing of surgical intervention should be made by a multispecialty heart valve team of cardiology, cardiothoracic surgery, and infectious disease specialists.
I	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE who present with valve dysfunction resulting in symptoms of HF.
I	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with left-sided IE caused by *S. aureus*, fungal, or other highly resistant organisms.
I	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE complicated by heart block, annular or aortic abscess, or destructive penetrating lesions.
I	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) for IE is indicated in patients with evidence of persistent infection as manifested by persistent bacteremia or fevers lasting longer than 5 to 7 days after onset of appropriate antimicrobial therapy.
I	C	Surgery is recommended for patients with prosthetic valve endocarditis and relapsing infection (defined as recurrence of bacteremia after a complete course of appropriate antibiotics and subsequently negative blood cultures) without other identifiable source for portal of infection.
I	B	Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is indicated as part of the early management plan in patients with IE with documented infection of the device or leads.
IIa	B	Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients with valvular IE caused by *S. aureus* or fungi, even without evidence of device or lead infection.
IIa	C	Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients undergoing valve surgery for valvular IE.
IIa	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is reasonable in patients with IE who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy.
IIb	B	Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) may be considered in patients with native valve endocarditis who exhibit mobile vegetations greater than 10 mm in length (with or without clinical evidence of embolic phenomenon).
IIb	B-NR	Operation without delay may be considered in patients with IE and an indication for surgery who have suffered a stroke but have no evidence of intracranial hemorrhage or extensive neurological damage.
IIb	B-NR	Delaying valve surgery for at least 4 weeks may be considered for patients with IE and major ischemic stroke or intracranial hemorrhage if the patient is hemodynamically stable.

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repeat surgery, but also multiple surgical procedures were often combined.[66]

In the 2017 updated guidelines, surgery remains a Class I indication for operable patients with severe symptomatic prosthetic valve stenosis and for operable patients with MHV with intractable hemolysis or heart failure attributed to severe prosthetic or paraprosthetic regurgitation (Table 12). Surgery is also reasonable for asymptomatic patients with acceptable operative risk with severe BHV regurgitation (Class IIa, LOE C-LD [updated from LOE C]).

At the time of publication of the 2014 guidelines, BHV thrombosis was not well appreciated. Bioprosthetic valve thrombosis presents differently and is dealt with differently than mechanical valves. In general, VKAs are not continued in bioprosthesis patients without risk factors for thrombosis postsurgery. Historically, bioprosthetic valve thrombus is rare (0.5% in aortic position and 6% in mitral). However, in modern registry data with routine multimodality surveillance, aortic thrombus was identified in 14% of TAVR and 7% of SAVR patients.[48] Symptoms, ranging from heart failure to stroke, remained rare (0.37–1%).[48,67]

With the availability of transcather-based valve therapies came alternatives to open surgical valve replacement.[68] The Valve-In-Valve International Database registry has collected data on the use of transcatheter-based VIV procedures. Data from the registry showed a 1-year survival rate of 83%, with the majority of survivors having a significant symptom improvement (92% NYHA class I–II).[45] A systematic review assessed 823 patients with transcatheter VIV procedure or surgical redo AVR.[69] The VIV patients were older and had more comorbidities. Regardless, periprocedural mortality was similar (VIV 7.9% versus AVR 6.1%; P=0.35), with significantly less stroke (1.9% versus 8.8%; P=0.002) and major bleeding (6.9% versus 9.1%; P=0.014) though higher paravalvular leak

rates (3.3% versus 0.4%; P=0.022). Interestingly, transvalvular gradients were not significantly different between groups (15.2 versus 13.5 mm Hg; P=0.55). Benefit has been noted in patients with stenosis, regurgitation, or mixed disease.

Careful assessment of both the valve and patient factors for consideration of the VIV procedure has been added to the 2017 updated guidelines for both bioprosthetic stenosis and regurgitation with a Class IIa indication (Table 12).

Bioprosthetic thrombus can present as increased leaflet thickening with restricted leaflet motion and increased valve gradients.[70] This occurs much earlier than valve degeneration, most commonly identified at 1 to 2 years, though reported out to 6.5 years.[67,70] With VKA treatment, most patients experience resolution of thrombus, as well as hemodynamic and symptom improvement.[48,67,70] In the 2017 updated guidelines, patients with suspected or confirmed BHV thrombosis who are hemodynamically stable and have no contraindications for anticoagulation should be treated with VKA (Class IIa; Table 12).

The recommendation for transcatheter-based therapies noted in the 2014 guidelines as a potential treatment option for paravalvular regurgitation (Class IIa) for patients with high operative risk and intractable class III/IV heart failure or hemolysis, remains unchanged in the 2017 updated guidelines.

Infective Endocarditis

Endocarditis continues to be a major clinical problem with prohibitive mortality rates. The 2014 valve guidelines provided extensive guidance for management in the acute phase of the illness, including aggressive antibiotic therapy, early removal of devices, and surgical consultation with consideration on timing of surgery, should any be required. These recommendations remain unchanged in the 2017 updated guidelines (Table 13).

The 2017 updated guidelines address the timing of operation in patients with IE who have suffered a stroke. For left-sided endocarditis, neurological complications are common (17–25%)[7,71] and associated with significant mortality (45% with versus 24% without neurological event).[71] A previous retrospective study observed that patients with embolic stroke had lower rates of cerebral complications if surgery was delayed more than 4 weeks (10% at 2–4 weeks and 2.3% at >4 weeks).[72] However, these early observational data were not risk adjusted. A more-recent retrospective analysis of patients with IE complicated by ischemic stroke included risk-adjusted analysis.[73] In this small study, 198 patients underwent valve replacement surgery with 58 undergoing surgery within 7 days poststroke. The risk for in-hospital mortality (odds ratio, 2.308; 95% CI, 0.94–5.65) or 1-year mortality (hazard ratio, 1.138; 95% CI, 0.80–1.65) was not significantly different between the 2 groups. Another observational study of 1345 patients showed that in patients with a hemorrhagic neurological event, mortality was prohibitive for those having surgery within 4 weeks (75%) and elevated, but slightly lower, for those after 4 weeks (40%).[71] As a result of these studies, the 2017 updated guidelines recommend operation without delay for those patients with IE who need cardiac surgery and have suffered a stroke but have no intracranial hemorrhage or extensive neurological damage (Class IIb, LOE B-NR) (Table 13).

Conclusion

The 2017 updated AHA/ACC valve guidelines provide treatment recommendations based on new data compiled since the 2014 document. Similar in both documents is the importance of including the patient as an active participant in the decision-making process. Stages of disease and involvement of the heart valve team also remain unchanged. New options for treatment, particularly percutaneous modalities now offer patients more choices. The 2017 updated guidelines highlight the established and novel treatments with defined levels of recommendation and strength of evidence to aid healthcare providers in navigating the complex options now available to treat VHD.

Disclosures

None.

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Key Words: anticoagulation • echocardiography • guideline • valve replacement • valve-in-valve