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OPINION

Aortic Valve Disease in the 2017 Focused Update: Questions Answered and Questions Raised

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The publication of the 2017 Focused Update of the 2014 American Heart Association (AHA)/American College of Cardiology (ACC) Guideline for the Management of Patients with Valvular Heart Disease provides an opportunity for clinicians to reflect upon how closely their decision-making matches recommendations and to reconcile points of departure.[1,2] The update includes new recommendations and changes to guidelines regarding the management of patients with aortic valve disease, treatment of bioprosthetic valve failure, and medical therapy of patients with valve disease or undergoing valve replacement (Table 1). In particular, the management of patients with aortic stenosis (AS) is undergoing rapid transition due to the maturation of transcatheter aortic valve replacement (TAVR), the changing nature of the patient population, and the availability of high-quality randomized controlled trials and large prospective registries reporting short- and long-term outcomes. The recognition of age-dependent differences in the natural history of AS and the still incompletely characterized syndrome of low-gradient severe AS complicate decisions regarding timing and type of treatment.[3–7] Comorbidities and advanced age make the assessment of risks and benefits a multidisciplinary exercise.

It is therefore not surprising that the 2017 Focused Update introduces additional complexity into the decision-making algorithm for the treatment of AS in patients of intermediate and high surgical risk. Randomized trials have clearly established the non-inferiority of TAVR relative to surgical aortic valve replacement (SAVR) with respect to survival, disabling stroke, and improvement in quality of life in these patient populations.[8–12] Recent trials and registry data have further demonstrated that improvements in technique and technology have reduced rates of mortality and disabling stroke with TAVR and have suggested possible superiority of transfemoral TAVR.[8,9,12,13] The 2017 Focused Update therefore assigns TAVR a Class I recommendation for high-risk patients with symptomatic severe AS and a Class IIa recommendation for intermediate risk patients. However, in light of the subsequent publication of the randomized SURTAVI trial, reaffirming the non-inferiority of TAVR in intermediate risk patients, the latter recommendation now already appears to be overly conservative.[10] This highlights an important problem with the guideline writing process, in which recommendations can quickly become outdated in a rapidly evolving field. In view of the current evidence, it would seem most rational for SAVR to be recommended in low-risk patients and both TAVR and SAVR to be recommended with equal strength in high and intermediate risk patients. A shared decision-making process, involving the heart valve team and focused on patient age and preferences, should inform individual judgments regarding the importance of a less invasive procedure versus limited data regarding TAVR durability beyond 5 years.

The 2017 Focused Update does not change recommendations for the treatment of patients with asymptomatic severe AS. Given the lack of randomized data comparing TAVR or SAVR with medical follow-up in this population, it is unclear why the recommendation for treatment of asymptomatic patients with very severe AS (peak velocity ≥ 5.0 m/s, mean gradient ≥ 60 mmHg) is restricted only to SAVR. A recent prospective registry demonstrated that 43% of older patients (>age 70) with severe AS and low to intermediate surgical risk under clinical and echocardiographic 6-month follow-up at a valve center transitioned from being asymptomatic to highly symptomatic (class III/IV) without passing through a phase of mild (i.e. class II) symptoms. This was particularly true when very severe AS (peak velocity ≥ 5.0 m/s) was present.[7] Importantly, advanced symptoms at presentation were also associated with increased 30-day and long-term mortality after AVR. The current indications for asymptomatic patients reflect markers of rapid progression to symptoms, which should be relevant regardless of treatment assignment to TAVR or SAVR. Indeed, new randomized trials are planned to examine the potential benefits of earlier treatment of asymptomatic patients with either SAVR or TAVR[14,15] (NCT03042104, NCT02436655, NCT01161732).

The 2017 Focused Update does not modify recommendations for the management of low-gradient (LG) (mean gradient < 40 mmHg, maximum velocity < 4 m/s), severe AS (valve area < 1.0 cm^2, indexed valve area < 0.6 cm^2/m^2). Since the release of the 2014 guidelines, however, several publications have examined the common clinical dilemma of patients with LG severe AS and normal ejection fraction. These studies have added to the conflicting data on the natural history and the relative benefit or lack thereof of valve replacement in this population compared to patients with classical high gradient AS and moderate AS.[5,6,16–22]

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Table 1. Aortic valve disease in the 2017 Focused Update.

New or significantly changed recommendations
TAVR for intermediate-risk patients,[a] Class IIa
TAVR for high-risk patients,[a] Class I
TAVR for high-risk patients with bioprosthetic AS or AI[b]
Age range for equipoise between mechanical and bioprosthetic SAVR expanded to 50–70 years
Anticoagulation after TAVR and SAVR for 3–6 months
SBE prophylaxis after TAVR
Therapeutic anticoagulation for patients with AF, CHA_2DS_2-VASc score ≥ 2 and aortic valve disease. DOACs are reasonable in this population.
Unchanged recommendations
Indications for aortic valve replacement
Management of asymptomatic, severe AS (SAVR only)
Management of low-gradient, severe AS with both normal and depressed LV systolic function

Note. [a]Symptomatic, severe AS. [b]Severely symptomatic, severe AS or AI.

Evidence regarding the role of low flow (SVi < 35 ml/m^2) in determining outcomes with AVR in this group has also been conflicting.[17,18] Multimodality imaging (calcification by computed tomography, fibrosis by magnetic resonance imaging) and sophisticated echocardiographic analysis should be considered to confirm the severity of AS in this scenario and stress testing may emerge as a useful test to exclude pseudo-severe AS.[23,24] At present, published data indicate that TAVR and SAVR are being done in similar frequency in patients with low gradient and normal or low flow.[17,18] It would therefore seem advisable to extend the current guideline to recommend that all patients with LG severe AS be evaluated by an experienced valve team. This will help to avoid both under-referral of patients based on SVi and over-referral for AVR of patients with moderate AS and alternate causes of symptoms.

The guidelines have also not changed for the management of LG severe AS with depressed LVEF. There is data, however, to suggest that in high surgical risk patients, outcomes including mortality and recovery of LV function, are equivalent or improved with TAVR compared to SAVR.[25,26] This patient group may be further risk stratified with dobutamine echocardiography; the subset of patients without contractile reserve have very high early mortality, although survivors appear to benefit from valve replacement compared with medical therapy.[27,28] In this very high-risk group, it may be reasonable to consider TAVR as the preferred approach.

In the 2017 Focused Update, valve-in-valve TAVR is assigned a Class IIa recommendation for severely symptomatic bioprosthetic aortic valve stenosis or regurgitation in high surgical risk patients. SAVR alone is recommended for asymptomatic patients with severe bioprosthetic aortic valve regurgitation. Depending on patient age and preference, valve-in-valve TAVR would seem to be a reasonable alternative across all surgical risk groups for symptomatic bioprosthetic aortic stenosis and regurgitation.[29–32] Indeed, in the recently published PARTNER 2 Valve-in-Valve Registry, the 30-day mortality rate of 2.7% (0.7% in the 269 patient Continued Access Cohort) compares extremely favorably with contemporary data from the STS registry, which showed mortality of 4.6% for reoperative SAVR in a younger, lower risk population.[29,33] The same consideration should also apply to asymptomatic patients with severe bioprosthetic regurgitation given the risk for sudden clinical deterioration in these patients.

In many of the above scenarios, patient preference will play an increasing role in the decision to perform TAVR. In fact, after TAVR received United States Food and Drug Administration approval for high risk and inoperable patients, the mean STS risk of patients undergoing TAVR in the STS/ACC TVT registry was 7.1% in 2012 and 6.7% in 2014, compared to >11% in the PARTNER trial that led to approval.[11,34,35] This likely reflects, in part, patient and physician preference in an elderly population with multiple comorbidities. It will be interesting to see if this trend continues after the recent approval for intermediate risk (STS PROM > 3%) patients. In fact, by 2014, 20% of patients undergoing commercial TAVR in the United States already had an STS risk score ≤ 4%.

The issue of valve durability and structural valve deterioration (SVD) remains an important one in advising TAVR in younger patients. It is estimated that the lifetime risk of SVD for patients undergoing SAVR at age 60 with a bioprosthesis is 20–25%, and this number rises to 45–50% with implantation at age 50.[36,37] The paucity of data on TAVR durability beyond 5 years versus the older patient's limited life expectancy and increased early morbidity with SAVR suggest that an age stratified approach to decision making should be considered in the application of the updated valve guidelines.[38–40] In fact, the *British Medical Journal* Rapid Recommendations guideline for patients with symptomatic severe AS at low or intermediate surgical risk concludes that TAVR is probably preferred over SAVR in patients above 75 years of age.[41] This is based on lower mortality and stroke rates with transfemoral TAVR versus SAVR in low- and intermediate-risk patients, balanced against uncertainty regarding TAVR durability.[12,13,41] It is clear that patient preferences must play an important role given the uncertainties and differences in individual preferences regarding issues such as avoiding open heart surgery and optimizing length of recovery.

The critical role of patient age in driving clinical decision-making is also apparent in the 2017 Focused Update recommendations for the choice between bioprosthetic and mechanical valves. The age below which a mechanical valve is preferred has now been decreased from 60 to 50 years. It is also recognized that a bioprosthetic valve may be preferred over the age of 70 years and is a reasonable alternative between the age of 50 and 70 years, based on individualized patient risk assessment and preferences. This change is justified based on the available evidence regarding the relative risks of structural valve deterioration and bleeding complications from therapeutic anticoagulation in this intermediate age range.[37,42–44] It is also a recognition of changing clinical practice patterns in the choice of valve type over the past 2 decades, which have only been accelerated by the recently recognized feasibility of valve-in-valve TAVR.[29,33,45,46] This is despite a lack of a significant change in the literature regarding the relative risks and benefits of bioprosthetic versus mechanical valves in 50 to 60-year-olds.[42–44,47] The durability of valve-in-valve TAVR and the risk of patient prosthesis mismatch in this scenario will continue to be important topics of research.

Finally, the 2017 Focused Update is notable for several important changes to recommendations for therapeutic anticoagulation in patients with aortic stenosis and those who undergo bioprosthetic valve replacement. It is now formally recognized that therapeutic anticoagulation is indicated for patients with atrial fibrillation, CHA_2DS_2-VASc score ≥ 2, and native aortic valve disease (Class I) and that the use of direct oral anticoagulants (DOACs) is reasonable in this population (Class IIa). The 2017 Focused Update recommends anticoagulation with a warfarin for 3–6 months after both bioprosthetic SAVR (Class IIa) and TAVR (Class IIb) in patients with low bleeding risk. This is based on observational studies suggesting a decreased occurrence of stroke and cardiovascular death during this period after bioprosthetic SAVR with warfarin and multidetector computed tomography findings suggestive of leaflet thrombosis after SAVR and TAVR that resolve with therapeutic anticoagulation.[41,48–54] Clearly, additional prospective data is necessary to clarify the clinical significance of this latter entity and determine indications for anticoagulation. This is especially true for elderly patients with elevated bleeding risk, who currently make up the majority of patients undergoing TAVR. Several ongoing randomized trials will investigate the use of DOACs in the TAVR patient population (NCT02556203, NCT02758964, NCT02664649). The evolution of medication recommendations further highlights the ongoing systematic acquisition of high quality clinical trial data that will continue to inform current clinical practice and alter future guideline recommendations.

In conclusion, the 2017 Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (VHD) is an excellent and comprehensive document that effectively summarizes the existing knowledge base. In certain areas, however, the guideline may be overly complex and is likely to quickly become outdated. Clinical practice will continue to have to adapt to rapidly accumulating clinical trial and registry data and should be based in a shared decision-making process that takes into account patient age, risk, and preferences.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the writing and content of this article.

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