Review: application of current imaging modalities in the management of left-sided valvular heart disease

Robert Zheng, Kenya Kusunose

Department of Cardiovascular Medicine, Tokushima University Hospital, Tokushima, Japan

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Correspondence to: Kenya Kusunose, MD, PhD. Department of Cardiovascular Medicine, Tokushima University Hospital, 2-50-1 Kuramoto, Tokushima, Japan. Email: kusunosek@tokushima-u.ac.jp.

Abstract: In terms of valvular heart disease (VHD) imaging, transthoracic echocardiography (TTE) is the preferred first choice because of its widespread availability. Other modalities, such as transesophageal echocardiography, computed tomography and magnetic resonance imaging, have played a supplementary role in diagnosis for severity, deciding the timing/type of treatment, detection of post procedural complications, and prognostic predictions. However, there are few consensuses on how to employ these modalities, as the evidence is not extensive as that for TTE. On the other hand, these imaging modalities also have their own unique strengths. If employed properly, these modalities have the potential to play a more prominent role in clinical decision making. In this review, we focus on the potential, limitations and application of current imaging modalities in the management of left-sided VHD

Keywords: Valvular heart disease (VHD); echocardiography; computed tomography (CT); magnetic resonance imaging (MRI)

Introduction

In the current field of valvular heart disease (VHD), the development of innovative techniques, such as transcatheter aortic valve replacement (TAVR) and transcatheter mitral valve repair (TMVR), have created new treatment options for high-risk patients previously considered unsuitable for invasive intervention. These advances have benefitted these patients, leading to improved quality of life (QOL) and better clinical outcomes. In terms of VHD imaging, transthoracic echocardiography (TTE) is the preferred first choice because of its widespread availability (*Figure 1*). Other modalities, such as transesophageal echocardiography (TEE), computed tomography (CT) and magnetic resonance imaging (MRI), have played a supplementary role in diagnosis for severity, deciding the timing/type of treatment, detection of post procedural complications, and prognostic predictions (*Figure 2*). However, there are

few consensuses on how to employ these modalities, as the evidence is not extensive as that for TTE. In this review, we focus on the potential, limitations and application of current imaging modalities in the management of left-sided VHD.

Strengths and limitations of imaging modalities

The strengths and limitations of each modality are listed in *Table 1*. TTE has been the first-line for imaging in VHD due to its inexpensiveness, simplicity and availability. It provides real-time hemodynamic information, and can be employed with exercise or dobutamine stress testing (1-4). It has decent spatial resolution, providing detailed images of valvular structures for determining the etiology of the disease. On the other hand, TTE tends to have a limited acoustic window, limited view of the right heart, and large artefacts due to calcification/devices. TTE also has a
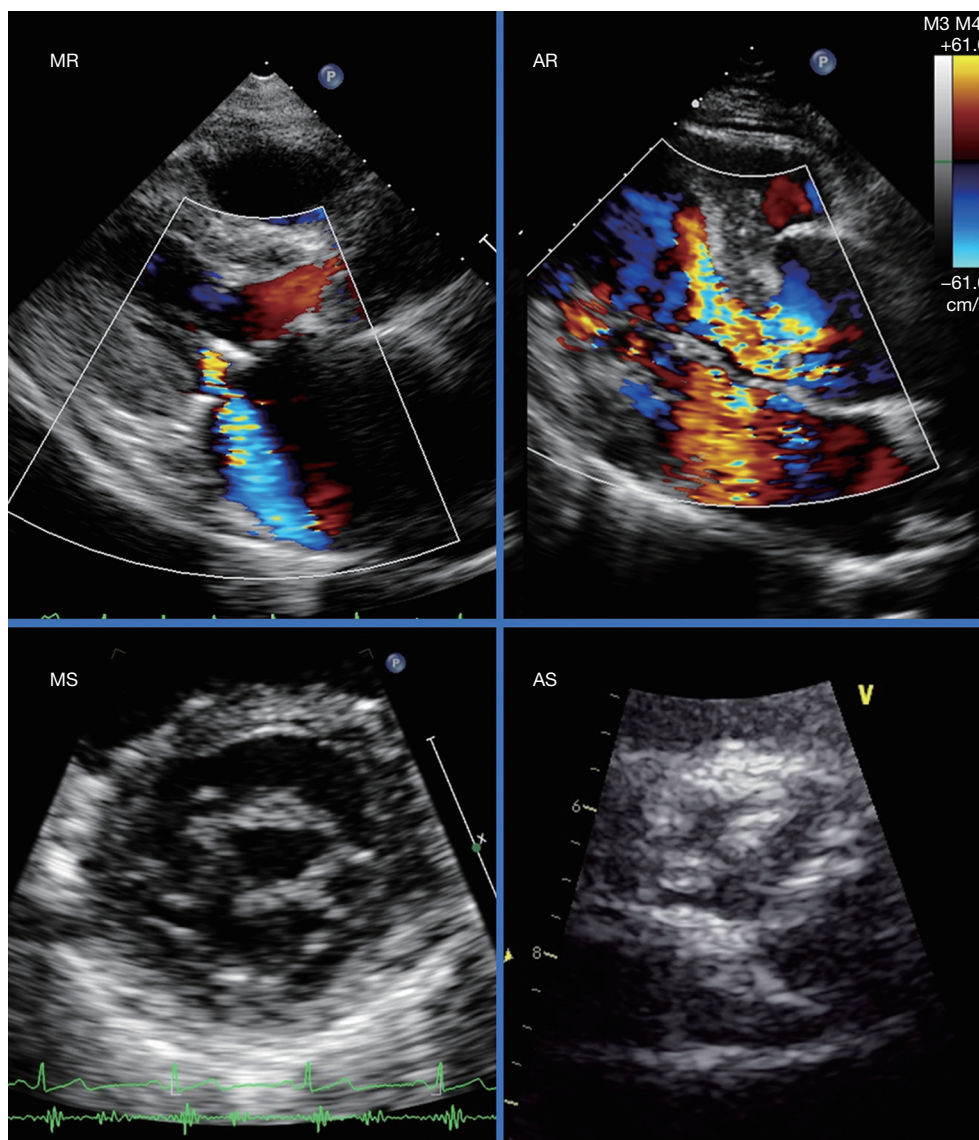
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Figure 1 Echocardiographic images for valvular heart disease. Echocardiography is the first-line imaging modality for assessment of valvular heart disease. AR, aortic regurgitation; MR, mitral regurgitation; AS, aortic stenosis; MS, mitral stenosis.

considerable inter-/intra-observer variability and is difficult to use in assessment of eccentric jet flows. Some parameters obtained by TTE are calculated based on anatomical assumptions, usually resulting in over/underestimation compared with measurements obtained with TEE, CT or MRI (5-7).

TEE does not have the same restrictions of acoustic windows like TTE, and can provide detailed imaging of the right heart. With 3D imaging, regurgitation jets and highly mobile structures (such as vegetation and embolism) are more clearly detailed. Measurements (dimensions, volumes

and velocities) show a good correlation with those obtained via CT or MRI. TEE also provides valuable real-time guidance for device placement in transcatheter procedures such as TAVR and TMVR. However, TEE usually requires sedation, making it unsuitable for highly frail patients or patients with an unstable hemodynamic state. TEE is also risky to perform in patients with esophageal hernias, varices and etc. (*Table 2*). This modality had many anatomical "blind spots", unable to provide accurate imaging of vascular structures outside of the heart. In addition, 3D TEE is useful to assess the tricuspid valve morphology for
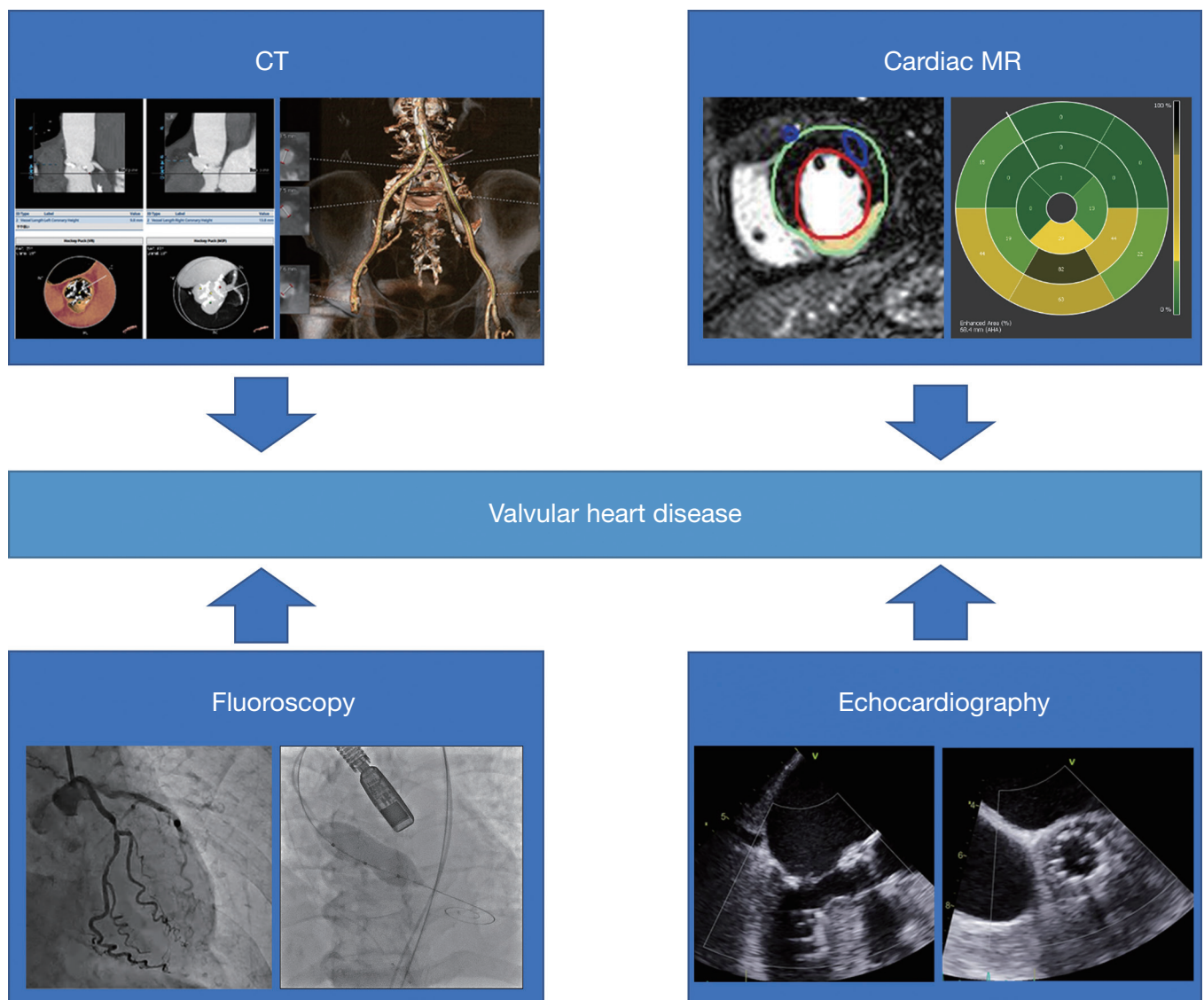
Figure 2 Multimodality assessment for valvular heart disease. Echocardiography, computed tomography and magnetic resonance imaging have played a supplementary role in diagnosis for severity, deciding the timing/type of treatment, detection of post procedural complications, and prognostic predictions. CT, computed tomography; MR, magnetic resonance.

the intervention (8).

CT with its high spatial resolution, is a swift and accurate tool for assessing the physical characteristics of the heart and surrounding structures (9). It provides additional detail on the degree/extent of calcifications and presence of coronary artery disease. Its excellent spatial resolution enables accurate measurements of valvular orifice and surrounding area, useful for planning the optimal approach and landing zones for device implantation. As a typical example of CT usage, Casset *et al.*, reported a reduction

in stroke occurrence, vascular complications, paravalvular aortic regurgitation (AR) after integrating CT data with measurements acquired via TTE and TEE (10). In spite of its superior spatial resolution, CT is unable to provide detailed information on the tissue composition of the valve and myocardium. Another drawback for this modality is the requirement of contrast agents and ionizing radiation.

MRI boasts a high reproducibility, simultaneously visualizes both the right and left heart and provides detailed information on myocardial mass and fibrosis. It does not use

Table 1 Characteristics of cardiac imaging modalities

Modality	TTE	TEE	CT	MRI
Strengths	Inexpensive, easy to perform	Greater image quality compared with TTE	Can provide additional information on vascular structures	High reproducibility
	Can provide information on hemodynamic effects	Enables 3D analysis of valve and jet flows	Images are obtained swiftly	Provides information on myocardial function/composition (fibrosis, remodeling)
	Can be employed with stress testing	Can view highly mobile or small structures (vegetation, embolism, etc.)	Provides information of possible routes of access, and can be utilized in simulations	No use of radiation, does not necessarily require contrast agents
	Provides real-time analysis	Provides real-time guidance for transcatheter intervention	Great accuracy in measuring physical dimensions	Simultaneous assessment of LV and RV function (gold standard for evaluation of ventricular function/mass)
	Provides information on valve structure	Can analyze RV function	Enables accurate analysis of calcified areas	Enables relatively accurate measurement of physical dimensions
				Can assess eccentric jets (by using stroke volumes)
Limitations	Limited acoustic window	Highly invasive and requires sedation	Requires use of contrast agent (difficult to use in patients with decreased renal function or allergy)	Limited availability (in terms of both hardware and software)
	Relatively large intra-/inter-observer variability	High risk in frail, hemodynamically, or unstable patients	Uses ionizing radiation	Requires high level of skill for analysis
	Calculations are based on anatomical assumptions, leading to over/underestimations	Has certain anatomical blind spots	Unable to analyze tissue characteristics	Difficult to use in patients with implanted devices, claustrophobia
	Large acoustic shadow by calcification or devices	Risk to employ in patients with esophageal hernia/varices	Difficult to employ in cases with multiple VHD	Difficult to assess calcification
	Difficult to assess RV			Difficult to use ECG gating in cases with arrhythmia
	Difficult to assess eccentric jets			Difficult to accurately measure peak flow velocities in turbulent jets
				Difficult to assess small, highly mobile structures due to insufficient spatial resolution
				Lack of consensus regarding grading of severity

Table 1 (*continued*)

Table 1 (*continued*)

Modality	TTE	TEE	CT	MRI
Role in prognosis	GLS may detect subclinical cardiac dysfunction and predict clinical outcomes post intervention	–	Large annular size may lead to greater paravalvular leakage post TAVR Can predict risk of LVOT obstruction post TMVR Degree of calcification correlated with paravalvular leakage	Can reveal extent of myocardial fibrosis/ remodeling, reverse remodeling may predict clinical outcomes post intervention
Role in post-operative management	Can be used to screen for the presence of post-procedural comorbidities	Can assess the location and degree of paravalvular leakage	Can provide guidance for planning paravalvular leakage closure	Can follow changes in aortic dimensions post AVR

TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; MRI, magnetic resonance imaging; CT, computed tomography; LV, left ventricular; RV, right ventricular; VHD, valvular heart disease; ECG, electrocardiogram; GLS, global longitudinal strain; TAVR, transcatheter aortic valve replacement; LVOT, left ventricular outflow tract; TMVR, transcatheter mitral valve repair; AVR, aortic valve replacement.

Table 2 Check list of TEE

Risk of procedure
Esophageal issues: hernias, dysphagia, ulcers and etc.
Cirrhosis or varices
Sleep apnea or oxygen requirement
Cervical spine issues
Dentures or loose teeth
History of thoracic radiation treatment
Coagulation therapy
Low platelet counts
For females <50 years, possibility of pregnancy
Allergies

TEE, transesophageal echocardiography.

ionizing radiation and does not necessarily require contrast agents. By using direct (for AR) and indirect [for mitral regurgitation (MR)] methods, MRI can accurately calculate regurgitation volumes, even in cases with multiple or eccentric jets. Major limitations for this modality are, high costs, limited availability (of both hardware and software, and analysis expertise), unsuitability with implanted devices and claustrophobic patients. Compared with CT, it has limited spatial resolution, making imaging of highly mobile

or thin structures (valve leaflets, vegetations, embolisms, and etc.) extremely difficult (11,12). Velocity and volume measurements tend to fluctuate in cases with arrhythmias or turbulent flows (13). Generally, measurements obtained with this modality are more accurate than TTE, however currently there is no consensus for cutoff values in determining disease severity. For example, Myerson *et al.* reported that AR quantified with cardiovascular magnetic resonance (CMR) identified clinical outcomes with high accuracy, 85% of subjects with regurgitant fraction >33% progressing to surgery, compared to 8% of subjects with regurgitant fraction <33% (14). Harris *et al.* reported that CMR-derived regurgitant volume for chronic AR was more strongly associated with clinical outcomes than that obtained with TTE (15). According to these results, we can apply the CMR assessment when the grading is undetermined in AR.

Fluoroscopy/catheterization can provide real-time analysis of the coronary arteries and hemodynamic state, and can be employed with stress testing. However, this highly invasive modality requires much radiation exposure and has a constant risk of bleeding/thrombotic complications.

What to look for?

The overview of check points for VHD imaging in TAVR

Table 3 Points of focus prior and post-intervention in AS

When	Points of focus
Prior to intervention	Severity (peak velocity, regurgitant volume, etc.)
	Morphology and number of leaflets
	Calcification of leaflets and surrounding structure
	Dimensions and shape of annulus and LVOT
	Possible routes of approach (in cases of transcatheter interventions)
	Etiology of the VHD in question
	LV, RV function
	Coincidental coronary lesions, thrombi, vegetations
	Signs of remodeling, fibrosis in myocardium
	Dimensions of Valsalva sinus, aorta, coronary height
Post-procedural follow-up	Transvalvular/paravalvular leakage
	Changes in position of prosthetic valve
	Changes in dimensions of aorta
	Changes in LV function (LVEF, remodeling)

AS, aortic stenosis; LVOT, left ventricular outflow tract; VHD, valvular heart disease; LV, left ventricular; RV, right ventricular; LVEF, left ventricular ejection fraction.

are shown in *Table 3*. In aortic stenosis (AS), in addition to peak aortic valve (AV) velocity and valvular orifice area, observations should be made on leaflet shape/calcification, shape and size of Valsalva sinus, appearance and angle of the ascending aorta and position of the coronary ostium. In cases where TAVR is a viable option, peripheral arteries should also be observed as possible points of access. Even in asymptomatic patients or moderate AS, signs of increased myocardial burden, such as changes in myocardial strain in TTE or myocardial fibrosis in MRI, play a crucial role in determining the optimal timing for intervention (16,17). In asymptomatic AS with extensive myocardial fibrosis, the current guideline recommendation for aortic valve replacement (AVR) is not feasible for early risk stratification (18). AS is characterized by a significant increase in diffuse myocardial fibrosis (DMF) then followed by focal myocardial fibrosis (FMF). DMF can be assessed with T1 mapping, while FMF is defined by late gadolinium enhancement. DMF is thought to be reversible, while

FMF is thought to be irreversible, with the latter associated with significantly poor postoperative outcomes (19-22). In a similar manner, regional and global longitudinal strain (GLS) are also reported to have a greater and earlier diagnostic power than left ventricular ejection fraction (LVEF) (23,24). There are also reports of using left atrial (LA) global strain and LA dilation for prediction of AS prognosis, however, whether this is a suitable sign for early intervention remains to be validated (25,26).

In AR, there have been similar findings of myocardial fibrosis to AS in MRI. In addition to valvular morphology and regurgitant volume, observation of the aorta is also important in determining the etiology of the disease. In chronic AR, LV volumetric data obtained via echocardiography (LV end-systolic volume index ≥45 mL/m^2) or CMR (LV end-diastolic volume >246 mL with regurgitant fraction >33%) may be useful for identifying patients at increased risk of clinical progression (27). Late-gadolinium enhancement in CMR has been associated with persisting symptoms, poor LV recovery, compromised event-free survival, and increased risk of mortality in surgical AR cohorts. Subnormal LV longitudinal deformation detected by speckle-tracking echocardiography may predict disease progression in asymptomatic patients (28,29). Both of these signs may occur prior to overt LV dysfunction, being possible determinants for early intervention (30).

In MR, assessment of the valve, left ventricle, left atrium, chordae tendineae and papillary muscles are all important to determine the etiology of the disease. It is also crucial to determine the type of MR (primary or secondary, ischemic or nonischemic) due to the differences in treatment options and post-procedural prognosis (31-33). Past reports have suggested that successful repair for secondary MR was less likely in the presence of mitral valve (MV) deformation, global LV remodeling and local LV remodeling (34). Similar to AR, MRI provides accurate quantifications of regurgitation volumes, with Myerson *et al.*, reporting that by using CMR quantification, 91% of subjects with regurgitant volume ≤55 mL survived to 5 years without surgery compared with only 21% with regurgitant volume >55 mL (35). If TMVR is considered, observation of the left ventricular outflow tract (LVOT) and mitral annulus are also necessary for predicting LVOT obstruction post procedure (36). As in the case of AS and AR, myocardial fibrosis may play a role in long-term clinical outcomes of MR, with its clinical value currently being validated in the mitral FINDER study (a multi-center, prospective, cross-sectional comparison of patients prior to and 9 months

following surgery for chronic severe primary degenerative MR) (37). In the echocardiographic field, GLS is also a strong predictor of post-operative outcome. Several investigators reported that LV GLS was a significant predictor of cardiac outcome, regardless of LV dysfunction, atrial fibrillation or surgery type (38,39).

In mitral stenosis (MS), valve morphology can provide information on disease etiology. Dilation of the left atrium is reported to increase the risk of atrial fibrillation and embolisms, and may be a sign for the necessity of intervention (40). The preferred method of treatment for MS is percutaneous mitral balloon valvuloplasty (PMBV). TTE and TEE play a crucial role in evaluating to suitability for PMBV. The Wilkins score, based on echocardiographic findings, such as leaflet mobility, valvular thickening, subvalvular thickening and calcification, is used to predict PMBV success, with a score of ≤8 predicting favorable outcomes. Assessment of contradictions (atrial thrombi, severe or bicommissural calcification, mitral valve area (MVA) >1.5 cm^2, greater than mild MR, absence of commissural fusion, severe concomitant aortic/tricuspid disease, and etc.) are also performed with echocardiography (41). The atrial remodeling may be different in MS compared with MR, with one group reporting a larger post-operative LAV reduction in MR compared with MS (42).

Mitral annular calcification (MAC) is estimated to be prevalent in 3–6% of patients undergoing MV replacement. The presence of extensive MAC is considered to be associated with worse surgical outcomes, with paravalvular leakage (PVL) and clinical deterioration (43). When considering interventional treatment in MV disease, mitral annular calcification may also become a factor in post-procedural complications, making it a necessity to evaluate the degree and extent of calcification in the mitral annulus along with the valve. Even in patients undergoing TAVR, the presence of MAC cannot be overlooked, with one group reporting severe MAC to be an independent strong predictor of overall mortality and new pacemaker implantation post-TAVR (44).

When and how to employ?

In the current clinical setting, TTE should be the preferred first choice for diagnosis of VHD. Other modalities can be considered when TTE were inconclusive. These modalities should play a more prominent role obtaining information crucial for clinical decision making (*Figure 3*). If the image

quality from TTE is insufficient, further evaluation can be provided with TEE or MRI. CT and fluoroscopy can be utilized to assess cardiac ischemia, while MRI can provide extensive imaging of the myocardium. In cases where there is a mismatch between severity determined by TTE and clinical symptoms, stress echocardiography can be considered to evaluate the hemodynamic effect of the disease, or MRI can be employed to reevaluate the flow volume obtained from TTE (45). When transcatheter intervention is taken into consideration, CT is useful for pre-procedural planning, searching for suitable vascular access routes and optimal landing zones. Signs of myocardial fibrosis, observed with contrast-enhanced MRI, provides hints for estimating post-procedural prognosis and the possibility of LV reverse remodeling.

Roles in post-procedural management

Especially in AS, important points prior to interventions and post procedural follow-up were shown in *Table 3*. Changes in the aorta and device, presence and degree of PVL, changes in LV function and mass should be assessed. Follow-up of dimensions in the aorta and valves can be performed with CT and MRI, which are highly reproducible. TTE can identify PVL, but fails to accurately quantify leakage severity in cases with multiple jets. Regurgitation volume of PVL can be more accurately assessed with MRI, and to some extent aortography (which can be performed immediately after device deployment). 3D imaging obtained via CT and TEE can help in determining the number and location of leaks. These images are crucial in planning secondary intervention for severe PVL (46). Myocardial strain evaluated with TTE, and reverse remodeling observed via MRI may provide estimates for LV function recovery and long-term prognosis. Nucifora *et al.*, reported a long-term improvement of LV myocardial deformation and regression of left ventricular hypertrophy (LVH) in both TAVR and surgical aortic valve replacement (SAVR) patients (47).

In TAVR, significant residual AR is associated with greater mortality. A meta-analysis conducted by Takagi *et al.* reported a 2-fold increase in 1-year all-cause mortality for patients with moderate to severe paravalvular AR post-TAVR (48). However, determining AR severity post-TAVR using TTE is challenging, due to the presence of multiple eccentric jets that are parallel and irregular in shape. Considerable artefacts caused by the prosthetic valve and calcifications also obscure significant regurgitant jets
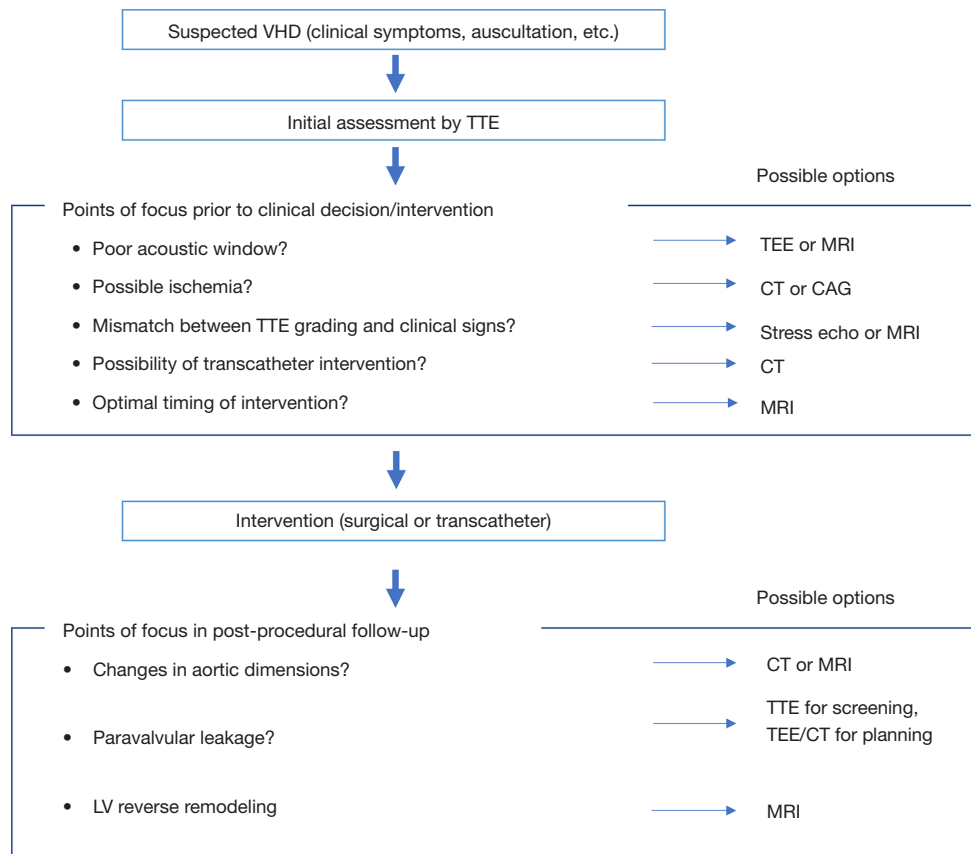
Figure 3 A chart of multimodality imaging for clinical decision making. Multimodalities should play a more prominent role obtaining information crucial for clinical decision making. TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; MRI, magnetic resonance imaging; CT, computed tomography; CAG, coronary angiography; LV, left ventricular.

and result in underestimation of severity (49). Ribeiro *et al.* reported that residual AR with a regurgitation fraction greater than 30% best predicted poorer clinical outcomes, with CMR performed 40 days post-TAVR showing a greater association than early TTE follow-up (50). Aortic root angiography also shows decent accuracy post-TAVR. However, this method is characterized by significant overlap among Sellers classifications and has a considerable intra-/inter-observer variability on assessing AR post-TAVR (51). In addition to residual AR, some attention should also be paid to concomitant valvular diseases, such as MR. However, the clinical value of these VHDs post-TAVR is still up for debate (52).

Conclusions

Currently, TTE is still the first-line imaging modality for assessment of VHD. In the guidelines, other imaging modalities would have been considered when TTE imaging was inconclusive, hence playing second fiddle to TTE. However, these modalities also have their own unique strengths. If employed properly, these modalities have the potential to play a more prominent role in clinical decision making.

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Footnote

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