JCS/JSCS/JATS/JSVS 2020 Guidelines on the Management of Valvular Heart Disease

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on behalf of the Japanese Circulation Society Joint Working Group

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Refer to Appendix 1 for the details of members.
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<tr>
<td>2D</td>
<td>two-dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>three-dimensional</td>
</tr>
<tr>
<td>ACC</td>
<td>American College of Cardiology</td>
</tr>
<tr>
<td>AF</td>
<td>atrial fibrillation</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>AR</td>
<td>aortic regurgitation</td>
</tr>
<tr>
<td>AS</td>
<td>aortic stenosis</td>
</tr>
<tr>
<td>AVA</td>
<td>aortic valve area</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>BNP</td>
<td>brain natriuretic peptide</td>
</tr>
<tr>
<td>BSA</td>
<td>body surface area</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary artery bypass grafting</td>
</tr>
<tr>
<td>CO</td>
<td>cardiac output (mL/min)</td>
</tr>
<tr>
<td>CQ</td>
<td>clinical question</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>DOAC</td>
<td>direct oral anticoagulant</td>
</tr>
<tr>
<td>EACTS</td>
<td>European Association of Cardiology and Thoracic Surgery</td>
</tr>
<tr>
<td>EOA</td>
<td>effective [valve] orifice area</td>
</tr>
<tr>
<td>EROA</td>
<td>effective regurgitant orifice area</td>
</tr>
<tr>
<td>ESC</td>
<td>European Society of Cardiology</td>
</tr>
<tr>
<td>FAC</td>
<td>fractional area change</td>
</tr>
<tr>
<td>FED</td>
<td>fibroelastic deficiency</td>
</tr>
<tr>
<td>HF</td>
<td>heart failure</td>
</tr>
<tr>
<td>HR</td>
<td>heart rate (beats/min)</td>
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<tr>
<td>JCS</td>
<td>Japanese Circulation Society</td>
</tr>
<tr>
<td>LA</td>
<td>left atrium/left atrial</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricle/left ventricular</td>
</tr>
<tr>
<td>LVEDD</td>
<td>LV end-diastolic diameter</td>
</tr>
<tr>
<td>LVEF</td>
<td>left ventricular ejection fraction</td>
</tr>
<tr>
<td>LVESD</td>
<td>LV end-systolic dimension</td>
</tr>
<tr>
<td>mPG</td>
<td>mean pressure gradient</td>
</tr>
<tr>
<td>MELD</td>
<td>Model for End-stage Liver Disease</td>
</tr>
<tr>
<td>MR</td>
<td>mitral regurgitation</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>MS</td>
<td>mitral stenosis</td>
</tr>
<tr>
<td>MVA</td>
<td>mitral valve area</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
</tr>
<tr>
<td>OMC</td>
<td>open mitral commissurotomy</td>
</tr>
<tr>
<td>PASP</td>
<td>pulmonary artery systolic pressure</td>
</tr>
<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
</tr>
<tr>
<td>PISA</td>
<td>proximal isovelocity surface area</td>
</tr>
<tr>
<td>PPM</td>
<td>patient-prosthesis mismatch</td>
</tr>
<tr>
<td>PR</td>
<td>pulmonary regurgitation</td>
</tr>
<tr>
<td>PS</td>
<td>pulmonary stenosis</td>
</tr>
<tr>
<td>PT-INR</td>
<td>international normalized ratio of prothrombin time</td>
</tr>
<tr>
<td>PTMC</td>
<td>percutaneous transseptal mitral commissurotomy</td>
</tr>
<tr>
<td>RA</td>
<td>right atrium/right atrial</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>RV</td>
<td>right ventricle/right ventricular</td>
</tr>
<tr>
<td>SAM</td>
<td>systolic anterior motion of the mitral leaflet</td>
</tr>
<tr>
<td>SAVR</td>
<td>surgical aortic valve replacement</td>
</tr>
<tr>
<td>SVD</td>
<td>structural valve deterioration</td>
</tr>
<tr>
<td>TAPSE</td>
<td>tricuspid annular plane systolic excursion</td>
</tr>
<tr>
<td>TAVI</td>
<td>transcatheter aortic valve implantation</td>
</tr>
<tr>
<td>TEE</td>
<td>transesophageal echocardiography</td>
</tr>
<tr>
<td>TR</td>
<td>tricuspid regurgitation</td>
</tr>
<tr>
<td>TS</td>
<td>tricuspid stenosis</td>
</tr>
<tr>
<td>TTE</td>
<td>transthoracic echocardiography</td>
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<td>VHD</td>
<td>valvular heart disease</td>
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</table>
1. Introduction

The “Guidelines on the Management of Valvular Heart Disease” were initially published as the “Guidelines on Non-pharmacological Treatment of Valvular Heart Disease” in 2002, revised in 2007, and again partially revised in 2012. However, advancements in the diagnosis and treatment of VHD have been rapid. The ACC/AHA guidelines were revised in 2014, with some updates in 2017, and the ESC/EACTS guidelines were revised in 2012 and again in 2017. TAVI was introduced in October 2013, and in April 2018 transcatheter treatment was introduced for MR. Evidence from these new transcatheter treatments has accumulated. In July 2018, valve-in-valve implantation became covered by insurance for valve dysfunction after bioprosthetic valve replacement. Regarding surgical treatment, progress has been remarkable over the past few years, including the spread of minimally invasive surgery, valve repair, or valve-sparing surgery for patients with AR, as have changes in the selection of prosthetic valves owing to improvements in prosthetic valve technology. In addition, new insights have been gained into the pathophysiology and prognosis of VHD, including low-flow/low-gradient severe AS, MR associated with AF, and isolated functional TR. Treatment for HF is essential for VHD with LV dysfunction, and many advances have also been made in the treatment of HF.

Thus, the increased range of treatments for VHD makes it necessary to determine the indications and optimal timing of interventions for each patient. At present, we are in the era of team-based medicine, and the importance of the “Heart Valve Team” is emphasized.

There are very few randomized trials on the treatment of VHD, and there is a lack of high-quality evidence regarding the surgical indications and timing. The accumulation of evidence from Japan is limited, but based on the insights

<table>
<thead>
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<th>Table 1. Class of Recommendation</th>
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<tr>
<td><strong>Class I</strong></td>
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<td><strong>Class II</strong></td>
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<tr>
<td><strong>Class IIa</strong></td>
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<tr>
<td><strong>Class IIb</strong></td>
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<td><strong>Class III</strong></td>
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<td><strong>Level B</strong></td>
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<td><strong>Level C</strong></td>
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<td><strong>Evaluation by systematic review</strong></td>
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<tr>
<td></td>
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<tr>
<td>CQ 1</td>
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<tr>
<td>CQ 2</td>
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<tr>
<td>CQ 3</td>
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<tr>
<td>CQ 4</td>
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<tr>
<td>CQ 5</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AS, aortic stenosis; AVA, aortic valve area; LVEF, left ventricular ejection fraction; LVESD, LV end-systolic dimension; MR, mitral regurgitation; TR, tricuspid regurgitation.
and clinical experience gained from previous observational studies, the present guidelines have been developed to reflect actual, current clinical practices.

New treatment techniques for VHD are expected to be introduced in the future, and a large amount of evidence is expected to emerge. The present guidelines should be understood to include the most recent data, as well as conventional evidence, to continue to develop the practice guidelines currently available.

This English version is a translated, abbreviated form of the Japanese version; the sections were selected based on their importance, with some parts omitted from the English version.

2. About the Recommendations

The Medical Information Network Distribution Service (Minds), which is operated by the Japan Council for Quality Health Care, has provided different levels of recommendation and evidence. However, we have applied the classes of recommendation and levels of evidence followed in conventional guidelines and are similar to those used in the present ACC/AHA and ESC guidelines (Tables 1,2), because emphasis is placed on widespread use of conventional recommendations and evidence levels within the field of cardiovascular disease, and these easily align with international guidelines.

Some have recommended the use of more scientific methods, such as systematic review, to determine recommendation guidelines.1 The present guidelines cover 5 CQs and comprise a systematic review. For each CQ systematic review, all evidence was assessed to form recommendations in accordance with the methods outlined in Minds 2014.1

Strength of Recommendation
1: Strongly recommended
2: Weakly recommended (proposed)

Strength of Overall Evidence
A (strong): Strong confidence in the estimated effect
B (moderate): Moderate confidence in the estimated effect
C (weak): Limited confidence in the estimated effect
D (very weak): Very little confidence in the estimated effect

Table 3 lists the 5 CQs and recommendations with the systematic review.

II. General Comments

1. Symptoms, Physical Findings, and Blood Tests

1.1 Medical History

The therapeutic strategies for VHD are determined by combining clinical evaluation and quantitative assessment. It is essential to take a detailed medical history, because the presence or absence of symptoms greatly affects the therapeutic strategy. In general, the clinical course of chronic VHD is gradual, so patients may not be aware of symptoms because they subconsciously avoid activities that cause the symptoms. Such a trend is seen most commonly in the elderly, and thus, needs to be paid careful attention.

Therefore, rather than simply assessing a patient’s subjective symptoms, questioning regarding signs similar or related to those being reported by the patient may help detect the slow progression of symptoms in daily life. If a patient has a history of HF and is now asymptomatic with medication, the patient should be considered as symptomatic. Documenting the history of complications and treatment is also crucial in differentiating symptoms and determining treatment strategies.

1.2 Physical Findings

The physical findings need to be detailed in order to diagnose VHD and assess its severity.2 When a heart murmur is heard, the phase, strongest point, strength, pitch and other characteristics, and the effects of respiration should be assessed. Although each VHD has its characteristic auscultatory findings, the phase of the murmur should be examined most precisely. In a patient with HF, the intensity of a heart murmur may be low, even in severe VHD. In addition, inspection and palpation are useful for evaluating VHD. Inspection and analysis of the jugular vein, which are useful in the evaluation of HF, are important. Evaluation of the location and characteristics of the apex beat and the characteristics of the carotid pulse by palpation are useful for the diagnosis of VHD.

1.3 Biomarkers

It has been reported that serum levels of BNP are useful for both assessing the severity of VHD and predicting the prognosis.3,4 The level may also be useful in determining therapeutic interventions, especially for patients with asymptomatic VHD.5-8 However, the optimal cutoff value for determining the therapeutic strategy in each VHD has not been clarified.8
2. Echocardiography (Tables 4, 5)

TTE is an essential imaging modality for the definitive diagnosis of VHD, evaluation of hemodynamics, and determination of therapeutic strategies. Therefore, TTE should be performed in all patients with known or suspected VHD (Class I). A comprehensive examination is recommended, including assessment of the mechanism of VHD, qualitative and quantitative evaluation of regurgitation and stenosis, and evaluation of chamber size, cardiac function, and hemodynamics. For patients with asymptomatic VHD, regular echocardiographic follow-up is recommended (Class I). Table 5 shows the approximate follow-up period according to severity.

If the TTE examination provides a suboptimal evaluation or further examinations are required, TEE is recommended (Class I). TEE is particularly useful for observing the mitral valve and LA. Recommendations for each VHD are described in the following sections.

### 2.1 Evaluation of Valvular Regurgitation

Valvular regurgitation is classified into 2 types: organic (primary regurgitation) accompanied by structural changes such as leaflet perforation and prolapse, and functional (secondary regurgitation) caused by ventricular and atrial remodeling despite no organic changes in the valve structure itself. Echocardiography is the first choice for assessing the mechanism and severity of regurgitation. When interpreting the mechanism and severity of regurgitation, a single index may not be sufficient to make an accurate diagnosis. Therefore, evaluation in combination with multiple findings or indices is needed. Color Doppler is the primary tool for evaluation and is commonly used in the clinical setting to assess the site, direction, and severity of the regurgitant flow. However, there are issues with this evaluation method, based on the regurgitant area. Therefore, a semiquantitative evaluation method measuring the width of the vena contracta of the regurgitant flow and quantification by the EROA, regurgitant volume, and regurgitant fraction are recommended. These quantitative indices are measured using the PISA method (Figure 1) and the volumetric method based on Doppler imaging (Figure 2). However, each method has multiple assumptions and sources of error that necessitate careful interpretation of the measurements.

LV size and LVEF are important in determining the therapeutic strategy in regurgitant valvular diseases. It is recommended that the LV diameter is measured at the top of the mitral leaflet. The LVEF should be measured using the modified Simpson’s method.

### 2.2 Evaluation of Valvular Stenosis

With the increase in the number of patients with AS, due to the aging population, and the rapid spread of TAVI use, echocardiography is required to make a more accurate diagnosis of AS. Estimation of the AVA is essential in the diagnosis of AS and there are 2 methods of measurement: (1) trace the 2D image using the planimetry method or (2) use the continuity equation using the Doppler method and 2D images. The continuity equation estimates the area of the functional valve orifice where the blood flow passes through the aortic valve at its most contractile point, whereas the planimetry method measures the anatomical valve orifice area. The functional valve orifice is located on the aortic side relative to the location of the anatomical valve orifice, and the AVA measured by the continuity equation is smaller than that with the planimetric method. Because it is often difficult to draw accurate cross-sections if there is advanced calcification, the use of the planimetric method is not particularly recommended for TTE. Conversely, it is necessary to keep in mind that errors may occur due to several factors in the continuity equation. For this reason, when there is a discrepancy between the estimated AVA and the clinical findings, echocardiographic remeasurement and AVA measurement by CT should be considered. In addition, these indices are affected by stress-related parameters, such as aortic pressure and CO, so careful interpretation of the measurements is necessary, considering the diversity of each pathophysiology.

For MS, evaluations using the mPG at the mitral valve and the pressure half-time method using the continuous-wave Doppler method are recommended. As with evaluation of the aortic valve, the planimetry method may cause errors in estimation of the MVA.

In the evaluation of regurgitation and stenosis, we need to understand the pitfalls of each measurement method. Each evaluation should be performed using multiple indices. If there are discrepancies among the results, the cause should be investigated, and evaluation using other modalities should be considered depending on the situation.

### 2.3 Evaluation of Pulmonary Hypertension and RV Function

Left-sided VHD may be accompanied by secondary pulmonary hypertension due to increased LA pressure. Pulmonary hypertension at rest and during exercise has been known to be associated with symptoms and prognosis, especially in AS and MR. Therefore, the PASP should be estimated for VHD. The estimated PASP can be obtained by calculating the RV systolic pressure using the simplified Bernoulli equation, which is based on the maximum velocity of the TR, the RA pressure estimated using the inferior vena cava.

#### Table 5. Frequency of Echocardiographic Examinations in Asymptomatic Patients With Valvular Heart Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Aortic stenosis</th>
<th>Aortic regurgitation</th>
<th>Mitral stenosis</th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Every 3–5 years</td>
<td>Every 3–5 years</td>
<td>Every 3–5 years</td>
<td>Every 3–5 years</td>
</tr>
<tr>
<td>Moderate</td>
<td>Every 1–2 years</td>
<td>Every 1–2 years</td>
<td>Every 1–2 years</td>
<td>Every 1–2 years</td>
</tr>
<tr>
<td>Severe</td>
<td>Every 6–12 months</td>
<td>Every 6–12 months</td>
<td>Every 1 year</td>
<td>Every 6–12 months</td>
</tr>
</tbody>
</table>

LV, left ventricle; MVA, mitral valve area; Vmax, maximum velocity.
maximum diameter, and the respiratory variability. An estimated PASP >35 mmHg is suggestive of pulmonary hypertension. However, in cases of an unclear TR waveform, PASP may be over- or underestimated. It should also be noted that in severe TR, the laminar regurgitant flow often results in an inaccurate estimation of the RV systolic pressure using the simplified Bernoulli equation. In patients without TR or with an unclear TR waveform, the mean pulmonary artery pressure can be estimated from the acceleration time of the pulmonary artery blood flow and the maximum velocity of the pulmonary regurgitant velocity waveform.

Pulmonary hypertension and tricuspid or pulmonary valve disease can cause RV dysfunction. Thus, RV function should be assessed in combination with the TAPSE, tissue Doppler-derived tricuspid annular systolic velocity, and FAC (Figure 3). However, in cases of significant TR, these indices may overestimate RV systolic function, so it may be challenging to evaluate RV systolic function correctly.

3. Other Noninvasive Investigations

3.1 Stress Testing

In patients with VHD, the severity of the condition may not match the clinical symptoms or findings. The purpose
of stress testing is to clarify the need for further intervention in such cases. There are 2 types of stress tests: exercise or pharmacological. Exercise stress tests that can assess symptoms and hemodynamic changes associated with exertion are preferred. Evidence has accumulated regarding the usefulness of exercise stress echocardiography, which can evaluate cardiac function and hemodynamics during exercise stress testing.

Figure 3. Representative methods to assess right ventricular (RV) systolic function. (A) Tricuspid annular plane systolic excursion (TAPSE, mm); the double arrow distance shows the TAPSE. The normal range is ≥17 mm. (B) Tissue Doppler-derived systolic velocity of tricuspid annulus (S', cm/s). The normal range is ≥10 cm/s. (C) RV fractional area change (FAC, %): FAC = (A1 − A2)/A1. A1, area at end-diastole; A2, area at end-systole. The normal range is ≥36%. LA, left atrium; LV, left ventricle; RA, right atrium.

Table 6 shows the recommended level of stress testing that is indicated for each type of VHD.

In AS, stress echocardiography is recommended for patients with asymptomatic severe AS to confirm the absence of symptoms, or for risk stratification for cardiovascular events (Class IIa). Further, in patients with low-flow/low-gradient AS and LV dysfunction, low-dose dobutamine stress echocardiography is recommended to distinguish true-severe AS from pseudo-severe AS and for confirming the LV contractile reserve.

In MR, stress testing is recommended for asymptomatic patients with severe primary chronic MR and for symptomatic patients with non-severe MR during resting echocardiographic examination (Class IIa).

Because secondary MR changes dynamically, exercise stress echocardiography is useful for understanding the pathophysiology and predicting the prognosis. However, there is still insufficient evidence for determining the thera-

Table 6. Recommendations of Valvular Stress Echocardiography

<table>
<thead>
<tr>
<th>Valve disease</th>
<th>Type</th>
<th>Indications</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral regurgitation</td>
<td>Chronic primary MR</td>
<td>In asymptomatic patients with severe MR or symptomatic patients with moderate MR, exercise testing is reasonable to confirm the absence/presence of symptoms, to assess changes of PASP and LV function with exercise</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Secondary MR</td>
<td>In asymptomatic patients with severe MR or symptomatic patients with moderate MR, exercise testing is reasonable to confirm the absence/presence of symptoms, to evaluate the changes in MR severity, and systolic pulmonary artery pressure during exercise, and to determine the indications for mitral valve surgery</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>Asymptomatic severe AS</td>
<td>Exercise testing is reasonable to confirm the absence of symptoms, to assess hemodynamic changes with exercise, and to stratify the risk of cardiovascular events</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Symptomatic low-flow/low-gradient severe AS with LVEF &lt;50%</td>
<td>Low-dose dobutamine stress echocardiography is reasonable to differentiate true- from pseudo-severe AS and assess LV contractile reserve</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
<td>In patients with discordance between symptoms and AR severity, exercise testing is used to assess symptoms, exercise tolerance, and LV response to stress</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

AS, aortic stenosis; AR, aortic regurgitation; CABG, coronary artery bypass grafting; COR, Class of Recommendation; LOE, Level of Evidence; LV, left ventricular; LVEF, LV ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; PASP, pulmonary artery systolic pressure.
4. Invasive Investigations (Table 7)

Because the diagnosis and severity of VHD can usually be assessed with TTE and TEE, invasive cardiac catheterization is not always necessary. However, assessment of severity and hemodynamics using cardiac catheterization is reasonable for patients who have difficulty evaluating by echocardiography for patients showing a discrepancy between their clinical symptoms and the echocardiographic findings (Class IIa).

In addition to coronary angiography, left ventriculography is used to evaluate LV size and LV contractility, wall motion abnormalities, and MR. This method also evaluates the cardiac load by measuring LV end-diastolic pressure and the severity of AS by measuring the pressure gradient between the aorta and the LV. Aortography is used in the evaluation of AR and the ascending aortic diameter. The severity of regurgitation is graded on a 4-level scale. It is important to place the pigtail catheter in the appropriate position and acquire images with the correct amount of contrast agent to be able to precisely examine the degree of regurgitation. In VHD, right cardiac catheterization is important for evaluating the pulmonary artery pressure and the pulmonary capillary wedge pressure. In MS, the MVA is calculated by measuring the pressure gradient between the LV and the pulmonary capillary wedge pressure. Severe MR may be characterized by an increased V wave of the pulmonary capillary wedge pressure.

Preoperative coronary angiography is recommended for patients with severe VHD with a history of coronary artery disease, suspected myocardial ischemia, or impaired LV function; males or post-menopausal females over 40 years of age; and patients with at least 1 cardiovascular risk factor (Class I). This procedure is also recommended for patients with suspected ischemia in moderate- to severe functional MR (Class IIa).

5. Risk Assessment

5.1 JapanSCORE and Comprehensive Risk Assessment

Risk assessment prior to heart valve surgery is important to ensure “quality control in surgery” (improvement of the quality of cardiac surgery and medical safety for patients). Predicted operative mortality can be calculated using existing risk calculators such as the JapanSCORE, EuroSCORE II, and STS score. Risk assessment before transcatheter treatment for VHD is traditionally conducted with the foreign risk calculators, but should also be performed with the JapanSCORE, a similar assessment based on Japanese clinical data. In addition to the 30-day operative mortality, the JapanSCORE 2 can predict the incidence of 7 major complications, namely, stroke, reoperation for bleeding, new requirement of dialysis, deep sternal infec-

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Table 7. Recommendations of Invasive Examination for Valvular Heart Disease

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative coronary angiography is recommended for patients with severe valvular disease who have any of the following: • History of coronary artery disease • Findings that suggest myocardial ischemia • Deterioration of left ventricular function • Males over 40 years old, postmenopausal females • One or more cardiovascular risk factors</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Assessment of severity and hemodynamics by cardiac catheterization is reasonable for patients who are difficult to evaluate by echocardiography or for patients showing discrepancy between clinical symptoms and echocardiographic findings</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>Coronary angiography is reasonable for patients with moderate to severe secondary mitral regurgitation and suspected involvement of myocardial ischemia</td>
<td>IIA</td>
<td>C</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; LOE, Level of Evidence.
Figure 4. Comprehensive risk assessment.
- Surgical risk should be evaluated by the Heart Valve Team.
- Representative assessment tools are shown for both Frailty and Cognitive function.

*1 Patient data include age, body surface area, sex, body mass index, current smoker status, history of diabetes mellitus and its treatment, chronic kidney disease (CKD) and hemodialysis, hypertension, infective endocarditis, chronic lung diseases, carotid artery disease, extracardiac vascular disease, history of cerebrovascular accident, consciousness disturbance within 24 h, history of heart valve surgery, previous coronary intervention, myocardial infarction, New York Heart Association (class 0–II, III, IV), angina pectoris, cardiogenic shock, history of arrhythmia, use of inotropic agents, mitral valve stenosis, aortic valve stenosis, number of diseased vessels in coronary artery, left ventricular function, valve regurgitation sites and the degree or regurgitation, emergency status, concomitant coronary artery bypass grafting, unavailable coronary artery surgery, surgical methods (e.g., replacement, repair, aortic root replacement), and double or triple valve surgery.

*2 GOLD=Global Initiative for Chronic Obstructive Lung Disease, Stage I=mild (%FEV1 ≥ 80%), Stage II=moderate (50% ≤ %FEV1 < 80%), Stage III=severe (30% ≤ %FEV1 < 50%), Stage IV=very severe (%FEV1 < 30%).

*3 CKD=chronic kidney disease eGFR categories (mL/min/1.73m²) description and range: G1=normal or high (≥ 90), G2=mildly decreased (60–89), G3a=mildly to moderately decreased (45–59), G3b=moderately to severely decreased (30–44), G4=severely decreased (15–29), G5=kidney failure (<15), 5D=dialysis.

*4 Frailty: 1=very fit, 2=well, 3=managing well, 4=vulnerable, 5=mildly frail, 6=moderately frail, 7=severely frail, 8=very severely frail, 9=terminally ill.

*5 HDS-R=revised Hasegawa dementia scale, MMSE=Mini-Mental State Examination, MoCA=Montreal Cognitive Assessment.
tion, prolonged ventilation >24h, gastrointestinal complication, and intensive care unit stay >7 days. These predictive data are useful in perioperative management. The JapanS-CORE2 is now available via a mobile software application and can be easily accessed on a smartphone. Although the input data used to calculate the score can vary, frailty (see Section 1.6: Special Considerations for Elderly Patients), procedure-specific factors, and alternative approaches, such as right minithoracotomy, are not included in this scoring system. In this regard, the 2014 AHA/ACC “Guideline for the Management of Patients With Valvular Heart Disease” proposes a “comprehensive risk assessment”, including evaluation of frailty, major organ damage, and procedure-specific factors in addition to predicted operative mortality. Figure 4 shows the comprehensive risk assessment according to the present guideline. In the clinical setting, the surgical risk assessment should be based on multidisciplinary and comprehensive discussions among the Heart Valve Team. It is important to note that there is no absolute way to evaluate frailty or cognitive function.

5.2 Caution Regarding Comorbidities, Steroid Users, and Anticoagulation Drugs

5.2.1 Cognitive Impairment

With the emergence of a “super-aged” society in Japan, an increasing number of patients with cognitive impairment are expected to undergo cardiac surgeries. Preoperative cognitive impairment indicates the risk of delirium after surgery. With a frequency of onset exceeding 10–20%, delirium is reported to increase operative mortality. Delirium is reported to increase operative mortality, prolonging the duration of hospital stay and increase the risk of postoperative cardiac events. Therefore, the preoperative assessment of cognitive function and postoperative delirium care are crucial to improve outcomes in elderly patients. Shortened operation time, early rehabilitation, perioperative pain management, and high-quality sleep are important in preventing postoperative delirium.

5.2.2 Diabetes Mellitus

Patients with diabetes mellitus are at high risk of surgical site infections such as mediastinitis. The perioperative blood glucose level should be maintained between 140 and 180 mg/dL to prevent both surgical site infections and hypoglycemia. The preoperative HbA1c level is a useful risk assessment marker to predict surgical site infection: ≥7.0% has been reported to increase the risk of mediastinitis.

5.2.3 Liver Cirrhosis

The surgical indications for patients with cirrhosis should be carefully considered because surgical intervention may lead to fatal liver dysfunction. An indocyanine green retention rate at 15 min of over 25%, Child–Pugh classification of B or C, MELD (Model for End-stage Liver Disease) score of over 13, and a low cholinesterase level are reported as markers of poor prognosis after surgery.

5.2.4 Blood Diseases

Blood diseases are reported to be related to perioperative infections and bleeding. To prevent perioperative bleeding, patients with idiopathic thrombocytopenic purpura can be treated with γ-globulin before surgery. Those with hemophilia B can be treated with factor IX before and after surgery. The risk of side effects, such as thromboembolism and acute renal failure, should be considered when administering γ-globulin.

5.2.5 Malignancies

Cardiopulmonary bypass in patients with malignancies is suspected to alter the immune response, tumor progression, and cancer cell metastasis; however, there is no evidence supporting these concerns. Heart valve surgery is therefore not contraindicated in patients with malignancies and should be considered comprehensively based on each patient’s life expectancy and general condition. In cases of hematological malignancy, the rates of postoperative bleeding and infection are as high as 23–57%. Patients with a high risk of thromboembolism, such as those with mechanical valve implantation, as well as those with a history of cerebral infection or a CHA2DS2-VASc score ≥2, should be considered. Warfarin should be adjusted to increase the activated partial thromboplastin time to 1.5–2.5-fold the normal control value, but the risk of bleeding complications should also be carefully considered. Unfractionated heparin should be discontinued 4–6 h before surgery. If prompt correction of the PT-INR is required in emergency cases, administration of vitamin K, factor IX complex, and fresh frozen plasma is recommended. Dabigatran should be discontinued 1–2 days before surgery if the creatinine clearance rate is >50 mL/min or 2–4 days before surgery if it is between 30 and 49 mL/min. If necessary, heparin replacement should be administered 12 h after the termination of dabigatran. Apixaban and edoxaban should be discontinued 48 h and 24 h before surgery, respectively, and replaced with heparin if necessary. Rivaroxaban should be discontinued at least 24 h before surgery.

5.2.6 Steroid Users

Patients with a long-term history of steroid use have a greater risk of compromised immunity, delayed wound healing, gastrointestinal ulcers, hyperglycemia, and acute adrenal insufficiency after surgery. In order to prevent these complications, decreasing the oral steroid dosage may be considered only if the underlying diseases can be properly managed. Perioperative steroid coverage is recommended for patients unable to restart oral steroids soon after surgery.

5.2.7 Oral Anticoagulation Drugs

Preoperative discontinuation of anticoagulation drugs is recommended. Warfarin should be discontinued 3–5 days before surgery and may be replaced with heparin if necessary. Heparin administration is recommended in patients with a high risk of thromboembolism, such as those with mechanical valve implantation, as well as those with a history of cerebral infection or a CHA2DS2-VASc score ≥2. The heparin dosage should be adjusted to increase the activated partial thromboplastin time to 1.5–2.5-fold the normal control value, but the risk of bleeding complications should also be carefully considered. Unfractionated heparin should be discontinued 4–6 h before surgery. If prompt correction of the PT-INR is required in emergency cases, administration of vitamin K, factor IX complex, and fresh frozen plasma is recommended. Dabigatran should be discontinued 1–2 days before surgery if the creatinine clearance rate is >50 mL/min or 2–4 days before surgery if it is between 30 and 49 mL/min. If necessary, heparin replacement should be administered 12 h after the termination of dabigatran. Apixaban and edoxaban should be discontinued 48 h and 24 h before surgery, respectively, and replaced with heparin if necessary. Rivaroxaban should be discontinued at least 24 h before surgery.

5.2.8 Dialysis

The 3 major causes of death after surgery in patients with dialysis are infection, low cardiac output syndrome, and respiratory complications. To improve outcomes, infection control, slow dehydration during dialysis and intensive respiratory management including rehabilitation are imperative. Nonobstructive intestinal ischemia is one of the critical complications after surgery, and its association with norepinephrine administration has been reported.

6. Special Considerations for Elderly Patients

The Japanese average life expectancy is expected to be increasing...
with recent improvements in health awareness, lifestyle, and medical standards. According to statistics from the Ministry of Health, Labor, and Welfare in 2017, the life expectancy was 87.26 years for females and 81.09 years for males, both being among the highest in the world with respect to longevity. According to a 2016 report, the healthy lifespan is 74.79 years for females and 72.14 years for males. Treatment options for the elderly are changing as the healthy lifespan increases, and it is necessary to actively evaluate frailty and cognitive function rather than simply classifying patients as elderly.

6.1 Assessing Frailty
This section is omitted from the English version.

6.2 Preoperative Frailty and Outcomes in Cardiac Surgery
This section is omitted from the English version.

6.3 Special Treatment Strategies for the Elderly
For elderly patients, not simply age and comorbidity, but also frailty (Figure 4) should be evaluated when predicting treatment outcomes. New, minimally invasive treatments with undetermined long-term but favorable short-term results are often beneficial for the elderly, given their relatively shorter remaining life expectancy compared with younger people. However, such treatment is generally expensive. Cost-effective treatment is an important issue for many elderly patients with a relatively short life expectancy. In elderly patients, VHD is often associated with other diseases. In such cases, it is necessary to consider which diseases define the prognosis in order to determine the order of priority to treat. Physicians should not hesitate to provide invasive treatment based on advanced age alone, but should also consider palliative alternatives. A treatment strategy for elderly patients should be fully discussed among the Heart Valve Team after a detailed evaluation of frailty, cognitive function, comorbidity, life expectancy determinants, and the patient’s own desires.

7. Importance of the Heart Valve Team (Heart Team)

Even experienced cardiologists sometimes hesitate when making decisions about treatment for VHD. In particular, for patients with asymptomatic, severe VHD or high surgical risk, difficult decision-making may be required for selecting treatment options, which include transcatheter therapy. There is also a risk of biased decisions, with physicians favoring their own specialty.

Decision-making in treating such complex and severe VHD cases must be done with the cooperation of cardiologists and cardiac surgeons. For some diseases, the extended Heart Valve Team may be required, including cardiologists, interventional specialists, cardiac imaging specialists, cardiac surgeons, anesthesiologists, radiologists, sonographers, and other healthcare professionals. The role of the Heart Valve Team is to consider the risks and benefits of different treatment options and to determine the best method without bias towards their own expertise. For example, determining the surgical indications for elderly patients with AS or choosing between TAVI and SAVR requires the Heart Valve Team to thoroughly discuss the possible surgical risks and treatment effects, as well as the patient’s age, severity of condition, frailty, cognitive function, and comorbidities. The Heart Valve Team must also fully explain the results of their discussion to the patients and families.

A well-balanced Heart Valve Team should be composed of experienced specialists from multiple fields and must be able to determine treatment strategies based on the guidelines after thorough evaluations and consultations. The Heart Valve Team is also required to provide highly specialized medical, transcatheter, or surgical treatment in a timely manner. Furthermore, the accumulation of case-related data and the creation of a national database will enable statistical evaluation of the effects and associated risks of the treatments. It is also important to register the medical results in the Japan Cardiovascular Surgery Database, as the information will help determine future treatment policies and lead to better medical care. In addition, it is desirable that the Heart Valve Team provide a systematic training program for cardiac surgeons, interventional specialists, and imaging specialists.

Although the term “Heart Team” is commonly used, it derives from discussions by cardiac surgeons and cardiologists on whether to choose CABG or catheter interventions for coronary artery diseases. With regard to valvular diseases, it is more important to discuss the severity of the disease, the features of valvular lesions, indications for intervention, and choice of surgical procedures. Therefore, it is essential to discuss these issues within an experienced and well-balanced team with diverse specialties as described above. The Heart Team for VHD described in the European and American guidelines is herein referred to as the “Heart Valve Team”, which means a group of experts who possess knowledge and experience related to VHD.
degenerative and rheumatic MR. MR associated with dilatation or dysfunction of the LV or left atrium is called secondary (functional MR). The underlying causes of MR are listed in Table 9.

The incidence of rheumatic MR has declined in developed countries because of the decreased occurrence of rheumatic fever, although the incidence of mitral prolapse and valve leaflet/annular sclerosis or calcification in the elderly is increasing.

Mitrail valve prolapse involves myxomatous degeneration through accumulation of mucopolysaccharides in the leaflets and chordae tendineae. It may be associated with abnormal connective tissue diseases, such as Marfan syndrome, but is often idiopathic. When rupture or elongation of the chordae tendineae is the primary cause, and degeneration of the leaflet itself is minimal, the prolapse and MR are often localized. These abnormalities are pathologically defined as FED (Figure 5). Conversely, when myxomatous degeneration of a valve leaflet is the primary cause, the leaflet thickens and expands, and billowing occurs (with the leaflet belly inflating toward the LA during systole). Multiple leaflet prolapse sites and multiple MR jets are seen in severe cases. These patients are diagnosed with Barlow’s disease, which is distinct from FED (Figure 5). The intermediate state between FED and Barlow’s disease is called “forme fruste” (French for “incomplete form”). Note that prolapse is defined as the tip of the leaflet exceeding the mitral valve annular plane during systole. By contrast, billowing is a term for the mitral valve morphology described above, irrespective of the presence or absence of prolapse.

Mitrail valve leaflet tethering due to LV dilatation and systolic dysfunction is the most well-known cause of secondary MR. Secondary MR associated with acute or prior myocardial infarction may be referred to as “ischemic MR”. However, that term may include primary MR due to papillary muscle rupture associated with acute myocardial infarction. Cases of LA dilatation due to AF indicate that secondary MR can also occur without LV systolic dysfunction, referred to as “atrial functional MR” and another type of secondary MR. Although there are multiple reports of the mechanism underlying this type of MR, a consensus remains to be established. However, “atrial functional MR” is commonly found with both LA and mitral annular dilatation.

The Carpentier classification considers MR origin based on leaflet motion. Normal leaflet motion, such as that seen with leaflet perforation due to infective endocarditis, congenital cleft, and/or AF-associated annular dilatation, is involved in type I. MR resulting from excessive leaflet motion (i.e., prolapse) is considered as type II. MR resulting from restricted leaflet motion and incomplete valve closure is considered as type III, which includes age-related or rheumatic lesion leading to restricted motion during systole and diastole (type IIIa), and valve tethering causing restricted motion during only systole (type IIIb) (Table 8).

In long-term chronic cases and in the elderly, several factors may occur simultaneously, such as changes in the leaflet, enlargement of the annulus, and LV dysfunction.

### 1.2 Acute and Chronic MR

The etiology of acute MR includes chordae tendineae rupture caused by idiopathic or infective endocarditis, trauma, or papillary muscle rupture associated with acute myocardial infarction. Acute severe MR often causes low CO and pulmonary congestion, and in severe cases, shock.

Conversely, chronic MR involves LV dilatation leading to a compensatory increase in the LV total stroke volume, which avoids low CO and/or pulmonary congestion. LV

---

### Table 8. Etiologies of Mitral Regurgitation

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Etiology</th>
<th>Mitral leaflet</th>
<th>Carpentier type</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV</td>
<td>Tethering due to LV dilatation and/or systolic dysfunction*</td>
<td>Reduced mobility</td>
<td>IIb</td>
</tr>
<tr>
<td>Papillary muscle</td>
<td>Rupture due to myocardial infarction</td>
<td>Prolapse</td>
<td>II</td>
</tr>
<tr>
<td>Cordae tendineae</td>
<td>Elongation or rupture due to degeneration (FED)</td>
<td>Prolapse</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>Rupture due to infective endocarditis</td>
<td>Prolapse</td>
<td>II</td>
</tr>
<tr>
<td>Mitral leaflet</td>
<td>Myxomatous change due to Barlow’s disease</td>
<td>Prolapse</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>Infective endocarditis</td>
<td>Perforation</td>
<td>I</td>
</tr>
<tr>
<td>Mitral leaflet and/or</td>
<td>Senile or rheumatic sclerosis and/or calcification</td>
<td>Reduced mobility</td>
<td>IIIa</td>
</tr>
<tr>
<td>cordae tendineae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA and mitral annulus</td>
<td>LA and mitral annular dilatation mainly due to atrial fibrillation¹</td>
<td>Reduced coaptation (+reduced mobility²)</td>
<td>I (+IIb)</td>
</tr>
</tbody>
</table>

* Etiologies of secondary (functional) MR. The others are etiologies of primary (degenerative) MR. † Atriogenic tethering of posterior mitral leaflet is also suggested as an etiology of functional MR occurring due to LA and mitral annular dilatation. ¹ Reduced mobility due to LA and mitral annular dilatation. ² Reduced mobility due to LA and mitral annular dilatation.

---

### Table 9. Classification and Causes of Mitral Regurgitation

<table>
<thead>
<tr>
<th>Primary (degenerative)</th>
<th>Secondary (functional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Prolapse</td>
<td>• Coronary artery disease, dilated cardiomyopathy</td>
</tr>
<tr>
<td>Idiopathic, Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome, trauma</td>
<td></td>
</tr>
<tr>
<td>• Rheumatic disease</td>
<td>• Atrial fibrillation</td>
</tr>
<tr>
<td>• Sclerosis or calcification of mitral leaflets and/or annulus</td>
<td></td>
</tr>
<tr>
<td>• Infective endocarditis</td>
<td></td>
</tr>
<tr>
<td>• Papillary muscle rupture due to myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>• Congenital lesion</td>
<td></td>
</tr>
<tr>
<td>Mitral cleft, parachute anomaly</td>
<td></td>
</tr>
<tr>
<td>• Autoimmune disease</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus, antiphospholipid syndrome (Libman-Sacks endocarditis)</td>
<td></td>
</tr>
<tr>
<td>• Drugs</td>
<td></td>
</tr>
</tbody>
</table>

---

IZUMI C, EISHI K, et al.
Figure 5. Fibroelastic deficiency (FED), forme fruste, and Barlow’s disease. Modified with permission from Adams DH, Rosenhek R, Falk V. Degenerative mitral valve regurgitation: best practice revolution. *Eur Heart J* 2010; 31: 1958 – 1966.127 Published on behalf of the European Society of Cardiology. All rights reserved. ©The Author 2010.

**Table 10. Grading the Severity of Mitral Regurgitation (MR) by Echocardiography**

<table>
<thead>
<tr>
<th>MR severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Pitfalls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structural</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV and LA size</td>
<td>Normal</td>
<td>–</td>
<td>Dilated</td>
<td>LV and LA size can be within the normal range for patients with acute severe MR. The grading of secondary MR cannot be estimated from LV and/or LA size</td>
</tr>
<tr>
<td><strong>Qualitative Doppler</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color flow jet area</td>
<td>Small, central, narrow, often brief</td>
<td>–</td>
<td>Large central jet (&gt;50% of LA)</td>
<td>Regurgitant grading tends to be underestimated from eccentric wall-impinging jet</td>
</tr>
<tr>
<td>Proximal flow convergence</td>
<td>Not visible, transient or small</td>
<td>–</td>
<td>Large throughout systole</td>
<td></td>
</tr>
<tr>
<td>Continuous wave Doppler</td>
<td>Faint or partial</td>
<td>–</td>
<td>Holosystolic and dense</td>
<td></td>
</tr>
<tr>
<td><strong>Semi-quantitative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vena contracta width (cm)</td>
<td>&lt;0.3</td>
<td>0.3 –0.69</td>
<td>≥0.7</td>
<td>Vena contracta width measured from a single plane is not suitable for the grading of secondary MR</td>
</tr>
<tr>
<td>Pulmonary vein flow</td>
<td>–</td>
<td>–</td>
<td>Minimal to no systolic flow or systolic flow reversal</td>
<td></td>
</tr>
<tr>
<td>Transmitral flow</td>
<td>–</td>
<td>–</td>
<td>E-wave elevation (&gt;1.2 m/s)</td>
<td></td>
</tr>
<tr>
<td><strong>Quantitative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EROA derived from PISA method (cm²)</td>
<td>&lt;0.20</td>
<td>0.20 –0.39</td>
<td>≥0.40</td>
<td>PISA method is not suitable for the grading of secondary MR</td>
</tr>
<tr>
<td>Regurgitant volume (mL)</td>
<td>&lt;30</td>
<td>30 –59</td>
<td>≥60</td>
<td>Regurgitant volume may be lower in patients with low-flow conditions in secondary MR due to LV dysfunction</td>
</tr>
<tr>
<td>Regurgitant fraction (%)</td>
<td>&lt;30</td>
<td>30 –49</td>
<td>≥50</td>
<td>Doppler-derived volumetric method comparing LV inflow and outflow is not suitable for MR grading in patients with cocomitant significant aortic regurgitation</td>
</tr>
</tbody>
</table>

EROA, effective regurgitant orifice area; LA, left atrial; LV, left ventricular; MR, mitral regurgitation; PISA, proximal isovelocity surface area. Produced by reference to Zoghbi et al. *J Am Soc Echocardiogr* 2017; 30: 303–371.10
2. Assessment of Severity

MR is classified as mild, moderate, or severe, which is evaluated mainly by TTE (Table 10). Various qualitative and quantitative evaluation methods have been proposed for assessing the severity of MR, each with certain advantages and disadvantages. Appropriate methods may vary by case. Therefore, the appropriate method for each case should be applied after understanding its strengths and weaknesses, and severity should be assessed comprehensively.

Qualitative evaluation is often used to assess the size of the MR jet using the color Doppler method. Color Doppler is easy to use, although it depends on the cross-sectional settings and the etiology and direction of the jet. Moreover, eccentric jets along the LA wall appear smaller than true regurgitations on color Doppler (due to the Coandă effect), and thus, MR will be underestimated. Other disadvantages of the color Doppler method include significant effects of the machine settings, such as color gain and pulse repetition frequency (velocity range). Quantitative evaluation methods include the PISA method and the Doppler-derived volumetric method. The PISA method is a quantitative method to calculate the EROA and the regurgitant volume, assuming that the proximal flow convergence is hemispherical. The Doppler-derived volumetric method is a quantitative method to determine the LV diastolic filling and systolic ejection volumes. Regurgitant volume is calculated as the difference between these volumes, whereas the regurgitant fraction is calculated using the LV diastolic filling volume. The PISA method should be used for the assessment of primary MR when the regurgitant orifice is localized. However, in the case of multiple MR jets, the PISA method is not suitable because calculating the EROA using only one of the proximal flow convergence points would underestimate the true EROA. The PISA calculations include measuring the MR velocity, and thus, it is not suitable when the MR jet velocity cannot be properly measured from a given angle due to eccentricity. Conversely, with secondary MR, a transverse gap along the coaptation of the anterior and posterior leaflets leads to a regurgitant orifice. Therefore, determination of the EROA, which is calculated assuming that the proximal flow convergence is hemispherical, by the PISA method is often inaccurate. Furthermore, the EROA in secondary MR shows dynamic changes during systole. This is also one of the causes of incorrect quantitative evaluation of secondary MR by the PISA method. Therefore, it is better to use the Doppler-derived volumetric method to quantify regurgitation in secondary MR. The disadvantage of the Doppler-derived volumetric method is that calculating MR concomitant with AR often results in inaccuracies.

3. Primary (Organic) MR

3.1 Pathophysiology and Natural History
This section is omitted from the English version.

3.2 Diagnostics

3.2.1 Symptoms and Physical Findings
This section is omitted from the English version.

3.2.2 Echocardiography
If MR is suspected from the physical findings, the next required examination is TTE (Class I). TTE is used to diagnose the etiology and severity of MR, and to evaluate cardiac function and hemodynamics.

The Carpentier classification is used for MR mechanism evaluation (see section III.2). Primary MR corresponds to types I, II, and IIIa. Classification of the MR mechanism is strongly linked to the choice of surgical treatment. In particular, it is important to identify the location of the prolapse or ruptured tendinous cord with type II.

Evaluation of the location and extent of the prolapse can be performed using multiple cross-sectional images. The regurgitation signal direction obtained by color Doppler is also essential in diagnosing the site of prolapse. In principle, the regurgitation jet flows opposite to the side of the prolapse. It is essential to select a cross-section that shows both the accelerated flow and the regurgitation jet in the same plane.

The grading of severity is shown in Table 10. The EROA (cm²), regurgitant volume (mL/beat), and regurgitation fraction (%) are calculated by the Doppler-derived volumetric method and the PISA method. The quantitative evaluation should then be compared to the semiquantitative findings, with the vena contracta width of the regurgitation jet and regurgitation jet area being compared with the LA area.

TEE is recommended as an alternative to TTE for patients with moderate or severe MR in whom conventional TTE is technically not feasible for assessing the severity and mechanism of the MR (Class I). TEE can provide higher image quality and is useful in cases wherein images cannot be obtained by TTE because of acoustic shadow. Detailed and systematically recorded images provide essential information for evaluation of the mechanism of regurgitation, as well as for estimating reparability. In particular, 3D TEE can provide more information in the preoperative evaluation of mitral valve repair (Class IIa), allowing for the surgeon’s view (or en face view) of the mitral valve.

However, it should be noted that due to sedatives administered changes in the hemodynamic status during the TEE tend to result in an underestimation of the degree of regurgitation. For example, with intraoperative echocardiography, the effects of general anesthesia and the decrease in blood flow because of extracorporeal cardiopulmonary bypass reduce the amount of regurgitation.

Exercise stress echocardiography is reasonable for patients with asymptomatic severe MR or symptomatic moderate MR to evaluate the hemodynamic physiology (Class IIa). It is also useful for evaluating hemodynamic changes and predicting the prognosis.
3.2.3 Other Diagnostic Tests
In recent years, cardiac MRI has been used to assess the size and contraction of the LV and RV as well as the severity of MR (Class IIb). This method is useful when TTE records are insufficient. However, there are limitations to the evaluation of the regurgitation mechanism.\(^{147-149}\)

Cardiac catheterization is often performed to diagnose the presence of coronary artery disease, and sometimes a pressure study is performed to estimate hemodynamic severity. Increased pulmonary capillary wedge pressure, notably an increased V wave, is closely related to shortness of breath symptoms. Left ventriculography may not accurately reflect the severity of regurgitation because it is sometimes affected by the size of the LA. Cardiac catheterization is reasonable if there is a discrepancy between the noninvasive tests and clinical findings or if evaluation with noninvasive tests is not technically feasible (Class IIa).

Cardiac CT may also help to diagnose mitral valve calcification, but currently, there are no clear data on its efficacy or accuracy.

Table 11 lists the recommendation for diagnostic testing for primary MR.

3.3 Surgical Treatment
3.3.1 Surgical Procedures and Results
This section is omitted from the English version.

3.3.2 Indications and Timing of Surgery (Figure 6, Table 12)
a. Chronic Primary MR
Careful evaluation of the symptoms is necessary because the indications for surgical intervention are mainly deter-
Table 12. Indications of Surgery for Severe Chronic Primary Mitral Regurgitation (MR)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV repair is recommended in preference to MV replacement, when a durable repair can be safely accomplished</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Concomitant MV repair or replacement is recommended for patients undergoing cardiac surgery for other indications</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery is recommended for symptomatic patients with LVEF &gt;30%</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>MV surgery is reasonable for symptomatic patients with LVEF ≤30%, when the Heart Valve Team judges that surgery is beneficial</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery is recommended for asymptomatic patients with LVEF ≤60% or LVESD ≥40 mm (LVESDI ≥24 mm/m²)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>MV surgery is reasonable for asymptomatic patients with LVEF &gt;60% and LVESD &lt;40 mm (LVESDI &lt;24 mm/m²) who have new onset of AF or resting PASP &gt;50 mmHg</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>MV repair is reasonable for asymptomatic patients with LVEF &gt;60% and LVESD &lt;40 mm (LVESDI &lt;24 mm/m²) who have neither new onset of AF nor resting PASP &gt;50 mmHg, when durable repair can be safely accomplished</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MV repair may be considered for asymptomatic patients with LVEF &gt;60% and LVESD &lt;40 mm (LVESDI &lt;24 mm/m²) who have neither new onset of AF nor resting PASP &gt;50 mmHg, in the following cases: *progressive LV dysfunction, or *PASP &gt;60 mmHg during exercise, or *left atrial dilatation (left atrial volume index ≥60 mL/m²)</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVESDI, LVESD index (=LVESD/body surface area); MV, mitral valve; PASP, pulmonary artery systolic pressure.

1) LVEF and LVESD

Poor postoperative LV function and prognosis has been demonstrated with preoperative LVEF ≤60% and/or LVESD ≥40 mm, and surgical intervention is indicated by the presence of these triggers (Class I). 152,153

Because the cutoff value of the LV diameter is selected according to the European and American literature, it is reasonable for patients with a small body size to refer to the adjusted values. In the present guideline, an LVESD index ≥24 mm/m² has been offered as a BSA indexed value for the LVESD ≥40 mm in patients with a BSA of <1.7 m².

Although the evidence is not definitive, it has been reported that an LV end-systolic volume of 40 mL/m² measured by 3D echocardiography reflects the postoperative prognosis better than conventional 2D measurements. 154

In addition, surgery can be considered when progressive reduction of LVEF or enlargement of LVESD is noted on serial echocardiographic examinations even if the LVEF >60% or the LVESD ≤40 mm criterion is not met (Class IIb).

2) Pulmonary Hypertension and AF

In cases of preserved LV function, new-onset AF or pulmonary hypertension (PASP >50 mmHg) at rest are indications for mitral valve surgery (Class IIa). 46,155,156 The actual onset of AF is often unclear in chronic severe MR.

Surgical intervention should be considered when main etiology of MR can be definitely determined as organic lesion such as flail leaflet, and improvement of prognosis is highly expected by intervention.

3) Early Surgery for Asymptomatic MR Without Triggers

It is still controversial whether early surgery is indicated for asymptomatic chronic severe MR caused by mitral valve prolapse without any triggers for surgical intervention. Early surgical intervention is recommended on the basis of an adverse long-term prognosis in patients with severe MR, even though cardiac function is maintained. 17 Some clinical studies have suggested a “watchful waiting” strategy with regular follow-up for asymptomatic severe MR when sinus rhythm can be maintained with LVEF >60% or LVESD <40 mm in the absence of pulmonary hypertension. 157 In recent cohort studies, however, surgery following the onset of symptoms was associated with a worse prognosis than that of early asymptomatic surgery. At this time, early surgery is preferred for asymptomatic severe MR if successful mitral valve repair with long-term durability can be expected. 152,158,160 Early surgery for asymptomatic severe MR cases with complex lesions, such as with Barlow’s disease and bileaflet prolapse, may not be recommended, and indications for early surgery should be carefully considered.

Accordingly, mitral valve repair is reasonable for asymptomatic patients with LVEF >60% and LVESD <40 mm (LVESDI index <24 mm/m²) without new-onset AF or a resting PASP >50 mmHg when durable repair can be safely accomplished (Class IIa). Repairability, durability, and surgical risk in each individual case should be carefully discussed by an experienced Heart Valve Team. When a “watchful waiting” strategy is applied for primary severe MR, semi-annual or annual evaluation of symptoms and echocardiographic findings are recommended to judge the proper timing of surgery. 157,161,162

CQ1 should also be referenced regarding early surgery discussion by the Heart Valve Team.
in asymptomatic severe MR.

4) Other Parameters
For asymptomatic severe MR, exercise stress echocardiography is useful for hemodynamic assessment in cases without resting pulmonary hypertension. An estimated PASP >60 mmHg during exercise stress is a benchmark for considering early surgery.50 (Class IIb). However, PASP during exercise should be interpreted with consideration of the effects of other factors, such as age and LV diastolic function. The BNP level may be helpful if the presence of symptoms associated with severe MR is uncertain or if early surgery is borderline suitable.5 LA enlargement (≥60 mL/m²) has been reported to predict a poor prognosis in patients even if they are asymptomatic and may be an indication of surgery (Class IIIb).163

When open-heart surgery is planned for treatment of other cardiac diseases, mitral valve surgery for severe MR should be performed at the same time (Class I). For moderate MR, concurrent surgery with surgery for other cardiac diseases is reasonable when the valve lesion is diagnosed as being repairable (Class IIA). If the valve lesion is not suitable for repair, indications for concurrent surgery should be carefully discussed by an experienced Heart Valve Team.

b. Acute MR
In acute MR, unlike in chronic MR, there is a sudden volume overload on the small, less compliant LA, possibly resulting in a rapid increase in LA pressure followed by acute HF. Sudden-onset HF due to acute severe MR is more difficult to control than HF caused by chronic severe MR and generally requires surgical intervention.

CQ1
Should early surgery be recommended for asymptomatic patients with severe primary MR with LVEF >60% and LVESD <40 mm who do not have new onset AF or pulmonary hypertension?

[Conclusion]
Early surgery is reasonable when a successful and durable repair surgery can be safely performed (2C).

[Strength of Recommendation]
2: Weakly recommended (proposed)

[Strength of Evidence]
C (weak): Limited confidence in the estimated effect

[Comment]
Patients with chronic severe primary MR, even without symptoms and LV dysfunction, have a high likelihood of developing “triggers” such as symptoms, LV dysfunction, AF, or pulmonary hypertension over the course of 6–10 years and require mitral valve surgery.17,157,162,164,165 Previous studies have reported that the overall survival of patients with the “watchful waiting” strategy (follow-up monitoring until the aforementioned triggers are reached and thereafter referred for surgery) was not statistically different from the expected survival.157,162 Conversely, several studies have reported that early surgery prior to the appearance of the triggers improves the prognosis.153,159,160 The advantages of mitral valve repair over prosthetic valve replacement166–169 are widely recognized and therefore repair surgery should be indicated for early surgery, which should be successful and durable and performed safely. The repair feasibility depends on the anatomy of the lesions. For early surgery, therefore, complex lesions that have a high likelihood of requiring mitral valve replacement should be avoided. Lesions limited to one scallop of the posterior leaflet may be a good candidate for early surgery. The ACC/AHA guidelines indicate that mitral repair is reasonable in patients without any triggers in whom the likelihood of a successful and durable repair is >95% with a mortality rate of <1% when performed at highly experienced facilities.29 It is important to recognize that the results of mitral valve repair depend on the experience of the Heart Valve Team, especially the surgeon’s skill and experience.170,171

[Evidence]
There are several reports supporting early surgery before the triggers are reached.

① Kang et al.56 divided patients with asymptomatic severe MR into 2 groups: an early surgery group with no triggers (LVESD <40 mm, LVEF >60%, absence of AF, and absence of pulmonary hypertension) and a group of patients who were referred for surgery when the triggers were reached. For the 207 propensity-matched pairs, the early surgery group had a significantly lower cardiac mortality rate (1% vs. 6% at 12 years; P=0.010) and cardiac event rate (4% vs. 19% at 12 years; P=0.001). The authors also reported in an age-based subanalysis that early surgery was particularly beneficial for patients aged ≥50 years.

② In research from the Mitral Regurgitation International Database registry from 6 centers in 4 countries, a subanalysis (790 patients in total) compared patients with early surgery with no triggers and patients who underwent medical treatment until the onset of triggers.159 At 10 years after the diagnosis, the survival rate was 87% and 82% (P=0.04) for the early surgery and triggered groups, respectively, and the heart failure incidence was 5% and 20% (P<0.001), respectively. This study suggested early surgery is associated with a better prognosis compared with initial medical management.

③ Enriquez-Sarano et al.158 defined the triggers as class I (symptoms, LVESD ≥40 mm, and LVEF ≤60%) or class II (AF and pulmonary hypertension) and stratified 1,512 primary MR patients into 3 groups: patients who underwent mitral valve surgery with a class I trigger; mitral valve surgery with a class II trigger; and early surgery with no trigger but with a high probability of valve repair. The postoperative hospital stay was the shortest for patients with early surgery. Survival rates at 15 years were 42%, 53%, and 70%, respectively, and the incidence of HF for each group was 35%, 27%, and 15%, respectively.153

[Note]
As mentioned, early surgery can be indicated for patients with severe MR with no triggers on the premise that a successful and durable repair is safely feasible. It has been reported that a recurrence of moderate or more than moderate MR after mitral valve repair is associated with adverse LV remodeling and an increased likelihood of death.172 Therefore, careful assessment is mandatory for determining the indications for early surgery. In addition, early surgery is indicated for patients with severe MR on the premise that the MR severity is adequately evaluated. When the severity of MR cannot be confidently diagnosed,
or there are difficulties in making a clear decision about early surgery, other triggers such as LA size,\textsuperscript{163,173-174} changes in pulmonary hypertension on exercise echocardiography,\textsuperscript{175} exercise capacity by cardiopulmonary exercise testing,\textsuperscript{59,176} myocardial strain,\textsuperscript{177,178} BNP,\textsuperscript{5} and change in LV function over time can be considered.

As the cutoff value for LV diameter, one of the triggers that is an indication for surgery, is selected based on European and American guidelines, it is reasonable for patients with a small body size to refer to the appropriate adjustment values. In the present guideline, an LVESD index $\geq 24$ mm/m$^2$ for patients with BSA $\leq 1.7$ m$^2$ is offered as a BSA-indexed value for an LVESD $\geq 40$ mm, which is one of the triggers that indicates LV remodeling.

### 4. Medical Therapy and Follow-up

This section is omitted from the English version.

#### 4.1 Pathophysiology and Natural History (Figures 7, 8)

This section is omitted from the English version.

#### 4.2 Diagnostics

##### 4.2.1 Symptoms and Physical Findings

This section is omitted from the English version.

##### 4.2.2 Echocardiography

In the management of HF, it is important to assess the possible etiology and hemodynamic status using the medical history, physical findings, ECG, or chest X-ray, and TTE. TTE plays a crucial role in the diagnosis of baseline heart disease and hemodynamic conditions in patients with HF. TTE can evaluate regional or diffuse LV wall motion abnormality, the degree of LV dysfunction with LV dilatation, and characteristic leaflet tenting/tethering without structural abnormality (Class I). The degree of tethering is generally evaluated by measuring the tenting area and height (or length) using 2D echocardiography (Figure 9). Although there is not a definitive recommendation regarding the measurement site, the tenting area and tenting height are commonly measured in the parasternal long-axis view at the center of the annulus in mid-systole.\textsuperscript{179} The greater the tethering degree, the greater the amount of MR.\textsuperscript{129} Severe tethering is associated with recurrence after mitral annuloplasty. Because of the multiple factors that can affect the postoperative result after mitral valve repair surgery, it is difficult to set a threshold of tenting area or length that accurately predicts postoperative recurrence.\textsuperscript{180-182}

Commonly in secondary MR, color Doppler echocardiography shows a regurgitant jet toward the center of the LA, in a slightly posterior direction. The regurgitant jet generally has a wide regurgitant orifice together with a coaptation line; it is well-observed in the bicommissural view (along the commissure–commissure plane) from the apical approach.

Multiplane TEE is useful for detailed observation of the valve's structure, regurgitation sites, and regurgitant severity.

#### 4.3 Secondary (Functional) MR Associated With LV Dysfunction

##### 4.3.1 Pathophysiology and Natural History

This section is omitted from the English version.

##### 4.3.2 Diagnostics

This section is omitted from the English version.

##### 4.3.3 Echocardiography

In the management of HF, it is important to assess the possible etiology and hemodynamic status using the medical history, physical findings, ECG, or chest X-ray, and TTE. TTE plays a crucial role in the diagnosis of baseline heart disease and hemodynamic conditions in patients with HF. TTE can evaluate regional or diffuse LV wall motion abnormality, the degree of LV dysfunction with LV dilatation, and characteristic leaflet tenting/tethering without structural abnormality (Class I). The degree of tethering is generally evaluated by measuring the tenting area and height (or length) using 2D echocardiography (Figure 9). Although there is not a definitive recommendation regarding the measurement site, the tenting area and tenting height are commonly measured in the parasternal long-axis view at the center of the annulus in mid-systole.\textsuperscript{179} The greater the tethering degree, the greater the amount of MR.\textsuperscript{129} Severe tethering is associated with recurrence after mitral annuloplasty. Because of the multiple factors that can affect the postoperative result after mitral valve repair surgery, it is difficult to set a threshold of tenting area or length that accurately predicts postoperative recurrence.\textsuperscript{180-182}

Commonly in secondary MR, color Doppler echocardiography shows a regurgitant jet toward the center of the LA, in a slightly posterior direction. The regurgitant jet generally has a wide regurgitant orifice together with a coaptation line; it is well-observed in the bicommissural view (along the commissure–commissure plane) from the apical approach.

Multiplane TEE is useful for detailed observation of the valve's structure, regurgitation sites, and regurgitant severity.
In addition, 3D observation is helpful in the assessment of valve morphology and regurgitation, and 3D TEE is mandatory for perioperative assessment of transcatheter mitral valve edge-to-edge repair surgery (Class I).

In the assessment of secondary MR, stress echocardiography is useful for evaluating the severity of the MR and the RV pressure during exercise (Class IIa). According to some reports, pharmacological stress echocardiography may be useful when reperfusion therapy is being considered for ischemic MR.

### 4.2.3 Other Diagnostic Tests
Cardiac MRI may be useful when the assessment of ventricular size and function by echocardiography is not conclusive (Class IIb). In functional MR, delayed enhancement may contribute to the assessment of myocardial fibrosis. Myocardial scintigraphy would also be useful to evaluate myocardial viability in patients with secondary MR due to LV remodeling.

Coronary angiography is required for the diagnosis of coronary artery disease, but it is not necessary if the number of coronary risk factors is low and the coronary CT scans are negative for coronary lesions. Because the degree of regurgitation and hemodynamics can be diagnosed by Doppler echocardiography, left ventriculography and right cardiac catheterization are not necessarily performed. These invasive tests (Class IIa) are recommended when noninvasive tests are not conclusive in the evaluation of MR severity or hemodynamic assessment.

Table 13 lists the tests recommended for secondary MR.

### 4.3 Surgical Treatment

#### 4.3.1 Surgical Procedures and Results
This section is omitted from the English version.

#### 4.3.2 Indications and Timing of Surgery (Figure 10, Table 14)
Eliminating MR may not be a perfect solution for secondary MR because it is a ventricular disease, not a valvular disease. Therefore, adequate medical treatment for HF is mandatory (Class I). In terms of surgical treatment, ischemic cardiomyopathy, in which recovery of LV function by simultaneous revascularization can be expected, and non-ischemic cardiomyopathy, in which surgery helps manage the MR only, should be considered separately. For ischemic MR without indications for revascularization, surgical indications should be considered using the same strategy as for non-ischemic cardiomyopathy.

PCI and CABG are revascularization methods for the treatment of ischemia. The difference between them is that CABG allows a concomitant valvular procedure and other surgical procedures whereas PCI can only improve the ischemia. The choice between CABG and PCI is based on whether it is necessary to perform a simultaneous operation on the mitral valve and whether CABG is safe for high-risk patients even if no mitral valve surgery is indicated. If CABG is not suitable because of patient risk, PCI should be selected to treat myocardial ischemia. Transcatheter mitral edge-to-edge repair should also be considered if indicated. Each case should be discussed individually in this regard.

#### a. Severe MR

1. **When Revascularization by CABG Is Indicated**

   Isolated CABG may improve LV function and reduce MR if the postero-inferior region is viable; however, in cases of severe MR, isolated CABG is usually not sufficient to eliminate MR. Secondary MR has been reported to worsen the prognosis after myocardial infarction, even in cases with mild or moderate regurgitation. Therefore, if the risk of using extracorporeal circulation is not high, mitral valve surgery is recommended for patients with LVEF >30% and severe MR with a high likelihood of persistence after CABG (Class I). If the LVEF is <30%, mitral valve intervention may be indicated according to LV myocardial dysfunction.
viability, the risk of using extracorporeal circulation, and the extent to which the MR is involved in HF (Class IIb).

Regarding mitral valve surgery, valve replacement or ring annuloplasty with subvalvular procedures can be performed in patients at high risk of MR recurrence (Table 15) and isolated ring annuloplasty can be performed in cases of low risk of MR recurrence.

**ii) When Revascularization by CABG Is Not Indicated**

If the patient is asymptomatic, careful periodic observation is recommended. If HF symptoms are present, careful and comprehensive medical treatment, including PCI, and cardiac resynchronization therapy, if indicated, should be considered (Class I). If controlling HF symptoms is difficult even after comprehensive medical treatments, MR intervention may be considered if the LVEF is >30% (Class IIb). The patient's general status and LV function should be considered by the Heart Valve Team when discussing the indications for transcatheter or surgical interventions. If the LVEF is ≤30%, some reports indicate that prognosis is not improved by invasive treatments compared with medical intervention. The Heart Valve Team should consider the patient's age and general condition to determine whether to perform LV assist device treatment, heart transplantation, mitral valve intervention (transcatheter or surgical), or rigorous medical treatment.

**b. Moderate MR**

**i) When Revascularization by CABG Is Indicated**

For moderate MR, it is highly likely that an isolated CABG will improve MR for patients in whom the posteroinferior region is viable or dysynchrony is not observed. Other

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**Table 14. Recommendations for Treatment for Secondary Mitral Regurgitation (MR) With LV Systolic Dysfunction**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal medical therapy (ACEIs, ARBs, β-blockers, mineralocorticoid receptor antagonists) of heart failure should be administered</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Cardiac resynchronization therapy should be performed for heart failure, if indicated (refer to Guidelines for Diagnosis and Treatment of Acute and Chronic Heart Failure (JCS 2017/ JHFS 2017))</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Mitral valve surgery is recommended for patients with severe MR and LVEF &gt;30% who have indication for CABG</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Mitral valve surgery may be considered for patients with severe MR and LVEF ≤30% who have indication for CABG</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Mitral valve surgery may be considered for patients with moderate MR who have indication for CABG and no viability in the posteroinferior wall</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>CABG without mitral valve surgery may be considered for patients with moderate MR who have indication for CABG and have viability in the posteroinferior wall</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Surgical or catheter intervention may be considered for patients with LVEF &gt;30% and severe MR who have no indication for coronary revascularization</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; CABG, coronary artery bypass grafting; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction.
considerations include the severity of the LV dysfunction and the probability of MR improvement by revascularization alone. CABG without mitral valve surgery may be considered for patients who have a viable posteroinferior wall (Class IIb). Conversely, mitral valve surgery may be considered for patients without a viable posteroinferior wall or those with a viable posteroinferior wall but without an adequate right or left circumflex coronary artery for bypass, if there is no increased risk for extracorporeal circulation (Class IIb). If mitral valve surgery is indicated, ring annuloplasty is the first choice.

### 4.4 Medical Therapy and Follow-up (Table 14)

This section is omitted from the English version.

### 5. Secondary (Functional) MR Associated With LA Dilatation: Atrial Functional MR

#### 5.1 Pathophysiology, Natural History, and Mechanism

Significant functional MR and functional TR without ventricular dysfunction can occur in patients with atrial dilatation and mitral/tricuspid annular dilatation accompanied by persistent AF. There is little systematic research on this type of TR and MR. However, in light of recent studies on MR due to atrial dilatation in persistent AF cases, this type of MR has garnered more attention. Many Japanese reports on this condition have contributed greatly to formulating the concept of this disease. The condition is often referred to as “atrial functional MR” or simply “atrial MR”. To distinguish this disease, the conventional functional MR associated with LV dysfunction can be referred to as “ventricular functional MR”. It is rare, but atrial dilatation due to LV diastolic dysfunction can also cause atrial functional MR in a sinus rhythm.

The frequency of moderate or severe atrial functional MR in patients with AF varies by population, but is generally low (2.8–15%). However, a higher proportion (28%) of moderate or severe atrial functional MR was observed in cases of longstanding, persistent AF over 10 years than in those with a duration of <10 years. In that report, the severity of both atrial functional MR and TR was an independent predictor of cardiac events. Moreover, the event-free rate was low, especially when moderate or severe MR and TR coexisted. Some other studies have reported that patients with AF who were hospitalized due to HF frequently showed significant atrial functional MR (37–44%), even at discharge after medical treatment, and that atrial functional MR was associated with readmission for HF during the post-discharge follow-up.

There are a number of studies on the mechanism of atrial functional MR. Failed coaptation of the anterior and posterior leaflets with LA dilatation and mitral annular dilatation is common across all studies. Disruption of the mitral annular saddle shape, reduction in mitral annular contractility, inadequate compensation for mitral annular dilatation resulting from the lack of leaflet remodeling, and atriogenic tethering of the posterior mitral leaflet have been proposed, together with other etiologies. Atriogenic tethering of the posterior mitral leaflet has been traditionally referred to as hamstringing of the posterior mitral leaflet observed in the giant LA (Figure 11). The main determinant and the relationship among the various etiologies still need to be established.

#### 5.2 Diagnosis

MR can be diagnosed as “atrial functional MR” when associated with LA dilatation without global/regional LV systolic dysfunction nor apparent structural abnormalities in the mitral leaflets and chordae tendineae. Cases of LV...
dilatation or dysfunction (LVEF <50%) may be excluded when atrial functional MR is strictly defined. However, even with atrial functional MR, mild LV dilatation and reduced LVEF may occur in longstanding chronic or advanced cases. Therefore, if the main mechanism is atrial dilatation, the MR can be referred to as atrial functional MR. As mentioned above, most cases of atrial functional MR occur in the context of AF, especially longstanding persistent AF. If posterior leaflet tethering or hamstringing is present, poor coaptation between the anterior and posterior leaflets may arise. The tip of the anterior leaflet will then deviate to the atrial side, overriding the posterior leaflet. This phenomenon can be referred to as anterior leaflet pseudoprolapse or overriding, which has been originally reported as a characteristic of ventricular functional MR (Figure 11).

5.3 Medical Therapy (Table 16)

Symptomatic patients with atrial functional MR should first receive standard medical therapy for HF, including diuretics (Class I). Invasive treatments should also be considered if patients with severe atrial functional MR are consistently symptomatic despite standard medical therapy for HF. According to a previous study, successful maintenance of sinus rhythm after catheter ablation resulted in reduction in the size of both the LA and mitral annulus, which in turn led to significant improvement in atrial functional MR. Therefore, the maintenance of sinus rhythm by catheter ablation may be an effective treatment for atrial functional MR (Class IIa). However, there are many cases in which LA dilatation is prominent and the probability of maintaining sinus rhythm by catheter ablation is low. In such cases, surgical treatment for MR is reasonable (Class IIa). However, the appropriate cutoff value of LA size for selecting catheter ablation or surgery remains undetermined.

Table 16: Recommendations for Treatment of Atrial Functional Mitral Regurgitation (MR)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard medical therapy for heart failure, including diuretics, should be performed for symptomatic patients with atrial functional MR</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>AF catheter ablation is reasonable for symptomatic patients with persistent AF and severe atrial functional MR if successful ablation and maintenance of sinus rhythm can be expected from the duration of AF and the left atrial size</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Mitral valve surgery is reasonable for patients with severe atrial functional MR who are consistently symptomatic despite standard medical therapy for heart failure*1</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

*This recommendation can also be applied to patients with chronic moderate atrial functional MR if the MR is severe at the worsening of heart failure or on exercise stress tests. 1Atrial functional MR is likely to accompany secondary atrial functional TR, and concomitant tricuspid surgery should be performed in patients with both atrial functional MR and TR. AF, atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; TR, tricuspid regurgitation.

5.4 Surgical Treatment

5.4.1 Surgical Procedures and Results

This section is omitted from the English version.

5.4.2 Indications and Timing of Surgery (Table 16)

Conventional treatment guidelines for functional MR with LV dysfunction cannot be applied to atrial functional MR because it is a completely different disease entity. Further, the data supporting treatment selection are still lacking. Consequently, consideration of surgery should be limited to patients with HF symptoms. Mitral valve surgery is reasonable if rhythm control therapy is not indicated and severe MR with HF symptoms persists despite medical therapies in patients with persistent AF (Class IIa). This recommendation can also be applied to patients with chronic moderate atrial functional MR if the MR becomes severe with worsening HF or during stress tests.

Atrial functional MR is likely to accompany secondary atrial functional TR. Patients with both atrial functional MR and atrial functional TR therefore require concomitant tricuspid surgery when they undergo mitral surgery. Mitral leaflet augmentation to increase the coaptation, the Cox maze procedure, or LA plication can be considered as a concomitant procedure based on a case-by-case evaluation. However, more evidence is needed to determine whether conservative or surgical interventions are superior for...
6. Transcatheter Treatment

6.1 Current Status of Transcatheter Treatment

This section is omitted from the English version.

6.2 Indications for Transcatheter Treatment

6.2.1 Primary MR

Transcatheter mitral valve edge-to-edge repair and conventional surgery were compared in the multicenter randomized EVEREST II trial. In the EVEREST II high-risk cohort study, the survival rate was favorable and the recurrence rate of HF was lower in the transcatheter treatment group than in the medical treatment group.

6.2.2 Secondary MR

There is high expectation of transcatheter mitral valve edge-to-edge repair for secondary MR with LV dysfunction. In the COAPT study, the transcatheter treatment group showed not only a reduction in the HF rate, but also a reduction in mortality.

6.2.3 Current Indications in Japan

A prospective multicenter study was conducted in Japan to confirm the safety and efficacy of transcatheter mitral valve edge-to-edge repair in patients with symptomatic severe MR. The participants included those with primary and secondary MR with LVEF >30% and who were considered as inoperable by the Heart Valve Team. The average participant age was 80 years, and approximately half of the participants had secondary MR. After treatment with transcatheter mitral valve edge-to-edge repair, 87% of the participants had MR ≤2+. There were no post procedure major adverse events or device complications at 30 days.

The difference in indications between Japan and Europe/USA is that the LVEF lower limit is 15% in Europe and 20% in North America, whereas it is 30% in Japan. In response to the results of these studies, the indications for transcatheter mitral valve edge-to-edge repair should be considered for symptomatic patients with severe secondary MR despite optimal medical therapy and cardiac resynchronization therapy, if indicated. Severity of secondary MR changes depending on the load conditions, and thus, evaluation with stress echocardiography is useful. The Heart Valve Team should thoroughly review and discuss this issue to determine the proper indications.

6.3 Current Indications in Europe/USA

The difference in indications between Japan and Europe/USA is that the LVEF lower limit is 15% in Europe and 20% in North America, whereas it is 30% in Japan. In response to the results of these studies, the LVEF lower limit may be reduced from 30% in Japan, but currently remains unchanged.
IV. Mitral Stenosis (MS)

1. Etiology

The incidence of rheumatic MS has decreased significantly in developed countries; however, MS due to annular calcification is increasing, especially in the elderly, though the condition rarely becomes severe. In some rare cases, MS is associated with congenital mitral valve abnormalities, such as undifferentiated papillary muscle, parachute mitral valves, mitral arcade, or double-orifice mitral valve, which are usually diagnosed during infancy or childhood.

2. Pathophysiology and Natural History

This section is omitted from the English version.

3. Assessment of Severity

In the 2014 AHA/ACC guidelines, severe VHD is defined as “the severity at which symptoms may appear and improve with intervention”; therefore, an MVA of 1.0–1.5 cm² is defined as severe MS, and MVA <1.0 cm² has been newly defined as very severe MS. In contrast, the conventional classification (moderate MVA 1.0–1.5 cm²; severe MVA <1.0 cm²) continues to be used in the 2017 ESC guidelines, and MS with an MVA <1.5 cm² is considered “clinically significant”.

Accordingly, this guideline defines an MVA <1.0 cm² as severe MS and an MVA 1.0–1.5 cm² as moderate MS (Table 18).

Given that the mean transmitral pressure gradient and diastolic pressure half-time are highly affected by valvular flow, LA/LV compliance, and heart rate, these parameters should be used as reference.

<table>
<thead>
<tr>
<th>Table 18. Grading the Severity of Mitral Stenosis (MS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>MVA</td>
</tr>
<tr>
<td>Mean transmitral PG</td>
</tr>
<tr>
<td>PHT</td>
</tr>
</tbody>
</table>

*Mitral valve PG and PHT should be used as a reference because of the influence of hemodynamics. MVA, mitral valve area; PG, pressure gradient; PHT, pressure half time.

4. Diagnosis and Follow-up

4.1 Symptoms and Physical Findings

This section is omitted from the English version.

4.2 Echocardiography

Echocardiography is useful in diagnosing MS and assessing the severity (Table 18) and hemodynamics; thus, TTE is indicated when the symptoms or physical findings change (Class I). It is recommended that TTE should be performed every 3–5 years for mild MS, every 1–2 years for moderate MS, and annually for severe MS. The reduction in the mitral valve cusps opening and thickening of the leaflet are considered signs of MS. In particular, characteristic doming of the anterior leaflet, commissural fusion, and subvalvular tissue changes such as chordal shortening/fusion, can be observed in rheumatic MS. The MVA can be measured by tracing the valve orifice with a short-axis view of the mitral valve level (using the planimetry method). The mean transmitral pressure gradient and pressure half-time are measured by the continuous-wave Doppler method. The MVA can be calculated from the pressure half-time, but it is noted that this measurement can be used in rheumatic MS and that the pressure half-time is affected by conditions other than MS that modify the LV or LA pressure. In addition, it cannot be used for evaluation immediately after PTMC. The planimetry method is the standard for MVA measurement, but it sometimes overestimates according to the measurement views used. Therefore, it is also helpful to use the continuity equation and/or the PISA method when there is a significant discrepancy between the measurement in planimetry and the pressure half-time methods.

TTE is useful in determining whether the mitral valve morphology is suitable for PTMC. Because it is a procedure...
that cleaves the commissural fusion, PTMC is indicated for rheumatic MS. Commissurotomy is difficult if calcification is present, and if the valve leaflet or subvalvular lesion is advanced, it is unlikely that a sufficient increase in the MVA can be obtained. When significant MR is present, PTMC should be avoided because it may exacerbate MR. The Wilkins score (Table 19) is known to be an objective method of assessing whether the mitral valve morphology is suitable for PTMC. If the score is less than 8 points, it is appropriate for PTMC. However, because the Wilkins score has the disadvantage of a lack of information on the commissure fusion, a score >8 does not necessarily indicate that PTMC cannot be performed.

TTE is usually sufficient for evaluating valve morphology and severity, and TEE does not need to be performed routinely. However, TEE is recommended for the evaluation of LA thrombus in cases of AF or when considering PTMC (Class I).

Exercise stress echocardiography is reasonable for evaluating the change in hemodynamics during exercise if there is a discrepancy between clinical symptoms and the severity of MS by echocardiography at rest (Class IIa).

### 4.3 Cardiac Catheterization

In recent years, the significance of cardiac catheterization for MS has decreased because the transvalvular pressure gradient, MVA, hemodynamics, and LV function can be evaluated by TTE. However, cardiac catheterization is reasonable for evaluating the severity and hemodynamics of MS when echocardiography is nondiagnostic or if there is a discrepancy between the clinical and echocardiographic evaluations (Class IIa). Ideally, the transvalvular pressure gradient is evaluated by simultaneously measuring the pulmonary capillary wedge pressure and the LV pressure. The MVA is calculated using the Gorlin formula after measuring CO by the thermodilution method or the Fick method (in the case of severe TR or intracardiac shunt).

\[
MVA (\text{cm}^2) = \frac{CO}{(DFP \times HR)} \times \frac{37.7}{\text{MVG}}
\]

where DFP is the diastolic flow period (s/beat) and MVG is the mean ventricular gradient (mmHg).

The transvalvular pressure gradient is the result of the total mitral valve blood flow, so it is necessary to note that the valve area is underestimated in patients with significant MR. In addition, hemodynamic measurement by catheter before and after exercise loading may be useful when there is a discrepancy between the symptoms and pressure data at rest.

Table 20 lists the recommendations for diagnostic testing for MS.

### 5. Surgical and Transcatheter Treatment

#### 5.1 Surgical Procedures and Results

This section is omitted from the English version.

#### 5.2 Results of PTMC

This section is omitted from the English version.

#### 5.3 Indications, Timing, and Selection of Intervention

##### 5.3.1 Indications and Timing of Intervention (Figure 12, Table 21)

The indications for intervention for MS are determined by symptoms and the MVA. Intervention is recommended for moderate and severe MS (MVA ≤1.5 cm²) with symptoms such as dyspnea on effort despite medical therapy (Class I). Intervention may be considered for mild MS (MVA >1.5 cm²) with symptoms and when meeting certain criteria (mean pressure gradient >15 mmHg or PASP >60 mmHg) during exercise stress testing (Class IIb).

Intervention is reasonable for asymptomatic patients with moderate or severe MS who develop new-onset AF or with recurrent embolization despite appropriate anticoagulant therapy (Class IIb). The progression of MS is very slow; thus, patients with MS limit their activity unconsciously and are often asymptomatic. Therefore, exercise testing with echocardiography is useful in determining the appropriate intervention. Intervention is reasonable for asymptomatic patients with moderate or severe MS when they become symptomatic or the transvalvular pressure gradient exceeds 15 mmHg or the PASP exceeds 60 mmHg during exercise stress (Class IIa). PTMC may be considered, irrespective of anatomical suitability, for critical symptomatic patients who are at high risk and contraindicated for surgery.

Surgical intervention is recommended during open-heart surgery for other indications (severe MS: Class I, moderate MS: Class IIa, Mild MS: Class IIb).

The etiology of MS is predominantly rheumatic; however, nonrheumatic MS due to age-related calcification in the leaflets or annulus is seen in the elderly and hemodialysis patients. In such cases, PTMC is often contraindicated because it causes MS without commissural fusion. It remains controversial whether nonrheumatic MS progresses more slowly than rheumatic MS.

##### 5.3.2 Selection Criteria for PTMC and Surgery

PTMC is relatively less invasive and several randomized comparative studies have shown results comparable to those of OMC. Conversely, cases suitable for PTMC are also well suited to OMC. If the MR is more than mild,
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OMC may be chosen, though it depends on the experience of the surgeon. Patients for whom PTMC or OMC are deemed inappropriate are often indicated for valve replacement. The choice of PTMC versus surgical treatment is determined by a complex weighing of the anatomical suitability and the surgical risk (Table 22).

The most important factor affecting the success or failure of PTMC is the valve morphology, and it is necessary to evaluate this in detail by TTE or other modalities. Evaluation of the valve morphology using the Wilkins score223 is well established, but physicians should also consider whether PTMC is appropriate by referring to other scoring systems such as the Iung score230 (Table 23). Although the mechanism of balloon dilatation of valve stenosis is considered to involve the splitting of the rheumatic, fused commissures and stretching of the entire valve orifice, the procedure may not have a proper effect and may lead to unfavorable splitting when the commissural fusion is very severe. In cases of restricted leaflet motion because of rheumatic changes or in cases of severe subvalvular lesion, the effect of valvotomy is limited. The pathophysiologies for which PTMC is inappropriate include (1) atrial thrombus, (2) MR > grade III, and (3) severe or bilateral commissural calcification. In cases of LA thrombus, dislodgement of the thrombus during the intervention is possible, and thus, these cases are strictly contraindicated for PTMC. PTMC should be performed following confirmation that the thrombus has been dissolved by anticoagulation therapy for 1–3 months. Associated MR > grade III may be exacerbated by PTMC and should undergo surgical treatment. Although the majority of aforementioned nonrheumatic MS conditions are not suitable for PTMC based on anatomical requirements, some cases may involve a combination of rheumatic and nonrheumatic etiologies.
Treatment strategies for such cases should be determined after considering the surgical risks.\textsuperscript{229}

5.3.3 Treatment Selection for Restenosis After PTMC
MS recurrence because of commissural fusion after PTMC or surgical commissurotomy should also be considered for PTMC if the above anatomical conditions are met.\textsuperscript{229} Typically, commissural calcification is more pronounced in such cases, and the procedural risk is higher than in the previous PTMC. In such cases, valve replacement is usually selected. However, patients may be elderly or have multiple coexisting diseases, thus treatment suitability should be determined by taking a comprehensive approach with consideration of the surgical risk and anatomical requirements.

6. Medical Therapy and Follow-up

This section is omitted from the English version.

V. Aortic Regurgitation (AR)

1. Classification and Etiology

1.1 Valvular AR and AR Due to Aortic Root Dilatation

AR is caused by insufficient coaptation of the 3 cusps because of congenital or acquired abnormalities of the aortic valve cusps or the aortic root. The mechanism is structural change of the valve cusp itself such as rheumatic or age-related degenerative changes, or aortic root dilatation with normal cusps (Table 24). AR associated with a ventricular septal defect is caused by valve prolapse due to right coronary cusp herniation in patients with outlet type (supracristal type) despite no structural changes of the aortic valve itself. Outlet type (supracristal type) is commonly found in Asian populations and should be recognized as a congenital disease and a potential cause of AR. Uncommonly, AR can also be seen in patients with perimembranous ventricular septal defect. Valve prolapse can be seen in patients with not only congenital bicuspid valves, but also acquired abnormalities such as myxomatous change of the aortic valve cusp, rupture of a fenestration that is located in a marginal region of the aortic valve cusps, rupture of fibrous strands, and localized aortic dissection.\textsuperscript{231}

A functional classification of AR mechanisms has been proposed, and AR is classified as types I–III based on the cusp motion\textsuperscript{232,233} (Figure 13). In patients with type I, the cusp motion is normal, and AR is caused by aortic root dilatation or cusp perforation. This type can be subdivided: type Ia: dilatation from the sinotubular junction to the ascending aorta; type Ib: dilatation of the sinuses of Valsalva and the sinotubular junction; type Ic: dilatation of the ventriculoaortic junction; and type Id: cusp perforation. Type Ia is often caused by arteriosclerosis, type Ib is often caused by Marfan syndrome, type Ic is caused by...
arteriosclerosis or annuloaortic ectasia, and type IId is caused by infective endocarditis or trauma. Type II is due to leaflet prolapse, and type III is due to leaflet restriction, which may be found in bicuspid, degenerative, or rheumatic valvular disease as a result of calcification, thickening, and fibrosis of the aortic valves. These classifications are considered by surgeons for surgical procedures.

### 1.2 Acute and Chronic AR

Acute AR is caused by a sudden onset of insufficient valve closing resulting from infective endocarditis, aortic dissec-
2. Pathophysiology and Natural History

This section is omitted from the English version.

3. Assessment of Severity

AR is classified as mild, moderate, or severe and is evaluated primarily by TTE. Qualitative, semiquantitative, and quantitative assessments are available using TTE, and severity is finally determined in combination with each result. However, if the results differ among those indices and TTE alone is insufficient to determine AR severity, results from other modalities such as TEE, cardiac MRI, and cardiac catheterization should be combined to definitively determine the severity (Table 25).

With TTE, the most frequent index for evaluating AR severity is the size of the AR jet (jet length and width) using the color Doppler method. This method is simple and easy to use, but tends towards underestimation in the case of an eccentric AR jet. Furthermore, AR severity evaluated by jet length is affected by diastolic blood pressure. The vena contracta method, which measures the width of the narrowest portion of the AR jet, is useful as a semiquantitative evaluation. In addition, the ratio of the width of the AR jet to the LV outflow tract and the ratio of area of the AR jet to the LV are also parameters of AR severity, but they are difficult to evaluate in cases of an eccentric jet or multiple jets. Quantitative evaluation includes the PISA and volumetric methods. The PISA method in AR is often difficult to measure in cases of severe calcification of the aortic valve or the presence of multiple jets. However, because the volumetric method is also affected by concomitant MR or an incorrect measurement of the annulus diameter, it is not optimal for determining AR severity using a single parameter.

It is also important to determine AR severity through combining the results of other modalities when the TTE results are inconclusive. TEE is generally better for evaluating aortic valve morphology than for AR severity, but it is possible to measure the vena contracta by 3D imaging for evaluation of AR severity. In addition, the phase-contrast method with cardiac MRI can be used to calculate regurgitant volume and fraction. The Sellers classification with aortography in cardiac catheterization is also an important method for determining the severity.

4. Diagnosis

4.1 Symptoms and Physical Findings

This section is omitted from the English version.

4.2 Echocardiography

TTE is an indispensable imaging test for assessing the severity and etiology of AR, evaluating LV size and func-

<table>
<thead>
<tr>
<th>Table 25. Grading the Severity of Aortic Regurgitation (AR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AR severity</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Aortic leaflets</td>
</tr>
<tr>
<td>LV size</td>
</tr>
<tr>
<td>AR jet width, (color flow)</td>
</tr>
<tr>
<td>AR flow convergence, (color flow)</td>
</tr>
<tr>
<td>Jet density (color wave Doppler)</td>
</tr>
<tr>
<td>Jet deceleration rate (color wave Doppler), PHT, ms</td>
</tr>
<tr>
<td>Diastolic flow reversal (descending aorta) (pulse wave Doppler)</td>
</tr>
<tr>
<td>Vena contracta width (cm)</td>
</tr>
<tr>
<td>Jet width/LVOT width (%) (central jet only)</td>
</tr>
<tr>
<td>Jet area/LVOT area (short axis) (%) (central jet only)</td>
</tr>
<tr>
<td>Rvol (mL/beat): volumetric or PISA</td>
</tr>
<tr>
<td>RF (%): volumetric</td>
</tr>
<tr>
<td>EROA (cm²): PISA</td>
</tr>
<tr>
<td>Transesopharyngeal echocardiography</td>
</tr>
<tr>
<td>Vena contracta width (cm)</td>
</tr>
<tr>
<td>Cardiac MRI</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
</tr>
</tbody>
</table>

EROA, effective regurgitant orifice area; LVOT, left ventricular outflow tract; PHT, pressure half time; PISA, proximal isovelocity surface area.
tion, and determining the timing of valve intervention (Class I).

### 4.2.1 Acute AR

Acute AR requires immediate identification of the severity and etiology, whereas severe AR is often difficult to diagnose because of the lack of LV enlargement and the attenuated color Doppler signal because of the rapid increase in LV end-diastolic pressure. Findings such as a shorter pressure half-time of the continuous-wave Doppler AR signal (<300 ms), shorter deceleration time of the mitral inflow E wave (<150 ms), and early closure of the mitral valve with subsequent diastolic MR indicate a marked rise in LV end-diastolic pressure. The degree of pulmonary hypertension can be estimated by the continuous-wave Doppler signal. Possible underlying causes of acute AR, such as infective endocarditis or aortic dissection, should be investigated, and TEE should be performed if diagnosis with TTE alone is difficult.

### 4.2.2 Chronic AR

The aortic valve/root morphology, etiology/severity of AR, size of the LV, and cardiac function should all be assessed. Table 25 lists the key TTE indices. If TTE provides enough information, no other imaging tests are required for follow-up evaluation. Exercise stress echocardiography is useful for evaluating subclinical cardiac dysfunction or symptoms in asymptomatic patients with severe AR. Exercise stress echocardiography allows for evaluation of the LV contractile reserve, and lack of contractile reserve has been found to predict LV systolic dysfunction development postoperatively or at follow-up. In addition, exercise stress echocardiography can reveal another cause for symptoms, such as ischemic heart disease, functional MR, LV diastolic dysfunction, or pulmonary hypertension. TTE is a central diagnostic modality, and TEE is used for detailed evaluation of the leaflet, regurgitation, and aortic root morphology (Class I). In particular, in cases for which aortic valve repair or valve-sparing root replacement can be indicated, the cause of regurgitation should be clarified and detailed measurements are required to determine the suitability for repair surgery and the surgical design, including the selection of the annuloplasty ring or vessel graft type and size. The most important preoperative measurement is the leaflet length (geometric height). Insufficient geometric height is not suitable for aortic valve repair. Effective height is the vertical distance from the annular plane to the leaflet tip at leaflet closure and is an index of leaflet prolapse and tethering. The diameter of the annulus, sinus of Valsalva, and sinotubular junction are also measured. The diameter of the annulus is calculated by measuring the annular perimeter or area, because the annulus is not circular. Evaluation of the geometric height and effective height and root measurements may not be possible by the 2D approach, and the optimal cross-section should be extracted and measured using a 3D approach. Cardiac CT is also useful, with image resolution higher than that obtained with 3D TEE (Class IIa).

### 4.3 Cardiac Catheterization

When the echocardiographic evaluation is suboptimal or when there is a discrepancy between the clinical assessment and the echocardiographic findings, cardiac catheterization is useful for evaluating the severity of both AR and hemodynamics (Class IIa).

The hemodynamic characteristics include wide pulse pressure. In severe AR, the LV diastolic pressure rises rapidly, and the LV pressure and aortic pressure are almost equal at end-diastole. AR severity is evaluated by the Sellers classification, which is based on the amount of contrast that appears in the LV after aortography. Left ventriculography allows for measurement of LVEF and LV size and is useful when other imaging modalities do not provide adequate information. Coronary angiography is used to assess coronary lesions, but it is not mandatory if the risk of coronary artery disease is low and coronary CT is negative for coronary lesions.

### 4.4 CT/MRI

Although it is possible to evaluate the aortic root and the ascending aorta by plain CT, detailed morphological evaluation of the leaflets and aortic root requires the use of contrast agents. Multidetector CT offers significantly
improved spatial and temporal resolution and allows for evaluation of the coronary arteries and cardiac function in addition to evaluation of the aortic valve complex. Cine MRI allows imaging with a high contrast between the blood and the myocardium without the use of contrast agents, enabling accurate measurement of the size of the LV and LVEF. In addition, a phase-contrast method can be used to calculate the blood flow in the aortic root to determine the regurgitant volume and the regurgitant fraction. Thus, MRI is a useful modality in cases of suboptimal echocardiographic images for assessment of the severity of AR, LV function, and LV size (Class IIa). Cardiac MRI with late gadolinium enhancement has been established as a method of detecting myocardial fibrosis. It has been reported that a greater amount of myocardial fibrosis quantified using delayed-contrast MRI was associated with a worse prognosis after aortic valve replacement. However, there is limited evidence to support this finding. Table 26 lists the recommendations for diagnostic testing for AR.

### 5. Surgical Treatment

#### 5.1 Surgical Procedures and Results

This section is omitted from the English version.

#### 5.2 Indications and Timing of Surgery (Figure 15, Table 27)

##### 5.2.1 Acute AR

Considering the causes (e.g., infective endocarditis, aortic dissection, or traumatic valve destruction), acute AR is often difficult to treat medically, thus physicians should consider performing surgery as soon as possible.

##### 5.2.2 Chronic AR

The surgical indications for chronic AR are determined by the presence of symptoms, LVEF reduction, LV dilatation, and performing other open-heart surgery (Figure 15).

**a. Symptoms**

When symptoms due to severe AR appear, aortic valve surgery is indicated regardless of LV function and size (Class I), except in cases of high surgical risk and contraindications for the procedure. Even in patients with preoperative severe LV dysfunction, surgery is recommended with maximal medical therapy before the operation.

**b. LV Dysfunction: LVEF <50%**

Early aortic valve surgery is indicated in asymptomatic patients with severe AR and LV dysfunction (LVEF <50%) if other causes of LV dysfunction such as coronary artery disease can be ruled out (Class I). In patients with LV dysfunction due to AR, surgery improves the postoperative prognosis compared with waiting for the appearance of symptoms or progression of LV dilatation.

Conversely, as mentioned above, physicians should consider whether the cause of LV dysfunction is AR, and it is important when using this criterion of LVEF to exclude the other causes of LV dysfunction. In patients with severe LV dysfunction (LVEF <30%), surgical indications should be determined for each case based on surgical risk, degree of myocardial damage, and the clinical course of the patient.

#### 5.3 LV Dilatation: LVESD >45 mm, LVEDD >65 mm

LVESD is a more useful index than LVEDD for surgical indication in patients with asymptomatic severe AR and preserved LV function (LVEF ≥50%). This is because an increase in afterload as well as in preload is the main factor in the LV dysfunction and dilatation in patients with chronic severe AR. In Europe and the USA, it has been often reported that LVESD >50 mm is a reasonable cutoff value when considering the postoperative prognosis. However, some studies in Japan have reported that LVESD >50 mm is a reasonable cutoff value when considering the postoperative prognosis.

Therefore, considering body size, it is appropriate to use a cutoff value for LVESD of 45 mm as a surgical indication (Class IIa) in this guideline.

Conversely, regarding LVESD with a BSA correction, the LVESD index of 25 mm/m² is used in the ESC and ACC/AHA guidelines, which is different from the LVESD index of 28 mm/m² calculated from the LVESD cutoff value of 45 mm in the present guideline and the average BSA of 1.6 m² for Japanese. In a Japanese study, an LVESD index of 26.7 mm/m² was used as the cutoff value for the occurrence of postoperative LV dysfunction.
Regarding LVEDD, there is little evidence for surgical indications, and it has been reported in a Japanese study that the LVEDD was not associated with postoperative prognosis. In the present guideline, an LVEDD >65 mm is used as a criterion for surgery (Class IIb), considering the difference in average body size between Western and Japanese populations.

**d. Indications for Other Open-Heart Surgeries Such as Ascending Aortic Replacement, Coronary Artery Bypass, and Mitral Valve Surgery**

When other open-heart procedures such as an ascending aortic replacement, coronary artery bypass, or mitral valve surgery are performed, aortic valve surgery is indicated in severe AR (Class I) and should be considered in moderate AR (Class IIa) to prevent perioperative hemodynamic failure due to AR and avoid reoperation for AR in the near future. In particular, with regard to ascending aortic dilatation, physicians need to follow up with a focus on the increase of the ascending aortic diameter as well as the surgical indications for AR itself in patients with a bicuspid valve or Marfan syndrome. The surgical indications depend mainly on the ascending aorta and aortic root dilatation and are described in the following sections.

**CQ2**

Should early surgery be conducted for asymptomatic patients with severe AR, LVEF ≥50%, and LVESD index >25 mm/m²?

**[Conclusion]**

Early surgery may be considered for asymptomatic patients with severe AR, an LVEF ≥50%, and an LVESD index...
Multivariate analysis revealed a significant correlation between LVEF and LV enlargement. Among the total cases, 58% were asymptomatic. Sambola et al. reported a worse prognosis with LVEF <55% (5.8% risk/year) in asymptomatic patients. Dujardin et al. observed only in those with a BSA <1.68 m². Only 23% of the patients in the study by Sambola et al were asymptomatic, versus 50% of the patients in the study by Dujardin et al.

The ACC/AHA 2014 guidelines suggested that LVESD >50 mm is a Class IIa indication for SAVR, and LVEDD >65 mm is a Class Ib indication. However, those guidelines also suggest that it is appropriate to consider BSA-corrected values in females or smaller patients. The 2017 ESC/EACTS guidelines state that Class IIa is warranted for LVESD >70 mm or LVEDD >50 mm. For smaller patients with BSA <1.68 m², a LVESD index >25 mm/m² is also indicated as Class IIa.

Mentias et al. investigated patients with severe AR and normal EF, using the data of 933 patients from the Cleveland Clinic who underwent SAVR and 484 conservatively treated patients. Among the total cases, 87% were asymptomatic. For patients with a LVESD index of 20–25 mm/m², which is below the conventional threshold, long-term survival was better in the surgery group than in the non-surgery group. Among the study population, 75% were males in their late 50s or older with an average BSA of ≈2.0 m². It should be noted that the study population had a relatively large body size, but this is the first study showing that surgery may be preferable even for patients with a LVESD index <25 mm/m². In addition, Yang et al. studied patients with severe AR and compared 361 patients who underwent SAVR and 387 conservatively treated patients. Among the total cases, 58% were asymptomatic. Multivariate analysis revealed a significant correlation between LVEF and LVESD as well as conventional Class I indications. Maeda et al. analyzed 268 patients with severe AR (162 asymptomatic patients). Patients with a LVESD index <25 mm/m² and LVEDD <65 mm (61 cases) demonstrated superior prognoses after 10 years as compared with patients with a LVESD index >25 mm/m² or LVEDD >65 mm (101 cases). This was a Japanese observational study with the average age being over 55 years, and males constituting a 70–80% proportion with a mean BSA of 1.63 m².

There are no RCTs comparing early surgical intervention and conservative treatment for patients with asymptomatic severe AR with normal LVEF and LV enlargement. The number of observational studies is also limited. There is no study regarding the optimal cutoff value of the LVESD index. All of the cited studies were retrospective, and therefore the evidence class was considered to be 2C.

### 6. Indications and Timing of Surgery for Aortic Dilatation and Specific Diseases (e.g., Marfan Syndrome, Bicuspid Valve) (Table 28)

#### 6.1 Ascending Aortic Dilatation With a Tricuspid Aortic Valve

##### 6.1.1 When Surgery Is Not Indicated for AR

Regardless of AR severity or aortic valve morphology, a maximum ascending aortic diameter ≥55 mm suggests that a preventative ascending aortic replacement should be considered. Preventative ascending aortic replacement should be considered in patients with >5 mm/year increase of maximum ascending aortic diameter even if the maximum ascending aortic diameter is <55 mm. Moreover, concomitant aortic valve surgery should be considered if the AR severity is more than moderate.

##### 6.1.2 When Surgery Is Indicated for Severe AR

If surgery is indicated for severe AR, simultaneous ascending aortic surgery should be considered in patients with a maximum ascending aortic diameter ≥50 mm. However, if the patient is elderly or the overall invasiveness and risk of surgery with an additional procedure is high, the indications for an ascending aortic replacement should be discussed by the Heart Valve Team.

#### 6.2 Ascending Aortic Enlargement With a Bicuspid Aortic Valve

##### 6.2.1 When Surgery Is Not Indicated for AR

In the presence of a bicuspid valve with additional risk factors or coarctation, an ascending aortic replacement should be considered in patients with an ascending aortic diameter ≥50 mm. Additional risk factors include a family history of aortic dissection, personal history of spontaneous vascular dissection, severe AR or MR, desire for pregnancy, systemic hypertension, and/or an aortic size increase >3 mm/year. Moreover, concomitant aortic valve surgery should be considered if the AR severity is more than moderate.

##### 6.2.2 When Surgery Is Indicated for Severe AR

If surgery is indicated for severe AR, simultaneous ascending aortic surgery should be considered in patients with a maximum ascending aortic diameter ≥45 mm.

#### 6.3 Ascending Aortic Enlargement in Marfan Syndrome

##### 6.3.1 When Surgery Is Not Indicated for AR

In the presence of Marfan syndrome, a preventative ascending aortic replacement is indicated regardless of background diseases in patients with an ascending aortic diameter ≥50 mm. In the presence of additional risk factors or genetic mutations, including Loeys-Dietz syndrome, an ascending aortic replacement should be considered for an ascending aortic diameter ≥45 mm. Additional risk factors include a family history of aortic dissection, personal history of spontaneous vascular dissection, severe AR or MR, desire for pregnancy, systemic hypertension, and/or an aortic size increase >3 mm/year. Moreover, among females with a small BSA or with the presence of a TGFBR2 mutation (related to familial thoracic...
aortic aneurysm or dissection) or severe extra-aortic features, an ascending aortic replacement may be considered if the AR severity is more than moderate (Class IIa).

### 6.3.2 When Surgery Is Indicated for Severe AR

If surgery is indicated for severe AR, simultaneous ascending aortic surgery is indicated in patients with a maximum ascending aortic diameter ≥45 mm (Class I). Moreover, among females with a small BSA or with the presence of a TGFBR2 mutation (related to familial thoracic aortic aneurysm or dissection) or severe extra-aortic features, an ascending aortic replacement may be considered in those with a maximum ascending aortic diameter of ≥40 mm (Class IIb).\(^{267,268}\)

### 6.4 Consideration of Body Size

In patients with a low BSA, slightly earlier timing for the surgery than that with the above criteria should be considered. In addition, serial dilatation of the aortic diameter should be taken into consideration. However, there is no evidence for criteria regarding smaller diameter or lower progression rate, and thus this is not defined in this guideline.

### 7. Medical Therapy and Follow-up

This section is omitted from the English version.
VI. Aortic Stenosis (AS)

1. Etiology

The primary etiology of AS varies greatly depending on the region and age. In developed countries such as Japan, where the average life expectancy is longer, age-related degeneration of the aortic valve accounts for more than 80% of severe AS requiring surgery. Rheumatic AS, which was once frequently seen, hardly occurs nowadays because adequate treatment for rheumatic fever is provided in childhood. Because age-related degeneration of the aortic valve is the primary etiology in developed countries, the frequency of AS increases with age. Although the incidence of severe AS in patients aged <70 years is <1%, it is approximately 7% in patients aged ≥80 years. Causes other than age-related and rheumatic AS include congenital factors such as unicuspid, bicuspid, and quadricuspid valves. Among these, bicuspid valves occur most frequently, with a prevalence of 0.5–2% and a sex ratio of 3:1, weighted towards males. Previous studies have reported that there are more patients with bicuspid aortic valves than with tricuspid valves among patients aged <70 years who receive aortic valve replacement. The prevalence of unicuspid valves is approximately 1/10 to 1/30 of that of bicuspid valves, and quadricuspid valves are very rare.

2. Pathophysiology and Natural History (Table 29)

This section is omitted from the English version.

3. Assessment of Severity (Table 30)

When a limitation to the opening of the aortic valve is confirmed, an AVA ≥1.0 cm² corresponds to mild or moderate AS. Severe AS is defined by an AVA of <1.0 cm² or an AVA indexed to BSA of <0.6 cm²/m². Severe AS can be roughly divided into a high-pressure gradient type, with a peak transvalvular velocity ≥4.0 m/s and a mean pressure gradient ≥40 mmHg, and a low-pressure gradient type with a peak velocity <4.0 m/s and a mean pressure gradient <40 mmHg. Low-flow/low-gradient severe AS is further divided into 2 types: low stroke volume with reduced LVEF or preserved LVEF and small LV cavity.

Table 29. Previous Reports on Prognosis of Asymptomatic Patients With Severe Aortic Stenosis (AS)

<table>
<thead>
<tr>
<th>Reference number (published year)</th>
<th>Definition of severe AS</th>
<th>No. subjects</th>
<th>Male (%)</th>
<th>Mean age (years)</th>
<th>Survival rate without events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 year</td>
</tr>
<tr>
<td>275 (2000) Vmax ≥4 m/s</td>
<td>128</td>
<td>53.9</td>
<td>60±18</td>
<td>All-cause death or AVR</td>
<td>67±5</td>
</tr>
<tr>
<td>25 (2005) Vmax ≥4 m/s</td>
<td>622</td>
<td>61.7</td>
<td>72±11</td>
<td>Cardiac death or AVR</td>
<td>80</td>
</tr>
<tr>
<td>276 (2010) Vmax ≥5 m/s</td>
<td>116</td>
<td>50.9</td>
<td>67±15</td>
<td>Cardiac death or AVR</td>
<td>64±4</td>
</tr>
<tr>
<td>278 (2010) AVA ≤0.75 cm² and Vmax ≥4.5 m/s and mPG ≥50 mmHg</td>
<td>95</td>
<td>46.3</td>
<td>63±12</td>
<td>Cardiac death or AVR</td>
<td>71±5</td>
</tr>
<tr>
<td>277 (2018) AVA &lt;1.0 cm²</td>
<td>861</td>
<td>57.7</td>
<td>72±12</td>
<td>All-cause death or AVR</td>
<td>54±2</td>
</tr>
<tr>
<td>279 (2015) AVA &lt;1.0 cm² or Vmax ≥4.0 m/s or mPG &gt;40 mmHg</td>
<td>1,517</td>
<td>39.8</td>
<td>77.8±9.4</td>
<td>All-cause death</td>
<td>87.7</td>
</tr>
</tbody>
</table>

AVA, aortic valve area; AVR, aortic valve replacement; mPG, mean pressure gradient; Vmax, maximum velocity.

Table 30. Grading the Severity of Aortic Stenosis (AS)

<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>Mild AS</th>
<th>Moderate AS</th>
<th>Severe AS</th>
<th>Very severe AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vmax (m/s)</td>
<td>≤2.5</td>
<td>2.6–2.9</td>
<td>3.0–3.9</td>
<td>≥4.0</td>
<td>≥5.0</td>
</tr>
<tr>
<td>Mean PG (mmHg)</td>
<td>–</td>
<td>&lt;20</td>
<td>20–39</td>
<td>≥40</td>
<td>≥60</td>
</tr>
<tr>
<td>AVA (cm²)</td>
<td>–</td>
<td>&gt;1.5</td>
<td>1.0–1.5</td>
<td>&lt;1.0</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Indexed AVA (cm²/m²)</td>
<td>–</td>
<td>&gt;0.85</td>
<td>0.60–0.85</td>
<td>&lt;0.6</td>
<td>–</td>
</tr>
<tr>
<td>Velocity ratio</td>
<td>–</td>
<td>&gt;0.50</td>
<td>0.25–0.50</td>
<td>&lt;0.25</td>
<td>–</td>
</tr>
</tbody>
</table>

AVA, aortic valve area; PG, pressure gradient; Vmax, maximum velocity; Velocity ratio, ratio of velocity at LV outflow tract to maximum velocity.
Low-flow/low-gradient severe AS should be differentiated from pseudo-severe AS, which is discussed later (see section VI.4.4).

In addition to the objective data, patients with severe AS are classified as symptomatic or asymptomatic according to whether they have symptoms due to AS such as HF symptoms, chest pain, and syncope. Symptomatic patients have worse prognoses than asymptomatic cases and should be considered more carefully.

---

### 4. Diagnosis and Follow-up

#### 4.1 Symptoms and Physical Findings

This section is omitted from the English version.

#### 4.2 Echocardiography

The diagnostic and severity assessments are primarily performed by echocardiography. Valve morphology (number of valve leaflets, presence of cusp fusion), the presence, distribution, and degree of calcification, and the valve opening are evaluated by TTE. When the findings indicate AS, the Doppler method should be used to assess severity (Class I). AVA is calculated using the continuity equation, for which measurements of peak transvalvular velocity, LV outflow tract flow velocity, and diameter are needed. The transvalvular velocity and pressure gradient are simple indices but may change due to hemodynamics; therefore, the AVA is also required for assessing severity. The AVA is also measured using the planimetry method, but it is often difficult to trace accurately if there is calcification. The Doppler beam must be parallel to the direction of the blood flow for accurate velocity measurements. In addition to the apical approach, multiple windows such as the right parasternal, the upper intercostal, and the suprasternal or other approaches should be considered to obtain the highest velocity. In particular, if the angle between the ascending aorta and the LV axis is relatively sharp (≤115°), as is the case with the sigmoid septum, a right parasternal approach is often useful for recording the peak velocity.200 LV function, wall thickening, dilatation of the proximal portion of the ascending aorta, other valve diseases, and the presence of pulmonary hypertension should also be evaluated. Because the bicuspid aortic valve may involve aortic lesions (dilatation, aneurysm, dissection), the aorta must be observed within the visible range. Grading for severity is shown in Table 30.34 Other parameters, such as valvuloarterial impedance and aortic valve resistance, are also important, but they are not routinely measured.34

The valve area measured by the continuity equation tends to be smaller than the valve area obtained by cardiac catheterization. One reason for this is the pressure recovery phenomenon, whereby the hydrostatic pressure rises at the spatial site of stenosis, and is theoretically observed when the valve opening is not orifice-like or when the ascending aorta is small (<30 mm in diameter), resulting in no significant distal turbulence. However, in calcific AS, which accounts for the majority of cases, the valve opening is usually considered orifice-like and turbulent flow is prominent; therefore, the valve area is less affected by the pressure recovery phenomenon. A formula for correcting for the pressure recovery phenomenon has also been proposed,34 and should be considered in the case of congenital AS, a small ascending aorta, or when there is a discrepancy between the valve area measured by the continuity equation and the clinical findings. TEE is recommended when the image quality of the TTE is poor and the TTE assessment is inconclusive (Class IIa). TEE is useful for evaluating the number of valve leaflets, valve morphology, calcification distribution, and dilatation of the ascending aorta.

Stress echocardiography should be performed when the findings of TTE at rest are inconclusive for an assessment of severity (Class IIa). Exercise stress echocardiography is reasonable for patients with AS to evaluate severity of stenosis and hemodynamics if TTE assessment is inconclusive or there is a discrepancy between TTE and clinical findings (IIa C).

### Table 31. Recommendations for Diagnostic Testing for Aortic Stenosis (AS)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTE is indicated for patients with known or suspected AS to evaluate severity and etiology of AS, LV size and LV function</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Periodic TTE is indicated for patients with moderate AS to evaluate severity of stenosis and for asymptomatic patients with severe AS to decide the timing of intervention</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Cardiac CT is indicated for patients who are candidates for TAVI to evaluate anatomy of aortic valve and aortic root</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Low-dose dobutamin stress echocardiography is reasonable to diagnose severity of stenosis and to evaluate contractile reserve for patients with low-flow/low-gradient AS and reduced LVEF</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Exercise stress test is reasonable for asymptomatic patients with severe AS to assess symptoms</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Exercise stress echocardiography is reasonable for asymptomatic patients with severe AS or asymptomatic patients with moderate AS to evaluate symptoms and hemodynamics during exercise</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Cardiac catheterization is reasonable for patients with AS to evaluate severity of stenosis and hemodynamics if TTE assessment is inconclusive or there is a discrepancy between TTE and clinical findings</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>TEE is reasonable to evaluate aortic valve and aortic root if TTE assessment is inconclusive due to technical difficulty</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Cardiac CT is reasonable for patients with low-flow/low-gradient AS with preserved EF to evaluate calcification of aortic valve</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; CT, computed tomography; EF, ejection fraction; LOE, Level of Evidence; LV, left ventricle; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

#### 4.3 Cardiac Catheterization, CT, and MRI

Cardiac catheterization is important for a preoperative diagnosis of AS. Coronary artery disease concomitant with AS should be closely assessed when determining the treatment strategy, and coronary angiography is the standard...
It is important to evaluate the presence of myocardial ischemia in patients with AS with coronary angiography and recognize the stenosis, though any interpretation should be made with caution in the presence of LV hypertrophy. A fractional flow reserve measurement may be difficult to perform in patients with AS because of concerns about blood pressure drop induced by coronary vasodilators. However, a nonpharmacological method has been recently reported to be useful. In addition, when the patient is elderly, or the risk of coronary angiography is high, coronary CT can be performed more safely with a high negative predictive value.

Coronary angiography does not necessarily need to be performed before surgery if the patient does not have chest pain and the coronary CT shows no significant stenosis. The concept of low-flow/low-gradient severe AS has been advanced in recent years, and an accurate severity assessment is important in determining the AS treatment. If severity is difficult to determine by echocardiography, hemodynamic assessment with a right cardiac catheter and simultaneous aortic and LV pressure measurements may be useful (Class IIa). Calcification scores based on cardiac CT are also useful in determining the severity.

Cardiac CT with ECG synchronization is useful for accurate valve morphology evaluation (especially bicuspid valves) (Class IIa). Evaluation of the aortic valve and aortic root are also important in the evaluation of the procedural risk of TAVI, as well as determining the type and size of valve and the approach (Class IIa).

Cardiac MRI may be useful in the detection and quantification of fibrosis in the myocardium. CT is useful for detecting valve thrombosis and vascular complications after SAVR and TAVI.

Table 31 lists the recommendations for diagnostic testing for AS.

### 4.4 Low-Flow/Low-Gradient AS

The diagnosis of severe AS is generally based on the AVA (<1.0 cm²), the mean transvalvular pressure gradient (>40 mmHg), and peak transvalvular velocity (>4.0 m/s).

If the measurements of valve area and pressure gradient/velocity are concordant, the assessment of severity is easy. However, these measurements are often discordant. In addition to possible measurement error, the velocity/pressure gradient may change depending on hemodynamics. Therefore, the pressure gradient does not increase if the stroke volume is low in severe AS, which is known as low-flow/low-gradient severe AS. Low-flow conditions include afterload mismatch, myocardial damage, and concomitant cardiac disease where the LVEF is reduced to <50%. Another condition is characterized by LVEF >50% but with a hypertrophied small LV leading to reduced stroke volume (paradoxical low-flow severe AS).
4.4.1 Low-Flow/Low-Gradient Severe AS With Reduced LVEF (<50%)

In patients with low stroke volume due to LV systolic dysfunction and an AVA <1.0 cm², dobutamine stress echocardiography can help distinguish between true-severe AS and pseudo-severe AS. When dobutamine infusion (maximum dose: 20 μg/kg/min) increases stroke volume by >20%, true-severe AS is diagnosed if the AVA is <1.0 cm² and the peak velocity is >4.0 m/s or the mean pressure gradient is >30–40 mmHg. A diagnosis of pseudo-severe AS is made if the AVA is >1.0 cm². If the stroke volume does not increase by >20% after the administration of dobutamine, it indicates the absence of contractile reserve. In this condition, it is difficult to distinguish between true-severe AS and pseudo-severe AS. Although the calcification score obtained by CT is a guide to such differentiation, the prognosis in this group has been shown to be poor even when SAVR is performed. However, recent reports indicate that the prognosis following TAVI is not influenced by the presence or absence of contractile reserve. Further consideration should be given to surgical indications in patients without contractile reserve.

4.4.2 Low-flow/Low-Gradient Severe AS With Preserved LVEF (≥50%) (Paradoxical Low-Flow Severe AS)

Paradoxical severe AS is defined as an AVA <1.0 cm², peak velocity <4.0 m/s, and a mean pressure gradient <40 mmHg despite preserved LVEF. A hypertrophied and small LV is characteristic of this group, resulting in low stroke volume (stroke volume index <35 mL/m²). The prognosis for this disease varies in published reports and is controversial. In cases of low-gradient severe AS with preserved LVEF, the prognosis has been reported to vary greatly depending on whether the stroke volume index is maintained or decreased. Therefore, in order to diagnose this group of patients, it is important to ensure that there are no errors in the measurement of stroke volume index or AVA. Many cases are accompanied by a history of hypertension. We should comprehensively determine whether or not true-severe AS using the calcification score, the degree of LV hypertrophy, relatively high mean pressure gradient (30–40 mmHg), and small valve area (AVA <0.8 cm²).

Figure 16 presents a flowchart for AS severity assessment.
patients were published that demonstrated the superior or noninferiority of TAVI to SAVR with regard to composite endpoints such as death, cerebral infarction, and heart failure-associated hospital readmission. The 30-day mortality rate of isolated SAVR in Japan was 1.9% and that of re-do surgery for AVR was 5.0%. The 30-day mortality rate of TAVI in Japan was \( \leq 2 \)% despite the fact that TAVI is indicated for higher-risk groups such as the elderly and patients with a history of previous open-heart surgery.

On the other hand, the current challenge for TAVI is the lack of long-term bioprosthesis durability data over a period >10 years. Accordingly, the ESC/EACTS guidelines set the age cutoff at 75 years, and the average age of the patients in the 2 low-risk RCTs was 73–74 years. In Japan, the average life expectancy is known to be 3–5 years longer than that in Europe and the USA, and life expectancy of the elderly in Japan aged \( \geq 75 \) years is 1–2 years longer than that in the USA and Europe.

The selection of SAVR or TAVI should be done after considering the patient’s age, the durability data available for each surgical valve or TAVI valve, surgical risk (STS score, EuroSCORE, and JapanSCORE, etc.), TAVI procedure risks, anatomical characteristics, comorbidities, and frailty, as well as the level of expertise of the physician in the required techniques (Table 33). Informed consent should be obtained after supplying patients with all the latest information on both the SAVR and TAVI treatments. Finally, the Heart Valve Team should be consulted prior to any decision being made. Given the various factors to consider and the lack of definitive evidence, the present guidelines do not establish a clear cutoff value of age for TAVI or SAVR. Rather, the present guidelines offer an index of prioritization that suggests using TAVI in patients aged \( \geq 80 \) years and SAVR in those aged \( <75 \) years. Because progress is being made every year in this field of clinical practice, a focused update should be implemented in accordance with these guidelines.

Both SAVR and TAVI are becoming increasingly safer every year, but with minimal improvements in the prognosis or activities of daily life, especially in the elderly. Invasive procedures for bedridden patients or those with dementia also result in a poor prognosis. Intervention in such cases should be strictly avoided. Therefore, based on an ethical and medical economic perspective, the use of such procedures should be determined after careful discussion with the Heart Valve Team.

When intervention is indicated for severe AS, simultaneous surgery of the ascending aorta is reasonable if the ascending aortic diameter is \( \geq 250 \) mm in the tricuspid aortic valve and \( \geq 45 \) mm in the bicuspid aortic valve. More details are provided in the AR section (V.6).

### 5.3.2 Indications for Intervention for Asymptomatic Severe AS

Whether early surgical intervention should be provided for asymptomatic severe AS has been controversial for decades, but no clear conclusion has yet been reached. In order to recommend early surgery for asymptomatic patients with severe AS, the benefits of early surgery, such as avoidance of sudden death or irreversible LV myocardial damage, must outweigh the risks of early surgery, such as operative mortality and postoperative complications associated with prosthetic valves. Previous observational studies have reported poor prognoses for asymptomatic patients with
Table 33. Factors to Be Considered by the Heart Valve Team When Deciding Between SAVR and TAVI for Patients With Aortic Stenosis

<table>
<thead>
<tr>
<th>Clinical patients’ factors</th>
<th>SAVR should be considered</th>
<th>TAVI should be considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger patients</td>
<td>• Younger patients</td>
<td>• Older patients</td>
</tr>
<tr>
<td>Suspicition of endocarditis</td>
<td>• Presence of severe comorbidity</td>
<td>• Favorable access for trans-femoral TAVI</td>
</tr>
<tr>
<td>Severe calcification, tortuosity, stenosis, obstruction of vessel</td>
<td>• Unfavorable conditions (except cardiac disease) for open heart surgery</td>
<td>• Unfavorable surgical access for SAVR</td>
</tr>
<tr>
<td>Severe mitral valve disease that could be treated surgically</td>
<td>• Washer in annulus</td>
<td>• Sequelea of chest radiation (severe adhesion in mediastinum)</td>
</tr>
<tr>
<td>Severe tricuspid regurgitation</td>
<td>• Previous cardiac surgery</td>
<td>• Previous history of intial coronary bypass grafts at risk when sternotomy is performed</td>
</tr>
<tr>
<td>Anieurnysm of the ascending aorta requiring surgical intervention</td>
<td>• Presence of worsening interstitial pneumonia</td>
<td>• Severe chest deformation or scoliosis</td>
</tr>
<tr>
<td>Septal hypertrophy requiring myocardectomy, etc.</td>
<td>• Bleeding tendency</td>
<td>• Unsafe aortic cross-clamping (porcelain aorta)</td>
</tr>
</tbody>
</table>

Factors to Be Considered by the Heart Valve Team When Deciding Between SAVR and TAVI for Patients With Aortic Stenosis

<table>
<thead>
<tr>
<th>Anatomical and technical factors related to SAVR and TAVI</th>
<th>SAVR should be considered</th>
<th>TAVI should be considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfavorable access for TAVI</td>
<td>• Favorable access for trans-femoral TAVI</td>
<td></td>
</tr>
<tr>
<td>Severe calcification, tortuosity, stenosis, obstruction of vessel</td>
<td>• Unfavorable surgical access for SAVR</td>
<td></td>
</tr>
<tr>
<td>High risk for coronary artery obstruction during TAVI</td>
<td>• Sequelea of chest radiation (severe adhesion in mediastinum)</td>
<td></td>
</tr>
<tr>
<td>Short distance between coronary ostia and annulus, relatively long cusp, small Valsalva, etc.</td>
<td>• Previous cardiac surgery</td>
<td></td>
</tr>
<tr>
<td>High risk for anulus rupture during TAVI</td>
<td>• Presence of intial coronary bypass grafts at risk when sternotomy is performed</td>
<td></td>
</tr>
<tr>
<td>Severe calcification in left ventricular outflow tract etc</td>
<td>• Severe chest deformation or scoliosis</td>
<td></td>
</tr>
<tr>
<td>Unfavorable valve morphology and size (annulus, aortic root, ST junction) for TAVI</td>
<td>• Unsafe aortic cross-clamping (porcelain aorta)</td>
<td></td>
</tr>
<tr>
<td>Presence of thorombi in left ventricle</td>
<td>• Small annulus highly expected patient-prosthesis mismatch</td>
<td></td>
</tr>
</tbody>
</table>

*Patient’s preference should be fully considered when making the decision between SAVR and TAVI. CABG, coronary artery bypass grafting; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

Severe AS who received conservative treatment, and have supported early surgery. RCTs such as the AVATAR study and the RECOVERY study, which compare “watchful waiting” and early AVR, are ongoing. RCTs comparing “watchful waiting” and early TAVI for asymptomatic severe AS are also in progress (the EARLY TAVR study) or planned (the EVE-TAVI study). Until the results of these studies are available, the Heart Valve Team is advised to discuss and decide the optimal therapeutic strategy based on each individual patient.

However, early surgery is recommended for some groups of asymptomatic patients with severe AS. Patients with reduced LVEF (<50%) and patients with symptoms on exercise testing have poor prognoses compared with those without these findings if managed conservatively; therefore, early surgery is recommended for these groups (Class I). LVEF <50% is known to be associated with poor prognosis, but recent studies have reported that LVEF <60% is also associated with a poor prognosis. Early surgery is reasonable in patients with a decrease in blood pressure on exercise testing. Among asymptomatic patients with severe AS, patients whose peak transvalvular velocity is highly increased (very severe AS) have a poor prognosis if managed conservatively. Conservation management of patients with a peak transvalvular velocity ≥5.0 m/s results in poorer prognoses than those with a peak transvalvular velocity <5.0 m/s; therefore, early surgery is reasonable for patients with a peak transvalvular velocity ≥5.0 m/s (Class Ia) (see CQ3). A rapid increase in the peak transvalvular velocity is also considered a prognostic factor. Early surgery may be considered if rapid progression of ≥0.3 m/s per year is observed (Class IIb). Regarding parameters other than peak aortic jet velocity, early surgery is reasonable in patients with a mean pressure gradient ≥60 mmHg or with an AVA ≤0.6 cm² because the prognosis of such patients are poor if managed conservatively (Class Ia). Early surgery is also reasonable if there is marked pulmonary hypertension (systolic pulmonary artery pressure ≥60 mmHg) caused by AS (Class Ia).

The biomarker BNP can predict symptoms and cardiovascular events in asymptomatic severe AS. The biomarker BNP is a simple, inexpensive, and repeatable test in outpatients, making it suitable for follow-up. The evaluation of the chronological change in the BNP level has been reported to be useful for prognosis prediction. Therefore, early surgery may be considered in patients with BNP level elevation. However, it is difficult to identify specific BNP levels that indicate surgical intervention because the cutoff values vary across published reports and no consensus has been reached.

In addition to AS severity, it is important to assess surgical risk when determining the surgical indications. Especially when the recommendation is Class II, surgery may be considered in patients with low surgical risk (as determined by the STS score, EuroSCORE, JapanSCORE, or catheter treatment procedure risk), whereas continued follow-up should be considered as an option in patients with high surgical risk.

The choice of either SAVR or TAVI for patients requiring intervention should be determined according to the criteria described in the previous section on symptomatic severe AS. According to the guidelines of the ACC/AHA and ESC, TAVI is indicated only for symptomatic AS. However, the definitions of symptoms are often vague, and it is difficult to determine whether AS is symptomatic or asymptomatic, especially in elderly patients. Given the current status of TAVI treatment in Japan, the Heart Valve Team is also required to determine the type of intervention when determining the indications for intervention in asymptomatic severe AS.

Concomitant SAVR is recommended in asymptomatic patients with severe AS undergoing coronary artery bypass surgery, ascending aortic surgery, or other valve surgery (Class I). In addition, concomitant SAVR is reasonable in patients with moderate AS if they are aged <70 years or if...
they are aged ≥70 years with a low risk of concomitant surgery (Class IIa).\textsuperscript{31,32}

6. Medical Therapy and Follow-up

This section is omitted from the English version.

CQ3 Should early operation be conducted for asymptomatic patients with very severe AS and preserved LVEF?

[Conclusion] If the transvalvular peak velocity is ≥5.0 m/s, the mean transvalvular pressure gradient is ≥60 mmHg or the AVA is ≤0.6 cm\(^2\), operation is recommended for asymptomatic patients at low surgical risk (2B).

[Strength of Recommendation] 2: Weakly recommended (proposed)

[Strength of Evidence] B (medium): Moderate confidence in the estimated effect

According to current guidelines in Europe and the USA, severe AS defined as an AVA <1.0 cm\(^2\), transvalvular peak velocity (V\text{\text{max}}) ≥4.0 m/s, and a mean pressure gradient (mPG) ≥40 mmHg warrants consideration of surgical intervention when symptoms are present or when the LVEF is <50%. In other words, an asymptomatic patient with severe AS and preserved LVEF does not necessarily warrant surgery. This is because the sudden death rate is ≈1% per year, even with severe AS, and if each patient is monitored carefully, survival during the asymptomatic period is similar to that of healthy people.\textsuperscript{333}

What then should we do for patients with more severe AS (very severe AS) that occurs in the absence of symptoms? Rosenhek et al divided 116 patients with asymptomatic AS and a V\text{max} ≥5.0 m/s into 2 groups according to V\text{max} ≥5.5 m/s or <5.5 m/s and found significantly poorer prognoses for patients with a V\text{max} ≥5.5 m/s. During an additional 6 months of follow-up, 6 patients suffered cardiac-related death (sudden death, n=1; heart failure, n=4; myocardial infarction, n=1).\textsuperscript{376} This indicates that even asymptomatic AS can result in cardiac-related death if the patient has very severe AS. Kang et al studied 197 cases of asymptomatic very severe AS (AVA ≤0.75 cm\(^2\), V\text{max} ≥4.5 m/s, and mPG ≥50 mmHg) divided into early surgery and conventional treatment groups. They found that the early surgery group had a superior prognosis and that the independent predictor associated with cardiac-related death in the conventional treatment group was V\text{max} ≥5.0 m/s.\textsuperscript{328} In a study that classified patients by mPG, 559 AS cases with preserved LVEF and no or minimal symptoms revealed a significantly lower 4-year survival rate when the mPG was >60 mmHg.\textsuperscript{324}

Regarding AVA, the smaller the AVA, the lower the 4-year cardiac events-free rate (34% for patients with AVA between 0.8 and 1.0 cm\(^2\), 26% between 0.6 and 0.8 cm\(^2\), and 11% at ≤0.6 cm\(^2\)), even in asymptomatic cases. Mortality was significantly higher when the AVA was <0.6 cm\(^2\), as opposed to >0.6 cm\(^2\).\textsuperscript{329} There are also a number of similar reports from Japan. In a single-institute retrospective study, the prognoses were compared between 166 cases of severe AS (V\text{max} ≥4.0 m/s, mPG ≥40 mmHg, AVA <1.0 cm\(^2\)) and 58 cases of very severe AS (V\text{max} ≥5.0 m/s, mPG ≥50 mmHg, AVA <0.6 cm\(^2\)). Very severe AS with symptoms had the worst prognosis, being similar to those with asymptomatic very severe AS and symptomatic severe AS, and a comparatively favorable prognosis was shown for asymptomatic severe AS.\textsuperscript{322} These results suggest that in Japan, early surgery should be considered for very severe asymptomatic AS. In addition, Japan’s multicenter CURRENT AS Registry shows that among 1,808 patients with asymptomatic severe AS, 291 who underwent early surgery experienced better prognoses compared with 1,517 patients who underwent a conservative course of observation. These results may be partly explained by the fact that they included 114 early surgery cases of very severe AS (V\text{max} ≥5.0 m/s).\textsuperscript{339} Indeed, some studies have reported that early surgery yields better prognoses in cases of very severe AS even when the LVEF is preserved without symptoms.\textsuperscript{344,335}

Considering these data, the ACC/AHA guidelines recommend surgery for patients with low surgical risk, V\text{max} ≥5.0 m/s, and mPG ≥60 mmHg as Class IIa.\textsuperscript{344} The ESC/EACTS guidelines recommend surgery for patients with low surgical risk that present with V\text{max} ≥5.5 m/s, prominent valve calcification, annual V\text{max} progression ≥0.3 m/s, marked increase in BNP (although the cutoff value has not been established), and pulmonary hypertension with a PASP >60 mmHg as Class IIa.\textsuperscript{341} The ACC/AHA guidelines note that an annual V\text{max} progression rate ≥0.5 m/s is classified as Class IIb, and no recommendations are given for pulmonary hypertension with a PASP ≥60 mmHg. In addition, the standards for very severe AS differ across the guidelines from Europe and the USA. The ACC/AHA guidelines indicate a V\text{max} ≥5.0 m/s, while the ESC/EACTS guidelines indicate a V\text{max} ≥5.5 m/s.\textsuperscript{8} Bobbot et al studied 558 patients with no or minimal symptoms, V\text{max} ≥4.0 m/s, and LVEF >50% and found a significant difference in survival between those with a V\text{max} ≥5.0 m/s and those with a V\text{max} <5.0 m/s. They did not find any difference between the V\text{max} 5.0–5.49 m/s group and the V\text{max} ≥5.5 m/s group.\textsuperscript{336}

Accordingly, the present guidelines refer to cases with a V\text{max} ≥5 m/s, mPG ≥60 mmHg, and an AVA ≤0.6 cm\(^2\) as very severe AS. If any of these parameters are met and the risk of surgery is low, surgery should be considered even if the patient is asymptomatic.

7. Tricuspid Regurgitation (TR)

It is reported that TR is a prognostic factor for various heart diseases,\textsuperscript{337,339} and the importance of evaluating TR is emphasized.

1. Classification and Etiology

TR is classified as primary (organic) or secondary (functional), with secondary TR accounting for 70–90% of all cases.\textsuperscript{340,344}
IZUMI C, EISHI K, et al.

1.1 Primary TR (Organic TR)
TR due to changes in the tricuspid leaflet and subvalvular tissue itself is referred to as primary TR; causes include infective endocarditis, trauma, iatrogenic causes (e.g., after pacemaker/defibrillator implantation, after RV biopsy), rheumatic, prolapse due to myxomatous change, congenital tricuspid valve lesions such as an Ebstein anomaly, carcinoids, and radiation therapy.

1.2 Secondary TR (Functional TR)
TR due to RV dilatation/dysfunction or RA dilatation without tricuspid leaflet abnormality is referred to as secondary TR. RV dilatation due to pressure and/or volume overload, dilatation of the RA due to AF, or disorders of the RV myocardium can result in tricuspid annular dilatation or tethering of the tricuspid valve, thereby worsening coaptation.

The most common condition that causes pressure overload to the RV is post-capillary pulmonary hypertension associated with left-sided heart disease, but it may also occur with pulmonary arterial hypertension or cor pulmonale (pre-capillary pulmonary hypertension). Atrial septal defect is a representative disease that causes volume overload to the RV. As the prevalence of AF increases with aging, AF-induced annular dilatation is a major cause of secondary TR. Secondary TR may often appear and progress late after left-sided valve surgery (mainly mitral valve surgery), without left-sided valve dysfunction. AF and preoperative hemodynamics are considered to be related to this process.

As a mechanism for TR, tethering is more pronounced in TR with pulmonary hypertension, whereas annular dilatation is the main mechanism in TR without pulmonary hypertension such as TR due to AF. However, tethering may occur after a long period of time as RV dysfunction develops. Valve morphology and RV function are important factors in determining the surgical indications, procedure type, and prognosis.

2. Pathophysiology and Natural History
This section is omitted from the English version.

3. Assessment of Severity
TR severity is primarily determined by echocardiography. However, there are several problems with TR severity assessment as follows. Although the severity of TR varies according to the pressure and/or volume loading conditions, such as in the treatment of HF, it is uncertain at what time the surgical indications should be determined. Many cases show multiple regurgitation jet signals, and the EROA is not circular. Quantitative evaluation of TR is difficult because of the high prevalence of AF and high respiratory variability. Quantitative evaluation of RV volume is also difficult with 2D echocardiography because the RV has complex geometry.
More accurate evaluation of RV volume can be achieved with cardiac MRI.
Grading the severity of TR is shown in Table 34. The severity of TR should be evaluated and determined using multiple parameters.

### 4. Diagnosis

In addition to confirming the symptoms and physical findings, imaging is important for diagnosis and the therapeutic strategy in TR (Table 35). Although TTE is the main imaging modality to evaluate TR, TEE, exercise testing, and cardiac MRI may also be used if necessary.

#### 4.1 Symptoms and Physical Findings

This section is omitted from the English version.

#### 4.2 Echocardiography

Echocardiography is the primary imaging technique for evaluating the severity and etiology of TR (Class I). In most cases, TTE alone is enough to assess TR, but TEE may be used as needed (Class IIb).

##### 4.2.1 TTE

The main focus of TTE evaluation in patients with TR is to assess the etiology and severity of the TR, RV size, and RV function, and to estimate the pulmonary artery and RA pressures. In secondary TR, the cause of regurgitation, such as left-sided heart disease or pulmonary hypertension, should also be assessed. These evaluations of TR follow the American Society of Echocardiography guidelines for the evaluation of native valvular regurgitation, cardiac chamber quantification, and the assessment of the right heart by echocardiography.

The first step is to determine whether the TR is primary or secondary, especially noting the presence of any structural abnormalities of the tricuspid valve. The presence of structural valvular abnormalities, annular dilatation, or valvular tethering should be carefully assessed in the multiple windows.

The regurgitant jet area measured by the color Doppler is widely used for assessing the severity of TR. However, measurement of the regurgitant jet area is often limited by multiple jets or a complex regurgitant orifice of the TR. In addition, in patients with elevated RA pressure from severe TR, the regurgitant jet area may decrease as the RV–RA pressure gradient decreases, resulting in an underestimation of TR severity. For this reason, the width of the TR jet vena contracta is often used as a semiquantitative parameter for TR grading. Continuous-wave Doppler and quantiative PISA are also used to assess TR severity. However, because each parameter has its intrinsic limitations, an integrative assessment of TR severity using multiple parameters is recommended, especially in cases where moderate or severe TR is suspected.

Evaluation of RV enlargement and function is essential in determining the optimal TR treatment strategy. The main reason for the difficulty in assessing RV function and volume by 2D echocardiography is the complex geometry of the RV. The echocardiographic parameters commonly used for evaluating RV systolic function are RV FAC, PAP, and other parameters.
TAPSE, and the systolic wave velocity of the tricuspid annulus (s′) by tissue Doppler imaging in the RV free wall. TAPSE and tissue Doppler-derived s′ values are parameters of RV longitudinal systolic function and correlate well with CO in the RV. However, in patients with moderate or severe TR, the tricuspid annulus shows exaggerated longitudinal motion, which can result in overestimation of RV systolic function. Therefore, the FAC is commonly used to assess RV function in patients with significant TR. However, it should be recognized that the FAC may also overestimate RV systolic function in patients with significant TR because of regurgitant blood flow to the RA low-pressure chamber during systole, as seen in LVEF in patients with significant MR. For assessing RV dilatation, RV diameter and area are measured in the apical 4-chamber view, while the presence of a D-shaped LV cavity due to RV volume and/or pressure overload should be confirmed in the short-axis view. Furthermore, 3D echocardiography is useful for accurately measuring the RV volume and the ejection fraction; the complexity of estimating RV volume and function with 2D echocardiography has been well documented. Currently, cardiac MRI is the standard method for RV volume evaluation, but 3D echocardiography may also be considered (Class IIb). Strain derived from 2D speckle-tracking echocardiography also provides excellent parameters of RV systolic function compared with conventional parameters. RV free wall longitudinal strain derived from 2D speckle-tracking imaging is calculated as the percentage of systolic shortening of the RV free wall from the base to the apex and is commonly used for assessing RV systolic function.

In particular, measurement of the tricuspid annular diameter is important in determining the indications for intervention in secondary TR. According to the ACC/AHA and ESC guidelines, the indications for surgical intervention are based on tricuspid annular dilatation (diameter >40 mm or >21 mm/m² indexed to BSA) assessed by echocardiography in the apical 4-chamber view. However, it has not been elucidated whether this value is appropriate for the Japanese population, which has a smaller body size than that of Western populations.

In secondary TR, tethering of the tricuspid valve should be also evaluated during mid-systole at the time of maximal valve closure in the apical 4-chamber view. In this view, the anterior leaflet (posterior leaflet in 20% of cases) is visualized at the side of the RV free wall, and the septal leaflet is visualized at the septal side. If the leaflets of the tricuspid valve are retracted in the direction of the apex by RV dilatation and valve leaflet coaptation is reduced, the valve is considered to have tethering. Preoperative tricuspid valve tethering height >8 mm reported as an important determinant of recurrence after tricuspid valve repair.

### 4.2.3 Exercise Stress Echocardiography

In asymptomatic or equivocally symptomatic patients, despite severe primary TR, exercise stress echocardiography may be effective in determining the surgical indications (Class IIb). Exercise stress echocardiography allows us to evaluate the relationship between TR severity and stress-induced symptoms or exercise tolerance. Studies on the Ebstein anomaly have shown that severe TR reduces CO from the RV during exercise stress, which can be improved by surgery.

### 4.3 Cardiac Catheterization

There are several limitations to the accuracy of echocardiographic estimations of pulmonary artery pressure, pulmonary vascular resistance, and RA pressure. Therefore, invasive right heart catheterization is useful and can be beneficial for assessing these hemodynamic parameters to determine the surgical indications for TR (Class IIa). Although right ventriculography can be used for evaluating TR severity and RV volume, these assessments are adequately made using echocardiography or cardiac MRI in most cases. Therefore, routine right ventriculography is not recommended for evaluating TR. However, right ventriculography might be useful in patients for whom echocardiography or cardiac MRI does not adequately determine the severity of the TR. In patients with severe TR, CO obtained based on thermodilution is inaccurate and the Fick method should be used instead.

### 4.4 Other Diagnostic Tests

Cardiac MRI permits accurate evaluation of RV volume and systolic function, and is the current gold standard. Cardiac MRI has also been reported as useful for assessment of hemodynamic parameters such as quantitative TR severity, tricuspid valve tethering, and pulmonary vascular resistance. Although it is not always necessary to perform cardiac MRI for the assessment of TR severity, it may be performed as needed if it is available (Class IIb). Evaluation of systemic venous congestion is also important for assessing the clinical severity of TR. Liver dysfunction due to congestion is a risk for perioperative mortality, and irreversible liver cirrhosis is a contraindication for surgery. Moreover, pancytopenia resulting from hypersplenism is associated with a risk of infection and bleeding and should be assessed in the consideration of the indications for surgical intervention. Some patients may not recognize their symptoms and in such patients, cardiopulmonary exercise testing is useful for the assessment of symptoms and exercise tolerance (Class IIb).

Table 35 lists the recommended TR tests.

### 5. Surgical Treatment

#### 5.1 Surgical Procedures and Results

This section is omitted from the English version.

#### 5.2 Indications and Timing for Surgery (Figures 18–20, Tables 37–39)

With a growing number of patients with TR, the number of patients who require surgical treatment has also been increasing. However, the indications for surgical inter-
5.2.1 Primary TR (Figure 18, Table 37)

This section describes the surgical indications for primary TR induced by structural abnormalities of the leaflets, including tricuspid valve prolapse, infective endocarditis, Ebstein anomaly, and blunt chest wall trauma. The indications for surgical intervention for functional TR associated with AF are described separately in another section.

TR may progress over time, even late after left-sided valve surgery, including mitral valve surgery, which is known to be one of the poor prognostic factors. In addition, reoperation for isolated TR after left-sided valve surgery is associated with a high perioperative mortality rate. Therefore, tricuspid valve repair (or replacement) is recommended for patients with severe primary TR undergoing left-sided valve surgery regardless of symptoms (Class I). Several studies report that tricuspid valve repair provides a better postoperative prognosis than replacement, thus tricuspid valve repair is preferable to replacement if feasible. Because moderate TR may have a risk of progression over time, tricuspid valve repair, if feasible, can be beneficial for patients with moderate TR at the time of left-sided valve surgery (Class IIa).

Meanwhile, right heart failure due to TR is known to respond well to medical therapy. Therefore, medical therapy is recommended in patients with severe primary TR in whom left-sided valve surgery is not being planned or considered. Tricuspid valve repair (or replacement) is recommended in cases with recurrent or persistent right heart failure despite optimal medical therapy or in cases where a lack of response to medical therapy for right HF is highly suspected (Class I). However, patients who have already developed severe irreversible RV dysfunction may not benefit from tricuspid valve surgery because of high perioperative risk, and the surgical indications should be carefully assessed in such patients. Similarly, tricuspid valve repair (or replacement) should be considered in cases of progressive RV dysfunction or dilatation regardless of the presence of symptoms (Class IIa), because the postoperative prognoses are poor for patients with advanced RV dysfunction before surgery. However, the specific cutoff values for RV dilatation or dysfunction have not yet been clarified.

Table 37. Indications of Surgery for Primary Tricuspid Regurgitation (TR)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
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<tbody>
<tr>
<td>Tricuspid valve repair (or replacement) is recommended for patients with severe TR undergoing left-sided heart surgery</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Tricuspid valve repair (or replacement) is recommended for patients who suffer from recurrent right heart failure due to severe TR despite medical therapy (or a lack of response to medical therapy is highly suspected)</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Tricuspid valve repair (or replacement) is reasonable for patients with severe TR and progressive RV dilation and/or systolic dysfunction regardless of the presence of symptoms</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Tricuspid valve repair is reasonable for patients with moderate TR undergoing left-sided valve surgery</td>
<td>IIa</td>
<td>C</td>
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</table>

*Except patients with irreversible severe RV dysfunction. COR, Class of Recommendation; LOE, Level of Evidence; RV, right ventricle.
Concomitant tricuspid valve repair should be considered for left-sided valve surgery (Class I). For moderate secondary TR, it is recommended for severe secondary TR at the time of left-sided valve surgery, either involving valve repair or replacement, is recommended (Class IIb). Because the criteria for tricuspid annular dilatation are not supported by definitive evidence, moderate secondary TR may worsen after left-sided valve surgery in patients without preoperative tricuspid annular dilatation. Thereafter, it has been shown that moderate secondary TR may worsen after left-sided valve surgery even in patients without preoperative tricuspid annular dilatation. It has been shown that moderate secondary TR may worsen after left-sided valve surgery in patients without preoperative tricuspid annular dilatation. It has been shown that moderate secondary TR may worsen after left-sided valve surgery in patients without preoperative tricuspid annular dilatation.

Recently, it was reported that persistent AF is associated with concomitant tricuspid valve repair and is an important determinant for surgical intervention with a cutoff value of 40 mm (in diameter) or 21 mm/m² (indexed to BSA) as measured by echocardiography in the apical 4-chamber view. However, to date, only one RCT has validated this value and a cutoff value of the tricuspid annular diameter was not adopted for moderate secondary TR in this guideline. Refer to CQ4 for further information.

The evidence supporting surgical intervention for mild secondary TR is even more limited. However, because mild TR may progress after left-sided valve surgery in patients with tricuspid annular dilatation, tricuspid valve repair may be considered for patients with mild secondary TR and tricuspid annular dilatation at the time of left-sided valve surgery (Class IIb). The criteria for tricuspid annular dilatation are not supported by definitive evidence as discussed in CQ4, this guideline adopts the cutoff value of 40 mm (in diameter) or 21 mm/m² (indexed to BSA), following the ACC/AHA and ESC guidelines.

Recently, it was reported that persistent AF is associated with TR progression late after left-sided valve surgery. Thus, patients with persistent AF may benefit from concomitant tricuspid valve repair for mild TR (Class IIb). The benefits of tricuspid valve replacement for mild or moderate secondary TR have not been proven and valve replacement is not recommended in this guideline.
renal dysfunction, resulting in increased perioperative risk. Moreover, tricuspid valve tethering due to progressive RV dilatation may present difficulties in tricuspid valve repair. Therefore, for secondary TR, it is important to consider the surgical indications at the optimal timing while monitoring the response to medical therapy, as reported by Latib et al. However, it should be recognized that optimal medical therapy and timing of surgical intervention have not been established and accumulation of more clinical evidence is needed.

The current major challenge regarding isolated secondary TR in clinical practice involves 2 presentations: progressive TR after left-sided valve surgery such as mitral valve surgery, and TR in elderly patients with AF. The present guideline provides recommendations for the surgical indications in these cases of isolated secondary TR. As for secondary TR with pulmonary hypertension, pulmonary hypertension itself is a major prognostic factor rather than the TR, and treatment should focus on the pulmonary hypertension.

As described above, the severity of secondary TR may vary depending on the hemodynamics. Here, we describe the indications for surgical intervention for secondary TR based on TR severity at the time when right HF worsens.

### a. Isolated TR After Previous Cardiac Surgery

Although many studies have demonstrated the risk of progression of secondary TR after left-sided valve surgery, surgical intervention for secondary TR after left-sided valve surgery was thought to be associated with high perioperative mortality. However, in recent years, the high perioperative mortality rate has been attributed to a deterioration in systemic conditions and RV dysfunction because of delayed surgical treatment. Therefore, surgical intervention at optimal timing is required to improve the prognoses of patients who developed significant TR after left-sided valve surgery. On the other hand, because severe secondary TR following heart surgery often responds to medical therapy, medical therapy should be attempted first. Surgical indications may be considered in patients who experience recurrent right HF despite medical therapy. Tricuspid valve repair (or replacement) is reasonable for patients with severe TR who suffer from recurrent heart failure despite medical therapy and without either of severe RV dysfunction, irreversible pulmonary hypertension, or irreversible liver dysfunction.

#### Medical therapy

- **Yes**: Recurrent right heart failure
- **No**: Medical therapy

#### Valve Repair (or Replacement)

- **Yes**: Secondary severe TR after previous cardiac surgery
- **No**: Tricuspid valve repair (or replacement) is reasonable for patients with severe TR who suffer from recurrent heart failure despite medical therapy and without either of severe RV dysfunction, irreversible pulmonary hypertension, or irreversible liver dysfunction.

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<tr>
<th>Recommendations</th>
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<th>LOE</th>
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<tbody>
<tr>
<td>Tricuspid valve repair (or replacement) is reasonable for patients with severe TR who suffer from recurrent heart failure despite medical therapy</td>
<td>IIA</td>
<td>C</td>
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</table>

**Isolated secondary TR due to AF**

- **Yes**: Progressive RV dilatation and/or dysfunction
- **No**: Medical therapy

#### Valve Repair

- **Yes**: Secondary severe TR due to atrial fibrillation
- **No**: Medical therapy

#### Valve Repair (or Replacement)

- **Yes**: Secondary severe TR due to atrial fibrillation
- **No**: Valve repair

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricuspid valve repair may be considered for patients with severe TR and progressive RV dysfunction and/or dilatation despite medical therapy regardless of the presence of symptoms</td>
<td>IIB</td>
<td>C</td>
</tr>
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</table>

AF, atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; RV, right ventricle.
RV function, the postoperative outcomes are poor.\textsuperscript{373,374,385} In cases of irreversible advanced pulmonary hypertension or liver dysfunction or in those where improvement in RV function after surgery cannot be expected, the balance between surgical risks and benefits should be comprehensively evaluated. Patients in whom no benefit of surgery is expected should be treated conservatively. The indocyanine green clearance test, Child-Pugh classification, and the MELD score are commonly used to evaluate liver function.\textsuperscript{363} However, the optimal test of liver function for predicting perioperative risk in TR surgery has not been established so far.

b. Isolated TR Associated With AF
AF causes tricuspid annular dilatation, often resulting in the development of significant TR.\textsuperscript{343} In severe TR associated with AF, medical therapy should be first attempted. Surgical intervention can be beneficial for patients who suffer from recurrent right HF despite medical therapy (Class IIa). Severe RV dysfunction and dilatation are associated with poor postoperative outcome.\textsuperscript{323,394} Thus, tricuspid valve repair may be considered before the development of right HF in patients with progressive RV dysfunction or dilatation despite medical therapy (Class IIb). In patients who have already developed pulmonary hypertension or liver dysfunction, the surgical indications should be carefully assessed based on the balance between the risks and benefits of surgery.

c. Future Directions in TR
Currently, open-heart surgery is the only available treatment option for TR in Japan. In recent years, TR treatment based on minimally invasive transcatheter techniques using several tools has been reported,\textsuperscript{384,386} and the indications for invasive treatment for TR may be more proactively assessed when these techniques are introduced in Japan.

CQ4
Should concomitant tricuspid valve repair be conducted for patients with mild TR and tricuspid annular dilatation (>40 mm or 21 mm/m\textsuperscript{2} in diameter)?

[Conclusion]
Concomitant tricuspid valve repair may be considered for patients with mild TR and significant tricuspid annular dilatation (>40 mm or 21 mm/m\textsuperscript{2} in diameter) (2C).

[Strength of Recommendation]
2: Weakly recommended (proposed)

[Strength of Evidence]
C (weak): Limited confidence in the estimated effect

[Comment]
Many observational studies have shown that even mild TR left uncorrected at the time of left-sided valve surgery may progress over time, resulting in a poor prognosis.\textsuperscript{337,349,351,367,368,375,387,390} On the other hand, if left HF improves after left-sided valve surgery, TR often improves.\textsuperscript{391} Therefore, it is necessary to identify patients at risk of postoperative TR progression among those with mild TR undergoing left-sided valve surgery and to perform prophylactic concomitant tricuspid valve repair. To date, tricuspid annular dilatation, decreased RV function, concomitant AF, and LA enlargement have been reported as risk factors for progression of TR following left-sided valve surgery.\textsuperscript{349,351,367,368,375,387,390} According to the current ACC/AHA\textsuperscript{144} and ESC\textsuperscript{c} guidelines for valvular disease, concomitant tricuspid valve repair is recommended as a Class IIa indication in patients with mild TR at the time of left-sided valve surgery and with tricuspid annular dilatation of >40 mm or >21 mm/m\textsuperscript{2} in diameter. The tricuspid annular diameter is assessed by echocardiography in the apical 4-chamber view, which is well correlated with the actual diameter measured intraoperatively.\textsuperscript{392} This cutoff value for tricuspid annular dilatation was first described in the 2007 ESC guideline for valvular disease\textsuperscript{393} and was based on 2 previous studies. Colombo et al\textsuperscript{381} reported 50 cases with a tricuspid annular diameter of >21 mm/m\textsuperscript{2} who underwent tricuspid annuloplasty with the De Vega method regardless of the TR severity at the time of mitral valve surgery. In that series of patients, none developed severe TR during the follow-up period and their clinical outcomes were favorable. However, the study lacked control cases and has limited significance as clinical evidence. In another study, Dreyfus et al\textsuperscript{382} retrospectively examined the association between tricuspid annular diameter by direct intraoperative measurements and progression of TR in patients who underwent mitral valve surgery. They concluded that a tricuspid annuloplasty should be performed at the time of mitral valve surgery to prevent progression of TR if the tricuspid annular diameter was greater than twice the normal size (>70 mm) regardless of the grade of TR. Their study did not examine the measurements of tricuspid annular diameter by echocardiography. On the other hand, only a few RCTs have examined the validity of the 40 mm or the 21 mm/m\textsuperscript{2} tricuspid annular diameter cutoff values. Benedetto et al\textsuperscript{380} conducted a prospective study enrolling 44 patients with less-than-moderate TR (≤2) and a tricuspid annular diameter ≥40 mm who underwent mitral valve surgery, randomizing them to receive or not receive tricuspid annuloplasty. At the 12-month follow-up, TR was absent in 71% versus 19% of patients in the tricuspid annuloplasty and control groups, respectively (P=0.001). Moderate to severe TR was present in 0% versus 28% of patients in the tricuspid annuloplasty and control groups, respectively (P=0.02). Although there was no significant difference in the improvement in NYHA functional class, the RV reverse remodeling was marked and the improvement in the 6-minute walk test was greater in the tricuspid annuloplasty group. Based on that study, if concomitant tricuspid valve repair is performed at the time of left-sided valve surgery in accordance with ESC or ACC/AHA guidelines, we may expect an improvement of symptoms or prognosis with improvement in RV function during the long-term follow-up, even if prognostic or symptomatic improvement over the short-term period of 12 months is not observed. In a report by Shi et al,\textsuperscript{394} 167 patients with moderate or less than moderate TR undergoing mitral valve surgery were randomized to 70 patients who received tricuspid annuloplasty and 97 patients who did not. During the long-term follow-up, the severity of TR was similar between the groups for patients with an annular diameter ≥21 mm/m\textsuperscript{2}, but the severity of TR was significantly less in the annuloplasty group in patients with a diameter >21 mm/m\textsuperscript{2}. However, that study included not only patients with mild TR but also those with moderate TR, and selection bias might have affected the results because the randomization was uneven and there were differences in the operating periods between groups. Therefore, we conclude that the evidence from this report
has limited reliability with regard to the scope of this CQ. Several observational studies of the cutoff values of the tricuspid annular diameter have been published.\textsuperscript{366,387,395–397} For example, Van De Veire et al found that concomitant tricuspid annuloplasty at the time of mitral valve surgery significantly prevented long-term TR progression and right ventricular remodeling in patients with mild TR and with an annular diameter >40 mm.\textsuperscript{390} On the other hand, David et al found that a tricuspid annular diameter of 40 mm was not a predictive factor for the development of moderate or severe TR in the long-term among 312 patients who underwent mitral valve repair without tricuspid annuloplasty.\textsuperscript{397} However, all of these studies were retrospective and included various potential biases, such as differences in operative techniques. In addition, there are studies that have reported contradicting results. It was suggested that mild TR (≤1+) may progress to moderate or severe if concomitant tricuspid annuloplasty is not performed, even in patients with an tricuspid annular diameter <40 mm.\textsuperscript{387} Another study showed no significant difference in the preoperative tricuspid annular diameter between patients who showed and did not show significant TR during long-term follow-up.\textsuperscript{395} It was also reported that tricuspid annular dilatation was a modest contributing factor for TR progression.\textsuperscript{393} Therefore, there are significant limitations in determining the indications for concomitant tricuspid valve repair based solely on the tricuspid annular diameter. Additionally, many previous investigations have suggested that mitral valve replacement has a higher risk of worsening postoperative TR than does mitral valve repair, implying that a variety of left-sided valve surgeries may not have the same effect on postoperative TR. For example, in patients after mitral valve replacement, it was reported that tricuspid annular dilatation was a high risk factor for worsening of postoperative TR,\textsuperscript{398} or that the mitral valve replacement itself was a contributing factor for the progression of postoperative TR.\textsuperscript{378} As for mitral valve replacement, it was shown in a propensity matched study that concomitant tricuspid valve repair for mild TR, regardless of the tricuspid annular diameter, might prevent progression of TR during long-term follow-up without increasing perioperative risk.\textsuperscript{379}

As described above, there is enough data showing that mild TR left uncorrected at the time of left-sided valve surgery may progress to moderate or severe TR during long-term follow-up, resulting in a poor prognosis, and that tricuspid annular dilatation may be associated with postoperative progression of TR. However, the evidence is considered insufficient to strongly recommend the indication of tricuspid valve repair for mild TR based only on the annulus diameter, and we concluded that this indication is “weakly recommended”.

6. Medical Therapy and Follow-up

This section is omitted from the English version.

VIII. Tricuspid Stenosis (TS)

1. Diagnosis

The most common etiology of TS is rheumatic disease. Isolated TS is rare, and TS is often found with other valvular diseases, particularly MS. Other etiologies include congenital disease, carcinoid syndrome, and drug-induced valvular disease. TS is usually accompanied by TR of varying degrees of severity. In addition, similarly to TR, the pathophysiology of TS includes decreased cardiac output due to impaired RV filling and systemic congestion due to increased venous pressure.

The most common diagnostic technique for TS is echocardiography (Class I). Echocardiographic findings in TS include sclerotic change, restricted motion, and doming of the tricuspid valve. However, TS may be overlooked if the tricuspid valve is not evaluated carefully due to the rarity of the disease. Although a mean tricuspid pressure gradient >5 mmHg is generally considered to indicate significant TS,\textsuperscript{398} there is little evidence demonstrating an association between the severity of isolated TS and prognosis, and the classification of TS severity has not been well validated. Table 40 shows the echocardiographic parameters indicating severe TS.\textsuperscript{398}

The tricuspid valve area can be calculated using the continuity equation or 3D echocardiography. In the continuity equation method, the valve area is calculated as stroke volume divided by the time–velocity integral of the transtricuspid flow using continuous-wave Doppler. Alternatively, this can be measured using the planimetry method using 3D echocardiography. Because of limited echocardiographic windows, the tricuspid valve area is rarely measured by 2D echocardiography. Routine cardiac catheterization only for the purposes of assessing TS severity is not recommended. Right heart catheterization may be considered for assessing the pressure gradient between the

<table>
<thead>
<tr>
<th>Table 40. Findings of Severe Tricuspid Stenosis (TS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Valve anatomy</strong></td>
</tr>
</tbody>
</table>
| • Thickened, sclerotic, calcified leaflets. Restricted motion of leaflets. | • PHT ≥190 ms  
• Valve area ≤1.0 cm\(^2\)  
• Tricuspid mean pressure gradient ≥5 mmHg  
• Tricuspid TVI >60 cm | • Dilation of right atrium and inferior vena cava |

Valve area can be measured by the continuity equation or planimetry method by 3D echocardiography. PHT, pressure half time; TVI, time-velocity integral.
RV and RA when there is a discrepancy between the TS severity as determined by echocardiography and the clinical findings (Class IIb).

### 2. Surgical Treatment

Very few cases require surgical treatment for severe TS, and few reports have been published on the topic. Surgical treatment is recommended for symptomatic severe TS. In many cases, tricuspid valvuloplasty is difficult because the valve is highly impaired and tricuspid valve replacement is required. As mentioned in the TR surgical treatment section (VII.5), there are no clear criteria for selecting the artificial valve replacement (bioprosthetic or mechanical valve). Rather, physicians must make their determination based on individual cases.

### 3. Medical Therapy

This section is omitted from the English version.

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### IX. Pulmonary Regurgitation (PR)

#### 1. Diagnosis

**1.1 Etiology**

Mild PR is frequently seen with normal pulmonary valves, but severe PR is a rare VHD. The structural abnormalities of the pulmonary valves that cause severe PR are usually congenital, such as in tricuspid valves, bicuspid valves, and hypoplasia. However, significant PR is frequently observed after pulmonary valvuloplasty in cases of tetralogy of Fallot. In addition, infective endocarditis, carcinoid syndrome, rheumatic heart disease, and use of the dopamine D1 and D2 agonist pergolide (often used in Parkinson's disease) can cause PR. Rarely, blunt thoracic trauma may cause pulmonary valve prolapse or crushing, leading to PR. Pulmonary hypertension can be a cause of secondary PR involving no apparent abnormality of the pulmonary valve.

**1.2 Assessment of Severity by Echocardiography**

There is little evidence for assessing the severity of PR by echocardiography, and its usefulness is limited. RV enlargement reflects PR severity, but pulmonary hypertension causes RV enlargement and dysfunction depending on the pressure overload. Therefore, RV enlargement is unlikely to reflect the severity of PR in patients with pulmonary hypertension. In contrast, acute PR may not cause RV enlargement. Although there is a limitation in the evaluation of PR severity based on RV enlargement, a basal RV diameter ≥42 mm and a middle diameter ≥35 mm in the apical 4-chamber view are proposed as criteria for RV enlargement in tetralogy of Fallot. The usefulness of RV function assessment using TAPSE or tissue Doppler in PR has not been recognized. The measurement of RV volume and RV ejection fraction by 3D echocardiography may be useful, but further accumulation of evidence is required. Color Doppler, pulsed Doppler, and continuous-wave Doppler at the RV outflow tract are commonly used to evaluate PR severity. The most reliable method of PR evaluation is to evaluate the ratio between the width of the regurgitation jet and the diameter of the pulmonary valve annulus. A ratio >0.7 indicates severe PR (Figure 21).

The continuous-wave Doppler waveform of severe PR has a high signal intensity and shows signs such as rapid...
deceleration and early termination (Figure 21). As a result, the pressure half-time of the PR waveform is shortened, suggesting severe PR in less than 100 ms of pressure half-time. However, because pressure half-time depends on the pressure gradient between the pulmonary artery and the RV, the specificity of the shortened pressure half-time decreases when RV diastolic pressure increases.\textsuperscript{403} There is also the PR index, which is the ratio of PR duration to diastolic time, and a PR index <0.77 indicates more than moderate PR (Table 41).\textsuperscript{30,31} The usefulness of TEE is limited in assessing PR.

### 1.3 Assessing PR by Cardiac MRI

Cardiac MRI is the most reliable quantitative evaluation method for PR. If PR evaluation is difficult by echocardiography, PR evaluation by MRI can be useful. MRI enables the measurement of stroke volume and regurgitant volume at the pulmonary valve using the phase-contrast method, and the regurgitant fraction can be obtained. A regurgitant fraction determined by MRI to be ≥40% is classified as severe, 20–40% is moderate, and <20% is mild (Table 41).\textsuperscript{404} In addition, the RV ejection fraction and RV volume measured by MRI are used as reference values to determine the indications for pulmonary valve reoperation in tetralogy of Fallot.

### 1.4 Comprehensive Evaluation of PR Severity

Because there is no established method for the quantification of PR by echocardiography, a comprehensive assessment should be performed using multiple indices (Table 41). It is reasonable to diagnose severe PR if all criteria for severe are met.\textsuperscript{30,31} However, if echocardiography cannot evaluate the severity or if the evaluation is inconclusive, especially in the late stages after pulmonary valve repair for tetralogy of Fallot, the severity of PR and RV function should be evaluated by MRI.\textsuperscript{30,31,401,404–407}

| Parameters Used in Assessing Severity of Pulmonary Regurgitation (PR) |
|---------------------------|----------------|----------------|----------------|
| Parameter | Mild | Moderate | Severe |
| RV size | Normal | Normal or dilated | Dilated |
| Ratio of PR jet width to PV annulus diameter | >0.7 | >0.7 | >0.7 |
| Density and contour of PR continuous Doppler flow | Faint or incomplete | Dense | Dense, early termination of diastolic flow |
| Pressure half time of PR Doppler flow | <100 ms | <100 ms | <100 ms |
| PR index | <0.77 | <0.77 | <0.77 |
| Pulsed wave Doppler flow reversal in the main or branch PA | Prominent | Prominent | Prominent |
| Pulmonic systolic flow VTI compared with systemic flow (LVOT) VTI | Slightly increased | Intermediate | Greatly increased |
| Regurgitant fraction by CMR | <20% | 20–40% | >40% |

CMR, cardiovascular magnetic resonance; LVOT, left ventricular outflow tract; PA, pulmonary artery; PV, pulmonary valve; RV, right ventricular; VTI, velocity-time integral. Produced by reference to Zoghbi WA, et al. 2017.\textsuperscript{30}

### 2. Surgical Treatment (Table 42)

Surgical treatment is indicated for patients with symptomatic PR. Pulmonary valve replacement is recommended for patients with symptomatic moderate or severe PR after transcatheter or surgical intervention for pulmonary stenosis (PS) (Class I).\textsuperscript{408} Surgical treatment is reasonable for asymptomatic patients with moderate or severe PR with RV dilatation and/or RV dysfunction (Class IIa). Surgical treatment may be reasonable in asymptomatic patients with moderate or severe PR with a ventricular tachycardia arrhythmia (Class IIb), in which case, concomitant surgical ablation should also be considered. Surgical treatment may also be considered in patients showing moderate or severe TR due to RV dilatation. According to some reports, pulmonary valve replacement before exceeding an RV end-diastolic volume of 170 mL/m\textsuperscript{2} and an RV end-systolic volume of 80 mL/m\textsuperscript{2} is recommended;\textsuperscript{409} however, the cutoff value for RV size that has not been established to date.

The advantage of using a homograft for pulmonary valve replacement has been shown,\textsuperscript{410} though it is rarely used in Japan. Because the durability of current bioprosthetic valves has improved and anticoagulant therapy is not required, some reports have revealed that the long-term results are better than those for mechanical valves.\textsuperscript{411,412} Other reports have shown that the reoperation rate is lower in patients with mechanical valves than in those with bioprosthetic valves, if adequate anticoagulation treatment is given.\textsuperscript{413} In Japan, bioprosthetic valves are more frequently used.\textsuperscript{414} Because pulmonary valve replacement is expected to improve symptoms, decrease RV end-diastolic and end-
systolic volumes, improve exercise tolerance, and decrease the incidence of ventricular tachycardia, it is important to perform pulmonary valve replacement at the appropriate timing.415-416

X. Pulmonary Stenosis (PS)

1. Diagnosis

RV outflow tract obstruction is classified as valvular, subvalvular, and supravalvular PS based on the stenotic location, and is most commonly caused by a congenital abnormality, accounting for 8% of all congenital heart disease cases.417 Valvular PS accounts for 80 to 90% of all RV outflow tract obstruction cases.418 Valvular PS is most commonly found as isolated valvular PS, but is also often associated with other congenital heart disease such as atrial septal defect, ventricular septal defect, or patent ductus arteriosus. In addition, multiple stenotic lesions are often present, such as valvular and subvalvular PS seen in tetralogy of Fallot.

The age of onset and symptoms depend on the degree of stenosis, unless there is other congenital heart disease. Patients with critical PS require emergency treatment during the neonatal period, whereas patients with mild PS remain asymptomatic throughout their lives. Most patients with mild or moderate PS are usually diagnosed as an incidental finding on auscultation.

Valvular PS is diagnosed based on thickened leaflets showing systolic doming on 2D echocardiography, and an accelerated jet across the stenotic valve on Doppler echocardiography. However, it is often difficult to distinguish valvular PS from subvalvular or supravalvular PS in adult patients. Careful observation of the location of a mosaic pattern of blood flow using color Doppler echocardiography and assessment of the location of the accelerated blood flow using pulsed Doppler echocardiography are useful for identifying an accurate stenotic lesion. The subxiphoid approach is useful in distinguishing valvular PS from subvalvular PS, but in adult patients there is often poor visualization in the subxiphoid view. Echocardiography cannot always accurately diagnose the stenotic lesion; cardiac MRI, cardiac CT, or cardiac catheterization is required in such patients. The severity of PS is graded by the peak transvalvular pressure gradient using Doppler echocardiography. A peak transvalvular pressure gradient <36 mmHg (peak jet velocity <3.0 m/s), 36–64 mmHg (3.0–4.0 m/s), or ≥64 mmHg (≥4.0 m/s) is graded as mild, moderate, or severe, respectively (Table 43).408,418 In addition, it is necessary to estimate the RV systolic pressure using the TR peak jet velocity. Whether or not there is a large discrepancy between the RV systolic pressure and the pressure gradient measured at the stenotic lesion should be confirmed. Especially when there are multiple stenotic lesions, the estimation of the pressure gradient at the stenotic lesions may be inaccurate; therefore, the severity of PS should be assessed by RV systolic pressure calculated from the TR peak jet velocity.53

2. Surgical and Transcatheter Treatment (Figure 22, Table 44)

It is difficult to standardize the indications for surgical intervention for patients with PS because there is insufficient evidence. Although each guideline has slightly different recommendations, intervention is recommended for patients with severe PS (symptomatic Class I, asymptomatic Class IIa) or symptomatic moderate PS (Class IIa). The indications for intervention in patients with PS are shown in Figure 22 and Table 44.

Since the first closed pulmonary commissurotomy in 1948, surgical intervention has been the only option for the treatment of patients with PS. However, since the first

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Table 43. Grading the Severity of Pulmonary Stenosis

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler peak gradient (mmHg)</td>
<td>&lt;36</td>
<td>36–64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Doppler peak velocity (m/s)</td>
<td>&lt;3</td>
<td>3–4</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>

Figure 22. Indications of surgical and transcatheter therapy for pulmonary stenosis (PS). Vmax, peak velocity.
transcatheter intervention for PS in 1982, this intervention has rapidly become popular than surgical treatment. Transcatheter intervention is available for most patients with PS, except those with annular hypoplasia, cusp dysplasia, or severe PR. Surgical intervention is only indicated in cases where the catheter intervention is difficult or unsuccessful, or for those who need surgical repair for concomitant congenital heart disease.

The safety of the transcatheter intervention has been established, and both the mortality and major complication rates are lower than 1%. In terms of efficacy, the transcatheter intervention for adults as well as pediatric patients has been reported to be effective. Care should be taken for complications such as PR after transcatheter intervention. In cases of concomitant infundibular stenosis (subvalvular stenosis), a sudden reduction in RV afterload may cause a transient deterioration in the infundibular stenosis. However, the stenosis usually improves after several months in many such cases. When surgical intervention is indicated, open pulmonary commissurotomy or pulmonary valve replacement is performed. Pulmonary valve replacement is often necessary in adults with calcification or structural deterioration of the valves. In terms of the type of prosthetic valve used, mechanical valves, which are generally considered durable, provide favorable results if sufficient anticoagulant therapy is provided. Conversely, some reports have revealed that bioprosthetic valves are effective without anticoagulation treatment because of low right heart pressure, and others have reported that the type of prosthetic valve used has no relationship to the long-term outcome. The freedom from reintervention rates 20 years after surgical intervention and catheter intervention are favorable at 88% and 84%, respectively.

### 3. Medical Therapy

This section is omitted from the English version.

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**XI. Combined or Multiple Valvular Disease**

#### 1. Problems in Combined or Multiple Valvular Disease

According to the 2016 Annual Report of the Japanese Society of Thoracic Surgery, 28.2% of valvular surgery was performed for combined valvular disease. The most common combination was mitral and tricuspid valves (55.8%), followed by mitral and aortic valves in 20.6%, and the aortic, mitral, and tricuspid valves in 15.9%. Thus, the combination of tricuspid valve and left-sided valvular diseases is common, accounting for 79.4% of surgeries for combined valvular disease.

Though combined valvular diseases are common, there is a lack of evidence for their diagnosis and treatment because of the various combinations. Especially in the combined valvular diseases of the aortic and mitral valves, the hemodynamic interactions between both valvular diseases may promote or conversely suppress the appearance of clinical findings in each lesion. Therefore, the physical findings, imaging, and catheterization data that have been validated for a single-valve disease may not provide accurate information in combined valvular diseases. It is necessary to be aware of the pitfalls for each combination (Table 45).

In addition to the combinations of severe and moderate valvular diseases, combined valvular diseases with multiple moderate valvular diseases also may cause reduced exercise tolerance, HF symptoms, LV dilatation and dysfunction, and pulmonary hypertension. Because each valvular disease is moderate, there is no evidence for the therapeutic strategies. However, the indications for surgery should be determined by comprehensively judging the effects of all lesions. Therefore, exercise tolerance, maximum oxygen uptake, evaluations of ventricular function and pulmonary hypertension at rest and during exercise, and serum BNP levels may be useful in determining therapeutic strategies.

#### 2. Disease-Specific Considerations

**2.1 Mixed AS and AR (ASR)**

Studies on ASR are few and therapeutic guidelines have not been proposed. Therefore, it is assumed that the treatment strategy for ASR will be based on treatment guidelines for the predominant disease. However, ASR may have a different clinical course from that of a case of only AS or only AR. Previous studies have reported that the prognosis of ASR with moderate AS and moderate AR is the same as for severe AS. Myocardial mass in ASR increases compared with AS only and AR only, because AS causes concentric hypertrophy by pressure overload, and AR causes eccentric hypertrophy by volume overload. The relationship between increased myocardial mass and poor prognosis of heart diseases is known. LV diastolic dysfunction accompanied by advanced LV hypertrophy is considered to be the primary cause of symptoms in ASR. Namely, a rapid increase in LV diastolic pressure due to
both LV diastolic dysfunction and volume load by AR may manifest as HF symptoms. Thus, conventional AS or AR guidelines are not sufficient for managing patients with ASR. Patients with ASR with moderate AS and moderate AR must receive careful and detailed follow-up as a severe aortic valvular disease, with evaluations of the myocardial mass and LV diastolic function in addition to the evaluation of valvular disease severity.

### 2.2 MS and MR (MSR)

The mechanism of concomitant MS and MR (MSR) is known to be rheumatic changes or mitral annular calcification due to aging. The mechanism of degenerative change due to aging is mitral annular calcification, in which fusion of the commissures rarely occurs. However, the differential diagnosis between degenerative change and rheumatic change is sometimes tricky among elderly patients. In order to detect the distribution of the calcification clearly, CT scans have been used as well as echocardiography.

MSR affects quantitative evaluation of MR using the Doppler method. MR increases the transmitial flow during diastole, resulting in an overestimation of MS severity. A comprehensive evaluation, including symptoms, rather than relying on a single Doppler index, is needed. Invasive pressure measurements by cardiac catheterization, not just evaluation by echocardiography, may help in assessing the severity. Evidence as to the optimal timing for surgery is limited. A comprehensive diagnosis from multiple viewpoints by the Heart Valve Team is required to determine the optimal timing of the operation.

Careful consideration should also be given to the choice of the surgical method. If rheumatic MS is the primary condition and less than moderate MR is present, the patient can be treated with PTMC. However, severe MR is a contraindication for PTMC. Furthermore, advanced techniques are indeed necessary in valvuloplasty for rheumatic mitral lesions. In addition to the preoperative evaluation, it is also necessary to include evaluation using intraoperative TEE.

### 2.3 MR and AS

#### 2.3.1 Pathophysiology

In recent years, in addition to SAVR, TAVI has been available for patients with severe AS. However, the presence of more than moderate MR affects the selection of SAVR or TAVI. It is important to evaluate this combined valvular disease, considering the tendency to “underestimate AS” and “overestimate MR”. MR is exacerbated and overestimated due to AS because of increasing the LV systolic pressure. Conversely, AS is underestimated because of decreasing aortic valve forward flow due to MR.

#### 2.3.2 Diagnosis and Surgical Indications

Taking the pathophysiology into consideration, the severity of AS should also be assessed by the degree of aortic valve calcification evaluated by CT. However, although AS does not improve with intervention for the mitral valve, MR may improve with intervention for the aortic valve; therefore, in this combined valvular disease, evaluating the severity and mechanism of MR is of particular importance. In other words, when surgery is indicated for severe MR, it is recommended to perform a dual valve replacement if the severity of AS is moderate or worse. However, in patients with severe AS, the indications for surgical intervention for MR (especially in the moderate stage) are determined by predicting the degree of improvement in MR with intervention for AS alone. The cause of MR is not only secondarily associated with LV dysfunction due to AS, but...
also primarily associated with valve prolapse, rheumatic change, and annular calcification. In the presence of decreased LV function due to severe AS, MR may improve after intervention for AS associated with improvement of LV function. It is important to carefully evaluate the preoperative mitral valve morphology on echocardiography because MR may not improve postoperatively in patients with significant degenerative changes of the mitral valve or mitral annular dilatation with AF.440,441

2.4 MR and AR

2.4.1 Pathophysiology
In this combined valvular disease, both AR and MR cause a volume overload to the LV resulting in LV dilatation. The degree of pressure overload depends on the predominant valvular disease, MR or AR.

2.4.2 Diagnosis and Surgical Indications
Regarding evaluation of the regurgitant severity, the volumetric method on echocardiography cannot be used for this combined valve disease, though the PISA method is appropriate. The phase-contrast method with cardiac MRI can be used to obtain more accurate data about regurgitant volume and fraction.

Because the surgical criteria for LV size and LVEF are different between asymptomatic AR and MR, the surgical indications should be determined by the predominant valvular disease. A dual valve surgery is recommended for more than moderate AR if surgical intervention is indicated for severe MR. Conversely, if surgical intervention is indicated for severe AR in patients with moderate MR, it is important to diagnose the cause of the MR, primary or secondary, as in the case of AS and MR. For secondary MR caused by LV dilatation due to severe AR, the MR may improve after surgery for the AR alone. The possibility of mitral valve repair should be determined by TEE.

2.5 AS and MS

2.5.1 Pathophysiology
Combined AS and MS is mostly caused by rheumatic disease, but the number of patients with degenerative AS and MS has been increasing in the aging population. In this combined valvular disease, AS tends to be “underestimated” because the aortic valve forward flow reduces, caused by reduced LV filling due to the MS. In addition, the MS tends to be “underestimated” because the transmural pressure gradient is underestimated by the increased LV end-diastolic pressure due to the severe AS.

2.5.2 Diagnosis and Surgical Indications
Regarding the evaluation of MS severity, it is important to measure the mitral valve area by the continuity equation and the planimetry method using 2D/3D cardiac echocardiography in addition to measuring the pressure gradient. The degree of aortic valve calcification evaluated by CT should also be considered. The extent of LV hypertrophy also helps assess the severity of the AS.

As for treatment options, PTMC should be considered first if the AS is mild and the morphology of the mitral valve is appropriate for PTMC in patients with rheumatic MS. Re-evaluation of AS severity should be done after performing PTMC.

With degenerative MS, the mitral annulus is severely calcified, not the valve leaflet. In patients with severe mitral annular calcification, it is difficult to suture a prosthetic valve to the mitral annulus, thus the surgical risk is high. The MS severity should be carefully assessed, and intervention for only the AS should also be considered if the severity of MS is mild or moderate in elderly patients. In this case, performing TAVI alone is also a treatment option. However, in patients with severe MS, intervention for AS alone leads to a poor prognosis.442

11. Prosthetic Valve Replacement

1. Types and Selection of Prosthetic Valves

Prosthetic valves can be mechanical or biological. Mechanical valves are more durable, but anticoagulation is required for life. In contrast, anticoagulants are not required for bioprostheses, but there is an issue with durability. Durability depends on the patient’s age at the time of surgery. However, progress in the production of prosthetic valves has been made, and other factors such as the emergence and popularization of transcatheter interventions for valvular disease, and the aging and longevity of the Japanese population may affect valve selection, which must be considered in the light of a variety of factors, and the final decision should be made by the patient with fully informed consent.8,443

1.1 Types and Progress of Mechanical Valves

Historically, ball valves and tilting disc valves have been used, but all current mechanical valves are bileaflet. In terms of durability, mechanical valves are significantly superior to a bioprosthesis. However, the biggest disadvantage of mechanical valves is the requirement for continuous anticoagulant therapy for life. Therefore, there is a higher risk of bleeding and thromboembolic events than with a bioprosthesis.

Recent advances in mechanical valves include the low-thrombotic On-X aortic valves. An RCT was performed comparing low-dose (PT-INR: 1.5–2.0) and standard-dose (PT-INR: 2.0–3.0) warfarin groups of high thromboembolism risk patients, showing that bleeding complications were significantly reduced in the low-dose group, but cerebral infarction and mortality rates were comparable in both groups.444 In patients with a low risk of thromboembolism, an RCT comparing dual antiplatelet therapy and standard warfarin therapy was discontinued because of the high incidence of thromboembolism and valve thrombosis in the dual antiplatelet group.445

1.2 Types and Progress of Bioprostheses

Bioprostheses are made of either bovine pericardial leaflets or porcine leaflets. A 20-year durability of bioprostheses
was reported in patients ≥60 years of age. Many studies have compared the hemodynamics of bovine pericardial valves and porcine valves, showing that the pressure gradient across the valve was lower and the EOA was larger in bovine pericardial valves compared with porcine valves. However, few studies showed a difference in LV mass regression, and the 10-year survival was comparable.

There are 2 types of bovine pericardial valve: (1) ordinary internally mounted and externally mounted valves; (2) internally mounted valve with pericardium on the inside of the stent post and an externally mounted valve with pericardium on the outside. Although the externally mounted valves have an advantage in hemodynamics, there are few reports on the long-term results beyond 10 years and reports of longer-term studies are pending. In addition, when performing the valve-in-valve procedure with TAVI for externally mounted valves, the risk of coronary obstruction is considered to be higher than with internally mounted valves, and it is important to consider various factors, such as the distance between the annulus and the coronary artery orifice and the size of the Valsalva sinus, for the valve-in-valve procedure.

The leaflet of the bioprosthesis is treated with various anticalcification media to prevent SVD. Recently, a bioprosthesis using specially treated bovine pericardium has become available. The pericardium is usually exposed to unstable aldehydes during fixation and storage, which binds calcium in the body. With this new bioprosthesis, a new method of preparation permanently blocks unstable aldehydes with capping, and excellent anticalcification effects have been found in animal experiments. Although clinical results are still scant, this valve is expected to be effective in avoiding SVD, especially in young patients.

### 1.3 Valve Selection (Table 46)

There are several studies comparing the long-term results between mechanical valves and bioprostheses in SAVR. In younger patients, mechanical valves are reported to have a survival benefit over bioprostheses, although some studies showed no difference in survival between mechanical valves and bioprostheses by age group. Reoperation was performed more frequently after bioprosthesis implantation, but the incidence of bleeding and embolic events was reported to be higher with mechanical valves.

In terms of actual usage, the proportion of bioprosthesis use increases as age increases, and the proportion of bioprosthesis use overall has increased in recent years, according to a report from the UK. In Japan, 2013–14 data from the Japan Cardiovascular Surgery Database also showed that the ratio of bioprosthesis use was 20% among patients in their 50s, 60% in the 60s, and >90% among those aged ≥70 years.

The ACC/AHA guidelines updated in 2017 recommend mechanical valves for those under 50 years of age and bioprostheses for those over 70 years of age. Valve selection should be individualized for patients between these ages. The 2017 ESC/EACTS guidelines recommend mechanical valves in the aortic position for patients aged ≤60 years, and in the mitral position for those aged ≤65 years of age, and they recommended bioprostheses in the aortic position for patients aged ≥65 years, and in the mitral position for those aged ≥70 years. As in the 2017 ESC/EACTS guidelines, the present guidelines recommend a bioprosthesis in the aortic position for patients aged ≥65 years, and in the mitral position for those aged ≥70 years; a mechanical valve in the aortic position in those aged ≥60 years, and in the mitral position for those aged ≥65 years (Class IIa). Physicians should be familiar with the advantages and disadvantages of each prosthetic valve type and consider not only age but also patient factors (e.g., lifestyle such as athletic preferences, hope of childbirth, etc.), comorbidities (e.g., bleeding disorders, thromboembolic disease), hospital access, and drug compliance. Patients who do not have adequate warfarin control (medication compliance, remote location) (Class I) or females who desire childbirth (Class IIa) are recommended for bioprostheses, but if a mechanical valve has already been implanted in the other position, a mechanical valve is often selected. It is also recommended that a bioprosthesis be used in patients who require redo surgery for a thrombosed mechanical valve despite good anticoagulant control (Class IIa). In all cases, sufficient information should be provided to the patient and discussed among the patient, family members, and physicians before the final decision is made by the patient (Class I).

As data on the long-term durability of TAVI valves, the durability of bioprostheses in young people, and long-term antithrombotic use for mechanical valves are revealed, the age cutoff values for artificial valves may change. It is also important to inform patients of the need for secondary and tertiary interventions when selecting bioprostheses for young patients.

The choice of artificial valves for patients on dialysis is controversial. According to the 2006 ACC/AHA guidelines, bioprostheses for patients with renal dysfunction, especially for patients on hemodialysis, are known to have durability issues. Although SVD by calcification is known to occur in bioprostheses and bleeding complications are common in mechanical valves, recent studies reported no difference in the surgical results between bioprostheses and mechanical valves and that it is not necessary to avoid bioprostheses for patients on hemodialysis. However, no conclusions have been reached on this topic. Physicians can only discuss the issues with patients on a case-by-case basis, and the present guidelines do not recommend either valve.

<table>
<thead>
<tr>
<th>Table 46. Recommendations for Prosthetic Valve Selection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendations</td>
</tr>
<tr>
<td>Valve choice should be finally determined by patients with fully informed consent</td>
</tr>
<tr>
<td>Bioprosthesis is recommended when anticoagulant therapy is contraindicated or cannot be fully controlled (poor compliance or remote area)</td>
</tr>
<tr>
<td>Bioprosthesis is reasonable for females who desire childbirth</td>
</tr>
<tr>
<td>Mechanical valve is reasonable for patients &lt;60 years in the aortic position and &lt;65 years in the mitral position</td>
</tr>
<tr>
<td>Bioprosthesis is reasonable for patients ≥65 years in the aortic position and ≥70 years in the mitral position</td>
</tr>
<tr>
<td>Bioprosthesis is reasonable in reoperation for mechanical valve thrombosis despite good anticoagulation control</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; LOE, Level of Evidence.
2. Prosthetic Valve Assessment and Follow-up

2.1 Basic Assessment of Follow-up
After prosthetic valve replacement, all patients must be followed for life for the early detection of prosthetic valve dysfunction, impaired cardiac function, or progressive disease of other heart valves. Therefore, regular follow-up TTE is necessary even in the absence of symptoms. Post-operative follow-up TTE is conducted within approximately 30 days postoperatively and 1 year postoperatively, then annually thereafter. In particular, follow-up on valve deterioration by echocardiography is important in cases where more than 10 years have passed since the surgery. If a new symptom presents, TEE should be used immediately to determine the cause.

TEE should be used in cases of suspected artificial valve malfunction or infective endocarditis. Both fluoroscopy of the mechanical valve and cardiac CT are useful in the event of suspected stenosis caused by prosthetic valve thrombus or pannus formation.

2.1.2 When Prosthetic Valve Thrombus Is Suspected
If prosthetic valve thrombosis is suspected in patients with new-onset dyspnea, then TTE, TEE, cinefluoroscopy, and cardiac CT may be used to quickly confirm the diagnosis. Prosthetic valve thrombosis is a problem often associated with mechanical valves, though they are also reported to occur with bioprosthetic valves. Bioprosthetic valve thrombosis with no clinical symptoms is often observed on CT, and in recent years has been reported after TAVI. Valve thrombus increases the transvalvular pressure gradient.

2.1.3 Hemolysis and Paravalvular Regurgitation
TTE should be used in cases of suspected hemolysis after prosthetic valve replacement, even if valve regurgitation is not observed. Re-do surgery should be considered if paravalvular regurgitation is caused by infective endocarditis or if the hemolysis causes refractory anemia or HF.

2.2 Antithrombotic Therapy
2.2.1 Selection and Control of Antithrombotic Drugs in Mechanical Valve Patients (Table 47)
Anticoagulant therapy with warfarin is required in all patients after mechanical valve replacement (Class I). However, thromboembolic events may appear at a rate of ≈1–3% per year despite using warfarin. In the ACC/AHA and ESC/STS guidelines for 2nd-generation mechanical bileaflet valves (e.g., Carbomedics valves, ATS valves, and St. Jude Medical valves), a target PT-INR of 2.5 (2.0–3.0) in the aortic valve position and a target PT-INR of 3.0 (2.5–3.5) in the mitral valve position is recommended. A history of embolism, presence of AF, MS, or an LVEF <35% are considered risk factors for embolism and require a target PT-INR 0.5 higher than the above ranges. For patients with a ball valve, a target PT-INR of 3.0 (2.5–3.5) in the USA and 3.5 (3.0–4.0) in Europe are recommended. In addition to warfarin, these guidelines also recommend the use of aspirin (75–100 mg). However, Japanese are known to have a higher risk of bleeding and a lower risk of embolism compared with Western populations. The optimal therapeutic range of warfarin or combinations of antiplatelet drugs should be modified from the US and European guidelines and should be considered for each individual case rather than for all cases in Japanese patients. In the present guideline, a PT-INR of 2.0–2.5 is recommended for the aortic valve position, and a PT-INR of 2.0–3.0 is recommended for the mitral valve position or the aortic valve position with a risk of embolism. However, the use of concomitant antiplatelet drugs is not recommended. For patients with apparent thromboembolic events, even during appropriate anticoagulant therapy, a PT-INR of 2.5–3.5 may be used (Class IIa) or a combination with aspirin may be considered (Class IIb).

The use of DOACs is not recommended for mechanical valve patients because in an RCT using warfarin and DOACs for mechanical valve patients, both embolism and bleeding events were higher in the DOAC group (Class III).

2.2.2 Indications and Selection of Antithrombotic Therapy in Bioprosthetic Valve Patients (Table 47)
The risk of thromboembolism is high within 3–6 months after bioprosthetic valve implantation. The incidence of cerebral infarction and death is significantly reduced with anticoagulant therapy for 6 months compared with 3

<table>
<thead>
<tr>
<th>Table 47. Antithrombotic Therapy for Prosthetic Valve Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanical valve</strong></td>
</tr>
<tr>
<td>Recommendations</td>
</tr>
<tr>
<td>Oral anticoagulant therapy with warfarin is recommended lifelong for all patients Target INR of warfarin control</td>
</tr>
<tr>
<td>• Aortic position: INR 2.0–2.5</td>
</tr>
<tr>
<td>• Aortic position and thrombotic risks: INR 2.0–3.0</td>
</tr>
<tr>
<td>• Mitral position: INR 2.0–3.0</td>
</tr>
<tr>
<td>Warfarin control of INR 2.5–3.5 is reasonable for patients with thrombotic event despite adequate anticoagulation therapy</td>
</tr>
<tr>
<td>Aspirin combination therapy may be considered for patients with thrombotic event despite adequate anticoagulation therapy</td>
</tr>
<tr>
<td>Single aspirin therapy is contraindicated</td>
</tr>
<tr>
<td>DOAC usage is contraindicated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bioprosthetic valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation therapy with warfarin control of INR 2.0–2.5 is reasonable for the first 3 months after surgery</td>
</tr>
<tr>
<td>DAPT (aspirin 75–100 mg+clopidogrel 75 mg) is reasonable for the first 6 months after TAVI, followed by lifelong single antiplatelet therapy (aspirin or clopidogrel)</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; DAPT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; INR, international normalized ratio; LOE, Level of Evidence; TAVI, transcatheter aortic valve implantation.
Table 48. Treatment for Overdose of Anticoagulant Therapy or Bleeding Complication in Patients With a Prosthetic Valve

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>General emergency management is indicated for bleeding complication</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Dose reduction or discontinuation of warfarin is indicated depending on bleeding severity and Vitamin K administration as required</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Dose reduction or discontinuation of heparin or reversal with protamine is indicated depending on bleeding severity</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Administration of fresh frozen plasma is reasonable when reversal of anticoagulation is urgent</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; LOE, Level of Evidence.

Table 49. Treatment for Prosthetic Valve Dysfunction

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve thrombosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose thrombolytic therapy or urgent/emergency valve replacement is recommended for symptomatic patients due to obstructive thrombosis of left-sided mechanical prosthesis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Valve stenosis/regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical replacement is recommended for severe prosthetic valve stenosis with heart failure symptoms</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Surgical replacement is recommended for severe prosthetic valve regurgitation with heart failure symptoms or hemolysis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Transcatheter valve-in-vein implantation is reasonable for high-risk symptomatic patients with severe bioprosthesis valve stenosis or transvalvular regurgitation in the aortic position</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

COR, Class of Recommendation; LOE, Level of Evidence.

months. Anticoagulant therapy with warfarin (PT-INR: 2.0–2.5) is recommended for the first 3 months (or 6 months if the patient has no risk of bleeding) after bioprosthetic valve implantation (Class IIa). Continuous anticoagulant therapy (PT-INR: 2.0–2.5) after 6 months is not recommended but may be considered in patients with thrombotic risk factors. After TAVI, dual antiplatelet drugs should be administered for 6 months followed by single-antiplatelet therapy for life (Class IIa). Recently, post-TAVI prosthetic valve thrombosis and restricted valve opening were reported at 7–40% and 18%, respectively. The 2017 AHA/ACC guidelines recommended anticoagulant therapy for 3 months after TAVI in patients with a low risk of bleeding. However, a study in Japan also reported that although 9.3% of TAVI patients experienced valve thrombosis within 30 days’ post-TAVI, the long-term prognosis did not differ from a group without valve thrombosis. The use of additional anticoagulants should be done with caution, because the risk of falling is higher among the elderly and the incidence of bleeding events is higher in the Japanese population than in Western populations. As with previous guideline, dual antiplatelet therapy for 6 months (class IIa) followed with single antiplatelet therapy for rest of their life is recommended in this guideline. This recommendation may change as with future coming evidence.

2.2.3 Excessive Dosage of Anticoagulant Therapy and Bleeding Complications (Table 48)

If the PT-INR exceeds 4.5 during warfarin administration, the risk of bleeding increases. If the PT-INR exceeds 6.0, the risk increases dramatically. In such cases, consider rapid reversal. If the PT-INR is 4.5–6 without active bleeding, stop warfarin or administer vitamin K depending on the risk of bleeding. If serious bleeding is observed, consider the administration of vitamin K and prothrombin complex concentrate. The recommendation of the present guideline follows the 2009 JCS guidelines for the management of anticoagulant and antiplatelet therapy in cardiovascular disease. Restarting anticoagulant therapy should be determined by the location of the bleeding, the type of intervention that has been done to stop the bleeding, and by establishing the underlying cause of the bleeding.

2.2.4 Interruption of Anticoagulant Therapy During Noninvasive Treatment or Noncardiac Surgery

 Interruption of warfarin may increase the risk of developing a thromboembolism during dental treatments such as a tooth extraction. Prospective studies have shown that dental extraction can be done without serious bleeding under warfarin if the PT-INR is between 2.0 and 4.0, although some reports recommend dental extraction at an PT-INR <2.5. As per the 2009 JCS guidelines for the management of anticoagulant and antiplatelet therapy in cardiovascular disease, we recommended that dental extraction should be done under continued use of warfarin controlling the PT-INR within the optimal therapeutic range. Antiplatelet drugs for patients undergoing noncardiac surgery should be discontinued 1 week prior to the procedure. If major surgery is performed, warfarin should be discontinued 72h prior to the procedure and the PT-INR should be controlled to <1.5. Continuous heparin administration is recommended during the perioperative period, while the PT-INR is <2.0. The heparin dose should be adjusted to maintain the activated partial thromboplastin time (aPTT) at 55–70s and should be discontinued 4–6h before surgery. After confirming there is no active bleeding after surgery, heparin should be restarted as soon as possible and then changed to warfarin. Anticoagulant and antiplatelet therapies should be continued during gastrointestinal endoscopy if performed only for observation. For endoscopic low-risk procedures such as biopsy and high-risk procedures such as polypectomy, warfarin should be discontinued for 3–4 days and adjust the dose to achieve a PT-INR of ≤1.5. Consider using heparin in cases of a high risk of thrombosis or embolism.

2.3 Diagnosis and Treatment of Thrombosis

Thrombosis in mechanical valves can cause fatal conditions such as HF or cardiogenic shock due to valve stenosis/obstruction. Patients may be asymptomatic but may show dull systolic or mechanical valve closure sounds on auscultation, and valve opening restriction or abnormal Doppler findings on TTE. Diagnosis should be made comprehensively, detected by increased pressure gradient and mobile tumor-like images on TTE, and a reduction in leaflet movement on fluoroscopy or cardiac CT. Pannus is another
condition involving restricted valve closure similar to valve thrombosis. Valve thrombosis may be suspected when the control of anticoagulant therapy is poor, symptoms appear early after valve replacement, or the onset is relatively rapid. It may, however, be difficult to differentiate between thrombosis and pannus and they may be concomitant.

Because the prognosis for valve thrombosis is poor for left-heart mechanical valves, symptoms suspected to be from valve thrombosis require an emergency initial action including low-dose fibrinolytic treatment or emergency surgery (Class I: Table 49). The 30-day mortality rate of emergency surgery was found to be high at 10–15% overall, though it was favorable for <5% of patients in the New York Heart Association (NYHA) I/II category.292–296 Until 2012, the 30-day mortality rate of obstructive left-heart mechanical valve thrombolytic therapy was 8%, with a hemodynamic success rate of 70%. However, the rate of concurrent thromboembolism and bleeding complications was high at 14%.485 In recent years, studies of low-dose fibrinolysis using the slow infusion protocol under echocardiographic guidance have been published, with mortality rates of <2% and success rates > 90%. Moreover, both thromboembolism and bleeding complications were reported to be <2%.487,488 Using that protocol, the study also showed favorable results even in cases of severe symptoms and with a large thrombus. However, whether to perform surgery or select fibrinolysis therapy should be determined on a case-by-case basis, considering the capability of each facility. Surgery is recommended in patients with low surgical risk, contraindication to thrombolysis, large thrombus (e.g., >0.8 cm² or >10 mm), high level of severity (hemodynamic instability, NYHA IV), and other concomitant VHD requiring cardiac surgery. Fibrinolytic therapy should be considered when skilled surgeons are unable or unavailable to perform immediate surgery, in cases of small thrombus or in hemodynamically stable patients. 

2.4 Nonthrombotic Prosthetic Valve Dysfunction (Stenosis/Regurgitation)

2.4.1 Definition and Pathophysiology of Prosthetic Valve Dysfunction

The definition of prosthetic valve dysfunction differs across reports, as does the frequency of dysfunction. As a result, the need to unify the definition of prosthetic valve dysfunction or failure has increased and several statements on this matter have been released from European and American academic societies.492–494 In both statements, SVD was clearly differentiated from infective endocarditis, paravalvular regurgitation, and patient–prosthesis mismatch (PPM), and SVD was described as a structural abnormality of the prosthetic leaflet.

With the new definition, it is important to correctly evaluate the severity of the stenosis and regurgitation, mainly based on echocardiographic assessment and the presence of symptoms.

A mechanical prosthetic valve is highly durable, but occasionally formation of a thrombus or pannus can cause leaflet malfunction. Formation of pannus is caused by various inflammatory responses to the materials of the prosthetic valve and thrombus can form on the surface of pannus. For bioprosthetic valves, SVD usually begins 5–7 years after implantation, mainly through degeneration and calcification, and no useful medical therapy has yet been established to prevent SVD. A bioprosthetic valve at the mitral position tends to be more prone to valve degeneration.

Porcine aortic valve leaflets and bovine heart pericardium are the main materials used for bioprosthetic valves. Externally-mounted leaflet valves such as the Trifecta, Mitroflow, and stentless Solo Smart, and sutureless valves such as the Perceval and Intuity valves are relatively new, and it remains unclear whether they can produce results comparable to those of other surgical bioprosthetic valves. Attention should be paid to the development of leaflet lacerations, particularly in the externally-mounted leaflet valves.490

Current transcatheter bioprosthetic valves are limited to aortic valve placement in Japan, and there are 2 types: balloon-expandable and self-expandable valves. Both valves can be affected by prosthetic valve failure from damage associated with crimping, asymmetric expansion, and valve-frame interaction.491

Paravalvular regurgitation is a complication that can be observed after valve replacement with either a mechanical or bioprosthetic valve. It can be caused by infective endocarditis, suture failure, mechanical stress, etc. Paravalvular regurgitation is a complication that occurs at a rate of 5–10% after aortic valve replacement and 10–20% after mitral valve replacement. The majority of cases are asymptomatic, and ~10% of patients with paravalvular regurgitation have symptoms of HF or hemolytic anemia.492

2.4.2 Diagnosis of Prosthetic Valve Dysfunction

Diagnosis of prosthetic valve dysfunction is mainly made by echocardiography, but CT and MRI sometimes play a significant role. CT can help distinguish between a thrombus and pannus and could help in recognizing paravalvular regurgitation.493 The quantification of prosthetic valve regurgitation using MRI is particularly important for prosthetic valves at the pulmonic valve position.494

Fluoroscopy is useful when evaluating the movement of the mechanical valve leaflets, the stent strut form, and calcification of a bioprosthetic valve.495 Each mechanical valve has a predefined threshold for the opening and closing angles. Excessive valve ring movement (>15°) is also recognized as dehiscence and usually accompanies a high degree of paravalvular regurgitation. Gallium scintigraphy or positron emission tomography CT can be useful for assessing the presence of infection.496

a. Diagnosis of Prosthetic Valve Stenosis

The opening of the prosthetic valve is mainly assessed by echocardiography to determine the EOA. However, it is difficult to accurately measure the diameter of the LV outflow in some situations and the degree of stenosis can be alternatively assessed using the Doppler velocity index or other methods. There is a predetermined normal EOA reference value for each valve type and size, with moderate prosthetic valve stenosis defined as <−1 standard deviation (SD) from the reference value and severe prosthetic valve stenosis as ≤−2 SD from the reference value. It is recommended to diagnose severe prosthetic valve stenosis when there is a peak transvalvular velocity ≥4 m/s and an EOA ≤0.8 cm² for the aortic position, and a peak transvalvular velocity ≥2.5 m/s and an EOA ≤1.0 cm² for the mitral position (Table 50).

PPM is not a valve failure itself, but may occur when an undersized valve compared to the patient’s body size has
been implanted. Therefore, if a relatively high-pressure gradient is recorded early after surgery, physicians should suspect PPM. Moderate PPM is relatively common (20–70%), but severe PPM is rare (2–10%). Severe PPM is defined as an EOA index <0.65 cm²/m² (for BMI <30 kg/m²) or <0.55 cm²/m² (BMI >30 kg/m²) at the aortic position, or an EOA index <0.90 cm²/m² (BMI <30 kg/m²) or <0.75 cm²/m² (BMI >30 kg/m²) at the mitral position.

b. Diagnosis of Prosthetic Valve Regurgitation

With mechanical valves, although small amounts of physiological regurgitation jet can usually be seen at the rotating axis (pivot) and inside the sewing cuff, pathological transvalvular regurgitation may be observed due to the formation of pannus, a thrombus, or vegetation. Although small amounts of physiological regurgitation may also be seen at the center of the bioprosthetic valve, advanced leaflet degeneration can lead to pathological regurgitation.

The severity of regurgitation is determined by the criteria shown in Table 51 for both mechanical and bioprosthetic valves. In addition, because of the increase in the number of TAVI cases in recent years, independent diagnostic criteria have been proposed for paravalvular regurgitation following TAVI. The localization of paravalvular regurgitation is numbered in a clockwise manner from the LA side with “12 o’clock” at the center of the aortomitral continuity. The severity of regurgitation is mainly determined by the echocardiographic findings, but the acoustic shadow caused by the metal structure of the prosthetic valve often complicates the evaluation and TEE can be

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### Table 50. Diagnosis of Prosthetic Valve Stenosis

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Possible obstruction</th>
<th>Significant obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve prosthesis</td>
<td>Acceleration time (ms)</td>
<td>&lt;80</td>
<td>80–99</td>
</tr>
<tr>
<td></td>
<td>Peak velocity (m/s)</td>
<td>&lt;3.0</td>
<td>3.0–3.9</td>
</tr>
<tr>
<td></td>
<td>Mean PG (mmHg)</td>
<td>&lt;20</td>
<td>20–34</td>
</tr>
<tr>
<td></td>
<td>Increase in mean PG during follow-up (mmHg)</td>
<td>&lt;10</td>
<td>10–19</td>
</tr>
<tr>
<td></td>
<td>EOA (cm²)</td>
<td>&gt;1.1</td>
<td>0.8–1.1</td>
</tr>
<tr>
<td></td>
<td>Measured EOA vs normal reference value (cm²)</td>
<td>Reference±1SD</td>
<td>&lt;Reference–1SD</td>
</tr>
<tr>
<td></td>
<td>DVI (VTIvo/VTIV)</td>
<td>≥0.30</td>
<td>0.25–0.30</td>
</tr>
<tr>
<td>Mitral valve prosthesis</td>
<td>Pressure half time (s)</td>
<td>&lt;130</td>
<td>130–200</td>
</tr>
<tr>
<td></td>
<td>Peak velocity (m/s)</td>
<td>&lt;1.9</td>
<td>1.9–2.5</td>
</tr>
<tr>
<td></td>
<td>Mean gradient (mmHg)</td>
<td>≤5</td>
<td>6–10</td>
</tr>
<tr>
<td></td>
<td>Increase in mean PG during follow-up (mmHg)</td>
<td>&lt;5</td>
<td>5–12</td>
</tr>
<tr>
<td></td>
<td>EOA (cm²)</td>
<td>&gt;2.0</td>
<td>1.0–2.0</td>
</tr>
<tr>
<td></td>
<td>Measured EOA vs normal reference value (cm²)</td>
<td>Reference±1SD</td>
<td>&lt;Reference–1SD</td>
</tr>
<tr>
<td></td>
<td>DVI (VTIV/VTIvo)</td>
<td>&lt;2.2</td>
<td>2.2–2.5</td>
</tr>
</tbody>
</table>

AV, aortic valve; DVI, Doppler velocity index; EOA, effective [valve] orifice area; LVOT, left ventricular outflow tract; PG, pressure gradient; VTI, velocity time integral.

### Table 51. Grading the Severity of Prosthetic Valve Regurgitation

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve prosthesis</td>
<td>AR jet width</td>
<td>Small</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Pressure half time of AR jet (ms)</td>
<td>&gt;500</td>
<td>200–500</td>
</tr>
<tr>
<td></td>
<td>Circumferential extent of PVL (%)</td>
<td>&lt;10</td>
<td>10–29</td>
</tr>
<tr>
<td></td>
<td>Vena contracta width (cm)</td>
<td>&lt;0.3</td>
<td>0.3–0.6</td>
</tr>
<tr>
<td></td>
<td>EROA (cm²) (PISA method)</td>
<td>&lt;0.10</td>
<td>0.1–0.29</td>
</tr>
<tr>
<td></td>
<td>RV vol (mL)</td>
<td>&lt;30</td>
<td>30–59</td>
</tr>
<tr>
<td>Mitral valve prosthesis</td>
<td>Color flow MR jet</td>
<td>Small</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Pulmonary vein flow</td>
<td>Systolic dominance</td>
<td>Systolic blunting</td>
</tr>
<tr>
<td></td>
<td>Mitral inflow (m/s)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>DVI (VTIvo/VTIV)</td>
<td>&lt;2.2</td>
<td>2.2–2.5</td>
</tr>
<tr>
<td></td>
<td>VC width (cm)</td>
<td>&lt;0.30</td>
<td>0.30–0.59</td>
</tr>
<tr>
<td></td>
<td>Circumferential extent of PVL (%)</td>
<td>&lt;10</td>
<td>10–29</td>
</tr>
<tr>
<td></td>
<td>EROA (cm²)</td>
<td>&lt;0.20</td>
<td>0.20–0.39</td>
</tr>
<tr>
<td></td>
<td>RV vol (mL) (volumetric or PISA method)</td>
<td>&lt;30</td>
<td>30–59</td>
</tr>
</tbody>
</table>

AR, aortic regurgitation; DVI, Doppler velocity index; EROA, effective regurgitant orifice area; LVOT, left ventricular outflow tract; PVL, paravalvular leakage; RV, right ventricle; VTI, velocity-time integral.
useful in such cases. In particular, a diagnosis of mitral valve paravalvular regurgitation can be exclusively achieved by TEE alone in the majority of cases. Conversely, aortic valve regurgitation can be more accurately detected by TTE, depending on the location. Quantification of artificial valve regurgitation is often difficult with TTE or TEE, and blood flow quantification using MRI often helps to identify the severity.

**2.4.3 Indications for Surgery and Transcatheter Intervention for Prosthetic Valve Dysfunction**

Severe prosthetic valve stenosis/regurgitation causes HF and hemolysis. If these symptoms are present, surgery or transcatheter treatment should be considered.

**a. Surgical and Transcatheter Interventions**

Surgery was originally the only treatment option available for severe prosthetic valve dysfunction, including paravalvular regurgitation. In recent years, however, the option of transcatheter treatment has emerged, including valve-in-valve treatment for bioprosthetic valve stenosis or transvalvular regurgitation, and transcatheter closure for paravalvular regurgitation.

Favorable results have been shown for re-do SAVR, but the operative mortality was reported to be higher than for the initial SAVR. The Valve-in-Valve International Data Registry report indicates that the surgical mortality rate among 459 patients who underwent the valve-in-valve procedure with a high surgical risk was lower than the expected mortality rate predicted by the STS score. Conversely, the outcomes of re-do SAVR were reported to be comparable to those for valve-in-valve treatment. There are also reports of poor prognoses when valve-in-valve is performed for small-sized bioprosthetic valve cases of PPM just after initial SAVR.

Re-do SAVR or valve-in-valve options should be determined on a case-by-case basis by the Heart Valve Team with consideration of the size and type of bioprosthesis, anatomical compatibility of the size of the Valsalva sinus, surgical risk, etc. Valve-in-valve for mitral bioprostheses has not been approved in Japan as of March 2020. However, the 1-year survival rate of this treatment was comparable to that for re-do valve replacement, despite involving higher risk patients compared with re-do valve replacement according to overseas retrospective observational studies.

Surgical procedures for paravalvular regurgitation include re-do mitral valve replacement and partial repair using a patch. These approaches may be selected based on the risk of surgery and the extent of the leak. In a long-term follow-up study involving 190 patients who underwent surgical procedures for paravalvular regurgitation, the operative mortality was 7%, 10-year survival was 56%, and the recurrence rate at 10 years was 32%. Among 122 long-term follow-up cases, the 30-day mortality was 10.7% and 12-year survival was 39%. Meanwhile, the long-term outcomes of transcatheter closure have not yet been shown, although short-term results have been reported as favorable. Among 308 cases, 91% had success in placing closure devices and the mortality rate was 3.9%. The median follow-up period was 110 days, with 25.3% of patients showing moderate or greater paravalvular regurgitation. Transcatheter closure of paravalvular regurgitation has not been approved in Japan as of March 2020.

**b. Indications for Intervention for Prosthetic Valve Dysfunction (Table 49)**

Re-do valve replacement is performed for severe prosthetic valve stenosis and/or regurgitation with HF symptoms (Class I). Re-do valve replacement should be performed for prosthetic valve regurgitation (often paravalvular) that causes severe hemolysis (Class I). In addition, transcatheter valve-in-valve treatment is performed for symptomatic severe aortic bioprosthetic valve stenosis and/or regurgitation with a high surgical risk (Class IIa). For asymptomatic severe prosthetic valve stenosis/ regurgitation, the Heart Valve Team should carefully determine the indications based on guidelines for native valve diseases, considering the risks with re-do surgery.

**2.4.4 Medical Therapy**

A moderate degree of stenosis due to PPM or SVD or a moderate degree of paravalvular or transvalvular regurgitation can be managed with medical therapy, including common HF drug therapy, especially diuretics and antihypertensive agents. Conversely, mechanical hemolysis may present with severe hemolytic anemia in cases of paravalvular regurgitation even at less than a severe degree. Severe hemolytic anemia may require surgical treatment, but is often challenging because of re-do surgery and coexistent comorbidities. In such cases, transfusion is the only therapeutic option, but frequent transfusions pose a risk of developing hemochromatosis and irregular antibodies. Hematopoiesis is usually amplified in cases of hemolytic anemia, but erythropoietin and iron administration are often effective. Because hemolysis occurs when blood passes through a small tunnel between the prosthetic valve and the tissue, beta-blockers may be effective for preventing progression of anemia by reducing stress on blood cells. If bradycardia is caused by beta-blockers, permanent pacemaker implantation may be required.

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**XIII. Management After Valve Repair**

**1. Mitral Valve Repair**

**1.1 Postoperative Assessment and Follow-up**

The evaluation of mitral valve repair is performed by echocardiography and should be done with prior information of preoperative cardiac function, anatomical lesion, etiology of MR, selected surgical procedures and when the surgery was performed.

**1.1.1 Intraoperative TEE After Mitral Valve Repair**

Assessment should be performed with the patient in a hemodynamically stable state after removal of the aortic cross-clamp. Even in cases of mild residual regurgitation, the reoperation rate is higher than without residual regur-
2. Aortic Valve Repair and Valve-Sparing Root Replacement

2.1 Postoperative Assessment and Follow-up

The postoperative evaluation of aortic valve repair is performed mainly by echocardiography, which should be done with the prior information of preoperative cardiac function, anatomical lesion, etiology of AR, and selected surgical procedures.

2.1.1 Intraoperative TEE After Aortic Valve Repair

Assessment needs to be performed with the patient in a hemodynamically stabilized state after removal of the aortic cross-clamp. Coaptation length ≥4 mm\(^2\) and effective height ≥9 mm\(^2\) have been reported as indicators for preventing recurrent AR late after aortic valve repair. Because the effective height correlates with BSA, \(\rho_{\text{A}}\) in patients with small body size appropriate adjustment may be needed when these indices are used. Other predictors of recurrent AR include a coaptation occurring below the level of the aortic annulus and residual AR. \(\rho_{\text{A}}\) Previous studies have identified that even a mild residual regurgitation is a risk factor for recurrent AR. \(\rho_{\text{A}}\) However, if the residual AR appears centrally with sufficient coaptation, mild AR (vena contracta <3 mm) can be acceptable. More than moderate regurgitation, or mild regurgitation but appearing eccentrically along the leaflet surface, indicates an incomplete repair such as residual leaflet prolapse, which requires revision of the repair or valve replacement. In cases of annuloplasty, the annular diameter needs to be measured by TEE to determine whether plication of the annulus has been adequately performed. Moderate or more than moderate AS (AVA <1.5 cm\(^2\)), which may occasionally result from excessive plication of the leaflet or the aortic root, requires consideration of re-repair or valve replacement. In cases of coronary artery reconstruction, cardiac CT is appropriate to rule out anastomotic failure. Leaflets and the aortic root can be visualized and evaluated by cardiac CT. Unlike the occurrence of recurrent MR after mitral valve repair, which plateaus 1–2 years postoperatively, that of recurrent AR tends to be consistent after surgery. Recurrent AR due to suture dehiscence or perforation at the repair site can lead to a rapid change in the severity of regurgitation. There are no clear criteria for follow-up intervals. It may be adequate to follow-up with TTE at discharge, 1–3 months after discharge, then every 6 months thereafter. If the TTE findings remain unchanged, annual follow-up may be reasonable.

2.1.2 Postoperative Follow-up

After repair surgery, a change in the pulse pressure and a diastolic murmur on auscultation should be carefully evaluated. LV function, residual regurgitation, and postoperative stenosis should be checked by TTE, usually 1 week postoperatively or before discharge. When the TTE image is suboptimal for visualizing postoperative hematoma around the aortic root, evaluation by CT before discharge is recommended. In patients who underwent coronary artery reconstruction, cardiac CT is appropriate to rule out anastomotic failure. Leaflets and the aortic root can be visualized and evaluated by cardiac CT. Unlike the occurrence of recurrent MR after mitral valve repair, which plateaus 1–2 years postoperatively, that of recurrent AR tends to be consistent after surgery. Recurrent AR due to suture dehiscence or perforation at the repair site can lead to a rapid change in the severity of regurgitation. There are no clear criteria for follow-up intervals. It may be adequate to follow-up with TTE at discharge, 1–3 months after discharge, then every 6 months thereafter. If the TTE findings remain unchanged, annual follow-up may be reasonable.
2.2 Indications for Reoperation

The cause of recurrent AR depends on the repair procedure, and its incidence varies according to the institution. Residual leaflet prolapse and its progression, suture dehiscence, perforation at the repair site, scarring or calcification of the leaflet, annular redilatation, infective endocarditis, and aortic dissection are reported as causes of recurrent AR.\textsuperscript{518,521–523} Re-repair is rarely feasible and AVR is selected for reoperation in most cases. The decision for reoperation can be made in reference to the initial AR surgery guideline. Symptomatic patients with severe AS require reoperation. In patients with less than severe but moderate or more than moderate recurrent/residual AR, who present with symptoms or progressive dilatation of the LV and/or decline of the LVEF, careful evaluation and consideration of reoperation should be undertaken, because the severity of the AR was possibly underestimated in such cases. Periodic monitoring of BNP function is useful for assessing LV function. TEE is reasonable for the patient with TTE imaging that is suboptimal for detailed evaluation of the recurrent/residual AR severity and etiology. When TEE imaging is also suboptimal due to acoustic shadowing resulting from the annuloplasty ring or the vessel graft, cardiac CT is useful for visualizing and evaluating the aortic valve. When there is a discordance between the symptoms and imaging findings, exercise stress echocardiography to observe changes in the symptoms and hemodynamics, is helpful to reveal the indications for reoperation.\textsuperscript{6}

XIV. Others

1. Treatment for Concomitant AF

1.1 Antithrombotic Therapy for AF

1.1.1 Risk Assessment for Cerebral Infarction With AF

Evaluating the risk of cerebral infarction in patients with nonvalvular AF in order to select the appropriate antithrombotic therapy is encouraged. However, evaluation is limited in cases of valvular AF. According to the 2013 JCS guidelines on the pharmacological treatment of AF, “valvular” includes both artificial valve replacement (both mechanical and biological) and rheumatic mitral valve disease (primarily stenosis). However, guidelines recently announced in the USA and Europe define “valvular AF” as AF with moderate or severe MS and mechanical valves. AF with native valve diseases and bioprosthetic valves is treated as “nonvalvular AF”. Although it is not based on established evidence, the prospective DOAC registry for AF includes valvular diseases, except moderate or severe MS and mechanical valves, and the efficacy and safety are similar to that in other nonvalvular AF cases. Therefore, the present guidelines also define “valvular AF” as AF with moderate or severe MS and a mechanical valve.

1.1.2 Antithrombotic Therapy for AF

Warfarin is the standard antithrombotic therapy for valvular AF. Warfarin therapy with a PT-INR 2.0–3.0 is recommended, especially given the high risk of embolism (Class I). Note that valvular AF does not apply to DOAC use (Class III). Nonvalvular AF follows the guidelines for the management of AF (except 3 months after bioprosthetic valve replacement – see section XII.2.2. Table 47).

Please refer to \textsuperscript{CQ5} for the use of DOAC in AF patients who undergo bioprosthetic valve replacement.

\textsuperscript{CQ5}

Can direct oral anticoagulants (DOACs) be used in patients with AF after bioprosthetic valve replacement?

[Conclusion]

DOACs can be used in patients with AF and bioprosthesis after the 3rd postoperative month (2C).

[Strength of Recommendation]

2: Weakly recommended (proposed)

[Strength of Evidence]

C (weak): Limited confidence in the estimated effect

Initially, and for many years, warfarin was the only oral anticoagulant. However, since 2011, DOACs that directly and selectively inhibit the thrombin or factor Xa coagulation cascade have become available for nonvalvular AF. Previous RCTs for nonvalvular AF demonstrated that DOACs were comparable to warfarin in terms of preventing embolic events and superior in terms of major bleeding.

When we discuss whether DOACs can be used in patients with AF after bioprosthetic valve replacement, the definition of “valvular AF” becomes an issue.

The European guidelines for the management of AF treat only mitral stenosis and mechanical values as valvular diseases, thus they treat patients with bioprosthetic valves as having “non-valvular” AF.\textsuperscript{525,526} In the ESC guidelines for the management of VHD,\textsuperscript{8} it is acceptable to use DOACs with bioprosthetic valves, although clear evidence is not provided.

There are few reports on using DOACs in patients with AF after bioprosthetic valve replacement. In large-scale RCTs comparing warfarin and DOACs in patients with AF, 13–26% of cases were described as having VHD and \textsuperscript{80} displayed VHD on echocardiography.\textsuperscript{527–530} The ENGAGE AF-TIMI 48 trial\textsuperscript{531} included 13% of patients with a history of moderate to severe VHD, most of whom were MR cases, and also included those with a history of valvular surgery. A subanalysis of the same clinical trial was performed with regard to patients after bioprosthetic valve replacement, and it showed no difference in the incidence of embolic events and major bleeding between DOACs and warfarin.\textsuperscript{532} In the ARISTOTLE study, a subanalysis of patients after bioprosthetic valve replacement and valve repair also revealed that DOACs were not inferior to warfarin.\textsuperscript{533} A single-center retrospective study\textsuperscript{534} investigated 73 patients with AF after bioprosthetic valve replacement who were treated with DOACs (44 on dabigatran, 25 on rivaroxaban, 4 on apixaban), and showed the efficacy of DOACs for thromboembolism. The majority (72.6%) of patients were on concurrent aspirin, and 1 transient ischemic attack (1.4%), 5 major episodes of bleeding
Factors.

The use of balloon-expandable valves, valve-in-valve, and thrombosis following TAVI was found to be 2.8%, and 68% with warfarin.

471 For heart mechanical valves, however, an RCT found the use of dabigatran was associated with increased rates of thromboembolic and bleeding complications, as compared with warfarin. 472 Therefore, DOACs should not be used for AF in patients with mechanical valves.

In nonvalvular AF, 90% of intracardiac thrombi forms in the LA appendage, 536 whereas bioprosthetic valve thrombus forms at the suture site and is often associated with a failed valve. 68,465 Recently, it was reported that valve thrombosis is frequently found by cardiac CT after TAVI. Among 890 cases undergoing cardiac CT following SAVR or TAVI, valve thrombosis was noted in 106 cases (12%), and the prevalence was higher with TAVI than with SAVR (TAVI 13%, SAVR 4%). Anticoagulant therapy decreased the frequency (15% on dual antiplatelet therapy, 4% on warfarin, 3% on DOACs). None of these cases presented clinical manifestations, and thrombosis resolved with anticoagulant therapy in all cases. 49 The frequency of valve thrombosis following TAVI was found to be 2.8%, and the use of balloon-expandable valves, valve-in-valve, and antiplatelet therapy alone were all reported to be risk factors. 539 It is believed that effectiveness for bioprosthetic valve thrombosis may be equivalent for warfarin and DOACs.

Therefore, DOACs can be used in patients with AF and bioprostheses after the 3rd postoperative month. However, as there is not enough evidence, it is deemed a “weak recommendation”.

### 1.2 Cox Maze Procedure, LA Appendage Closure, and Resection During Valvular Surgery Concomitant With AF

#### 1.2.1 Overview

Surgical strategies, such as the Cox maze procedure or LA atrial appendage closure/resection, for patients with AF and VHD should be determined based on the potential efficacy to prevent thromboembolic events and the risk of these procedures. Although the Cox maze procedure is one of many surgical rhythm control methods for AF, in this section, “the Cox maze procedure” is used to represent surgical rhythm management for AF in general.

1.2.2 Indications for the Cox Maze Procedure During Mitral Valve Surgery (Table 52)

In an RCT by Gillinov et al, 538 260 mitral valve surgery patients with persistent AF were divided into either a surgical ablation (atrial Cox maze or pulmonary venous isolation) or no ablation group, with a comparison of the AF rates at 12 months later. The rate of patients without AF was higher in the ablation group than in the non-ablation group (63% vs. 29%). However, the rate of pacemaker use was significantly higher in the ablation group (21.5% vs. 8.1%). There was no significant difference in the rates of 1-year mortality, cerebral infarction, or re-admission for HF. Other randomized and observational studies have shown that surgical ablation at the time of mitral valve surgery significantly increased the rate of postoperative sinus rhythm compared with mitral valve surgery alone. 539

In the short term, the Cox maze procedure performed with mitral valve surgery is a treatment that increases the postoperative sinus rhythm rate without increasing the surgical risk. The Cox maze procedure should be considered for chronic/persistent AF during mitral valve surgery (Class IIA). The Cox maze procedure or pulmonary venous isolation may be considered for paroxysmal AF (Class IIB).

Older age, larger LA, and a long history of AF are known predictors of an unsuccessful Cox maze procedure. 545,546 However, the cutoff values are unclear, and the Heart Valve Team should thoroughly review the indications for the Cox maze procedure in each case. It remains unclear whether the Cox maze procedure at the time of mitral valve surgery improves long-term survival. 547,551

1.2.3 Indications for the Cox Maze Procedure During Aortic Valve Surgery (Table 52)

There are fewer studies on performing the Cox maze procedure during aortic valve surgery than during mitral valve surgery. In 2 single-facility observational studies, the group undergoing the Cox maze procedure at the time of SAVR showed a significantly higher rate of sinus rhythm than the group without the Cox maze procedure; there was no difference in mortality or complication rates. 552,553 As in mitral valve surgery, LA size is a predictor of an unsuccessful Cox maze procedure. 554,555 In aortic valve surgery, the LA is often not as large as the mitral valve, and that may contribute to the success rate. 555 The Cox maze procedure for chronic/persistent AF during aortic valve surgery should be considered (Class IIA). However, the effect on long-term survival remains unclear.

1.2.4 LA Appendage Closure/Resection During Valvular Surgery (Table 52)

LA appendage closure for nonvalvular AF is equivalent to anticoagulation treatment in preventing embolism, with fewer bleeding events and deaths reported than with anticoagulant therapy. 556 However, there are no large-scale RCTs to evaluate the effectiveness of LA appendage closure/resection during valvular surgery. According to observational studies, LA appendage closure/resection has contributed to fewer postoperative embolism events, though other studies indicate negative results. 557,559 LA appendage closure/resection should be considered during valvular surgery concomitant with AF (Class IIA).

### Table 52. Concomitant Maze Procedure and LAA Resection/Closure With Valve Surgery

<table>
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<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
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<td>Concomitant maze procedure is reasonable for permanent or persistent AF at the time of mitral valve surgery</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>Concomitant maze procedure or pulmonary vein isolation may be considered for paroxysmal AF at the time of mitral valve surgery</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Concomitant maze procedure is reasonable for permanent or persistent AF at the time of aortic valve surgery</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>Concomitant LAA resection/closure is reasonable for AF at the time of any valve surgery</td>
<td>IIA</td>
<td>C</td>
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</table>

AF, atrial fibrillation; COR, Class of Recommendation; LAA, left atrial appendage; LOE, Level of Evidence.
4. Evaluation in Noncardiac Surgery

4.1 Preoperative Assessment and Intraoperative Monitoring

Patients with VHD have a high perioperative cardiovascular risk in noncardiac surgery. Careful auscultation is advised to confirm the presence of a murmur, even in patients without a prior history of VHD. In general, functional murmur is rarely above the level of Levine III/VI. Because the magnitude of the murmur can be affected by body size, even a low level of murmur does not completely rule out organic abnormality. Therefore, in patients with VHD, as well as those with a murmur, TTE should be performed prior to surgery to assess the presence and severity of the VHD as well as LV function. It should be considered whether or not intervention for VHD is required prior to noncardiac surgery based on symptoms, severity of VHD, and noncardiac surgical risk (Table 53).

4.2 Disease-Specific Considerations

4.2.1 AS

Chronic pressure overload in AS patients reduces LV compliance, which requires enough preload and atrial contraction for LV filling. It is therefore important to maintain normal sinus rhythm. If hypotension is caused by supraventricular tachycardia or AF, electrical defibrillation should be done as soon as possible. Fluid management is important; fluids should be administered so that cardiac output is maintained, but excessive fluids should be avoided.

Emergency noncardiac surgery in patients with severe AS should be performed by a cardiovascular anesthesiologist under hemodynamic or TEE monitoring. The indications for elective noncardiac surgery should be determined by the presence of symptoms and the type of surgery. In asymptomatic severe AS, SAVR/TAVI is recommended.

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Table 53. Risk Estimate of Noncardiac Surgery According to Type of Surgery or Intervention

<table>
<thead>
<tr>
<th>Low risk &lt;1%</th>
<th>Intermediate risk 1–5%</th>
<th>High risk &gt;5%</th>
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<tbody>
<tr>
<td>• Superficial surgery</td>
<td>• Intraperitoneal: splenectomy, hiatal hernia repair, cholecystectomy</td>
<td>• Aortic and major vascular surgery</td>
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<tr>
<td>• Breast</td>
<td>• Carotid symptomatic (CEA or CAS)</td>
<td>• Open lower limb revascularization or amputation or thromboembolectomy</td>
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<tr>
<td>• Dental</td>
<td>• Peripheral arterial angioplasty</td>
<td>• Duodeno-pancreatic surgery</td>
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<td>• Endocrine: thyroid</td>
<td>• Endovascular aneurysm repair</td>
<td>• Liver resection, bile duct surgery</td>
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<tr>
<td>• Eye</td>
<td>• Head and neck surgery</td>
<td>• Esophagectomy</td>
</tr>
<tr>
<td>• Reconstructive</td>
<td>• Neurologic/orthopedic: major (hip and spine surgery)</td>
<td>• Repair of perforated bowel</td>
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<td>• Carotid asymptomatic (CEA or CAS)</td>
<td>• Urologic or gynecologic: major</td>
<td>• Total cystectomy</td>
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<td>• Gynecologic: minor</td>
<td>• Renal transplant</td>
<td>• Pneumonectomy</td>
</tr>
<tr>
<td>• Orthopedic: minor (meniscectomy)</td>
<td>• Intrathoracic: non-major</td>
<td>• Lung or liver transplant</td>
</tr>
<tr>
<td>• Urologic: minor (transurethral resection of the prostate)</td>
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</table>

CAS, carotid artery stent; CEA, carotid endarterectomy. Kristensen SD, et al. 2014 Reprinted and translated by permission of Oxford University Press on behalf of the European Society of Cardiology. OUP and the ESC are not responsible or in any way liable for the accuracy of the translation. The Japanese Circulation Society is solely responsible for the translation in this publication/reprint.
prior to noncardiac surgery. If SAVR/TAVI is high-risk because of anatomical characteristics and patient background, percutaneous balloon aortic valvuloplasty should be considered (Figure 23). In asymptomatic severe AS, it is possible to safely perform elective noncardiac surgery. For high-risk noncardiac surgery with significant volume overload, SAVR/TAVI prior to noncardiac surgery may be considered in the absence of symptoms.

### 4.2.2 MS

Management of patients with MS is similar to that of AS; maintaining preload and normal sinus rhythm is important. Noncardiac surgery can be performed safely in patients with mild MS (valve orifice area >1.5 cm²), asymptomatic patients, and patients with a PASP <50 mmHg. PTMC prior to surgery should be considered in patients with symptoms or a PASP >50 mmHg if planning a high-risk noncardiac surgery.

### 4.2.3 AR and MR

In AR and MR, afterload reduction leads to an increase in CO as well as a decrease in regurgitation. In cases of chronic regurgitation, preload should be maintained.

Central venous pressure, pulmonary artery pressure, and LV size and function should be monitored using echocardiography and invasive catheterisation.

Noncardiac surgery can be performed safely in asymptomatic severe AR or MR when LV function is maintained. Valve surgery prior to noncardiac surgery may be considered for symptomatic patients or patients with reduced cardiac function. However, if HF is being managed by medical therapy, valve surgery prior to noncardiac surgery is rarely required. If LV dysfunction is advanced (LVEF <30%), noncardiac surgery should only be performed after optimal medical therapy for HF and only when it is absolutely necessary.

### 5. Prevention of Infective Endocarditis

This section is omitted from the English version.

### 6. Prevention of Rheumatic Fever

This section is omitted from the English version.

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**References**


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69. Chakravarty T, Søndergaard L, Friedman J, et al; RESOLVE, 2014; 851 – 858. PMID: 20137394


329. Nakatsuma K, Taniguchi T, Morimoto T, et al; CURRENT


556. Reddy VY, Doshi SK, Kar S, et al; PREVAIL and PROTECT AF Investigators. 5-Year outcomes after left atrial appendage closure: From the PREVAIL and PROTECT AF trials. *J Am Coll Cardiol* 2017; **70**:2964 – 2975. PMID: 29103847


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### Appendix 2 Disclosure of Potential Conflicts of Interest (COI):

**JCS/JSCS/JATS/JSVS 2020 Guidelines on the Management of Valvular Heart Disease**

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<td>External Evaluation Committee Members</td>
<td>Takashi, Akatsuka</td>
<td>QiVIA Services Japan K.K.</td>
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*Note: The table details various affiliations and potential conflicts of interest among the authors.*
<table>
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<th>Author</th>
<th>Employment/leadership position (gets an income)</th>
<th>Stakeholder</th>
<th>Patent royalty</th>
<th>Honorarium</th>
<th>Payment for manuscripts</th>
<th>Research grant</th>
<th>Scholarship (educational) grant</th>
<th>Endowed chair</th>
<th>Other rewards</th>
<th>Potential COI of the head of the organization/department in which the participant belongs (when the participant is in the position of cooperative research with the head of the organization/department)</th>
</tr>
</thead>
</table>

Notation of corporation is omitted.  
No potential COI for the following members.  
Group Leaders: Kiyoyuki Eishi  
Members: Kyomi Ashihara  
Members: Takeshi Kimura  
Members: Masaaki Okano  
Collaborators: Yukio Abe  
Collaborators: Kikuko Obase  
Collaborators: Takashi Miura  
Collaborators: Makoto Miyake  
External Evaluation Committee Members: Kiyoshi Yoshida