Introduction

Aortic stenosis (AS) has been the most common valvular heart disease in the past decades (1). As a result of the PARTNER trial (2), transcatheter aortic valve implantation (TAVI) provides an effective and less invasive alternative to surgical aortic valve replacement (SAVR) for inoperable and high-risk patients with symptomatic AS (3). As the use of TAVI for intermediate-risk patients has also been found acceptable based on a recent clinical trial (4), indications for TAVI may be increasing in the future.

Echocardiography is vital in the assessment of AS patients from pre- to post-procedure for TAVI. Initial evaluation is mainly performed by transthoracic echocardiography (TTE) to assess patient suitability for TAVI, including the severity of AS, assessment of the aortic valve complex and aortic valve morphology, and quantification of mitral regurgitation (MR) and left ventricular function. Transesophageal echocardiography (TEE) is usually used as an intra-procedural monitoring tool to provide feedback during the procedure, to assess prosthetic function, and to detect complications rapidly before and after balloon aortic valvuloplasty (BAV) or transcatheter heart valve (THV) deployment. In this review, the role of echocardiography in the pre-, intra-, and post-TAVI procedure periods is described in detail.

Abstract: Transcatheter aortic valve implantation (TAVI) is an effective and less invasive treatment for the increasing population of individuals with severe aortic stenosis (AS). Echocardiography is crucial in the assessment of AS patients from pre- to post-procedure. Transthoracic echocardiography (TTE) may be used to assess patient suitability for TAVI, as well as evaluate the severity of AS, the aortic valve complex, aortic valve morphology, mitral regurgitation (MR), and left ventricular function. Transesophageal echocardiography (TEE) is usually used as an intra-procedural monitoring tool to provide feedback during the procedure, to assess prosthetic valve function, and to detect complications rapidly before and after balloon aortic valvuloplasty (BAV) or transcatheter heart valve (THV) deployment. In this review, the role of echocardiography in the pre-, intra-, and post-TAVI procedure periods is described in detail.

Keywords: Echocardiography; aortic stenosis (AS); transcatheter aortic valve implantation (TAVI)
Pre-procedural echocardiography in TAVI

The pre-procedural echocardiographic evaluation for TAVI is mainly performed with TTE to assess valvular and ventricular morphology and function. The general approaches for assessing AS, AR, and MR are published by the American Society of Echocardiography (5).

Severity of AS

Current indications for aortic valve replacement (AVR), including TAVI, are based on the severity of AS in symptomatic patients, including patients with evidence of left ventricular compromise [left ventricular ejection fraction (LVEF) <50%] (6). According to the guidelines, severe AS is defined as a calculated aortic valve area (AVA) of ≤1.0 cm² (≤0.6 cm²/m²), a peak transvalvular velocity of ≥4 m/s, or a mean aortic valve gradient of ≥40 mmHg (6).

Although most patients with severe AS exhibit a high transvalvular gradient, some patients with a lower gradient (peak transvalvular velocity of <4 m/s) but severe AS are found in the situation of low aortic transvalvular flow (stroke volume index <35 mL/m²) either with an impaired LVEF (classical low-flow low-gradient severe AS) or with a normal LVEF (paradoxical low-flow low-gradient severe AS) (7). While the former is primarily due to low stroke volume (SV) with overt left ventricular (LV) systolic dysfunction, the latter is mainly due to low SV with a smaller LV and a restrictive physiology (8). Thus, it is important to distinguish between true severe AS and pseudo-severe AS. Dobutamine stress echocardiography has been useful in differentiating between them (it is negative in the pseudo-severe condition) (5) and predicting the risk of adverse events in the severe condition (9,10). Projected AVA has been proposed to standardize the calculation of AVA at a transvalvular normal flow rate of 250 mL/s and distinguish between them (10,11). This concept is theoretically attractive because it offers a rational solution to the common problem of achieving different. Although it is controversial whether the prognosis of paradoxical low-flow low-gradient severe AS is better than that of low-flow high-gradient severe AS (8,12), Herrmann et al. demonstrated improved survival in patients with low-flow low-gradient severe AS following TAVI compared with medical therapy at 2 years (56.5% vs. 76.9%) in a sub-analysis of the PARTNER trial (13).

Beyond these pathophysiological findings, special attention to the following points needs to be paid to this inconsistency in grading the severity of AS. At first, multiple measurements with TTE are made using different acoustic windows to measure the maximum velocity and highest mean gradient across the stenotic valve. Thaden et al. showed that in 100 consecutive patients with severe AS, the right parasternal window was superior for identifying maximal velocity. When sampling maximal velocity only from the apical window, nearly a quarter of patients were misclassified, of whom two-thirds were underestimated as moderate AS and one-third were misclassified from high-gradient severe AS to low-gradient severe AS (14).

Measurement of the LV outflow tract (LVOT) dimensions is measured in mid-systole at the same time in the cardiac cycle as the maximum LVOT velocity just below the insertion of the aortic valve leaflets (15), and it may have relatively high inter-observer variability (16). Furthermore, since the LVOT is elliptical in patients with AS, and measurement using two-dimensional (2D)-TTE is often the shortest dimension, stroke volume and calculated AVA by the continuity equation may be underestimated (17). When three-dimensional (3D)-TTE reveals the elliptical LVOT and its area is measured, AS grading accuracy may be improved (18).

Aortic valve complex

Assessment of the aortic valve complex, which includes the LVOT, aortic annulus, aortic valve cusps, sinus of valsalva, sinotubular junction, and position of the coronary arteries, is important in deciding the size of the THV to avoid complications such as paravalvular regurgitation, annular rupture, or coronary artery occlusion (19-22).

The most important approach for THV sizing is measurement of the aortic annulus, which is a “virtual ring” at the level of the hinge point of the three aortic valve cusps (23). Since the annulus is often asymmetric and oval, annular diameters should be largest in the coronal plane and shortest in the sagittal plane (24-26) (Figure 1). The conventional measurement for annular size has been mid-systolic diameter in the long axis plane (parasternal for TTE, mid-esophageal for TEE) that bisects the largest dimension of the aortic annulus (27). Recently, the annular diameter calculated from the annular perimeters or area measurements delivered by multiple detector computed tomography (MDCT) has become the gold standard (28,29). In general, the annular diameter measured by 2D-TTE has been shown to be smaller than that by 2D-TEE, and aortic annular area by

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2D-TEE to be underestimated than that by 3D-TEE or 3D-TTE in comparison to MDCT (30-32). Either by echocardiography or by MDCT, the following annular measurements were performed: perimeter, area, and orthogonal maximum and minimum diameters. Average diameter was calculated from perimeter (perimeter/π) and area \[ \left( \frac{\text{area}}{\pi} \right) \]. Mean diameter was calculated as the average of the maximum diameter and minimum diameter. Oversizing of the THV can result in aortic annular rupture, and undersizing can lead to increased paravalvular leak (PVL), valve ‘pop-out’ or migration (20). For each type of THV, the recommended device/annulus oversizing is required to prevent PVL calculated from the aortic basal ring perimeter, area, or mean diameter.

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Coronary obstruction is related to the displacement of a calcified native aortic valve leaflet into the coronary ostium. Ribeiro et al. reported in the recent meta-analysis that it occurred more frequently in the left coronary artery (83%), the height of the left main above the annulus was on average 10.3 mm (range, 7 to >12 mm), and approximately 60% of occlusions occurred with a coronary height >10 mm (22).

Calcification within the aortic complex should be noted because when it involves the LVOT, aortic leaflets, or proximal root, it is predictive of postprocedural AR (33,34), annular rupture (19,35), root perforation, aortic wall hematoma, and dissection (36). Calcifications around the coronary ostia may lead to coronary obstruction (37).

**Aortic valve morphology**

Bicuspid aortic valve disease is challenging for TAVI, and has been so far an exclusion criterion in randomized TAVI trials (2). Although there are some reports of TAVI being successfully performed for a bicuspid valve (38,39), there are some issues due to asymmetry of the aortic valve opening, including greater severity of post-TAVI PVL and higher mortality and incidence of device malposition (39,40). In the multicenter retrospective analysis of 139 patients with bicuspid valve, Mylotte et al. reported a procedural mortality of 3.6%, incidences of THV embolization and conversion to surgery of 2.2%, and 1-year mortality rate of 17.5%. The incidence of PVL was 28.4% (more than mild) and 8% (more than moderate). There was no difference in PVL between self-expanding and balloon-expandable valves (P=0.99) (40). TAVI for bicuspid valve remains controversial.
Significant MR is frequent in patients with severe AS. Prevalence is up to 74% of elderly candidates for SAVR or TAVI (41). Thus, accurate evaluation for MR on pre-procedural echocardiography is important.

MR can be often classified into primary degenerative and secondary functional subsets. Nombela-Franco et al. demonstrated in their review that MR severity improves after TAVI, especially in patients with LV dysfunction and functional MR (41). Other studies also suggested that outcomes were better with functional than with degenerative MR (42,43). However, Chakravarty et al. evaluated the impact of MR on outcomes after TAVI by performing a meta-analysis of 8 studies involving 8,927 patients, and showed that the increased mortality associated with moderate-to-severe MR was not influenced by the cause of MR [functional or degenerative MR; RR 0.90, 95% confidence interval (CI): 0.62 to 1.30, P=0.56]. They concluded that baseline moderate-to-severe MR and significant residual MR after TAVI are associated with an increase in mortality after TAVI (44). The management of patients with severe AS and concomitant MR remains challenging.

Successful TAVI is associated with a significant improvement in LV systolic and diastolic function (45-47). Webb et al. demonstrated that LV EF increased after TAVI from a mean of 53% to 57% (P<0.0001) within days and was sustained up to 1 year in 50 patients referred for TAVI. In particular, an LV EF ≤40% at baseline was documented in 21% of patients before successful valve implantation, falling to 12%, 13%, 0%, and 6% prevalence at discharge and 1, 6, and 12 months, respectively (45).

Patients with severe AS and reduced LV EF have a poor prognosis with conservative therapy but high operative mortality when treated surgically. Even in patients with severe LV dysfunction (LVEF ≤35%), AVR is associated with a large mortality benefit (48,49). Passeri et al. demonstrated that in 342 inoperable patients for SAVR undergoing TAVI or standard therapy, baseline LV EF dysfunction did not affect survival after TAVI but was associated with increased cardiac mortality at 1 year with standard therapy [59.3% vs. 45.8% with normal LV EF; hazard ratio (HR) =1.71 (95% CI: 1.08 to 2.71); P=0.02]. TAVI improves survival in patients with severe LV dysfunction (50).

Improvement of LV diastolic function should play an important role in reducing postoperative morbidity and mortality. Gonçalves et al. reported acute improvement of LV diastolic function immediately after successful TAVI in a group of 61 AS patients with preserved LVEF. They showed a reduction in hemodynamic invasive LV end-diastolic pressure a few minutes after TAVI and a significant improvement in the LV restrictive filling pattern without a significant decrease in E/E ratio (46). In 135 patients with successful TAVI, Vizzardi et al. demonstrated that LV mass index decreased from 191±58 (baseline) to 132±30 g/m² (6 months after TAVI) (P<0.001) and that 97 patients (72%) showed improvement in LV diastolic filling pattern (47).

Combined valvular and subvalvular LV outflow obstruction can be the result of either independent processes of valvular AS and coincident hypertrophic obstructive cardiomyopathy (HOCM), or the development of subvalvular LV outflow obstruction as a result of LV hypertrophy that occurs as a result of the increased afterload of AS (51). Echocardiography can adequately document the presence of obstructive flow pattern with the jet peaks late in systole (52) and specific echocardiographic parameters can guide interventionalist or surgeon whether TAVI can be performed without complication. Or, SAVR should be performed along with surgical myectomy to relieve LVOT obstruction post AVR (51).

Intra-procedural echocardiography in TAVI

TEE is usually used as an intra-procedural monitoring tool to provide feedback during the procedure, to assess the prosthetic valve function, and mainly to detect complications rapidly before and after BAV or THV deployment, although general anesthesia is required for TEE in elderly patients with severe AS and multiple co-morbidities.
compromise of the mitral apparatus by stiff wires, cannulae, LV dysfunction, increases in blood pressure, severe AR, systolic anterior motion following the abrupt reduction in afterload, or the THV itself (53).

**Wire insertion and position**

It is often difficult to pass a guidewire retrogradely through the narrow aortic valve in patients with AS. This is a routine first step in TAVI, and TEE can provide the information on guidewire location, with simultaneous multiplane imaging (Figure 2).

2D- and 3D-TEE can easily visualize the position of the retrograde stiff wire with the coiled section of the tip at the apex in the LV for stability (Figure 3). Since wire injury or entanglement within the mitral apparatus may cause worsening of MR, TEE can help avoid it.

When the TAVI approach is done via a trans-apical approach, additional imaging is required. To ensure optimal location of the apical puncture, a cannulation site in the anterior apex is pushed by the surgeon’s finger (Figure 4). When the guidewire or stiff wire is run through the “shortcut” in the LV, TEE should be performed to ensure avoiding the mitral valve apparatus (Figure 5).

**BAV**

BAV is often performed before TAVI to facilitate delivery of the THV and to expand the calcified aortic valve annulus after creating fractures of the calcified leaflets and increasing leaflet flexibility. Observation with TEE during and following BAV is important to assess the functional results of the dilation and to detect possible adverse events, including post-valvuloplasty AR, acute coronary occlusion, and cardiac tamponade.

**THV deployment**

To precisely position the THV is critically important. Although fluoroscopy plays a central role, TEE is an adjunct...
imaging in confirming the correct position during the THV deployment. To perform TEE may improve procedural results mainly thanks to its rapid detection of complications. Currently, there are three types of THV, those are the balloon-expandable, self-expanding, and mechanically expanded THV. How to deploy them is technically different for each.

**Immediate post-THV deployment**

Immediately after THV deployment, TEE rapidly provides an accurate assessment of valve position, shape, leaflet motion, maximal velocity, mean pressure gradient, and effective orifice area (EOA). Balloon post-dilation is usually needed when valve shape is too oval due to underexpansion and maximal velocity or mean pressure gradient is too high, measured by trans-gastric TEE view which is sometimes technically difficult to detect. Additionally, TEE can assess for complications, such as post-procedural AR, mitral valve damage, pericardial effusion, ventricular dysfunction, and aortic rupture or dissection.

**Complications**

**AR**

Both transvalvular and paravalvular AR may occur after THV deployment. Numerous studies have shown an association between post-procedural AR and increased short- and long-term mortality (54,55).

Transvalvular AR is commonly associated with the stiff wire across the valve (Figure 6), and often improves after it is removed.

It is often difficult to evaluate the severity and location of paravalvular AR because the anatomy and physiology of regurgitant jets differ from those in conventional SAVR with a sewing ring. It is usually important to detect the true orifice of paravalvular AR to prevent the overestimation of AR severity using the long-axis view by rotating the TEE probe from medial to lateral, the short-axis view at the level of the aortic annulus, or simultaneous multiplane imaging (Figure 7). Deep gastric views can be also helpful in detecting AR, but jet area and length cannot be used for AR severity (56). Current guidelines state that a circumferential extent <10% of paravalvular AR can be associated with mild,
10% to 20% with moderate, and > 20% with severe (57) (Figure 8). However, paravalvular AR is commonly eccentric and can have multiple jets, and it is therefore uncertain how these jets should be summed (56).

There are three important factors in paravalvular AR: undersizing of the prosthesis, severity of aortic calcification, and prosthesis position in relation to the annulus (20). The first, undersizing of the prosthesis relative to the annulus size, is a common cause of paravalvular AR after TAVI. Détaint et al. demonstrated the effect of undersizing using the cover index \[100 \times (\text{prosthesis diameter} - \text{TEE annulus diameter})/\text{prosthesis diameter}\], and found this to be an independent predictor of moderate or severe AR post THV deployment \([\text{odds ratio} 1.22; 95\% \ CI: 1.03–1.51, P<0.02]\) (21). The second, aortic valve calcification, also influences the severity of paravalvular AR post TAVI. Colli et al. demonstrated that the calcification score by TEE allowed prediction of the risk of paravalvular AR after TAVI \([\text{odds ratio} 8.5; 95\% \ CI: 1.2–58.9; P<0.0001]\) (58). Finally, post-TAVI AR is influenced by prosthesis position in relation to the annulus. When the THV is misplaced higher or lower, the skirt of the valve does not serve its function as an adequate seal around the annulus, resulting in AR. In cases of significant paravalvular AR, additional balloon dilatation or a second THV implantation is sometimes needed.

Mitral valve damage
Severe MR due to valvular perforation (Figure 9) or ruptured chordae might occur during the procedure. Frequent evaluation of the severity of MR and the anatomy of the mitral apparatus is always important.

Pericardial effusion
Pericardial effusion can indicate localized bleeding during the procedure. Whenever pericardial effusion is suddenly observed, evaluation for tamponade physiology and etiology, such as chamber perforation or aortic dissection, is required.

Ventricular dysfunction
Coronary obstruction due to displacement of the calcified native valve leaflets over the coronary ostia during the procedure can result in regional wall motion abnormalities. It is necessary to confirm regional or global wall motion abnormalities of the LV and RV, and to assess blood flow in the coronary ostia using color Doppler imaging.

Aortic rupture or dissection
Extensive annular calcification or prosthesis oversizing increases the risk of aortic rupture (Figure 10) or dissection after BAV or THV deployment. The aortic root and ascending aorta should be carefully examined to determine whether periaortic hematoma, aortic dissection, or rupture including ventricular septal defect or LV to left atrial shunt has occurred. They will likely cause massive bleeding and tamponade.

Post-procedural echocardiography in TAVI
Surveillance TTE should be considered as the primary imaging modality for the assessment of prosthetic valve function. The Valve Academic Research Consortium (VARC)-2 suggested the following schedule: immediately (before discharge) following THV implantation; 1, 6, and 12 months after implantation; and yearly thereafter (59). Additionally, an urgent TTE should be performed when a new murmur or new congestive heart failure symptoms appear in patients with THV.

In general, most surgical biological valves have limited durability and degenerate within 10–20 years (60). Since THV involves prosthetic valves made from cow or pig tissues, late degeneration may occur as the major
Prosthesis-patient mismatch

Prosthesis-patient mismatch (PPM) occurs when the EOA of the implanted prosthesis is too small in relation to body size. The severity of PPM is graded using EOA indexed to body surface area (EOAi) \((56, 59)\) with absence defined as \(>0.85 \text{ cm}^2/\text{m}^2\), moderate as \(0.65 \leq \text{EOAi} < 0.85 \text{ cm}^2/\text{m}^2\), and severe as \(<0.65 \text{ cm}^2/\text{m}^2\). PPM affects LV mass regression \((61)\) and long-term survival \((62)\) after SAVR. In the PARTNER trial, Hahn et al. demonstrated that TAVI patients had less PPM than SAVR patients over 2 years (moderate 34%, severe 23% for TAVI vs. 48%, 23% for SAVR, \(P=0.019\)) and PPM in TAVI patients is associated with lower mortality \((63)\). Pibarot et al. demonstrated in a post hoc analysis of the PARTNER cohort A trial that the incidence of PPM was higher in SAVR than in TAVI (28% vs. 20%) with a more significant difference when dealing with small aortic annulus diameters (<20 mm) (34% vs. 19%) \((64)\). They concluded that TAVI might be preferable to SAVR in patients with a small aortic annulus who are susceptible to PPM to avoid its adverse impact on LV mass regression and survival \((64)\).

Structural valve deterioration

Structural valve deterioration (SVD) is defined as any change in function of a THV resulting from any valve abnormality, including THV stenosis and regurgitation exclusive of infection or thrombosis. In their study of 8,914 TAVI patients, Foroutan et al. concluded that SVD is probably an infrequent event within the first 5 years, and...
longer follow-up (>10 years) is required (65).

**THV stenosis or regurgitation**

THV stenosis may sometimes occur as a result of calcification, or less frequently due to pannus (Figure 11). If the peak aortic velocity is >3.0 m/s or mean gradient is >20 mmHg, THV stenosis can be suspected (Table 1) (56,59). Although peak velocity and mean gradient are flow-dependent parameters, Doppler velocity index (DVI) is
independent of flow and the size of the inserted valve. Thus, DVI can be more useful in detecting valve dysfunction. A normal DVI indicates basically normal prosthetic valve function. When the EOAi is low in the setting of a normal DVI, the patient is considered to have a PPM (59). THV regurgitation may occur as a consequence of wear and tear, such as leaflet prolapse (Figure 12) or calcification. A transcatheter valve-in-valve procedure may be chosen for the treatment of THV stenosis and regurgitation.

**IE**

IE is a serious complication after TAVI as well as after SAVR (Figure 13). From a large multicenter registry of 7,944 patients, Amat-Santos et al. reported an incidence of IE at 1 year following TAVI of 0.5% with a median time from implantation of 6 months (66).

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Table 1 Transcatheter heart valve (THV) stenosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Mild stenosis</th>
<th>Moderate/severe stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak velocity (m/s)</td>
<td>&lt;3</td>
<td>3–4</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&lt;20</td>
<td>20–40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Doppler velocity index†</td>
<td>&gt;0.35</td>
<td>0.35–0.25</td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>Effective orifice area (BSA &gt;1.6 cm²)</td>
<td>&gt;1.1</td>
<td>1.1–0.8</td>
<td>&lt;0.8</td>
</tr>
<tr>
<td>Effective orifice area (BSA &lt;1.6 cm²)</td>
<td>&gt;0.9</td>
<td>0.9–0.6</td>
<td>&lt;0.6</td>
</tr>
</tbody>
</table>

†, for left ventricular outflow tract (LVOT) >2.5 cm, significant stenosis criteria is <0.20. BSA, body surface area.

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Aortic root rupture with periaortic hematoma. Aortic root rupture with periaortic hematoma (yellow arrow) after transcatheter heart valve deployment was observed in this case. LV, left ventricle; LA, left atrium; Ao, aorta.

**Clinical & subclinical THV thrombosis**

Recently, hypoattenuated leaflet thickening (HALT) and reduced leaflet motion (RELM) of bioprosthetic aortic valves associated with normal transvalvular gradients have been reported as affecting THV. The prevalence of this finding ranged from 4% to 20% (67-69). Latib et al. first
reported the treatment and clinical outcomes of THV thrombosis from a multicenter registry (69). The overall incidence of THV thrombosis was 0.6% (n=26) out of 4,266 patients. The most common clinical presentation was exertional dyspnea (n=17; 65%), whereas 8 (31%) patients had no worsening symptoms. Echocardiography detected a markedly elevated mean aortic valve pressure gradient, presence of thickened leaflets or thrombotic apposition of leaflets in 20 (77%) and a thrombotic mass on the leaflets in the remaining 6 (23%) patients. Of 26 patients, 23 (88%) were successfully treated with anticoagulation; two patients underwent a transcatheter valve-in-valve procedure and one patient underwent SAVR (69).

Figure 12 Transcatheter heart valve (THV) regurgitation. THV leaflet prolapse (orange dotted lines, yellow arrow) occurred 5 years after THV deployment (A). Severe THV regurgitation (pink arrow) could be observed (B). LV, left ventricle; Ao, aorta.

Figure 13 Infective endocarditis. Two months after transcatheter heart valve (THV) deployment, the patient presented with malaise, breathlessness and elevated markers of infection. TEE revealed small mobile echogenic masses attached to the THV leaflet (A). In the surgical findings, vegetation (yellow arrow) was identified on the valve leaflets and THV stent frame (B). LV, left ventricle; LA, left atrium; Ao, aorta; THV, transcatheter heart valve.

Conclusions

TAVI provides an effective, less-invasive alternative to SAVR for an increasing population of individuals with severe AS. TTE may be used to assess patient suitability for TAVI, and TEE can detect complications rapidly during TAVI. After THV deployment, TTE can evaluate prosthetic valve function. Echocardiography always serves an important function in the assessment of AS patients in any situation, from pre- to post-procedure for TAVI.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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