Consistency of transesophageal echocardiography and angiography in grading (using the Valve Academic Research Consortium 3 criteria) of perivalvular regurgitation during transcatheter aortic valve replacement

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Abstract

The aim of this study was to evaluate the consistency between transesophageal echocardiography (TEE) and angiography in grading of paravalvular regurgitation (PVR) during transcatheter aortic valve replacement (TAVR) according to the Valve Academic Research Consortium 3 (VARC-3) criteria. 31 patients who underwent TEE and angiography during TAVR were retrospectively included. Circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area were measured by TEE. Weighted kappa coefficient was used to analyze the consistency of the two techniques. PVR was found in 16 of 31 patients. TEE assessed mild PVR in 14 cases and moderate PVR in 2 cases. Angiography assessed mild PVR in 12 cases and moderate PVR in 2 cases. The grading of TEE and angiography were the same in 29 cases, of which 15 were absent, 12 were mild, and 2 were moderate. The weighted kappa coefficient for both techniques was 0.88 (P < 0.001). The Kendall’s W coefficient of the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area was 0.285 (P < 0.005). TEE and angiography had strong consistency in the grading (using the VARC-3 criteria) of PVR during TAVR. TEE was a potential diagnostic tool for classifying PVR.

Introduction

Paravalvular regurgitation (PVR) is a usual complication of transcatheter aortic valve replacement (TAVR), and it will seriously affect the efficacy of TAVR. A growing number of studies showed that PVL classification was increasingly associated with short-term and long-term mortality⁴⁻⁶. Angiography and transesophageal echocardiography (TEE) were both recommended imaging modalities to grade PVR post-TAVR⁷⁻⁵. In some studies, graded assessment of PVR by Angiography correlated well with transthoracic echocardiography in patients post-TAVR⁶. Several studies have reported moderate agreement between Angiography and postoperative transthoracic echocardiography in the graded assessment of PVR⁷. However, the immediate assessment of paravalvular regurgitation during TAVR was more important for surgery, and the consistency between Angiography and TEE in assessing paravalvular regurgitation during TAVR had not been reported. Compared with angiography, TEE can not only be performed intraoperatively, but also does not have the risk of allergic reaction induced by iodinated contrast agent or the risk of renal insufficiency caused by overdose⁸⁻⁹. Recently, the Valve Academic Research Consortium 3 (VARC-3) updated the grading criteria for paravalvular regurgitation post- TAVR¹⁰. The aim of the study was the consistency between TEE and Angiography in assessing PVR during TAVR.

Materials and methods

Study population
The retrospective study had been approved by the Ethics Review Committee of the Fifth Affiliated Hospital of Sun Yat-Sen University. Waiver of informed consent was granted. The study retrospectively collected patients diagnosed with severe aortic valve stenosis or severe regurgitation in the Fifth Affiliated Hospital of Sun Yat-Sen University from August 2019 to November 2021. Based on the aortic valve annulus size, coronary ostium height, valve type, and surgical approach, the cardiac multidisciplinary team discussed and decided to perform TAVR on these patients. All patients underwent angiography and TEE examination immediately during prosthetic valve implantation. Two patients were unable to undergo angiography because of renal failure, and two patients were unable to undergo TEE because of esophageal varices. 31 patients who underwent TEE and angiography post-TAVR were finally included (Figure 1). Among them, Venus A-Valve was used in 24 cases, J-Valve in 5 cases, and Edwards Sapien3 in 2 cases.

Angiography

Angiography was performed within 10 minutes of the completion of prosthetic aortic valve placement. The catheter was placed in the upper third of the self-expanding valve frame, and at least 20 mL of contrast medium was injected into the aortic root at a rate of 20 mL/s. Angiography was retrospectively evaluated by an investigator with many years of experience in angiography and was blinded to TEE data.

Transesophageal echocardiography

TEE was performed immediately after the completion of angiography. TEE adopts Philips IE Elite ultrasonic diagnostic apparatus, X7-2t transesophageal ultrasonic probe, and the probe frequency is 2-7MHz. After intravenous anesthesia, the probe was slowly placed in the middle of the esophagus through the oropharynx, and the parameters of paravalvular regurgitation were measured in the midesophageal aortic valve short-axis views and in the midesophageal aortic valve long-axis views.

Two sonographers independently retrospectively evaluated TEE images, both blinded to angiography data. According to the VARC-3, parameters of PVR were measured, including the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area. In addition, left ventricular ejection fraction (LVEF), left ventricular outflow tract (LVOT), aortic valve area (AVA), and aortic annulus size were measured. Basic patient information, including age, gender, body mass index (BMI), New York Heart Association (NYHA) cardiac function class, and myocardial infarction (MI), hypertension, diabetes, chronic obstructive pulmonary disease (COPD) or Chronic kidney disease (CKD) were also recorded.

PVR grading scheme

PVR was graded according to Sellers and VARC-3 criteria:

Sellers class I was no obvious regurgitation; Sellers class II was a regurgitant jet with faint opacification of the left ventricle; Sellers class III was defined as dense opacification of the left ventricle and no distinct jet was usually visualized; Sellers IV was the left ventricle is opacified more densely than the aorta.

The circumferential extent of PVR: absent, not quantifiable; mild, <10%; moderate, 10% to <30%; severe, ≥30%. Calculation method of the circumferential extent of PVR: the sum of the circumference lengths of each regurgitation jet (excluding the non-regurgitation space between the separate regurgitation jets) divided by the circumference of the outer edge of the transcatheter valve (Figure 2).

Regurgitant volume(ml/beat): absent, <15; mild, 15 to <30; moderate, 30 to < 60; severe, ≥60. Regurgitant volume was calculated by subtracting the stroke volume measured in the left ventricular outflow tract from the stroke volume measured in the right ventricular outflow tract.

Regurgitant fraction: absent, <15%: mild, 15% to <30%; moderate, 30% to < 50%; severe, ≥50%. Regurgitant fraction was calculated by dividing the regurgitation volume by the left ventricular outflow tract stroke volume.

The effective regurgitant orifice area(mm²): absent, <5: mild, 5 to <10; moderate, 10 to <30; severe,
Calculation method of the effective regurgitant orifice area: divide the regurgitant volume by the time-velocity integral of the aortic regurgitant flow using continuous wave Doppler.

The final paravalvular regurgitation grading was based on the same grading results of 3 of the 5 measurement indicators, including aortography, the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area.

Inter-observer intraclass correlation efficient of TEE assessment

ICC analysis of data assessed by two sonographers showed that the ICC for paravalvular regurgitation beam circumference was 0.87; the ICC for regurgitation was 0.92; the ICC for fractional regurgitation was 0.88; the measured ICC was 0.91. In the study, the ICC of the two measurements was high, and the average of the two measurements was taken as the final measurement result.

Analysis

For numerical variables, normal distributions were determined using histograms and the Shapiro-Wilk test. For categorical variables, frequencies and percentages are used. For the central tendency and dispersion of numerical variables, the mean and standard deviation are used to describe. Weighted kappa analysis was used to evaluate the consistency of AR grades between TEE and aortography. The Kendall’s W test was used to analyze the consistency of the AR degree grading of the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitation orifice area measured by TEE. All statistical analyses were performed using SPSS 22.0 software package, and P<0.05 was considered statistically significant.

Result

Thirty-one patients were included, with a mean age of 65 years (range 50-86 years). There were 15 males and 16 females. The characteristics of the patients and the parameters of the aortic valve are listed (Table 1).

PVR was found in 16 of 31 patients (Table 2). In mild PVR, the average circumferential extent of PVR was 5.7±1.9, the average regurgitation volume was 15.4±7.5, the average regurgitation fraction was 15.2±7.5, and the average effective regurgitant orifice area was 6±1. In moderate PVR, the average circumferential extent of PVR was 16.5±3.3, the average regurgitation volume was 42.5±2.5, the average regurgitation fraction was 35.9±3.1, and the average effective regurgitant orifice area was 21±1. Severe PVR was absent in 31 patients.

PVR measured by TEE was absent in 15 of 31 patients, mild in 14 of 31 patients, and moderate in 2 of 31 patients (Table 3). PVR measured by angiography was absent in 15 of 31 patients, mild in 12 of 31 patients, and moderate in 2 of 31 patients. PVR measured by TEE and angiography was absent in 15 of 31 patients, mild in 12 of 31 patients, and moderate in 2 of 31 patients (Figure 3).

Among the 31 patients, two patients showed inconsistencies between TEE and angiography for PVR (Table 4).

The weighted kappa coefficient for both techniques was 0.88, P < 0.001. The Kendall’s W coefficient of the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area measured by TEE was 0.285, P<0.005.

Discussion

In the study, we found that 1) TEE can be used to assess the grading of PVR during TAVR; 2) TEE has strong consistency with angiography; 3) there is consistency among the parameters of PVR, including the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and effective regurgitation orifice area. The results showed that TEE and angiography were completely consistent in the grading results of absent PVR and moderate PVR; TEE and angiography were almost identical in the grading results of mild PVR. The study demonstrated strong agreement between TEE and angiography, and the four parameters of PVR measured by TEE were consistent in assessment the grading of PVR, which provides an effective way for the clinical evaluation of PVR during TAVR.
PVR is a common complication during TAVR, and the degree of PVR is significantly associated with post-operative mortality. Grube, E, et al. reported moderate and severe PVR in 17% of patients treated with TAVR. A study that included data from 25 centers reported that the effect of aortic regurgitation on mortality was proportional to the severity of regurgitation, and that even mild aortic regurgitation increased long-term mortality. Therefore, the graded assessment of PVR is increasingly significant. In 1964, Sellers et al. reported a method for grading PVR based on the intensity and duration of left ventricular visualization after aortic root injection of contrast agent. Although angiography is considered a semi-quantitative means of assessing the degree of PVR, studies reported that angiography had a tendency to underestimate the grade of PVR.

The VARC-3 proposes a quantitative grading standard for PVR, and TEE is recommended for grading PVR. Tateishi, H. et al. reported a good correlation between angiography and TEE for graded assessment of the circumference of PVR. However, they did not use TEE to measure regurgitation, fractional regurgitation, and effective regurgitation orifice area, and their ultrasound data were not obtained intraoperatively. In the study, we measured the more detailed parameters of PVR by measuring the perivalvular regurgitation volume, regurgitation fraction, and effective regurgitation port area according to the VARC-3 criteria. Abdelghani, M. et al reported poor agreement between angiography and echocardiography (using the Valve Academic Research Consortium 2 criteria) in PVR grading during TAVR. But they did not use TEE as an assessment method, and the acquisition of ultrasound data was non-immediate intraoperatively. In our study, we found that TEE and angiography were in perfect agreement for the absence of and moderate PVR in 17 of 31 patients; the assessment of weekly regurgitation was almost consistent, with 12 consistent and 2 inconsistent. We used angiography and TEE to measure and grade PVR within 10 minutes of prosthetic valve placement, and the data obtained may be responsible for the strong agreement. Due to the high cost of transcatheter imaging, exposure to radiation, and invasiveness, the technique is relatively unsafe and unsuitable for repeated procedures. Studies have reported that 12-62% of patients treated with TAVR have some degree of pre-existing renal dysfunction, and these patients are even at increased risk of AKI if exposed to transcatheter contrast media. Several studies have reported that exposure to iodinated contrast media and its amount are two important predictors of AKI. The results found strong consistency between TEE and angiography in assessing PVR during TAVR. Therefore, we suggested that TEE may be an alternative to angiography to assess PVR during TAVR, reducing the risk of AKI and the side-effect of iodinated contrast agents to other organs.

Valve Academic Research Consortium 3 proposed that the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area were parameters for evaluating PVR. However, it is unclear for the relationship between these indicators, and the weight of them in assessing PVR. In the study, we found that the four indicators were consistent in the assessment of PVR. The results demonstrated that the circumferential extent of PVR, regurgitation volume, regurgitation fraction, and the effective regurgitant orifice area measured by TEE had similar clinical value for the assessment of PVR.

In the present study, we found that the TEE and transcatheter angiographic assessment were inconsistent in 2 patients. The results of angiography in these 2 patients showed absent PVR, and the results of TEE assessment showed mild PVR. The possible reasons for the are as follows: 1) Small amount of PVR were readily unavailable to produce visual grading effect through angiography; 2) the implantation of the prosthetic valve is mainly carried out under the guidance of angiography, so the contrast medium The dosage should be kept as low as possible, especially in high-risk patients with chronic renal failure and/or acute kidney injury; 3) TEE responds to the Doppler effect The display of small amounts of regurgitation may be more sensitive.

Limitations

Some limitations in the study should be pointed out. Firstly, the overall sample size was small, and further statistical analysis of the advantages and disadvantages of TEE versus angiography cannot be performed. Secondly, the study lacks patients with severe regurgitation. However, severe regurgitation immediately
during TAVR means that the valve has failed. We had not yet cases of severe regurgitation due to the
detailed preoperative evaluation of TAVR in our center. Thirdly, an inherent limitation of the study is that
it did not include hemodynamic indices, namely Aortic regurgitation (AR) Index, with cardiac MRI results.
However, the AR Index is often used to judge prognosis rather than diagnose the degree of PVR\textsuperscript{19}. And the
AR Index cannot distinguish between PVR and transvalvular regurgitation. In addition, cardiac MRI is not
suitable for immediate intraoperative evaluation because TAVR is performed under angiography.

**Conclusion**

TEE and angiography had strong consistency in the grading (using the VARC-3 criteria) of PVR during
TAVR. TEE was a potential diagnostic tool for classifying PVR during TAVR.

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### Tables

Table 1. Baseline and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65±8.73</td>
</tr>
<tr>
<td>Female</td>
<td>16 (52%)</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2±2.7</td>
</tr>
<tr>
<td>EuroSCORE II (%)</td>
<td>1.4±0.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (58%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>COPD</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>CKD</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>MI</td>
<td>11 (35%)</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>11 (35%)</td>
</tr>
<tr>
<td>III</td>
<td>12 (39%)</td>
</tr>
<tr>
<td>IV</td>
<td>8 (26%)</td>
</tr>
<tr>
<td>AVA (cm²)</td>
<td>4.13±0.83</td>
</tr>
<tr>
<td>Aortic annulus diameter (mm)</td>
<td>24.06±2.75</td>
</tr>
<tr>
<td>LVOT</td>
<td>23.83±2.5</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>59.61±14.25</td>
</tr>
</tbody>
</table>

BMI, body mass index; EuroSCORE, European System for Cardiac Operative Risk Evaluation Score; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; MI, myocardial infarction; NYHA, New York Heart Association; AVA, aortic valve area; LVOT, left ventricular outflow tract; LVEF, Left ventricular ejection fraction.

Table 2. TEE and angiography parameters of patients with PVR.
Patients ID | TEE | TEE | TEE
---|---|---|---
| Circumferential extent of paravalvular regurgitation (%) | Regurgitant volume (mL/beat) | Regurgitant fraction (%) |
1 | 6.2 | 18 | 17 |
2 | 2.8 | 5 | 4.3 |
3 | 19.8 | 45 | 39 |
4 | 3.4 | 4.5 | 3.8 |
5 | 13.2 | 40 | 32.8 |
6 | 8.6 | 25 | 24 |
7 | 5.5 | 17 | 16 |
8 | 3.3 | 6 | 5 |
9 | 8.3 | 20 | 22 |
10 | 6.2 | 20 | 22 |
11 | 5.9 | 13 | 12 |
12 | 3.7 | 9 | 8 |
13 | 4.4 | 10 | 15 |
14 | 8.6 | 28 | 27 |
15 | 7.4 | 25 | 23 |
16 | 5.5 | 15 | 14 |

TEE, transesophageal echocardiography; PVR, paravalvular regurgitation; EROA, effective regurgitation orifice area.

Table 3. Comparison of PVR grading between TEE and angiography.

<table>
<thead>
<tr>
<th>Angiographic grading</th>
<th>Absent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEE</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15 (48.4%)</td>
</tr>
<tr>
<td>Absent</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14 (45.2%)</td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2 (6.5%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>17 (54.8%)</td>
<td>12 (38.7%)</td>
<td>2 (6.5%)</td>
<td>0</td>
<td>31</td>
</tr>
</tbody>
</table>

TEE, transesophageal echocardiography; PVR, paravalvular regurgitation.

Table 4. Characteristics of patients with inconsistent PVR grading of two imaging.

<table>
<thead>
<tr>
<th>Patients ID</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>gender</td>
<td>Female</td>
<td>male</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66</td>
<td>71</td>
</tr>
<tr>
<td>EuroSCORE II (%)</td>
<td>2.0</td>
<td>3.0</td>
</tr>
<tr>
<td>BMI</td>
<td>22.5</td>
<td>26.7</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>MI</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Hypertension</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CKD</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>COPD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>73</td>
<td>45</td>
</tr>
<tr>
<td>LVOT</td>
<td>22</td>
<td>22</td>
</tr>
</tbody>
</table>
Patients ID | 4 | 8
---|---|---
Aortic annulus diameter (mm) | 22 | 25
AVA (cm²) | 3.4 | 4.5

PVR, paravalvular regurgitation; BMI, body mass index; EuroSCORE, European System for Cardiac Operative Risk Evaluation Score; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; MI, myocardial infarction; NYHA, New York Heart Association; AVA, aortic valve area; LVOT, left ventricular outflow tract; LVEF, Left ventricular ejection fraction; +, patient had the disease; -, patient did not had the disease yet.

**Figure legends**

Fig. 1. Patients select process. TEE, transesophageal echocardiography.

Fig. 2. TEE measured the circumferential extent of PVR. The position, numbers and circumferential extent of PVR (black arrow) was shown in the midesophageal aortic valve short-axis views. The circumferential extent of PVR was calculated as the circumferential lengths of regurgitant jet (blue line) divided by the circumference of the outer edge of the transcatheter valve (grey dotted line circle). The calculation of the circumferential extent of PVR was unified from Valve Academic Research Consortium 3. TEE, transesophageal echocardiography. PVR, paravalvular regurgitation.

Fig. 3. TEE and angiography evaluated mild PVR (A-C) and moderate PVR (D-F) during TAVR. Mild PVR was shown with four bundles (black arrows) in the midesophageal aortic valve short-axis views (A) and the largest bundle (black arrow) in the midesophageal aortic valve long-axis views (B), angiography (C) showed contrast with faint opacification of the left ventricle (white arrows). Moderate PVR was shown with one bundle (black arrows) in the midesophageal aortic valve short-axis views (D) and in the midesophageal aortic valve long-axis views (E), angiography (F) showed contrast with dense opacification of the left ventricle (white arrows). TEE, transesophageal echocardiography. PVR, paravalvular regurgitation.

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