The value of real-time three-dimensional transesophageal echocardiography in the assessment of paravalvular leak origin following prosthetic mitral valve replacement

Mitral kapak replasmanı sonrası gelişen paravalvüler kaçak yerinin belirlenmesinde gerçek zamanlı üçboyutlu transözofageal ekokardiyografinin yeri

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Objectives: Two-dimensional (2D) echocardiographic approaches are not sufficient to determine the origin of paravalvular leak (PVL) that occurs after prosthetic mitral valve replacement (MVR). In this study, we investigated the role of real-time three-dimensional transesophageal echocardiography (RT-3D TEE) in detecting the origin and size of PVL occurring after prosthetic MVR.

Study design: The study included 13 patients (7 females; 6 males; mean age 56±10 years; range 37 to 71 years) who developed PVL within a mean of 8.3±3.8 years following mechanical prosthetic MVR. Nine patients (69.2%) had atrial fibrillation, and four patients (30.8%) had normal sinus rhythm. Four patients (30.8%) had hemolysis. Paravalvular leak was mild, moderate, and severe in two, six, and five patients, respectively. Real-time 3D TEE was performed using a 3D matrix-array TEE transducer immediately after detection of PVL on 2D TEE examination. Localization of PVL was made using a clock-wise format in relation to the aortic valve and the size of dehiscence was measured.

Results: The mean PVL width measured by 2D TEE was 3.00±0.92 mm. The mean length of dehiscence was 13.6±8.8 mm, and the mean width was 3.88±2.04 mm on RT-3D TEE. The PVLs were mainly localized in the posterior and anterior annular positions between 12 to 03 hours (n=7) and 06 to 09 hours (n=3) on RT-3D TEE, respectively, which corresponded to the posteromedial or anterolateral sectors of the posterior annulus.

Conclusion: Considering that only the width of the PVL defect can be assessed by 2D TEE, delineation by RT-3D TEE includes the localization of PVL together with the length and width of the defect.

Key words: Echocardiography, three-dimensional; echocardiography, transesophageal; heart valve prosthesis/adverse effects; mitral valve insufficiency/etiology; prosthesis failure.

Amaç: İkiboyutlu (2B) ekokardiyografik yöntemlerle, prostetik mitral kapak değişiminden sonra görülebilen paravalvüler kaçak (PVK) yeri tam olarak gösterilememektedir. Bu çalışmada, protez kapak değişimi sonrası PVK gelişen olgularda, PVK kaynağının ve boyutunun gösterilmesinde gerçek zamanlı üçboyutlu transözofageal ekokardiyografinin (3B TÖE) değeri araştırıldı.

Çalışma planı: Çalışmaya, mekanik kapak değişiminden ortalama 8.3±3.8 yıl sonra PVK gelişen 13 hasta (7 kadın, 6 erkek; ort. yaş 56±10; dağılım 37-71) alındı. Dokuz hastada (69.2%) atriyal fibrilasyon bulunurken, dört hasta (%30.8) normal sinüs ritmindeydi. Dört hastada (%30.8) hemoliz vardı. İki hastada hafif, altı hastada orta, beş hastada ileri derecede PVK vardı. İkiboyutlu TÖE ile PVK saptanmasından hemen sonra hastalara 3B matriks dizilimli TÖE transdüser ile gerçek zamanlı 3B TÖE yapıldı. Paravalvüler kaçak yeri, aort kapağına göre konumlandırılan saat kadranı düşünülerek işaretlendi ve ayrışma boyutları ölçüldü.

Bulgular: İkiboyutlu TÖE'de ortalama PVK genişliği 3.00±0.92 mm ölçüldü. Gerçek zamanlı 3B TÖE'de ise ayrışma boyu 13.6±8.8 mm, genişliği 3.88±2.04 mm bulundu. Paravalvüler kaçak yeri 3B TÖE'de sırasıyla posteriyor ve anteriyor anülüs taraflarında, 12-03 (n=7) ve 06-09 (n=3) saatleri arasında ve mitral arka yaprak anülüsünün posteromedial ve anterolateral komissürlerinde yoğunlaşmaktaydı.

Sonuç: İkiboyutlu TÖE'de PVK'nin sadece genişliğinin ölçülebildiği göz önüne alındığında, gerçek zamanlı 3B TÖE ile PVK'nin hem yeri belirlenebilmekte, hem de defektin boy ve genişliği hesaplanabilmektedir.

Anahtar sözcükler: Ekokardiyografi, üçboyutlu; ekokardiyografi, transözofageal; kalp kapağı protezi/yan etki; mitral kapağı yetersizliği/etyoloji; protez başarısızlığı.

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The incidence of paravalvular leak (PVL) has been reported as approximately 17% after 15 years of prosthetic mitral valve replacement (MVR)[1,2] and, when detected, it is an important complication requiring intervention. Paravalvular leak is most commonly seen in the commissural regions and posterior annulus.[3] Sutures may separate easily since the region involving the posterior annulus is longer than the anterior region and the posterior region is more affected by annular dilatation.[3] Paravalvular leak typically leads to mitral regurgitation and related symptoms. It may cause decreased functional capacity of the patients and hemolysis in varying degrees. Two-dimensional transesophageal echocardiography (2D TEE) is significantly superior to 2D transthoracic echocardiography (2D TTE) in terms of accurate estimation of regurgitation, distinguishing between central/paravalvular leaks, and determination of the degree and causes of the regurgitation.[4] Though differential diagnosis of pathologies responsible for paravalvular regurgitation including separation of sutures, fistulas, perivalvular abscess, and dehiscence is possible by 2D TEE, the PVL origin and the length of the defect cannot be shown anatomically. In line with improvement in the quality of echocardiographic imaging, real-time three-dimensional transthoracic echocardiography (RT-3D TTE) and real-time three-dimensional transesophageal echocardiography (RT-3D TEE) have been used recently.[5-7] It is possible to obtain 3D cardiac images from any plane with 3D TTE and 3D TEE.[5-7] Therefore, 3D TEE makes it possible to obtain cross-sectional visualization of the mitral valve and PVL origin, which are not possible with 2D TEE. Consequently, the size of the defect which is a key guide in the treatment plan of PVL can directly be measured.

This study was designed to assess the importance and role of RT-3D TEE in the detection of PVL origin and in determining anatomical localization and size of dehiscence in patients with a history of MVR.

PATIENTS AND METHODS

Patients. The study included 13 patients (7 females; 6 males; mean age 56±10 years; range 37 to 71 years) who underwent mechanical prosthetic MVR due to various reasons (10 rheumatic, 2 infective endocarditis, 1 degenerative) and developed PVL as detected by transthoracic echocardiography. Two patients also underwent aortic valve replacement. Five patients underwent more than one operations. The patients were recruited from the Departments of Cardiology and Cardiovascular Surgery of Koşuyolu Kartal Heart Training and Research Hospital, and all were referred for a clinically indicated TEE. The study protocol was approved by the institutional review board and written informed consent was obtained from each patient at the time of enrolment for the TEE procedures.

Assessment with TEE. Mitral regurgitation was evaluated according to the existing criteria. Mitral ring dehiscence was diagnosed as a segment of separation between the prosthetic ring and the patient's native mitral annulus (Fig. 1a). Doppler color flow imaging was used to show the presence of mitral regurgitation flow through the dehisced segment (Fig. 1b). The position, shape, and area of each dehiscence were measured and tabulated.

Real-time 3D TEE was performed using an iE33 ultrasound system equipped with a 3D-matrix TEE transducer (Philips Medical Systems, Andover,

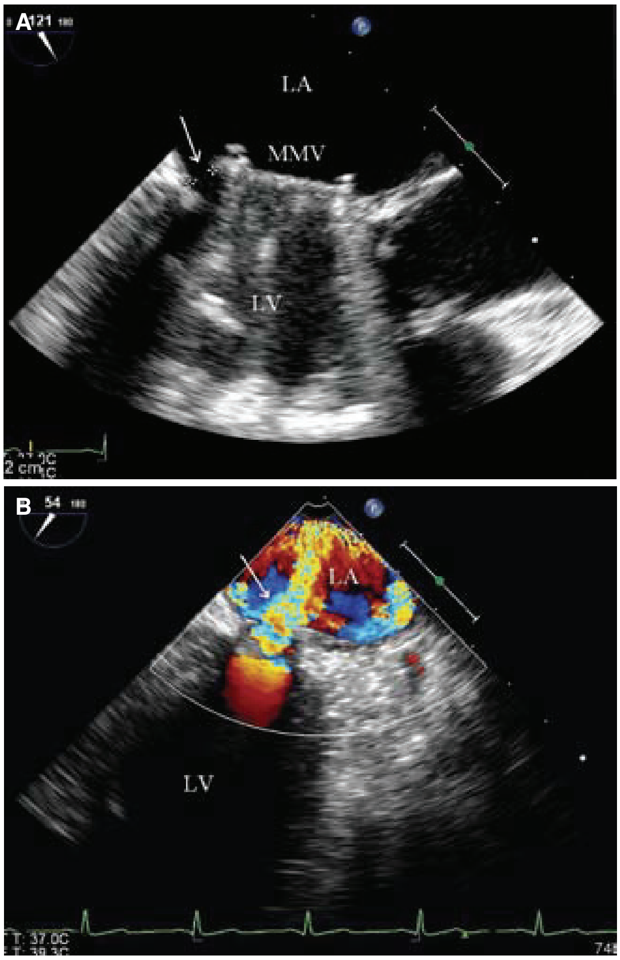

Figure 1. (A) Two-dimensional transesophageal echocardiographic image showing paravalvular leakage due to mechanical mitral valve dehiscence (arrow) and its width. **(B)** The severity of mitral regurgitation (arrow) circling along the left atrium. MMV: Mechanical mitral valve; LV: Left ventricle; LA: Left atrium.

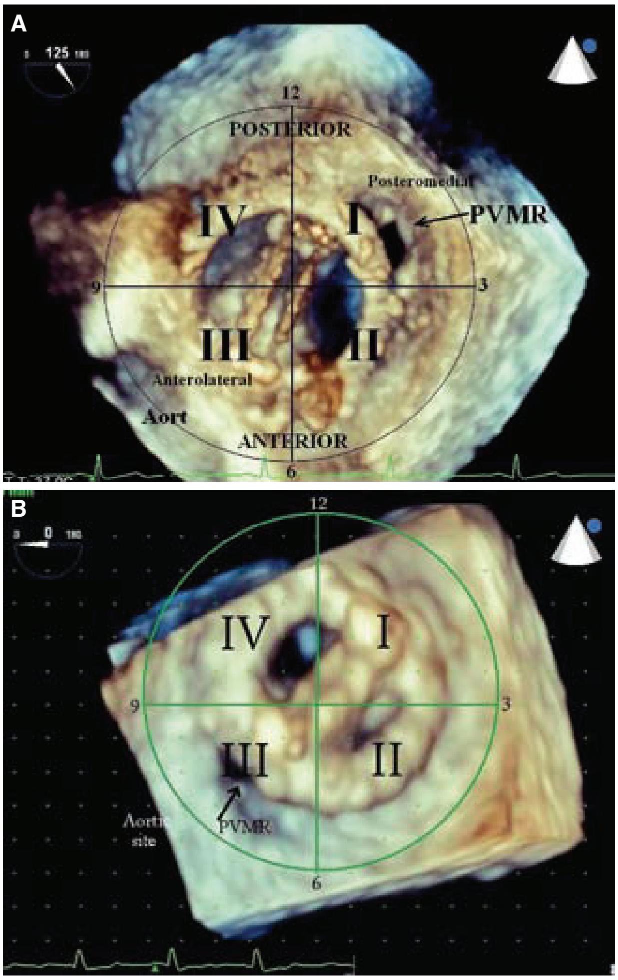

Figure 2. (A) All images of paravalvular leak localization were arranged in relation to the lower left side of the aorta (between 06-09 hours clockwise) and paravalvular leak positions were defined on a clock format scale. **(B)** The grid method applied on the clock format scale. PVMR: Paravalvular mitral regurgitation.

USA) immediately after completing a comprehensive 2D-TEE examination according to the standard protocol. Initially, gain settings were optimized using the narrow-angle gain mode. The narrow-angle gain mode without the need for electrocardiography allowed us to obtain real-time 3D images of an approximately 30º x 60º pyramidal volume. To magnify the pyramidal volume, 3D zoom mode was used for prosthetic valve visualization. The size of the pyramidal volume could be changed from 20º x 20º to 90º x 90º, depending on equipment settings in the zoom mode. Images were assessed offline.

Localization of PVL was made using a clock-wise format in relation to the aortic valve. At this position, the PVL origin was described based on the position on the clockwise scale which was partition of the mitral annulus adopting a clock format and the size of dehiscence was measured (Fig. 2a, b; Fig. 3).

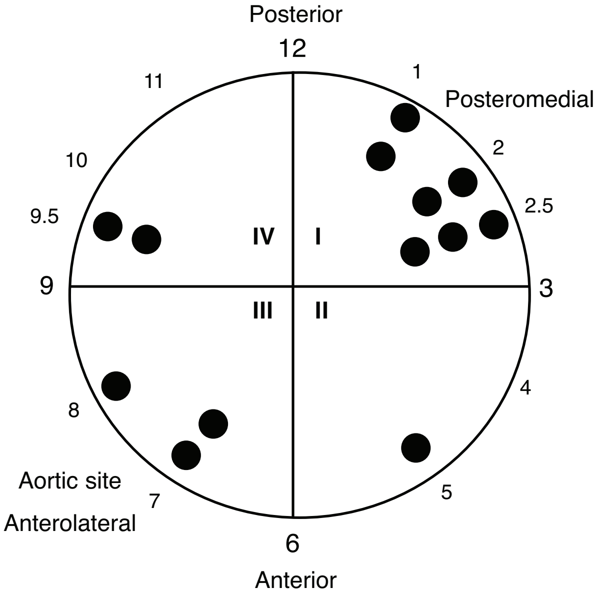

Figure 3. This schematic view shows paravalvular leak positions which mainly correspond to the posterior and anterior annular sites between 12 to 03 hours and 06 to 09 hours on three-dimensional transesophageal echocardiography (each full circle indicates one case).

The grid method. Image pages were divided automatically by the instrument into 2 mm or 5 mm squares based on the size of the images. The size of the image (such as defect, mass, and anatomical structure) was estimated by these squares (Fig. 2b).

Continuous and categorical variables were described as mean ± standard deviation and percentages, respectively.

RESULTS

The mean time from MVR to the detection of PVL was 8.3±3.8 years (range 1 to 13 years). In mitral valve replacement, St. Jude, Carbomedics, and Medtronic prosthetic valves were used in nine, two, and two patients, respectively. Two patients had mild, six patients had moderate, and five patients had severe PVL. Two of the patients with severe PVL underwent surgical reoperation, whereas three patients were scheduled for percutaneous paravalvular closure.

Nine patients (69.2%) had atrial fibrillation, while four patients (30.8%) had normal sinus rhythm. Four patients (30.8%) had hemolysis. Transthoracic echocardiographic and hematological/laboratory findings are presented in Table 1. Ten patients (76.9%) were in New York Heart Association (NYHA) class I, two

Table 1. Transthoracic echocardiographic, hematological, and laboratory findings

	Mean±SD	Range
Transthoracic echocardiographic findings		
Left atrium (mm)	5.4±0.8	4.4 - 7.2
Left ventricular end-diastolic diameter (cm)	5.7±0.8	4.7 - 7.7
Left ventricular end-systolic diameter (cm)	3.8±0.8	3.2 - 6.1
Interventricular septum thickness (cm)	1.0±0.2	0.8 - 1.3
Left ventricular posterior wall thickness (cm)	1.0±0.1	0.8 - 1.2
Ejection fraction (%)	55.8±10.4	30 - 65
Degree of tricuspid regurgitation	3±1	0 - 4
Pulmonary artery systolic pressure (mmHg)	53.5±13.9	35 - 80
Hematological and laboratory findings		
Hemoglobin (mg/dl)	11.3±2.4	6.5 - 14.3
Hematocrit (%)	33.7±66.3	21.1 - 41.2
Platelet count (/μl)	217,923±72,185	112,000 - 315,000
Leukocyte count (/μl)	6,666±2,245	3,300 - 11,000
International Normalized Ratio	2.6±0.9	1.4 - 4.4
Lactate dehydrogenase (U/l)	587.2±181.0	321 - 855
Creatinine (mg/dl)	1.0±0.3	0.6 - 1.6
Urea (mg/dl)	41.5±15.3	21 - 72
C-reactive protein (mg/dl)	0.9±0.6	0.3 - 2.1

(15.4%) were in class II, and one patient (7.7%) was in class III. Ejection fraction, left atrial size, and mean pulmonary artery systolic pressure were 55.8±10.4%, 5.4±0.8 cm, and 53.5±13.9 mmHg, respectively.

Two- and three-dimensional TEE data used to establish the origin of paravalvular mitral regurgitation are presented in Table 2. The mean PVL width measured by 2D TEE was 3.00±0.92 mm. The mean length of dehiscence was measured as 13.6±8.8 mm, and the mean width was 3.88±2.04 mm on 3D TEE. On 2D TEE, the PVL was mostly observed on the appendix side (8 patients). The PVLs were mainly localized in the posterior and anterior positions between 12 to 03 hours (first quarter, 7 patients) and 06 to 09 hours (third quarter, 3 patients) on RT-3D TEE, respectively, which corresponded to the posteromedial or anterolateral sectors of the posterior annulus (Fig. 3).

DISCUSSION

In this study, it was found that RT-3D TEE was successful in defining the anatomic origin and size of PVL as compared to 2D TTE and 2D TEE, following prosthetic MVR. Furthermore, our study showed that PVL occurred more frequently at the anterolateral and posteromedial segments of the mitral annulus.

Table 2. Findings of two- and three-dimensional transesophageal echocardiography used to establish the localization of paravalvular mitral regurgitation (MR)

		Two-dimensional		Three-dimensional	
Case	MR degree	Localization	Width (mm)	Localization (clockwise)	Length (mm) x Width (mm)
1	2	Appendix	1.2	2	4.0 x 2.0
2	4	Appendix	3.5	5	15.0 x 4.0
3	4	Appendix	3.0	2.5	10.0 x 4.0
4	4	Appendix	5.0	2.5	35.0 x 7.0
5	3	Aorta	3.5	7	10.0 x 3.0
6	4	Appendix	3.0	1	4.0 x 7.0
7	3	Aorta	2.5	9.5	18.0 x 3.0
8	2	Aorta	3.0	9.5	5.0 x 1.0
9	4	Appendix	4.0	2	25.0 x 7.0
10	3	Aorta	2.5	7	10.0 x 2.5
11	3	Appendix	2.0	2.5	16.,0 x 2.0
12	3	Aorta	3.0	8	16.0 x 3.0
13	3	Appendix	2.8	1	10.0 x 5.0

Although uncommon, PVL may develop in both mechanical and biological prostheses.[1,2,7] Infection is the leading cause of PVLs. Following prosthetic MVR, destruction may develop in the valve ring due to infective endocarditis or postoperative endocarditis, resulting in dehiscence in tissue and paravalvular regurgitation and leak in the suture line. Annular calcification is another major risk factor. Debulking of the calcified valve may lead to tissue destruction in the suture line, and calcified foci which are not removed adequately may result in much greater decreases in tissue stability due to disrupted sutures. Twenty percent of the patients with PVL have annular calcification.[8] Since the etiology of our patients was predominantly of rheumatic origin, this may not reflect the actual cause of PVL as previously reported. Minor leaks are not clinically significant, whereas major leaks which are less common may require intervention due to symptomatic heart failure and severe hemolytic anemia. Treatment of PVL may be in the form of running monofilament suture techniques, prosthetic MVR, or percutaneous closure, which has recently gained popularity.[9-11] Twenty-two percent of the patients are diagnosed with PVL within the first week following prosthetic MVR, while 52% are diagnosed within the first year.[9-11] The mortality rate of prosthetic mitral valve reoperations is 6.2% under elective conditions and up to 13.3% under emergency conditions,[12] making percutaneous closure increasingly more popular.

Two-dimensional echocardiography allows direct visualization of endocardial and epicardial margins and other anatomical structures without the need for geometrical assumptions. On the other hand, 3D echocardiography proved to be a more accurate tool compared to 2D echocardiography in the assessment of ventricular volumes, ventricular systolic functions, heart valves, congenital cardiac anomalies such as atrial septal defect and ventricular septal defect, and central leaks associated with prosthetic valves.[13-15] Full-volume, biplane and triplane images can be obtained in the same cardiac cycle by the 3D echocardiographic technique which utilizes matrix array transducers. Thus, it is possible to obtain more detailed data about mitral valve functions.

Similar to visualization of natural valves by RT-3D TEE, the view of prosthetic valves may be fitted in zoom volume sector with adjustment of zoom sector and density settings.[16] Unlike rotational 3D data, zoom 3D TEE volume data can be obtained in one cycle and displayed without delay. Elicitation of valvular data by using the zoom technique was accomplished successfully particularly in patients with atrial fibrillation, since obtaining one-time data within the same cardiac cycle eliminated potential artifacts.[16,17] Consequently, as it was shown in this study, it is possible to obtain unparalleled views of mechanical (and bioprosthetic) valves including rings and struts via RT-3D TEE transducers. Excellent images of mechanical mitral valves can be obtained both from the left ventricle and left atrium by this technique. Compared with the left atrium, visualization scores of mechanical mitral valves obtained from the left ventricle would probably be lower due to acoustic shadowing.

Real-time 3D TEE transducer will be beneficial for establishing percutaneous or surgical treatment strategies for complications due to paravalvular mitral regurgitation related to prosthetic mitral valves, since it provides excellent spatial delineation about prosthetic decomposition and related structures. The prosthetic valve or dynamics of annuloplasty may be measured and the association with other cardiac structures may be assessed by 3D volumetric visualization of the mitral valve apparatus.[16,17] However, like native aortic and tricuspid valves, prosthetic valves cannot be visualized clearly in these localizations. This is considered to result from relative distance from the transducer and oblique angle of ultrasonographic waves. Hence, further technological developments are necessary for the ideal clinical use of RT-3D TEE in order to assess prosthetic valves like aortic and tricuspid valves.

There are few studies on the relationship between the anatomy and dynamics of the mitral annulus and prosthetic valve that predisposes to PVL.[18-20] In our study, the occurrence of PVL was mainly between 12 to 03 hours and 06 to 09 hours. This may be attributed to histological features. It has been reported that collagen fibers in the mitral valve annulus are not distributed homogeneously.[21,22] Of three layers of the mitral annulus, the amount of fibrosa is less in the posterior sector of the annulus. Additionally, the mitral annulus does not exhibit a uniformly well-formed chord-like fibrous structure, particularly along the posterior sector of the annulus.[22] These histological factors may render the posterior annulus vulnerable to mechanical stresses, predisposing it to PVL occurrence. Paravalvular leak may also develop due to technical or surgeon-related causes as shown by some investigators.[9,23]

Limitations of the study. The main limitation of RT-3D TEE is the limited capacity to visualize the anterior cardiac structures (aortic and tricuspid valve) compared to posterior structures (such as mitral valve). In addition, it may not be possible to view fast-moving structures such as vegetation and to evaluate dynamic behaviors due to low temporal resolution of zoomed images. Wide-angle full-volume recording at a frame rate of >30 Hz may be used to improve temporal resolution. However, the risk for combined artifacts increases due to the need for many samples of cardiac cycles between 4-7 beats and more than 70% of patients may have such artifacts.[16] Based on our experience in Koşuyolu Hospital, these artifacts do not affect the diagnostic value of the tests in many patients. This limitation is particularly important in the evaluation of 3D color data where seven cycles are recorded. These artifacts may be overcome by short-term interrupted respiration during the procedure.

Additionally, the RT-3D TEE technology slightly prolongs the duration of TEE assessment. However, with the use of standard imaging protocols in the future, manual imaging analysis will no longer be used, which is expected to shorten the duration of 3D TEE assessment. Currently, RT-3D TEE provides valuable information on the basis of, and complementary to 2D TEE findings.

Furthermore, planimetric areas of PVL cannot be measured real-time by 3D TEE. However, the origin and degree of leakage can be determined by the full-volume method. The anatomical dehisced areas can only be estimated roughly by using the grid method.

False PVL images may be obtained when the gain settings are markedly reduced. The more the reduced gain settings, the more the false PVL images. However, this limitation may be overcome when the learning curve is completed.

In conclusion, RT-3D TEE is superior to 2D TEE in localizing and measuring the size of PVLs that develop following prosthetic MVR. At present, however, this technology should be considered complementary rather than comparative to 2D TTE and 2D TEE. Fast evaluation and immediate online display will make RT-3D TEE the modality of choice for planning mitral valve interventions and postinterventional follow-up.

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