Transprosthetic Cuff Leakage of a Bovine Pericardial Aortic Bioprosthesis

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The Carpentier-Edwards PERIMOUNT Magna aortic heart valve is the most frequently implanted bioprosthesis. However, the existence of transvalvular cuff leakage necessitating a second cross clamp has been recently reported. The aim of this study is to seek the mechanism, occurrence rate, and influence of cuff leakage on the clinical course. Between September 2012 and August 2018, 754 consecutive patients underwent aortic valve replacement using a Magna aortic prosthesis at a single cardiovascular center. The overall mean patient age was 75 (69–80) years, and the percentage of female gender was 45.5% (343/754). The etiology included aortic stenosis in 506 patients (67.1%) and aortic insufficiency in 248 patients (32.9%). The implanted valve size was 19 mm, 21 mm, 23 mm, 25 mm, and 27 mm in 125 (16.6%), 243 (32.2%), 228 (30.2%), 130 (17.2%), and 28 (3.7%) patients, respectively. The incidence of cuff leakage was 1.59% (12/754). The origin was left-right commissure in all cases, and the jet passed toward the anterior mitral leaflet. In 9 patients (75%), cuff leakage faded completely within 3 months after surgery. Additionally, residual leak was not associated with hemolysis and cardiac events in all cases. Transvalvular cuff leakage should be perceived as a benign leakage. Nonperivalvular oblique jet from the left-right commissure toward the anterior mitral leaflet in transgastric long-axis view is likely to be cuff leakage, and follow-up with protamine administration for mild leak is suggested as the first-line choice of treatment rather than a second aortic clamp.

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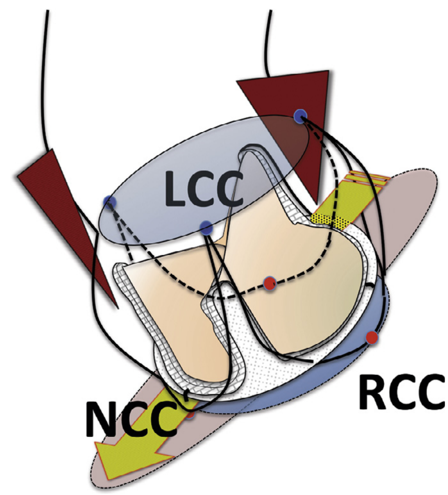
Keywords: Aortic valve replacement, Cuff leakage, Bovine bioprosthesis, Echocardiogram



Cuff leakage from the Carpentier-Edwards PERIMOUNT Magna aortic bioprosthesis.

Central Message

Follow-up with protamine administration is recommended for transprosthetic cuff leakage toward the anterior mitral leaflet in the Carpentier-Edwards PERIMOUNT aortic prosthesis.

Perspective Statement

Transprosthetic cuff leakage of the Carpentier-Edwards PERIMOUT aortic prosthesis occurred in 1.59%, and the clinical course was good. It should be widely known that nonperivalvular oblique jet from the left-right commissure toward the anterior mitral leaflet is likely to be cuff leak. Follow-up with protamine administration is advisable as the first-line choice rather than a second aortic clamping.

Abbreviations: AVR, aortic valve replacement; TEE, transesophageal echocardiogram

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INTRODUCTION

The Carpentier-Edwards PERIMOUNT Magna aortic bioprosthesis (Edwards Lifesciences, Irvine, CA) is the most frequently implanted prosthetic valve with proven durability, implantability, and hemodynamic performance.[1,2] In aortic valve replacement (AVR), it is well known that mild central transvalvular leakage is a structural feature, purposefully designed to improve durability.[3] However, nontransvalvular

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and nonparavalvular leakage has been recently reported after implantation of the Carpentier-Edwards aortic bioprosthesis.[4–8] The diagnostic features of this transprosthetic cuff leakage are as follows: (1) neither paravalvular nor transvalvular, (2) noncentral and eccentric jet, (3) mostly dissipating after heparin neutralization, and (4) benign in most cases. The left-right commissure is the frequent site of cuff leakage, and the oblique jet flows toward the anterior mitral leaflet. Still undetermined, the leakage is thought to result from the weak point of the cuff at the gap between the metal stent and silicone ring.[7] Additionally, although cases have been reported as rare, the occurrence rate after AVR, follow-up, and strategy for the cuff leakage has yet to be confirmed. To avoid unnecessary intervention, the criteria should be evaluated not only for cardiac surgeons but also for anesthesiologists and cardiologists involved in the intraoperative transesophageal echocardiogram (TEE) examination. Based on these findings, the aim of this study is to evaluate the occurrence rate of the cuff leakage from the Carpentier-Edwards aortic bioprosthesis and investigate its features.

PATIENTS AND METHODS

Cohort and Data Collection

This study is a retrospective evaluation of cuff leakage from the Carpentier-Edwards aortic bioprosthesis. Between September 2012 and August 2018, 754 consecutive patients underwent AVR using the Carpentier-Edwards Magna aortic prosthesis at the Sakakibara Heart Institute of Okayama, Japan. The overall mean patient age was 75 (69–80) years, of which 45.5% (343/754) were female. The etiology included aortic stenosis in 506 patients (67.1%) and aortic insufficiency in 248 patients (32.9%). The implanted valve size was 19 mm, 21 mm, 23 mm, 25 mm, and 27 mm in 125 (16.6%), 243 (32.2%), 228 (30.2%), 130 (17.2%), and 28 (3.7%) patients, respectively. Patient characteristics are presented in Table 1. Data collection was performed as approved by the institutional review board on September 27, 2018. This study was approved by the institutional ethics committee in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Consent for usage of patients' data was obtained from all patients.

Table 1. Patient Demographics

Variables	($n = 754$)
Age (y)	75 (69–80)
Female	343 (45.5%)
Body surface area (m^2)	1.55 (1.43–1.70)
Hypertension	193 (25.6%)
Hyperlipidemia	316 (41.9%)
Diabetes mellitus	216 (28.6%)
Dialysis	58 (7.7%)
Aortic stenosis	506 (67.1%)
Bicuspid aortic valve	123 (16.3%)
Infectious endocarditis	11 (1.5%)
Ejection fraction (%)	64 (56–70)
Implanted valve size	
19 mm	125 (16.6%)
21 mm	243 (32.2%)
23 mm	228 (30.2%)
25 mm	130 (17.2%)
27 mm	28 (3.7%)

Surgical Aortic Valve Replacement

Surgical AVR with the Carpentier-Edwards Magna aortic prosthesis was performed by standard supra-annular position with 12–15 pairs of noneverting mattress pledgetted sutures of 2-0 nesporen. In patients with aortic stenosis, the calcification of the aortic annulus was carefully resected using the Cavitron Ultrasound Surgical Aspirator (CUSA Excel Plus, Integra LifeSciences Corporation, NJ).

Definition of Transprosthetic Cuff Leakage

After cardiopulmonary bypass was terminated, the anesthesiologist and cardiologist carefully examined the aortic prosthesis using the TEE. Nonparavalvular and nontransvalvular leakage from the cuff at the left-right commissure to the anterior mitral leaflet was defined as transprosthetic leakage.[4–8] Color Doppler flow TEE mid-esophageal aortic valve long-axis view with a multiplane angle of 120–140°, a field depth of 10 cm, and velocity range of 60–70 cm/s was effective to represent the leakage. Additionally, LIVE xPlane using iE33 (Philips Medical Systems, Bothell, WA) simultaneously displayed orthogonal sections (short-axis view at a multiplane angle of 45°) and provided optimal views to detect the transprosthetic cuff leakage. The direction of the leakage was commonly perpendicular (Fig. 1, Supplementary Videos 1 and 2).

The structural cause of the leak is thought to be a gap between the silicone ring and the metal stent. The metal stent forms an arch curve at the commissure. By peeling the surficial cuff at the commissure post, the pervious space covered by fabric is revealed (Fig. 2).

Statistical Analysis

Continuous data are presented as median and interquartile values (the first to the third quartile). Categorical variables are given as a count and percentage of patients. All data were analyzed using the Statistical Analysis Systems software JMP 12.0 (SAS Institute Inc., Cary, NC).

RESULTS

Characteristics of Cuff Leakage Patients

Transprosthetic cuff leakage was observed in 12 patients, and the occurrence rate was 1.59%. The median age of patients with cuff leakage was 74.5 (70–76) years, which included 3 female, 9 hypertension, 6 hyperlipidemia, 1 diabetes mellitus, and 1 dialysis. Etiology was 4 aortic stenosis, including 1 bicuspid aortic valve and 8 aortic insufficiency. The implanted valve sizes were 3 (21 mm), 5 (23 mm), 3 (25 mm), and 1 (27 mm).

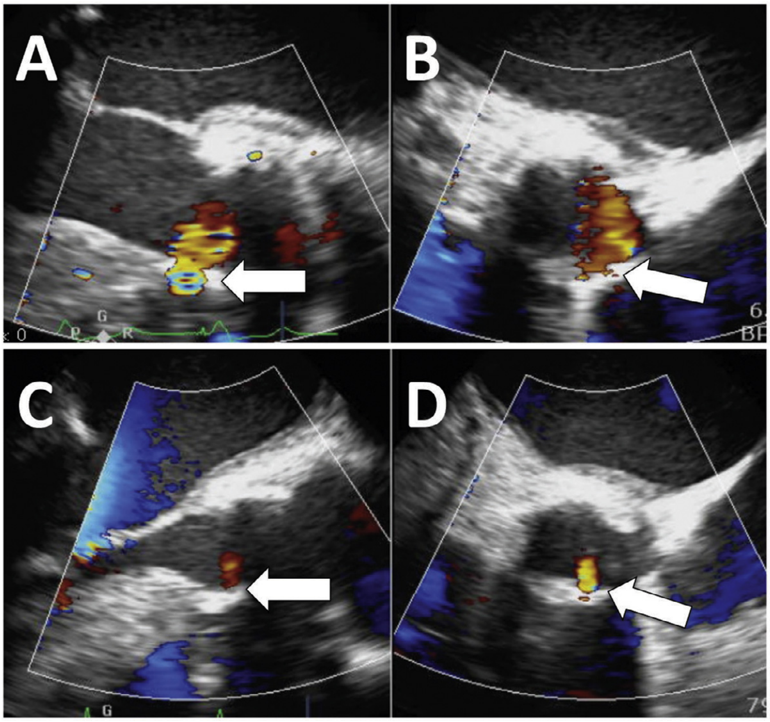


Figure 1. Intraoperative transesophageal echocardiogram of a patient with typical transprosthetic cuff leakage (white arrows). The origin of cuff leakage was left-right commissure, and the jet passed toward the anterior mitral leaflet at long-axis view (A) and short-axis view (B). After protamine administration, the leakage significantly decreased (white arrows) at long-axis view (C) and short-axis view (D).

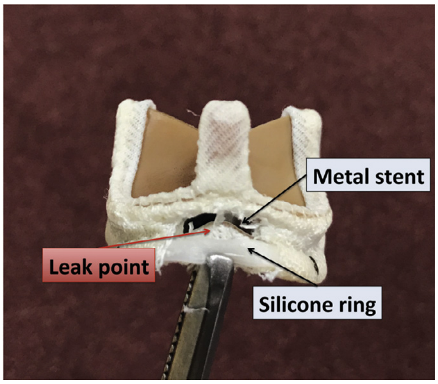


Figure 2. After peeling the surficial cuff at the commissure post of the Carpentier-Edwards PERIMOUNT aortic bioprosthesis, the pervious space covered by fabric is revealed. Red arrow shows the pervious area between the silicone ring and the metal stent. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

Preoperative Echocardiographic Parameters in Patients With Cuff Leakage

The median of left ventricular diastolic, systolic size, and ejection fraction was 57 (28.8−63) mm, 38.5 (28.8−45.5) mm, and 63.5% (53.8−68.5), respectively. No abnormal findings were found in the preoperative transthoracic echocardiogram (Supplementary Table 1).

Intraoperative Transesophageal Echocardiography in Patients With Cuff Leakage

In all cases, the intraoperative TEE revealed an oblique jet from the left-right commissure to the anterior mitral leaflet after termination of cardiopulmonary bypass. In the initial 3 patients, additional sutures were placed after a second cross clamping; however, cuff leakage had not completely tapered during the surgical procedure. Transprosthetic cuff leakage was observed without additional intervention in the remaining subsequent 9 patients. In 2 patients, cuff leakage dissipated completely during surgery after protamine administration (Fig. 3, Supplementary Videos 3 and 4).

Clinical Course and Follow-Up Echocardiography in Patients With Cuff Leakage

Follow-up transthoracic echocardiography showed an absence of cuff leakage in 4 patients at 1 week, 2 patients at 1 month, and 1 patient at 3 months after AVR. In contrast, a trivial jet was observed in 2 patients at 8 months and at 3 years after surgery, and a mild jet remained in 1 patient at 2 months after implantation. There were no patients with hemolysis and cardiac events caused by regurgitation during follow-up. Overview of patients with cuff leakage is shown in Table 2.

DISCUSSION

The Carpentier-Edwards PERIMOUNT Magna aortic heart valve has been the most used bioprosthesis in the world.[9−12]

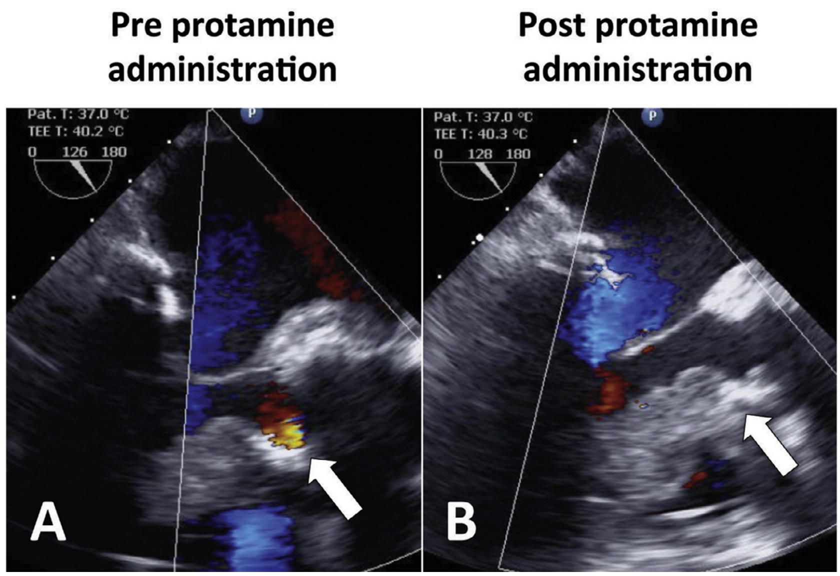


Figure 3. Seventy-six years, male. Twenty-one millimeter Carpentier-Edwards PERIMOUT Magna aortic bioprosthesis was implanted for aortic stenosis. Intraoperative transesophageal echocardiogram of a patient with transprosthetic cuff leakage (white arrow) (A). Cuff leakage faded completely during operation after protamine administration (white arrow) (B).

Table 2. Detailed Data of Patients With Transprosthetic Cuff Leakage

	Age (y)	Gender	BSA (m^2)	Etiology	Annulus Diameter (mm)	Valve Size (mm)	Reintervention	Follow-Up TTE
1	61	F	1.59	AI with BAV	20	21	After second cross clamp, 2 additional sutures were placed	Absence, 1 mo after surgery
2	76	M	1.45	AS	19.5	21	After second cross clamp, 2 additional sutures were placed	Absence, 3 mo after surgery
3	75	M	1.72	AI	24	25	After second cross clamp, 2 additional sutures were placed	Mild jet, 2 mo after surgery
4	76	M	1.51	AI	23	23	Observation	Absence, 1 wk after surgery
5	70	M	1.78	AI	22	23	Observation	Absence, 1 wk after surgery
6	63	M	1.89	AI	25	27	Observation	Absence, 1 mo after surgery
7	77	M	1.85	AI	25	25	Observation	Trivial jet, 3 y after surgery
8	74	M	1.46	AI	23	23	Observation	Trivial jet, 8 mo after surgery
9	80	M	1.53	AS	23	25	Observation	Absence, 1 wk after surgery
10	73	M	1.57	AI	21	23	Observation	Absence, during operation
11	76	F	1.38	AI with IE	20	23	Observation	Absence, during operation
12	70	F	1.60	AS	20	21	Observation	Absence, 1 wk after surgery

Since it is difficult to diagnose the leakage as nonperivalvular transprosthetic cuff leakage, we surgeons truly vacillate between observation and additional intervention when this type of leakage is encountered. Therefore, to avoid a second cardiac arrest, it is important to understand and prevent cuff leakage. In the present study, new observations of cuff leakage were documented: the incidence rate was 1.59% (12/754), the origin was left-right commissure in all cases, and the jet flowed toward the anterior mitral leaflet. In 8 patients (67%), cuff leakage disappeared completely within 3 months after AVR. Finally, residual cuff leakage was not associated with hemolysis and cardiac events.

Five cases discussing transprosthetic cuff leakage from the Carpentier-Edwards Magna aortic bioprosthesis have been reported,[4–8] the overview of which is summarized in Supplementary Table 2. We underscore Kuroda et al, who reported that a mid-esophageal short-axis and transgastric long-axis view could display the cuff leakage clearly.[5] In all reports, the eccentric jet flowed toward the anterior mitral leaflet, and it did not cause adverse postoperative events. However, additional sutures were placed after reclamping in 2 cases, and in 1 case another same-size valve was reimplanted. In fact, we also chose to perform a second cross clamping for additional stitches in the initial 3 cases. No abnormal findings in the initial explanted bioprosthesis were reported by Arakawa et al,[8] whereas Tokunaga et al described that a clear gap between the silicone ring and the metal stent was a cause of their leakage, which was repaired using a 5-0 prolene stitch.[7] This remark is key; however, there are still queries. One, especially, if the weak point of the cuff is widest just below each stent-post, then this can lead to the cuff leakage, but why is the left-right commissure the frequent site? It could be that regurgitation from other commissures (right-non and non-left) is a blind spot for TEE. Kunisawa et al reported a major leakage at the left-right commissure, and small jets at other commissures.[4] In our institute, 2 different experts diagnosed different leakages from other commissures that could not be detected in all cases using intraoperative TEE. Dr Liakopoulos indicated that extensive force on surgical suture can lead to local dehiscence within the sewing cuff, and grading by using the Paravalvular Leak Academic Research Consortium criteria before and after protamine administration was a promising approach.[13,14] Another possible answer to consider is the anatomical and technical attributes of the aortic annulus: it is not flat, and the nadir of the noncoronary cusp is commonly located at the lowest level, compared to the remaining cusps. If the Carpentier-Edwards aortic bioprosthesis is implanted flatly to all the nadirs, the space between each stent-post and aortic wall is similar (Fig. 4A). Conversely, when the Carpentier-Edwards aortic bioprosthesis is secured at the nadir of the noncoronary cusp and implanted obliquely, the stent-post of left-right commissure is placed at a higher level. Consequently, the angle between the stent-post and aortic wall increases, and the weak point of the cuff may be stretched at the left-right commissure compared to the remaining commissures (Fig. 4B). Therefore, the horizontal aortic root and nonhorizontal stitch at the left-right commissure may be one of the triggers for leakage. As for a preventive strategy for transprosthetic cuff leakage, selection of an appropriately sized valve is required to avoid undersizing. The stretching of the cuff confirms the vulnerable point of the Carpentier-Edwards aortic bioprosthesis (Fig. 5A). A precautionary stitch would be advisable for the gap between the silicone ring and metal stent at the left-right commissure and a horizontal stitch for the aortic annulus to prevent cuff leakage. Additionally, a stitch at the edge may increase the risk of cuff leakage (Fig. 5B); therefore, the stitch should be placed close to the stent-post and reinforcement with pledget may be more effective as a preventative option (Fig. 5C and D).

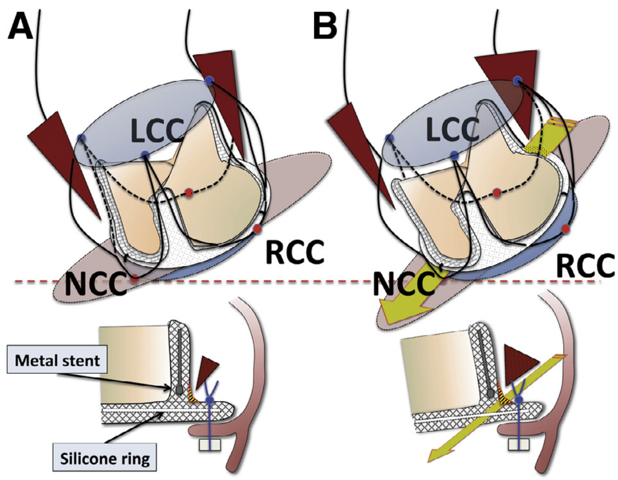


Figure 4. (A) If the aortic prosthesis is implanted flatly to tall nadirs, the space between each stent-post and aortic wall is similar between respective commissures (red arrowheads). (B) When the aortic prosthesis is secured at the nadir of the noncoronary cusp and implanted obliquely, the angle between the stent-post and aortic wall increases at the left-right commissure (red arrowheads). The weak point of the cuff between the metal stent and silicone ring (shaded yellow area) may be stretched at the left-right commissure compared to the remaining commissures, and can lead to the transprosthetic leakage (yellow arrows). LCC, left coronary cusp; NCC, noncoronary cusp; RCC, right coronary cusp. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

Study Limitations

There were several limitations. First, the cohort included patients who were not directly checked by a second cross clamping. Therefore, diagnostic error could not be completely excluded. Additionally, the use of clinical echo may be inadequate to provide solid scientific data. Second, we cannot deny the possibility of overlooked transprosthetic cuff leakage in some cases. Since there were a small number of patients with cuff leakage, regression analysis could not detect the significant risks of cuff leakage. Finally, 4 different surgeons performed AVR in our institute; therefore, technical differences may have influenced results.

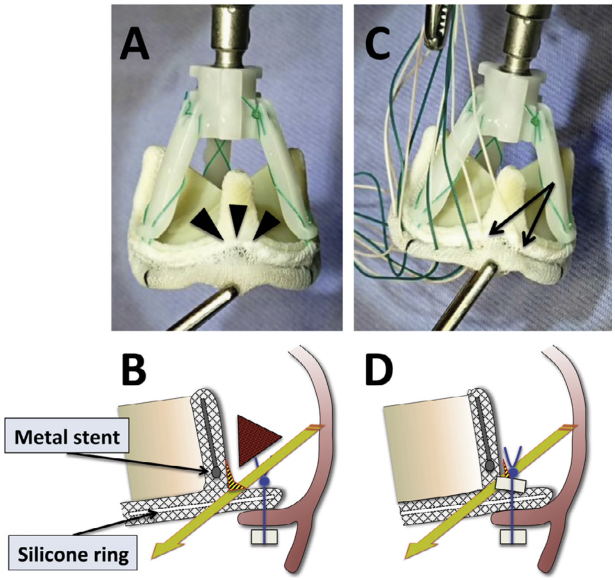


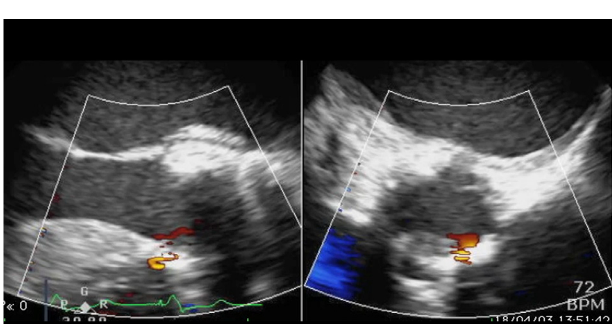
Figure 5. The sparse point of the Carpentier-Edwards PERIMOUT Magna aortic bioprosthesis (black arrowheads) (A). A stitch at the edge may increase the risk of transprosthetic cuff leakage (B); therefore, the stitch should be placed close to the stent-post and reinforcement with pledget may be more effective as a preventative option (C and D).

CONCLUSIONS

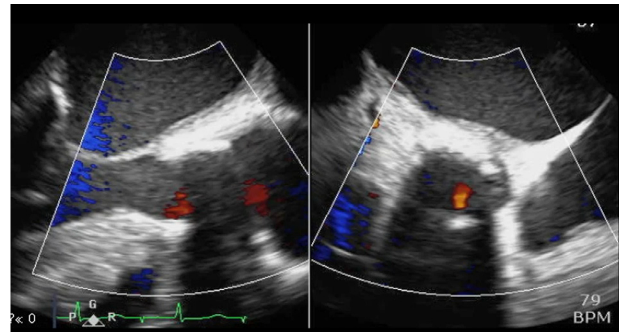
The incidence of transprosthetic cuff leakage from the Carpentier-Edwards aortic bioprosthesis was 1.59%. The cuff leakage is not associated with adverse events in most cases. Therefore, it is important that mild cuff leakage be widely known as a benign leakage by not only cardiac surgeons but also anesthesiologists and cardiologists involved in the intraoperative TEE evaluation. The nonperivalvular oblique jet from the left-right commissure toward the anterior mitral leaflet in the transgastric long-axis view is likely to be cuff leakage, and follow-up with protamine administration for mild cuff leakage is advisable as the first-line choice of treatment rather than a second aortic clamping. However, this may not be the case when leakage is moderate.

SUPPLEMENTARY MATERIAL

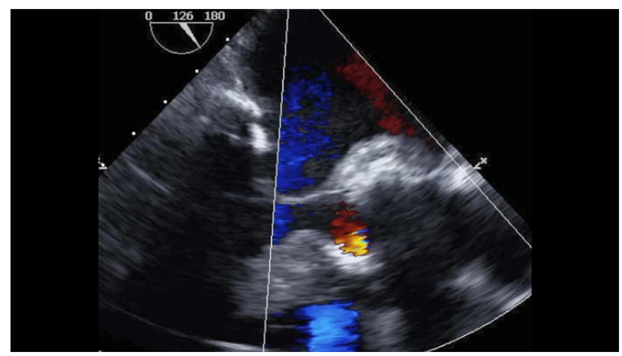
The following is the supplementary data to this article:



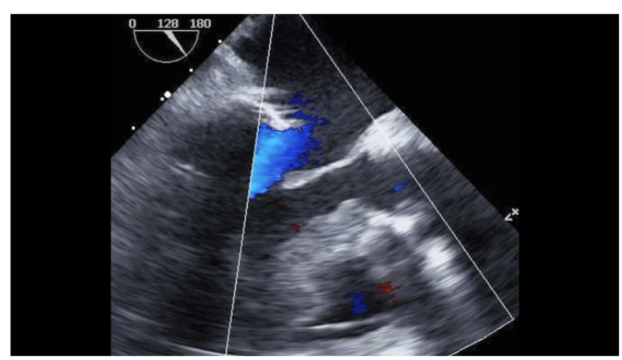
Video 1. Intraoperative transesophageal echocardiogram before protamine administration.



Video 2. Intraoperative transesophageal echocardiogram after protamine administration.



Video 3. Intraoperative transesophageal echocardiogram before protamine administration.



Video 4. Intraoperative transesophageal echocardiogram after protamine administration.

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