Early postoperative paravalvular leak among Egyptian population: An observational study

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Objectives: Several reports described the incidence of postoperative paravalvular leakage (PVL) early after valve replacement surgery, however, there is a paucity of data regarding the outcomes and complications correlated to the severity of PVL. The aim of the current study was to evaluate the incidence, causes, and short term outcome of early postoperative PVL.

Methods: Data were collected from patients presenting to the cardiovascular department at Cairo University Hospital for aortic and/or mitral valve replacement surgery from May 2014 to May 2015. Transthoracic echocardiography (TTE) was done for all patients early postoperative. Transesophageal echocardiography (TEE) was done if diagnosis was not confirmed by TTE. All patients with detected PVL were subjected to TTE and TEE after a 3 month follow-up period.

Results: Two hundred patients were enrolled in the study. Seventy five percent of patients were known to have rheumatic heart disease, while 16.5% had infective endocarditis. The mitral valve was replaced in 40% of patients, the aortic valve was replaced in 36%, and other patients had both valves replaced. Early postoperative period PVL was detected in 25 patients. The most common underlying etiologies were rheumatic heart disease and infective endocarditis. PVL was common in patients with both valves replaced compared with either mitral or aortic valve replacement. Infective endocarditis as underlying valve disease was significantly high in patients with PVL compared with those without ($p < 0.001$).

Conclusion: The incidence of PVL was high in patients with both valves replaced compared with either mitral or aortic valve replacement. Moreover, every patient with PVL should be properly investigated for infective endocarditis. Surgical intervention, although associated with high morbidity and mortality, reduces PVL recurrence.

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Introduction

The presence of paravalvular leaks (PVLs) is a well-known complication after both aortic (AVR) and mitral (MVR) valve replacements. It occurs because of the incomplete apposition of the sewing ring to the native annular tissue. PVLs can be seen either immediately after valve replacement in the operating room or during the follow-up period. The immediate PVLs usually are associated with technical difficulties related to calcification of the native annulus. Late PVLs are commonly a consequence of suture dehiscence caused by prosthetic valve endocarditis or the gradual resorption of incompletely debrided annular calcifications [1]. Although most PVLs are asymptomatic and have a benign clinical course, an estimated 1–5% of patients with PVLs can develop serious clinical consequences [2].

Patients with symptomatic PVLs present with congestive heart failure from volume overload in 90% of cases and hemolytic anemia from shear stress on the red blood cells ranging from one-third to three-quarters of cases. Hemolysis can be identified by serum lactate dehydrogenase level >460 U/L and any two of the following criteria blood hemoglobin <13.8 g/dL for males or <12.4 g/dL for females, serum haptoglobin <50 mg/dL, and reticulocyte count >2%. Severe hemolytic anemia may even manifest as congestive heart failure [3].

Furthermore, PVL, like any intracardiac defect creating a significant turbulent flow, is an important pre-existing condition in the context of bacteremia to develop infective endocarditis [2].

Transthoracic echocardiography (TTE) along with transoesophageal echocardiography (TEE) can be utilized to determine these spatial characteristics and prosthetic valve function. Three-dimensional TEE is superior to two-dimensional TEE for evaluation of PVL regurgitation because it provides improved localization and analysis of the PVL size and shape, especially in patients with multiple PVLs [4].

Until recently, surgery has been the only available therapy for the treatment of clinically significant PVLs despite the significant mortality associated with reoperation [5,6]. The transcatheter closure of PVLs is performed using trans-septal, retrograde transaortic, and/or left ventricular (LV) transapical approaches. The choice of approach depends on the valve involved, the location of the leak, the presence of mechanical valves hindering entry, and the vascular access

Abbreviations	
PVL	Paravalvular leak
TTE	Transthoracic echocardiography
TEE	Transoesophageal echocardiography
AVR	Aortic valve replacement
MVR	Mitral valve replacement
PWD	Pulsed wave Doppler
CWD	Continuous wave Doppler
EOA	Effective orifice area
VTI Pr V	Velocity-time integral through the prosthetic heart valve
DVI	Doppler velocity index
LDH	Lactate dehydrogenase
RHD	Rheumatic heart disease
IE	Infective endocarditis

difficulties of an individual patient. There are several complications that can occur either during transcatheter closure or in follow-up. Complications include the need for emergency cardiac surgery in 0.7–2% and death in 1.4–2% [7].

The aim of the current study was not only to evaluate the incidence, causes, and short-term outcome of PVL with variable degree of severity in patients with prosthetic cardiac valves, but also to describe the association of hemolytic anemia with different grades of PVL.

Patients and methods

Study design

This was an observational study in which we collected data from patients with mechanical or biological valve prostheses complicated with PVL presenting to the Cardiovascular Department at Cairo University Hospital, Egypt for aortic and/or mitral valve replacement surgery from May 2014 to May 2015. Patients were subjected to history taking and physical examination. Demographic parameters were recorded, including age, sex, and body mass index. Written informed consent was obtained from all participants. The study protocol was approved by the Ethics Committee at Cairo University Hospital. Patients who were not willing to participate in the study or refused to undergo TEE were excluded.

Laboratory data

Hemolytic anemia was detected by blood analysis for hemoglobin, bilirubin (total and direct), lactate dehydrogenase, and reticulocyte count. Patients with suspected infective endocarditis (IE) had three sets of blood cultures that were

Table 1. Baseline clinical evaluation for all patients.

Variable	All patients (n = 200)	Patients with postoperative paravalvular leak (n = 25)
Age (y)	38.9 ± 12.3	34.48 ± 9.39
Sex		
Male	108 (54%)	16 (64%)
Female	92 (46%)	9 (36%)
Underlying valve etiology		
Rheumatic valve lesion	150 (75%)	18 (72%)
Infective endocarditis	33 (16.5%)	16 (64%)
Bicuspid aortic valve	16 (8%)	3 (12%)
Clinical presentation		
Heart failure	194 (97%)	24 (96%)
Infective endocarditis	29 (14.5%)	14 (56%)
Embolic events	25 (12.5%)	14 (56%)

Table 2. Surgical data for all patients and patients with paravalvular leak.

Variable	All patients (n = 200)	Paravalvular leak patients (n = 25)
Valve replaced		
Mitral	80 (40%)	3 (12%)
Aortic	77 (36%)	7 (28%)
Both	43 (21.5%)	15 (60%)
Type of valve replaced		
Mechanical	198 (99%)	25 (100%)
Bioprosthesis	2 (1%)	0 (0%)

withdrawn in aerobic and anaerobic media from three different venipuncture sites under complete aseptic precautions.

Echocardiography analysis

All patients had TTE before valve replacement and early postoperative before discharge to screen for early PVL. If there was any clinical suspicion of PVL such as symptoms of heart failure, newly developed murmur at auscultation, or laboratory findings of anemia, an additional TTE was performed. If findings were inconclusive, TEE was performed. Echocardiography was performed with all patients in the left lateral decubitus position. Standardized measurement and evaluation of the size of all cardiac chambers, LV wall thickness and function, left atrial size, and estimation of pulmonary artery systolic pressure were done by commercial scanner (iE33 Philips Medical
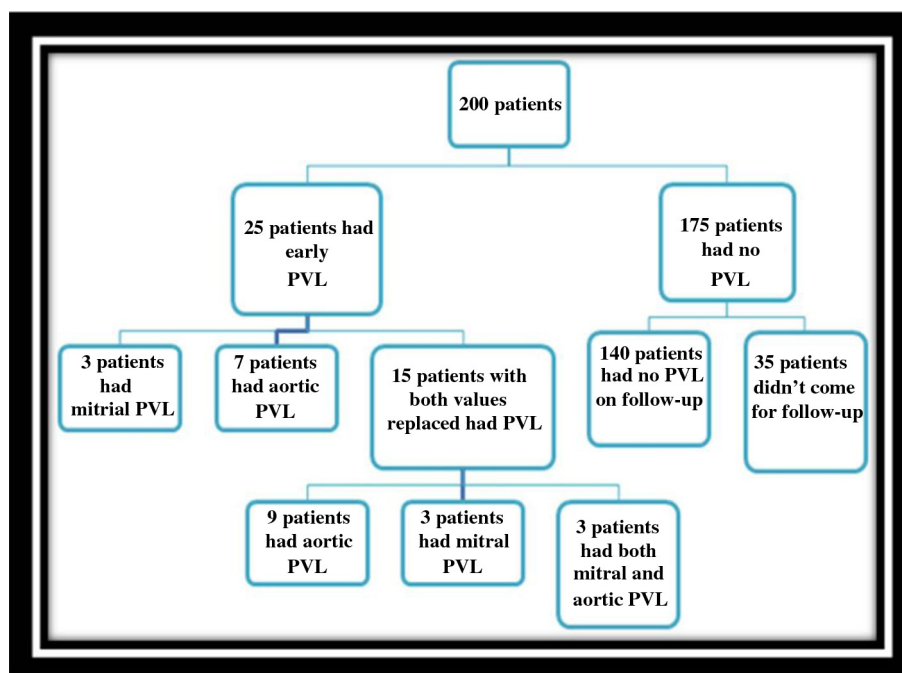

Fig. 1. Flow chart for all patients included in the study. PVL = paravalvular leak.

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Table 3. Patients with and without paravalvular leak according to the type of previous surgery.

|		Group I n = 175		Group II n = 25		P
		Count	%	Count	%	
Mitral valve replaced	Yes	16	9.1	17	68.0	<0.001
(previous surgery)	No	159	90.9	8	32.0	
Aortic valve replaced	Yes	4	2.3	22	88.0	<0.001
(previous surgery)	No	171	97.7	3	12.0	
Mitral commisurotomy	Yes	5	2.9	0	0.0	1.000
(previous surgery)	No	170	97.1	25	100.0	
Mitral valve repair	Yes	3	1.7	0	0.0	1.000
(previous surgery)	No	172	98.3	25	100.0	
	No	174	100.0	24	96.0	

Results shown are mean ± standard deviation.
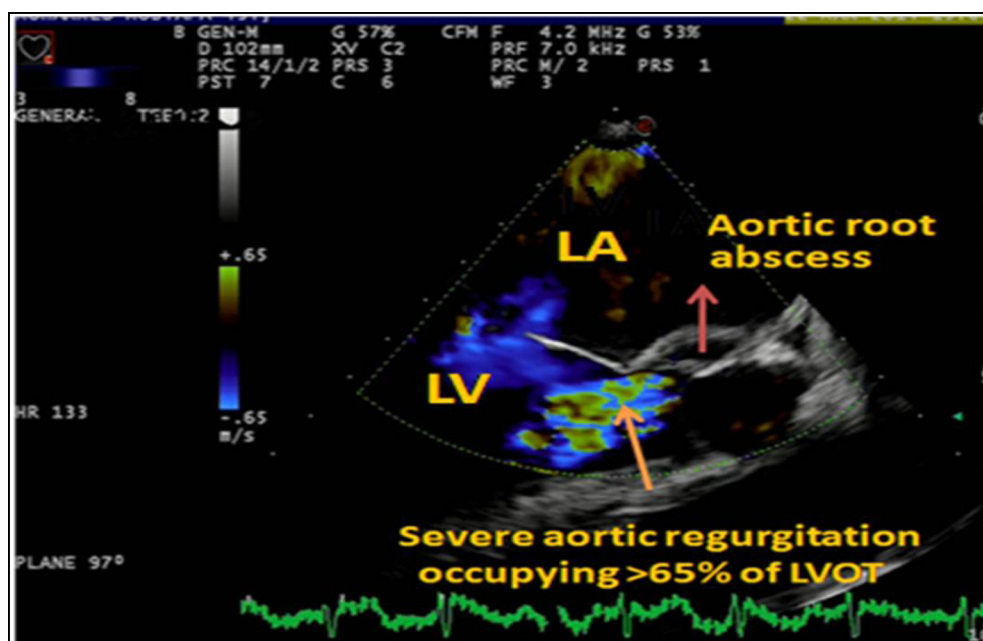
Fig. 2. Preopertive long axis tranesophageal study showing aortic root abscess. Transesophageal images of a patient with significant aortic regurgitation and aortic root abscess, with an underlying pathology of infective endocarditis. LA = left atrium; LV = left ventricle; LVOT = left ventricle outflow tract.

Systems, Andover, MA, USA) according to the recommendations of the American Society of Echocardiography [8].

Statistical analysis

Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data, and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the nonparametric Kruskal–Wallis and Mann–Whitney tests. For comparing categorical data, the χ^2 test was performed. Fisher's exact test was used instead when the expected frequency was <5. A p value <0.05 was considered statistically significant. Data were coded and entered using SPSS version 22 (Chicago, IL, USA).

Results

The study included 200 patients who underwent mitral and/or aortic valve replacement at Cairo University Hospital, New Kasr Al Ainy Teaching Hospital, and National Heart Institute Cairo, Egypt from May 2014 to May 2015 (Fig. 1). Patients were divided into Group I with 175 patients with replaced prosthetic heart valve with no PVL, and Group II with 25 patients with early PVL. All patients were subjected to clinical evaluation and echocardiography assessment before and after
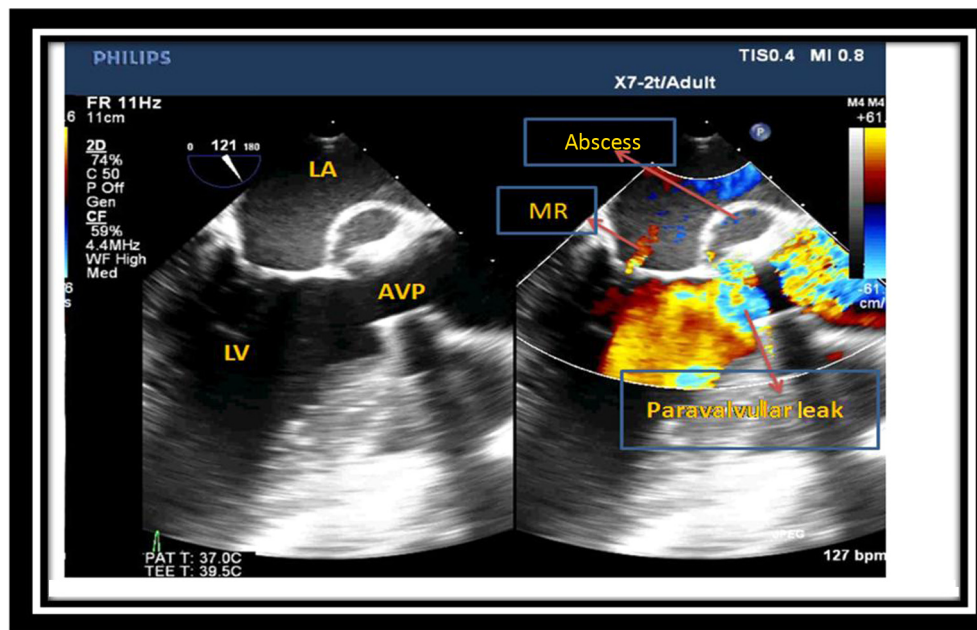
Fig. 3. Early postoperative paravalvular leak due to infective endocarditis showing aortic root abscess. Long-axis view of transesophageal echocardiography showing abscess cavity related to prosthetic valve in aortic position, with severe paravalvular leak and central ject of mild mitral regurgitation. AVP = aortic valve prosthesis. LA = left atrium; LV = left ventricle; MR = mitral regurgitation.

Table 4. Vegetations affecting mitral and aortic prostheses among two study groups.

Variables		Group I		Group II		P
		Count	%	Count	%	
Masses on mitral prosthesis	Yes	1	0.9	3	17.6	0.008
	No	107	99.1	14	82.4	
Masses on aortic prosthesis	Yes	0	0.0	3	13.6	0.005
	No	100	100.0	19	86.4	

surgery, before discharge from hospital, and after 3 months follow-up. The mean age of the patients was 38.9 ± 12.3 years (Table 1). The mitral valve, aortic valve, and both valves were replaced in 80, 77, and 43 patients, respectively (Table 2). Rheumatic heart disease (RHD) and IE were the most common underlying pathology for valve replacement (Fig. 2). Heart failure symptoms were the most common presentation followed by symptoms suggestive of IE.

Laboratory workup revealed that hemoglobin was significantly low in patients with PVL compared with those without PVL (9.8 vs. 11.2 g/dL, $p = 0.02$). Moreover, total bilirubin, LDH, and reticulocyte count were elevated in patients with PVL ($p = 0.313$, $p = 0.002$, and $p = 0.045$, respectively). There was trend in renal impairment defined as elevation of serum creatinine >1.3 mg/ dL (according to reference value in our laboratories) or glomerular filtration rate <60 mL/ $min/1.73 m^2$ among patients with PVL compared with patients without PVL ($p = 0.027$).

The incidence of early PVL was higher in patients who had both mitral and aortic valves replaced compared with those with only one valve replaced. Previous valve replacement was significantly higher in patients with PVL compared with those without PVL ($p < 0.001$) with no significant difference in other valve surgeries (mitral valve repair or comissurotomy) (Table 3).

IE was significantly high in patients with PVL compared with patients without PVL ($p < 0.001$). Aortic root abscess was found in 5.6% of patients with IE without PVL ($n = 1/18$) compared with 53.3% of patients with IE and PVL ($n = 8/15$; $p = 0.004$) (Fig. 3).

Vegetation detected by echocardiography was statistically significant for patients in Group II (P value 0.008 and 0.005 for mitral and aortic prosthesis respectively) (Table 4).

Echocardiography showed that peak gradients were significantly elevated in patients with PVL compared with those without PVL ($p < 0.001$ and $p < 0.002$ for mitral and aortic prosthesis, respec-

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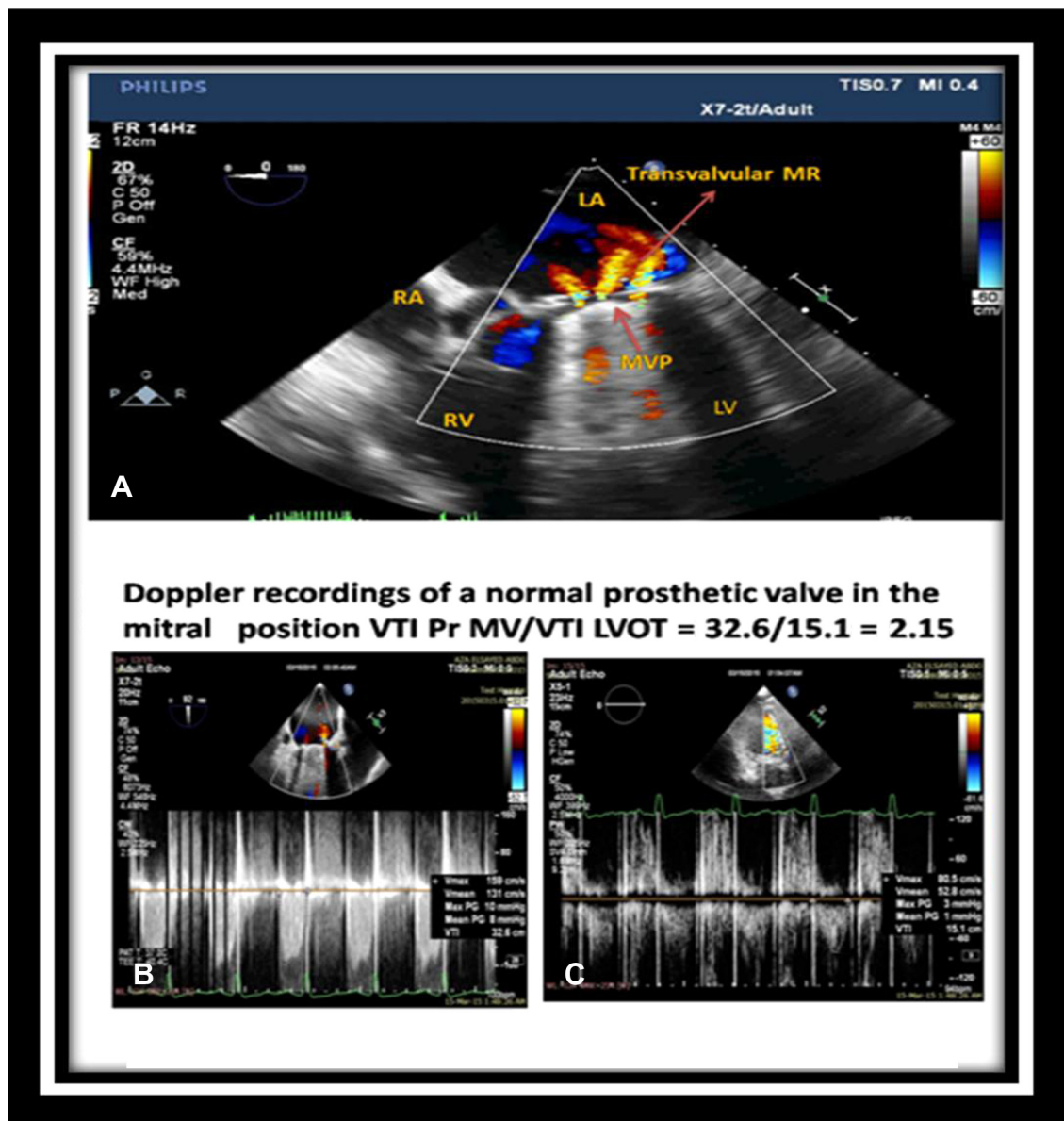EGYPTIAN POPULATION: AN OBSERVATIONAL STUDY

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Fig. 4. Well-functioning mitral valve prosthesis with physiological jet (upper panel) and normal Doppler velocity index (lower panel). LA = left atrium; LV = left ventricle; MR = mitral regurgitation; MVP = mitral valve prosthesis; RA = right atrium; RV = right ventricle; LVOT = left ventricle outflow tract; VTI = velocity time integral; VTI Pr MV = velocity time integral through the prosthetic heart valve in mitral position.

tively). Mean gradients were significantly elevated in patients with PVL compared with those without PVL ($p < 0.001$ and $p < 0.015$ for mitral and aortic prosthesis, respectively). However, there was no significant difference regarding LV dimensions, left atrial size, aortic root diameters, or LV ejection fraction between patients with and without PVL (Table 5).

Follow-up of patients with postoperative PVL showed well-functioning prostheses in 175 patients with no PVL detected by TTE or TEE (Figs. 4 and 5). Mortality was present in 16% of patients with early prosthetic PVL ($n = 4/25$) due to sepsis. Repeat surgery was done in 11 patients

with PVL and was successful in seven patients with no residual leak detected in the early postoperative period and during follow-up. Heart failure symptoms were the most common presentation for patients with residual PVL who did not undergo surgery.

The progression of severity in patients with mitral valve PVL varied. Among six patients with mild mitral PVL, one patient died due to associated severe aortic PVL, one patient had no leak on follow-up without intervention; and four patients still had mild PVL. One patient with moderate mitral PVL did not show disease progression and two patients with severe mitral PVL had no

Table 5. Echocardiographic data of the two study groups.

Variables	Group I		Group II		p
	Mean	SD	Mean	SD	
Peak gradient (mitral valve)	10.94	4.08	16.06	4.46	<0.001
Mean gradient (mitral valve)	4.69	1.47	8.24	3.21	<0.001
Peak gradient (aortic valve)	25.48	12.60	37.32	18.50	0.002
Mean gradient (aortic valve)	14.49	7.66	20.68	11.90	0.015
Left ventricular diastolic dimensions	5.37	0.91	5.33	0.97	0.686
Left ventricular systolic dimensions	3.79	0.98	3.72	1.00	0.677
Aortic root diameter	2.86	0.50	2.71	0.54	0.128
Left atrial diameter	4.71	1.06	4.38	0.90	0.277
Ejection fraction	55.17	11.70	57.72	11.96	0.279

Results shown as mean ± SD, unless noted otherwise.
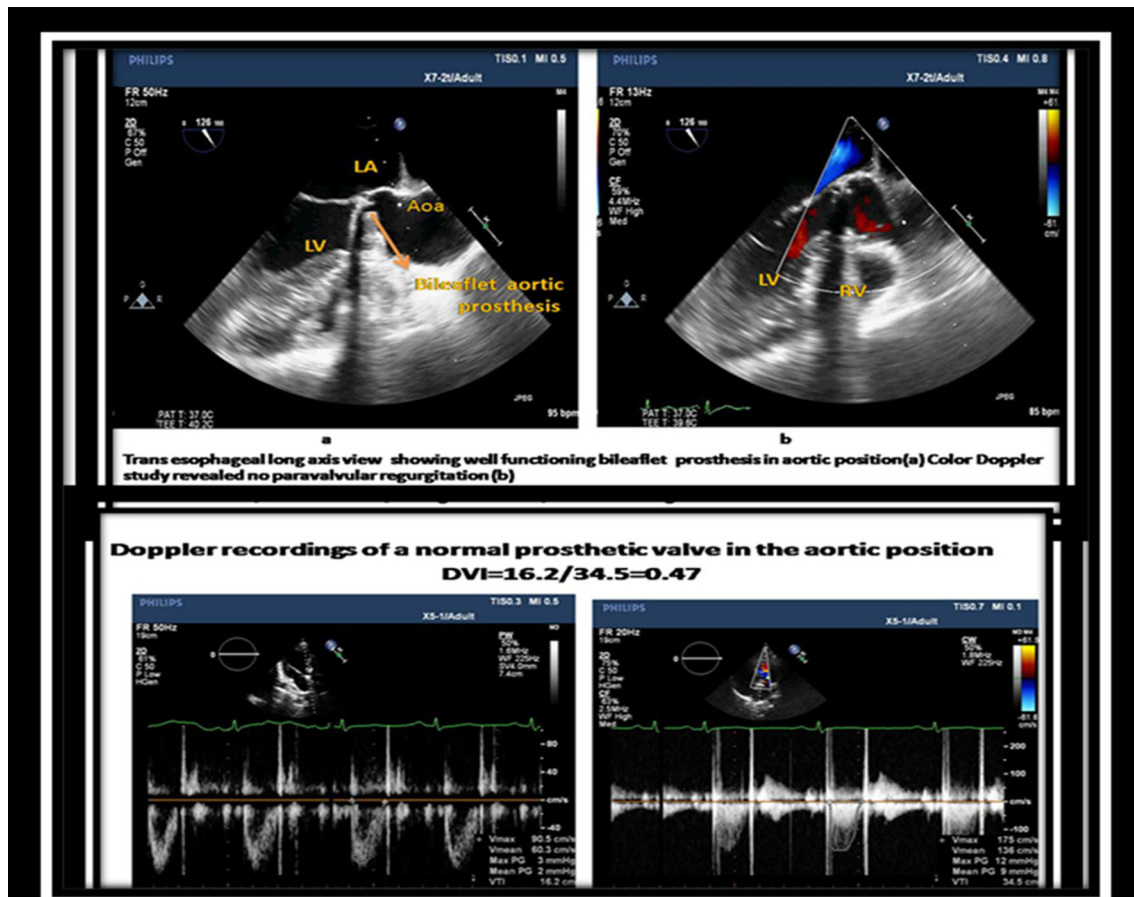SD = standard deviation.

Fig. 5. Well-functioning aortic valve prosthesis with no paravalvular leak LA = left atrium; LV = left ventricle; RV = right ventricle; Aoa = ascending aorta.

leak after surgical repair. As for aortic valve PVL, 19 patients had aortic leak. Three of eight patients with mild leak did not show disease progression, one patient with mild leak died after surgery for aortic root abscess, and one patient with mild aortic leak progressed to severe disease. Patients with mild or moderate PVL not referred for surgery were kept on drugs for heart failure and to reduce afterload.

Discussion

Prosthetic PVL is a serious complication after surgical valve replacement secondary to inappropriate

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sealing of the prosthetic ring to the native cardiac tissue producing periprosthetic regurgitation. Although most of the cases are mild and asymptomatic regurgitations that are usually detected as an incidental finding, a small percentage of patients show large and clinically significant regurgitations.

The real incidence of PVL is unknown and differs widely between different registries. PVLs are more commonly detected in mechanical valves, especially in the mitral position. Mitral PVL occurs in 7–17% of cases, while aortic PVL occurs in 2–10% of cases [9,10].

The current study found that the incidence of mitral PVL in the early postoperative period was 3.25%. This is less than what has been reported for early mitral PVL, which varies from 5% to 32% [11]. This can be explained because we only considered patients who had the mitral valve replaced. However, if we calculated the incidence in patients with both valves replaced, the result was 12.2%, which is close to what has been reported. However, the incidence of aortic PVL was 9%. This matches the reported incidence for aortic PVL, which varies from 2% to 17% [12].

The current study found that the incidence of PVL was higher in the aortic prosthesis compared with mitral prosthesis. Previous studies have reported that the overall incidence of PVLs was similar after mitral valve replacement (13%) and aortic valve replacement (11%), and that PVL was more common after bioprostheses insertion in the mitral position and mechanical prostheses in the aortic position. However, they explained that this may be related to mitral annular calcification when compared with the aortic group; technical difficulties during the excision of calcified native mitral valve; and implantation of new bioprostheses were attributed to the higher prevalence of PVLs in this group of patients [13]. One of our study limitations was lack of bioprostheses in our institution.

IE was the most important underlying valve etiology for PVL, which is in accordance with previous studies [14] that found that IE was associated with the highest incidence of PVL. Mullany et al. [15] reported the development of early PVL in IE patients with sustained positive blood culture, despite adequate antibiotic therapy, and advised prolonged antibiotic therapy following diagnosis of PVL and prior to surgery. Moreover, it has been reported that total excision of infected and devitalized tissue should be followed by valve replacement and repair of associated defects to secure valve fixation to avoid leaks in complex cases with locally uncontrolled infection [16,17].

Although there is widespread agreement among cardiologists and surgeons that severe PVLs should be corrected immediately, there is no consensus regarding the optimal management of patients with mild-to-moderate PVLs. In many of these cases, the risk of untreated PVLs has to be balanced against the consequences of prolonged cardiopulmonary bypass time, which may carry significant incremental risks. Furthermore, there are several reports describing the incidence of perioperative detection of PVLs after valve replacement surgery; however, there is a paucity of data regarding the incidence of PVLs and their association with immediate postoperative outcomes. To the best of our knowledge, no studies have addressed the incidence of early PVL in patients with both mitral and aortic valve replacement. In our study, the incidence was high (35%), compared with patients with one valve replaced.

Conflict of interest

The authors have no conflicts of interest to declare.

Acknowledgments

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