

# The relation between location of paravalvular leakage and time to reoperation after mitral valve replacement

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## ABSTRACT

**Objective:** A relation between the location of the paravalvular leakage (PVL) and time to reoperation after mitral mechanical valve replacement was investigated.

**Methods:** In an observational retrospective study plan, from 59 patients who underwent reoperation only 47 patients having clinical and echocardiographic follow-up for five years were included into study. Depending on echocardiographic evaluation of location of leak, patients were divided into Group 1 (Leaflet) and Group 2 (Commissural). Demographics, preoperative variables, causes of reoperation, the time period between diagnosis of PVL and reoperation were recorded. Unpaired t test or Mann-Whitney U test were used for comparison of variables between groups.

**Results:** A PVL was diagnosed after a median time of 180 days (range: 1 day-28 years) after the first mitral valve replacement. The median follow-up period was 5 years (range: 1-16 years). Age, gender, left ventricular ejection function, number and size of leaks did not differ between groups ( $p>0.05$ ). The time period between diagnosis and reoperation time was longer in Group 1 in comparison to Group 2 ( $39.0\pm9.9$  vs.  $19.5\pm12.8$  months,  $p=0.002$ ). The 30-day mortality for valve reoperation was 4.3% (2/47). In Group 1, 2 patients (2/21, 9.8%) died whereas, no death was observed in Group 2 (0/26, 0%) ( $p=0.002$ ).

**Conclusion:** The time period between diagnosis and reoperation was longer in leaflet leak group in comparison to commissural leak group. We suggest echocardiographic evaluation should include location of the paravalvular leakage during follow-up of patients with PVL after mitral valve replacement. (*Anadolu Kardiyol Derg* 2014; 14: 61-7)

**Key words:** paravalvular leak, mitral valve surgery, reoperation, transthoracic echocardiography

## Introduction

A perfectly functioning ideal prosthetic valve that has a long-lasting duration without causing any complications is still not available. Paravalvular leak (PVL) is a serious complication after mitral valve replacement operations and the factors that are responsible for its occurrence has been reported as; 1-annular calcification, 2-infection, 3-suture technique, 4-size and shape of prosthesis (1-3). The reported incidence of PVL varies between 7 and 15% (1-5). One of the most frequent determinants of reoperation after mechanical mitral valve replacement is shown to be PVL (6).

There are two significant causes of reoperation and these are; 1-structural valve degeneration in patients with bioprosthetic valves and 2-valve thrombosis in patients with mechanical

valves (7). For the first and second reoperations valve dysfunction was the main reported cause however, PVL and infective endocarditis were more frequent for the remaining additional reoperations (8, 9). The independent predictors of mortality in patients who underwent valvular reoperations for prosthetic valve dysfunction has been reported as; 1- advanced NYHA (New York Heart Association) functional class and 2- higher serum creatinine levels. The mortality rates observed were 9 % for reoperations in the aortic position and 12% in the mitral position (10, 11).

Depending on the degree of periprosthetic regurgitation, PVL can impair cardiac function and reduce the patient's functional capacity. Surgical reoperation is the gold standard of therapy for PVL but is associated with high perioperative mortality risk (1, 6, 8).

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In the first 6 months after the original procedure, it is usually possible to detect PVL as it is diagnosable by the echocardiographic findings however, many patients remain asymptomatic and do not require further surgical intervention. In patients who have clinical symptomatic, it is possible to find either one or more of the clinical findings of heart failure, hemolytic anemia, arrhythmias, or infective endocarditis (1, 4). Many patients with symptomatic PVL may benefit from a second surgical intervention by sternotomy or right thoracotomy for repair of the PVL or replacement of the valve (1, 4, 6).

Surgical repair of the PVL is associated with a better long-term survival when compared with patients who received conservative therapy (2). The choice of operation involves repair of the leak or re-replacement of the valve and depends on the surgical findings related to etiology, condition of the native mitral annulus, location and size of the leak, and surgical exposure.

Although there are several studies on operative techniques, a relation between the location of the PVL (leaflet or commissure) and time to reoperation has not been investigated before.

In a retrospective observational study design, our goal was to investigate whether a relation exists between the location of the PVL (leaflet or commissure) and time to reoperation in patients who underwent re-operation for mitral valve replacement. For this purpose, echocardiographic studies of patients who had a diagnosis of PVL were collected during follow-up clinical visits.

## Methods

### Study design

This is an observational retrospective study.

### Study population and protocol

At Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital a retrospective observational study on 1453 patients who underwent mitral valve surgery between the period of January 2000 and December 2009 was conducted after local ethical committee approval. Eighty two patients with mitral mechanical valve replacement and PVL were identified and only 59 patients underwent reoperation. However, from 59 patients who underwent reoperation only 47 patients were included into the study. Twelve patients were excluded as either they did not have a complete clinical and echocardiographic follow-up every 6 months or refused to participate into the study.

The inclusion criteria into the study include; patients with mitral mechanical valve replacement (MVR) and PVL who underwent reoperation.

The exclusion criteria include; more than one valve replacement, pathologic organic lesions within mitral valve leaflets, history of ischemic mitral insufficiency, recent (<3 months) admission to hospital due to myocardial infarction, coronary artery bypass grafting (CABG) or unstable angina, permanent atrial fibrillation, thrombus in the left atrial appendage, significant tricuspid regurgitation, presence of a foreign body in the

coronary sinus or the great cardiac vein, serum creatinine level >2.1 mg/dL, history of infective endocarditis, patients who refuse to participate into the study, and patients without echocardiographic or clinical follow-ups.

Depending on echocardiographic evaluation patients who underwent reoperation were evaluated according to leak location and divided into Group 1 (Leaflet leak) and Group 2 (Commissural leak). These patients were classified according to nature of the valve, location and number of PVL.

### Clinical and follow-up data collection

Patients were evaluated according to demographic data, etiological factors of mitral valve operation, operation types, causes of reoperation, concomitant diseases and risk factors.

The data that were recorded include; 1- first operation time, 2- the time period between first operation and diagnosis of PVL, 3- the time period between diagnosis of PVL and reoperation were recorded. Preoperative, operative, and postoperative characteristics of the patients, operative mortality, and early survival were examined.

A leaflet leak is defined as; detection of some degree of mitral regurgitation (MR) at the opening region of the anterior and posterior leaflets. The commissures define a distinct area where the anterior and posterior leaflets come together at their insertion into the annulus. A commissural leak is defined as; detection of some degree of mitral regurgitation at the insertion into the annulus (12, 13).

Follow-up data of these 59 patients were obtained by clinical interview. Survival data were 97.2% complete, and 12 patients were lost to follow-up. After detection of PVL on mechanical valve, patients were followed up periodically. Stated follow up till operation time was due to patients condition. Worsening symptoms with development of new systolic murmurs, complicated with congestive heart failure, NYHA ≥ III (New York Heart Association Class) were the main diagnostics parameters for reoperation in patients undergoing mitral valve repair or replacement (2, 14). The examination findings and degree of leak were recorded in each visit.

### Baseline variables and definitions

The initial clinical and echocardiographic evaluation and follow-up visits include; demographic data, etiological factors of mitral valve operation, operation types, causes of reoperation, concomitant diseases and risk factors, left ventricular ejection function, number and size of leaks. Identification time was defined as; the elapsed time from the previous valve surgery to the diagnosis of PVL. Reoperation time was defined as; the elapsed time from the previous valve surgery to second reoperation, or last operation for correction of valvular leak. Identification to operation time was defined as; the elapsed time from diagnosis of valvular leak to reoperation for correction of valvular leak. Number of PVL was defined as one or more leak. Hospital mortality was defined as death for any reason occurring within 30 days after opera-

tion. Late mortality is defined as any subsequent death. Late complications are defined as those that occurred after hospital dismissal. The hemogram including hemoglobin, hematocrit, serum indirect and total bilirubin values as well as serum lactate dehydrogenase (LDH) values are followed in each clinical follow-up visit (15).

### **Transthoracic echocardiography examination**

A complete transthoracic echocardiography (TTE) study was performed in all patients. Echocardiographic study includes; standard imaging views (parasternal long- and short-axis views, apical 2-, 3-, 4-, and 5-chamber views). Measurements of left ventricular end-diastolic dimension (LVESD) and left ventricular end-systolic dimension (LVEDS), left atrial diameter, interventricular septum thickness and posterior wall thickness were performed using the M-mode view. Two-dimensional imaging in the parasternal long-axis view was used to measure mitral annulus and LVOT (left ventricular outflow tract). The apical four-chamber view was used to calculate LV end systolic and end-diastolic volume, maximum and end-systolic left atrial area, and medio-lateral and supero-inferior left atrial dimensions. Measurements of peak and mean mitral inflow velocity, trans-aortic flow, peak LVOT flow velocity and its integral, peak MR jet velocity and its integral, and pulmonary venous systolic and diastolic flow integral were performed using pulsed-wave Doppler spectrum. Left ventricular ejection fraction (LVEF) was calculated using the Simpson method (16).

### **Operative procedure**

The surgical technique for the operation included aortic or femoral arterial and bicaval venous cannulation, moderate hypothermia and retrograde continuous retrograde blood cardioplegia. MVR was performed after TTE assessment. PVL on mitral valve was initially evaluated through the left atriotomy. Leakage points were classified as commissural and leaflet. After careful analysis of the anatomic and functional valvular leakage points to ensure that each valve was suitable for repair or replacement, repair was performed as reattachment of the valve towards the annulus with single stitches or routine valve re-replacement was performed. Valve re-replacement was preferred for patients who have more than one leakage point. Repaired leakage points were evaluated with TEE at the end of the operation.

### **Study end-points**

The primary end point was valve-related mortality (inclusive of reoperative mortality) as defined by "Guidelines for Reporting Morbidity and Mortality After Cardiac Valvular Operations" from the The Society of Thoracic Surgeons, The American Association for Thoracic Surgery, and European Association for Cardio-Thoracic Surgeons (14). Valve-related mortality included death caused by structural valve deterioration, nonstructural dysfunction (periprosthetic leak), thrombosis, thromboembolism, hemorrhage, or prosthetic valve endocarditis and death related to reoperation for a valve-related complication.

Valve-related mortality was inclusive of sudden unexplained, unexpected deaths. Valve-related reoperation was reoperation for any valve-related complication. Valve-related morbidity was considered as permanent valve-related impairment as a result of permanent neurologic or other functional deficit caused by structural valve deterioration, nonstructural valve dysfunction, valve thrombosis, thrombotic embolism, bleeding, prosthetic valve endocarditis, or reoperation.

### **Statistical analysis**

All analyses were performed using SPSS Statistical Package 17.0 (SPSS Inc., California, USA). For each continuous variable, normal distribution was analyzed by Kolmogorov Smirnov and Shapiro-Wilk tests. The comparison of between groups were investigated using one way Student t-test for normally distributed parameters. Mann-Whitney U test was used for parameters that are not normally distributed. The categorical variables between the groups were analyzed by using Chi-square or Fisher exact test. Data are presented as mean and standard deviation (SD), median (minimum-maximum) or as frequencies and percentages. Late survival and time-dependent events were assessed by Kaplan-Meier survival analysis. P values <0.05 were considered statistically significant.

## **Results**

### **Baseline characteristics and etiological factors**

The mean age of the study group of patients were  $47.30 \pm 11.19$ . The gender distribution was 23 (48.9 %) males and 24 (51.1%) females. The overall mean age was  $51.4 \pm 10.1$  years for mechanical mitral valve prostheses. During this period the mechanical prostheses were as follows: St Jude Medical (St Jude Medical Inc, Minneapolis, Minn; n=19) and Carbo- Medics (Sorin CarboMedics Inc, Austin, Tex, n=28). The overall median valve size at the initial procedure were 29 mm (range; minimum-maximum: 27-33) for mechanical prostheses. MR aetiology in these patients was diagnosed by surgical findings, pathological reports, and pre-/intra-operative echocardiograms. The distributions of the important demographic and clinical findings for the study of patients are listed in Table 1. Age, gender, left ventricular ejection function, number and size of leaks did not differ between groups ( $p>0.05$ ). Symptoms at the time of diagnosis of PVL after valve replacement were major fatigue in 36 of patients (76% of patients), vertigo in 27 patients (58%), dyspnea in 40 patients (85%) and NYHA class III/IV in 47 patients (100%).

The patients who had PVL after the first operation, the etiological factors were identified as; rheumatic heart disease in 36 patients (55.3%), mitral valve prolapsus in 3 patients (6.4%), idiopathic mitral insufficiency in 8 patients (17%). The distribution of mitral valvular pathology was as follows; 14 patients had only mitral valvular stenosis (29.8%), 12 patients had degenerative mitral insufficiency (25.5%) and the other 21 patients (44.7%) had both mitral stenosis and insufficiency. Mitral annular calcification was observed in 39 (83%) patients during first operation.

### The comparison of the perioperative data

The perioperative data of the study groups are provided in Table 2.

The procedures carried out in the surgically treated group included the reattachment of the prosthesis with pledged interrupted sutures in 28/47 patients (59.5 %) and replacement of the prosthesis with pledget suture in 19/47 patients (40.5%). Re-leak after surgical closure of the primary mitral PVL was found in 2/47 patients. Causes of MR in the two patients with disrupted repairs

**Table 1. The preoperative data and demographics of all patients**

Variables	Patients (n=47)*
Age, years	51.36±10.12
Sex, M/F	27/20
Weight, kg	59.78±8.41
Height, cm	164.52±5.16
BMI, kg/m <sup>2</sup>	23.58±3.63
Native valve diseases, n (%)	Rheumatic 32 (60.1) Degenerative 7 (14.9) Ischemic 5 (10.6) Infective endocarditis 3 (6.4)
Number of leak,n (%)	1 leak 38 (80.9) >1 leak 9 (19.1)
NYHA class, n (%)	III 20 (42.6) IV 27 (57.4)

Values are expressed as; mean±SD (standard deviation); (n,%); number, percentage, BMI - body mass index; M/F - male/female; NYHA - New York Heart Association

**Table 2. The perioperative data of the study group of patients**

Variables	Patients (n=47)
Diagnosis time, month	6.0 (1.0-340.0)
Operation time, month	18.0 (2.0-345.0)
Time period between diagnosis and operation time, month	10.0 (0.0-28.0)
Hct, %	34.1±4.4
Total bilirubin, mg/dL	1.2 (0.62-3.56)
Indirect bilirubin, mg/dL	0.22 (0.10-1.57)
LDH, mg/dL	721.0 (254.0-3525.0)
Blood transfusion, unit	2.7±3.8
Cardiopulmonary bypass time, min	124.9±13.6
Cross-clamp time, min	69.0 (40.0-95.0)
Intensive care unit stay, hour	129.0 (70.0-151.0)
Hospital stay, day	2.0 (2.0-18.0)
Leak repair, n (%)	28 (59.57)
Valve replacement, n (%)	19 (40.23)
Mortality, n (%)	2 (4.3)

Values are expressed as median (minimum-maximum), mean±SD, and number (percentage)

Hct - hematocrit; LDH - lactate dehydrogenase

were dehiscence of the annuloplasty ring and breakdown of a chordae shortening procedure to the anterior leaflet in one patient each. Both of these patients are in Group 1. In these two patients, pledged interrupted sutures were used. The patients died within 48 hours after the re-operation due to development of re-leak after surgical re-operation. The hemodynamic parameters showed deterioration within one hour after surgery in the intensive care unit. In spite of full inotropic support, the patient's hemodynamic data did not improve and patients were lost after cardiopulmonary resuscitation.

The comparison of perioperative parameters after division of the two groups depending on the location of leak is shown in Table 3. Group 1 has a longer mean time of diagnosis for PVL in comparison to Group 2 ( $p=0.001$ ). The time period between diagnosis and reoperation time was longer in Group 1 in comparison to Group 2 ( $p=0.002$ ). In Kaplan Meier analysis (Fig. 1), the time period between diagnosis and reoperation time is used to show its relation to 30-day survival after re-operation. The 30-day mortality for valve reoperation was 4.3 % (2/47). In Group 1, 2 patients (2/21, 9.8%) died whereas, no death was observed in Group 2 (0/26, 0%) ( $p=0.002$ ) (Table 2). Direct suture repair was used in 28 patients (59.6%) and while mortality was not observed in this group of patients, 19 patients (40.4%) underwent re-replacement and the mortality was observed in 2 patients (10.5 %). There is no difference between the failure rates of the two groups.

In comparison to preoperative values, an increase in mean hematocrit levels ( $p< 0.0001$ ) and a decrease in LDH values ( $p<0.0001$ ) were found after surgery (Table 3).

### The comparison of the echocardiographic data

The comparison of the echocardiographic findings of the two groups (leaflet leak and commissural leak) before operation are shown in Table 4. There is no significant difference between Group 1 and 2 regarding LVEDD, LVESD, LVEF and LA parameters ( $p>0.05$ ).

### Discussion

The most important finding of our study is, the time period between diagnosis and reoperation time was higher in leaflet leak group in comparison to commissural leak group. There is only one study in literature where the importance of the time period between diagnosis and reoperation time was discussed. Our study has a similar sample size to their study and our findings are comparable to their findings (2). In our study, we have demonstrated that in follow-up of patients an echocardiographic evaluation including the location of PVL should be a requirement.

After a second complete mitral PVL repair or replacement After a second complete replacement of the mitral valve mortality rate has been reported to be as high as 22% (17). Because of this, after diagnosis of PVL, a certain time period elapses before reconsideration for re-replacement of the mitral valve. Fifteen years after mitral valve replacement (MVR), 17% of patients will present with a PVL (18). Interestingly, 25% of all PVLs are diag-

**Table 3. The comparison of perioperative parameters after division of the two groups depending on the location of leak**

Variables	Group 1 Leaflet leak	Group 2 Commissural leak	*P
Diagnosis time, months	20.0 (1.0-189.0)	4.0 (1.0-340.0)	0.001
Operation time, months	28.0 (3.0-195.0)	8.0 (2.0-345.0)	0.002
Time period between diagnosis and re-operation time, months	39.0±9.9	19.5±12.8	0.002
Hct, %	32.0 (20.0-41.0)	34.5 (27.0-43.0)	0.069
Total bilirubin, mg/dL	1.44(0.80-3.20)	1.14 (0.62-3.56)	0.123
Indirect bilirubin, mg/dL	0.23 (0.10-0.65)	0.22 (0.14-1.57)	0.880
LDH, mg/dL	812.0 (278.0-3525.0)	689.0 (254.0-1534.0)	0.416
Blood transfusion, unit	3.0 (0-22.0)	1.5 (0-6.0)	0.073
Cardiopulmonary bypass time, min	127.0 (90.0-143.0)	129.5 (70.0-151.0)	0.256
Cross clamp time, min	69.0 (45.0-90.0)	70.0 (40.0-95.0)	0.614
Intensive care unit stay, days	2.0 (2.0-14.0)	2.0 (2.0-18.0)	0.706
Hospital stay, days	11.0 (2.0-25.0)	8.0 (6.0-41.0)	0.816

Values are expressed as median (minimum-maximum) and mean±SD  
 \*t-test for independent samples or Mann-Whitney U test  
 Hct - hematocrit; LDH - lactate dehydrogenase

nosed in the immediate postoperative period. Based on the patient's symptoms and on the degree of hemolysis, a reoperation may become necessary (19). In our study group of patients, 9 (18%) of the patients had a diagnosis of PVL within 10 days after discharge from the hospital.

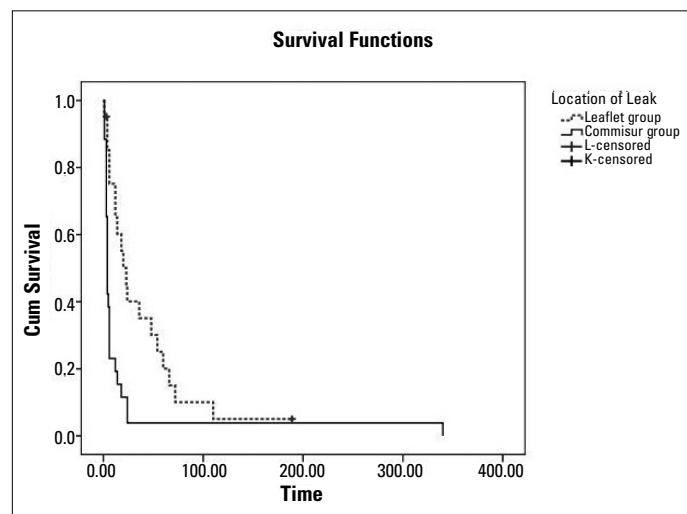
Reoperation for repair of PVL is associated with higher morbidity and mortality than the original procedure, with in-hospital mortality rates of 13%, 15%, and 37% for the first, second, and third reoperations, respectively (20). Twenty-two percent of patients with PVLs are diagnosed in the first week after MVR, and another 52% are diagnosed within the first postoperative year. Patients requiring operative repair are older, have symptomatic heart failure, hemolytic anemia, and larger leaks. Surgical intervention to repair the leak improves symptoms of congestive heart failure, augments the hematocrit value, decreases the need for blood transfusion, and is an independent predictor of long-term survival when compared with medical therapy. Choice of operation involves either direct suture repair of the leak site, which carries a failure rate of 13%; or replacement of the valve, which carries a failure rate of up to 35% (21). In our study group of 47 patients we preferred to have direct suture repair in 28 patients (59.6%) and failure was observed in 1 patient (3.57%) however, and 19 patients (40.4%) underwent re-replacement and the failure was observed in 1 patients (5.26%) and there is no difference between the failure rates of the two groups.

The mechanism of red cell destruction is a high velocity eccentric stream of blood impacting on a small area of a prosthetic ring or pledget. This process retards endothelialization of

**Table 4. The comparison of the echocardiographic findings of the two groups (leaflet leak and commissural leak) before operation**

Variables	Group 1 Leaflet leak	Group 2 Commissural leak	*P
LVEDD, mm	54.81±5.53	55.92±5.05	0.475
LVESD, mm	42.43±5.95	43.92±5.24	0.365
EF, %	53.0 (45.0-60.0)	50.0 (45.0-60.0)	0.399
LA, mm	44.0 (37.0-65.0)	46.5 (35.0-60.0)	0.101

Values are expressed as median (minimum-maximum) and mean±SD  
 \*t-test for independent samples or Mann-Whitney U test  
 EF - ejection fraction; LA - left atrium; LVEDD - left ventricular end-diastolic dimension; LVESD - left ventricular end-systolic dimension

**Figure 1. Time period between diagnosis and reoperation (month)**

the ring. Reoperation with re-repair or mitral valve replacement is safe and effectively relieves the hemolysis (15, 22). In our study we have also observed that re-operation in patients with MVR and PVL provided improvement in hematocrit values whereas a decrease in serum LDH values.

Mitral annular calcification was found to be a potential risk factor for PVLs with bioprosthetic mitral or aortic valves (23). Our study also provides data that in patients with mitral valve mechanical prosthesis, mitral annular calcification is an important risk factor for PVLs as 39 of the 47 patients (83%) showed annular calcification at the first operation. The authors suggest that mitral annular calcification should be completely removed from the annulus in the first operation otherwise the remaining parts can cause a reason for development of PVL.

Patients with low LVEF are at high operative risk, as low LVEF is a predictor of increased mortality and particularly post-operative mortality. In these circumstances, percutaneous repair might prove safer but equally effective. Significant limitation of spatial changes of LV during the cardiac cycle and LV dysfunction may result in annular dilatation and papillary muscle displacement (23, 24). In our study, although there was no statistically significant difference between leaflet and commissural

leak groups, we observed progressive increase in LVEDD values in our study group of patients with PVL in comparison to the time point where diagnosis of PVL was made. Our data parameters were shown in Table 4. This suggests that echocardiographic findings provide important parameters during follow-up of patients and also during critical decision for re-operation.

Therefore, closer follow-up after first mitral valve operation appears justified in patients with mild paravalvular regurgitation and surgical intervention is required only for those who develop symptoms, hemolysis, and/or progressive LV dysfunction (16, 25, 26).

### **Study limitations**

The limitations of our study includes; 1-In our study, we did not include investigation of different methods of surgical technique and related complications. 2- We did not investigate whether the number of leaks correlate with severity of clinical symptoms. It has been reported that there is no relation between number of leaks and severity of clinical symptoms. Multiple leaks were more likely to cause significant hemolysis (2, 25, 26).

### **Conclusion**

Our study on the importance of location of PVL during decision for reoperation after mitral valve replacement showed that the time period between diagnosis and reoperation time was higher in leaflet leak group in comparison to commissural leak group. In follow-up of patients an echocardiographic evaluation including the location of PVL should be a requirement.

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