Long term outcomes of surgical revascularization for isolated left main coronary artery stenosis: a single-center surveillance study

İzole sol ana koroner arter darlığının uzun dönem cerrahi revaskülarizasyon sonuçları: Tek merkezli sağkalım çalışması

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ABSTRACT

Objective: The objective of this study was to retrospectively analyze the clinical course and postoperative long-term survival of patients diagnosed with isolated left main coronary artery (LMCA) stenosis after surgical revascularization.

Methods: A total of 38 patients (27 males, 11 females) who were diagnosed with isolated LMCA stenosis and underwent surgical revascularization were enrolled in the study. Isolated LMCA stenosis was classified into 2 groups: ostial stenosis and nonostial stenosis. Coronary events were defined as death of cardiac origin, the need for a new myocardial revascularization procedure, or the occurrence of myocardial infarction in the course of follow-up. The postoperative assessment period included short- and long-term follow-up. The study endpoint was defined as all-cause mortality.

Results: Among the 38 patients who participated in the study, 25 suffered from ostial LMCA stenosis. The early postoperative mortality rate before hospital discharge was 2.6%. Median duration of postoperative long-term follow-up was 73.43 months (range: 0.17–187.23). Median duration of long-term follow-up free from coronary events or percutaneous coronary interventions was 73.43 months. Postoperative 2-year survival rate was 97.4%, and 5-year survival rate was 92.1%. The postoperative survival period and period free of coronary events of patients with isolated ostial LMCA stenosis did not differ significantly from those of patients with nonostial stenosis (p=0.801, p=0.970, respectively).

Conclusion: Postoperative short- and long-term prognosis of isolated LMCA stenosis appears good in terms of mortality and coronary event symptoms.

ÖZET

Amaç: Bizim bu çalışmadaki amacımız sol ana koroner arter (LMCA) darlığı olan hastaların cerrahi revaskülarizasyon sonrası klinik seyir ve uzun dönem sağkalım sonuçlarını geriye dönük olarak incelemektir.

Yöntemler: Bu çalışmaya tek başına LMCA darlığı tanısı konulan ve cerrahi revaskülarizasyon yapılan 38 hasta (27 erkek, 11 kadın) alındı. Tek başına LMCA darlığı iki grupta sınıflandırıldı: Ostial ve nonostial darlık. Takip seyrinde; kalp nedenli ölüm, yeni bir miyokart revaskülarizasyonu ihtiyacı veya miyokart enfarktüsü gelişimi koroner olay olarak tanımlandı. Ameliyat sonrası değerlendirme periyodu erken ve uzun dönem takiplerinden oluşmaktaydı. Çalışmanın sonlanım noktası tüm nedenlere bağlı ölüm olarak tanımlandı.

Bulgular: Çalışmaya katılan 38 hastanın 25'inde LMCA ostial darlığı mevcuttu. Hastaneden taburcu edilmeden önceki erken dönem ameliyat sonrası mortalitesi %2.6 idi. Ameliyat sonrası uzun dönemde medyan takip süresi 73.43 (dağılım, 0.17-187.23) aydı. Revaskülarizasyon sonrası koroner olaysız veya perkütan koroner girişimsiz geçen medyan süre 73.43 aydı. Ameliyat sonrası iki yıllık sağkalım oranı %97.4; beş yıllık sağkalım oranı %92.1 idi. Ostial ve nonostial darlığı olan hastaların koroner olaysız geçen süreleri ve ameliyat sonrası sağkalım sonuçları arasında anlamlı farklılık yoktu (sırasıyla, p=0.801 ve p=0.970).

Sonuç: Mortalite ve koroner olaylar açısından bakıldığı zaman tek başına LMCA darlığının ameliyat sonrası kısa ve uzun dönem prognozu iyi gözükmektedir.

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Isolated stenosis of the left main coronary artery (LMCA) commonly results from atherosclerosis, though it can also be associated with syphilitic aortitis, congenital anomalies, Takayasu's arteritis, aortic valve disease, and iatrogenic causes such as cardiac surgery or mediastinal irradiation.[1–5] The standard of care for treating patients with this condition is urgent coronary artery bypass grafting (CABG), but patch angioplasty is an alternative operative treatment for patients presenting with ostial lesions.[3] There is a paucity of literature regarding the long-term survival of patients with isolated LMCA stenosis who have undergone CABG. The objective of the present study was to retrospectively analyze the clinical course and long-term outcomes of patients who received surgical revascularization for treatment of isolated LMCA stenosis.

Abbreviations:

CABG	*Coronary artery bypass grafting*
EF	*Ejection fraction*
IOS	*Isolated ostial stenosis*
LMCA	*Left main coronary artery*
LAD	*Left anterior descending*
MI	*Myocardial infarction*

METHODS

Study design and patient selection

Images of patients diagnosed with isolated LMCA stenosis via emergent or elective coronary angiography from 2002 to 2012 in our cardiology clinic were analyzed retrospectively. This study was conducted according to the Principles of the Declaration of Helsinki. Isolated LMCA stenosis was defined as >50% reduction in the vessel lumen that was not accompanied by significant stenosis in the remaining coronary arteries. Patients with concomitant stenosis >20% in the epicardial coronary arteries and/or their side branches were excluded from the study to avoid skewing the data. In addition, cases in which intracoronary nitroglycerin was not used were not included in the study in order to exclude possible catheter-induced ostial LMCA vasospasm. A total of 43 patients with similar coronary angiographic findings were enrolled in the study. Patients excluded from postoperative long-term survival assessments included those who refused surgical treatment or received the following procedures: valve replacement, aneurysm resection, and ascending aorta replacement with myocardial revascularization. Of the enrolled patients, 38 qualified for long-term outcome assessments. Demographic and clinical information such as age, sex, presence of risk factors for atherosclerosis, and preoperative symptoms were determined by referring to electronic medical records. Surviving patients were contacted by telephone, and their medical information was confirmed and updated as necessary. Isolated LMCA stenosis was classified into 2 groups: ostial stenosis and nonostial stenosis. Ostial LMCA stenosis was defined as the presence of an atherosclerotic lesion in the first 3 mm of the LMCA. Nonostial stenosis was defined as stenosis beyond the first 3 mm of the LMCA at its proximal, midportion, and distal segments (Figures 1 and 2). Patients with ostial stenosis were classified as a subgroup because these patients are known to have specific characteristics. The severity of LMCA stenosis was classified by dividing the patients into 2 groups based on the degree of occlusion: 50–70% stenosis and >70% stenosis. Preoperative ejection fraction (EF) values were calculated via transthoracic echocardiography or left ventriculography, and patients were stratified based on EF levels of <50% or ≥50%. Procedure details were

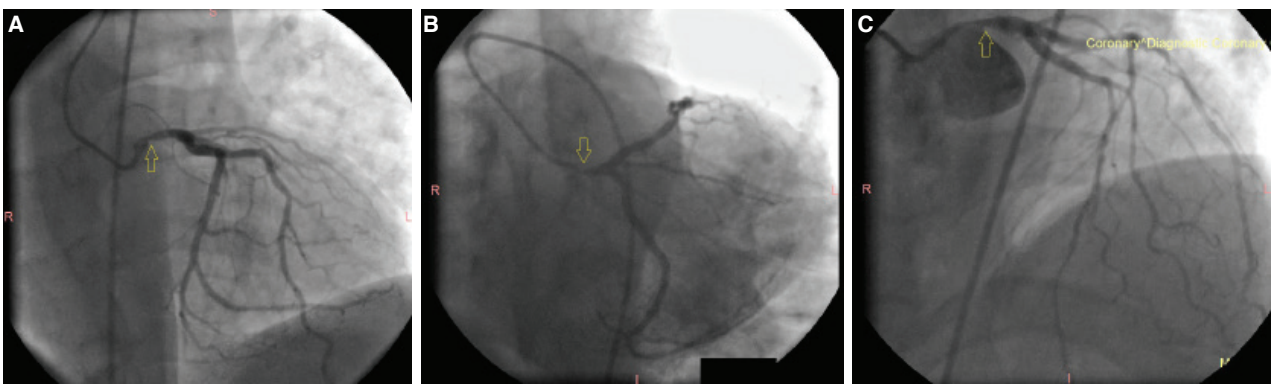

Figure 1. (A-C) Selective left coronary angiography images of different patients with ostial LMCA stenosis.

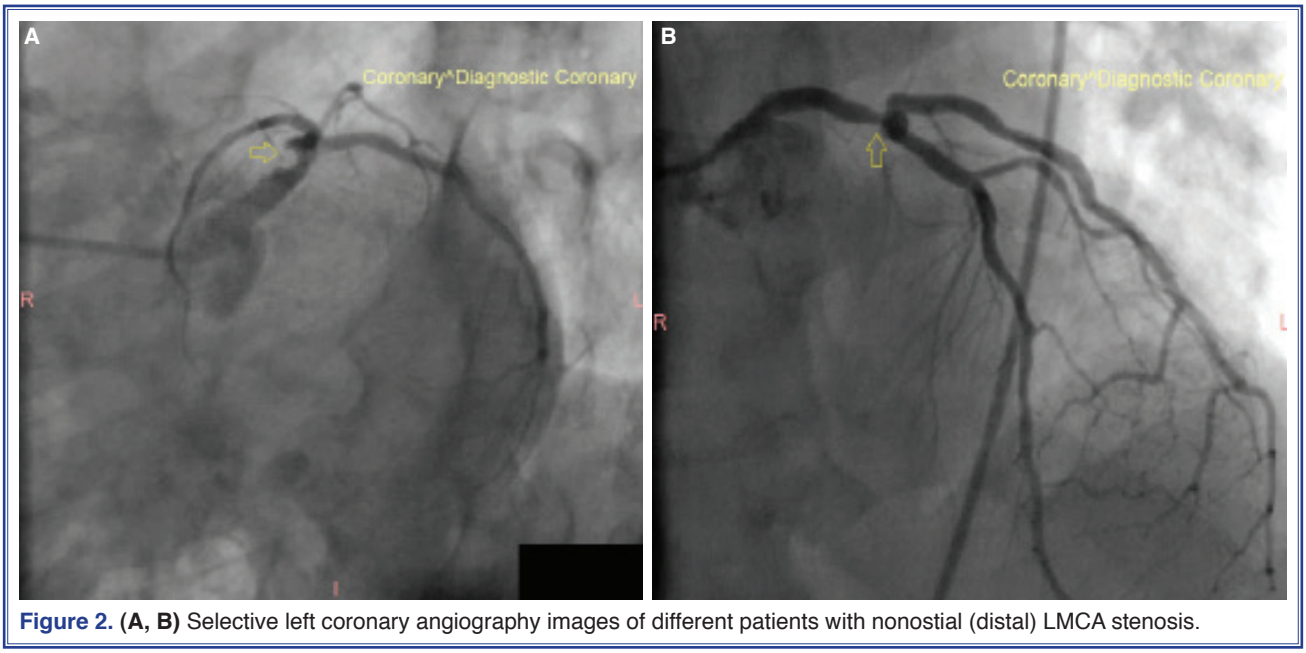

Figure 2. **(A, B)** Selective left coronary angiography images of different patients with nonostial (distal) LMCA stenosis.

documented as to whether the operation was emergent and surgery was required within 24 hours of receiving coronary angiography results, what specific grafts were utilized, whether the surgery was open and performed while the heart was beating, and if there was early postoperative mortality. Coronary events were defined as death of cardiac origin, the need for a new myocardial revascularization procedure, or the occurrence of myocardial infarction (MI) in the course of follow-up. The postoperative assessment period included immediate, short-, and long-term follow-up. The study endpoint was defined as all-cause mortality.

Statistical analysis

Data means, standard deviations, and ratios were utilized to express descriptive data. Shapiro-Wilk test was used to determine normality of the continuous variables. Normally distributed continuous variables were analyzed with independent samples t-test. Pearson's chi-square test and Fisher's exact test were used to determine the association between qualitative variables. Cumulative survival rate was calculated by the Kaplan-Meier method. Log-rank test was used to compare the long-term survival and coronary event free time distributions of patients with ostial and nonostial stenosis. For all tests, a two-tailed p value <0.05 was considered to be statistically significant. All analyses were performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Preoperative findings and surgical treatment

The study sample consisted of a total of 38 patients (11 women and 27 men) with a mean age of 58.1±10.8 years. The presenting symptom of 34 patients (89.4%) was either unstable or exercise-induced angina pectoris. Of all the patients, 23.7% had a history of MI preceding the operation, and 15.7% demonstrated low preoperative left ventricular EF values <50%. LMCA stenosis >70% was identified in 73.7% of patients. A diagnosis of isolated LMCA ostial stenosis was given to 65.7% of patients (Table 1). Only 1 female patient had a history of mediastinal irradiation (as a therapy for breast cancer) before developing coronary artery disease. Otherwise, no specific etiology for LMCA stenosis could be established for the remaining patients; however, most cases were attributed to atherosclerotic disease.

Nineteen operations were performed emergently. A total of 38 patients were operated for LMCA stenosis, including both ostial (25 patients) and nonostial (13 patients) lesions. The left anterior descending coronary artery (LAD) was bypassed in 37 patients; patch angioplasty was performed in only 1. Of the 37 patients who underwent LAD bypass, the internal thoracic artery was utilized in 33 cases, and a venous graft was used in the other 4 cases. Of these 4 cases,

Table 1. Preoperative and postoperative characteristics of patients with isolated LMCA stenosis

	All patients (n=38)		Non-ostia lstenosis (n=13)		Ostial stenosis (n=25)		*p*
	n	%	n	%	n	%	
Demographic data							
Age (year±SD)	58.13±10.83		63.15±10.07		55.52±10.45		[c]0.058
Women/men	11/27		2/11		9/16		[a]0.268
CAD risk factors							
Hypertension	23	60.5	9	69.2	14	56	[b]0.429
Diabetes mellitus	10	26.3	2	15.4	8	32	[a]0.441
Family history	15	39.5	5	38.5	10	40	[b]0.927
Dyslipidemia	22	57.9	6	46.1	16	64	[b]0.290
Smoking	25	65.8	9	69.2	16	64	[a]1.000
Preoperative symptoms							
Myocardial infarction	9	23.7	5	38.5	4	16	[a]0.226
Angina pectoris	34	89.5	11	84.6	23	92	[a]0.595
Dyspnea	4	10.5	2	15.4	2	8	[a]0.595
LMCA stenosis percentage (%)							
50–70%	10	26.3	4	30.8	6	24	[a]0.709
>70%	28	73.7	9	69.2	19	76	
Preoperative left ventricle EF (%)							
<50%	6	15.8	3	23.1	3	12	[a]0.392
≥50%	32	84.2	10	76.9	22	88	
Myocardial revascularization							
Emergency	19	50	7	53.8	12	48	[b]0.732
Beating	3	7.9	2	15.4	1	4	[a]0.265
LAD venous grafts	4	10.5	2	15.4	2	8	[a]0.595
Radial grafts (Cx-radial)	4	10.5	1	7.7	3	12	[a]1.000
Patch angioplasty	1	2.6	0	0	1	4	[a]1.000

Data are numbers (% of the subjects) unless otherwise indicated.
a: Fisher's exact test is used; b: Pearson chi-square test is used; c: Independent samplest test is used.
SD: Standard deviation; CAD: Coronary artery disease; LMCA: Left main coronaryartery; EF: Ejection fraction; LAD: Left anterior descending artery; Cx: Circumflex artery.

2 cases were emergently operated, and left internal mammary artery flow was not sufficient in the remaining 2 cases. In 4 patients, the circumflex artery was bypassed with the radial artery. Of the 25 patients who presented with isolated LMCA ostial stenosis, only 1 underwent direct left main patch angioplasty. LAD was bypassed with the internal thoracic artery in 22 patients, and LAD was bypassed with a venous graft in 2 patients (Table 1). Median duration of postoperative long-term follow-up was 73.43 months (range: 0.17–187.23 months).

Coronary events and mortality rate

Early postoperative mortality preceding hospital discharge was 2.6%, as 1 patient died on the fourth postoperative day due to refractory sepsis. Median duration of time free of coronary events following surgery was 73.43 months. Figures 3 and 4 illustrate the Kaplan-Meier survival curve and graph detailing patients with LMCA stenosis. No statistically significant differences were observed between patients diagnosed with ostial or nonostial LMCA

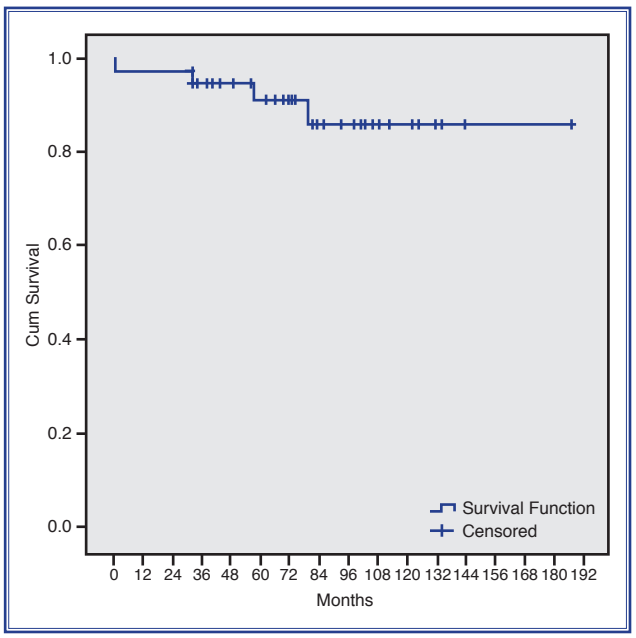

Figure 3. Kaplan-Meier cumulative survival curve for patients with LMCA stenosis.

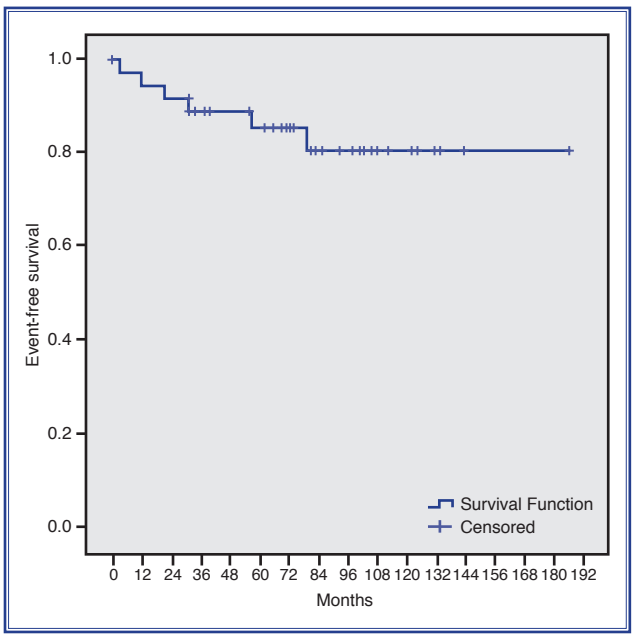

Figure 5. Kaplan-Meier survival curve and graph detailing the duration of time free of coronary events for patients with LMCA stenosis.

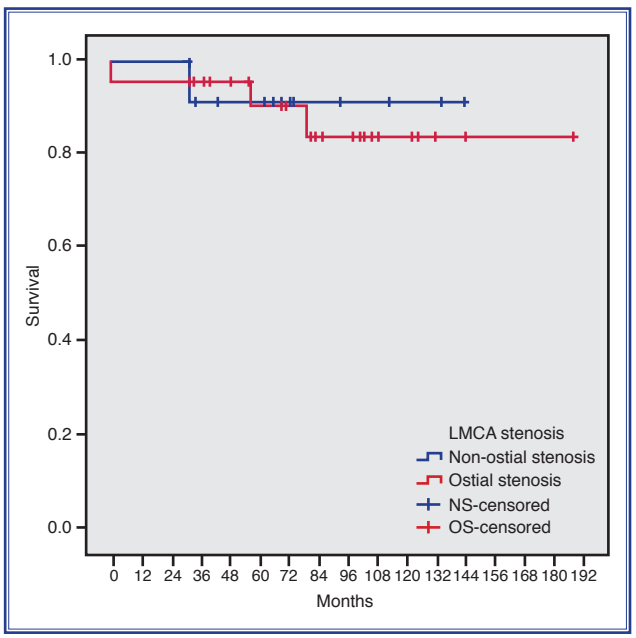

Figure 4. Kaplan-Meier survival curve for patients with non-ostial and ostial LMCA stenosis.

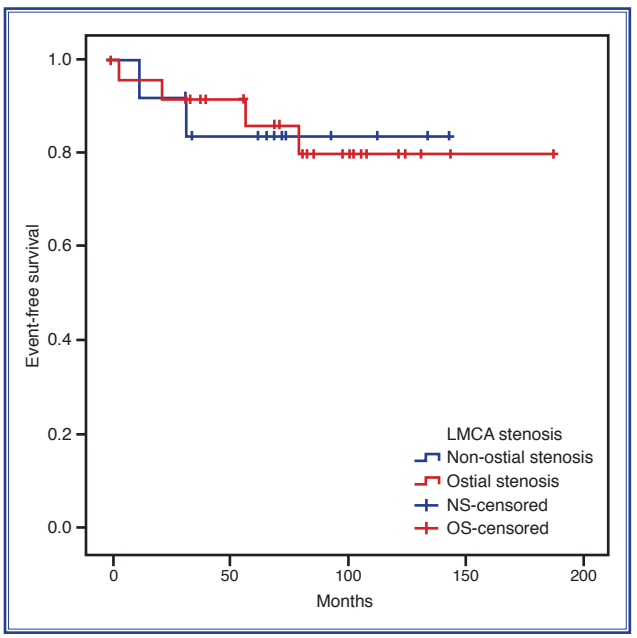

Figure 6. Kaplan-Meier survival curve and graph detailing the duration of time free of coronary events for patients with non-ostial and ostial LMCA stenosis.

stenosis in terms of duration of time free of coronary events and life expectancy (Tables 2 and 3). Figures 5 and 6 illustrate the Kaplan-Meier survival curve and graph detailing the duration of time free of coronary events for patients with LMCA stenosis. Six patients suffered from coronary events in the postoperative long-term period, and of these patients, 3 died primarily due to MIs. Postoperative 2-year survival rate was 97.4%, and 5-year survival rate was 92.1%.

Table 2. Comparison of time free of coronary events between patients with nonostial and ostial stenosis

Left main coronary artery	Mean			*p*
	Estimate	95% CI		
		LB	UB	
Nonostial stenosis (n=13)	123.82	99.06	148.58	0.970
Ostial stenosis (n=25)	158.99	133.91	184.08	
Overall (n=38)	159.12	138.60	179.64	

Log-rank test is used. CI: Confidence intervals; LB: Lower board; UB: Upper board.

Table 3. Comparison of long-term survival between patients with nonostial and ostial LMCA stenosis

Left main coronary artery	Mean			*p*
	Estimate	95% CI		
		LB	UB	
Nonostial stenosis (n=13)	133.99	116.58	151.40	0.801
Ostial stenosis (n=25)	165.81	143.34	188.28	
Overall (n=38)	168.07	150.38	185.76	

Log-rank test is used. CI: Confidence intervals; LB: Lower board; UB: Upper board.

DISCUSSION

Isolated LMCA stenosis is a rare presentation, accounting for 1% of all coronary artery diseases, and has a poor prognosis when treated only medically.[6,7] If these patients are treated with drugs, 15-year cumulative survival rates are 27%.[7] Angiographic studies demonstrated that the prevalence of severe LMCA stenosis is 5%, and isolated severe LMCA stenosis constitutes only 3.5–5.9% of these patients.[8,9]

Isolated severe LMCA stenosis is defined as >50% reduction of LMCA lumen that is not accompanied by significant stenosis of any of the other coronary arteries or side branches. A subgroup of patients with isolated severe LMCA stenosis may be diagnosed with isolated ostial stenosis (IOS), with a reported angiographic prevalence of 0.2–0.88%.[2,10,11] IOS occurs predominantly in women who are premenopausal, which may indicate that inflammation accelerates intimal thickening in female patients who would otherwise have had little if any coronary risk factors.[2,10,12] In many cases, ostial LMCA stenosis is atherosclerotic in origin, but other etiologies including syphilis, iatrogenic causes such as exposure to therapeutic radiation, and congenital heart disease have been implicated.[1–4,13–15] Pathohistological examination of ostial LMCA lesions showed intimal proliferation with lipid-laden histiocytes or foam cells, which indicated the presence of coronary atheromas.[10,16] The standard of treatment for isolated severe LMCA stenosis is CABG; however, alternative surgical treatments exist, including patch angioplasty, which is generally preferred for patients with ostial, proximal, or midportion stenosis of the main trunk. Conventional grafting provides retrograde perfusion to an extensive myocardial area and leads to a forward competitive flow of the non-occluded coronaries, thus consuming the grafts. Surgical reconstruction of the LMCA with patch angioplasty is an alternative method that eliminates these drawbacks. Many trials showed that patch angioplasty made with saphenous vein or pericardial patch is a safe and effective method for the treatment of isolated LMCA stenosis.[17,18] Nonetheless, with

marked technological advances in less invasive percutaneous strategies such as drug-eluting stents, and potent adjunctive pharmacology, percutaneous coronary intervention has been increasingly accepted as an alternative to CABG or patch angioplasty for selected cases with LMCA disease.

There are few studies that have compared the clinical characteristics and long-term survival of patients with isolated ostial and nonostial LMCA stenosis, probably due to its low prevalence. Many of the studies focused on the short- and long-term survival of patients with IOS after myocardial revascularization, especially after surgical angioplasty.[4,19–21] The largest study that investigated the postoperative long-term survival of isolated ostial and nonostial LMCA stenosis was conducted by Allones et al., which had a sample size of 106 patients. Early postoperative mortality (hospital mortality) was 4.7%, and long-term survival of patients with isolated ostial LMCA stenosis did not differ significantly from that of patients without ostial stenosis.[9] No statistically significant differences were appreciated between the patients with coronary events and the patients without coronary events in terms of sex, age, hypertension, diabetes mellitus, family history of atherosclerosis, dyslipidemia, smoking, number of previous MIs, preoperative EF, LMCA stenosis percentage, and use of LAD-venous graft. Furthermore, it was observed that IOS was commonly identified in middle-aged women.[9] Our results demonstrated that IOS was more prevalent in middle-aged men; while this differs from the findings of Allones et al. and others, our findings were not statistically significant. Early postoperative mortality preceding hospital discharge was 2.6%, as 1 patient died on the fourth postoperative day due to refractory sepsis. In this patient, fever, leukocytosis, and elevation of C-reactive protein levels occurred on the first postoperative day. Required cultures were obtained, and the source of the infection was found to be hospital-acquired methicillin-resistant *Staphylococcus aureus*. Despite appropriate and sufficient antibiotic treatment, the patient developed refractory sepsis and died because of subsequent septic shock. The duration of time free of coronary events and long-term survival of patients with isolated ostial LMCA stenosis did not differ significantly from that of patients without ostial stenosis. Postoperative 2-year survival rate was 97.4%, and 5-year survival rate was 92.1%. No statistically significant differences were found between the patients with coronary events and those without coronary events in terms of sex, age, smoking, diabetes mellitus, family history of atherosclerosis, dyslipidemia, number of previous MIs, preoperative EF, and LMCA stenosis percentage. Most importantly, our study excluded patients with stenosis ≥20% of the epicardial coronary arteries and/or their side branches. Apart from this, cases for which intracoronary nitroglycerin was not used were not included in the study in order to exclude the possibility of catheter-induced LMCA vasospasm during angiography. To our knowledge, the present study is the second largest study, following that of Allones et al., regarding the comparison of long-term survival of patients with isolated ostial and nonostial LMCA stenosis after revascularization.

Study limitations

This retrospective cross-sectional study has a relatively medium-sized sample due to the low prevalence of isolated LMCA stenosis. Therefore, future prospective studies with larger sample sizes are required to increase statistical power and validate our results. Secondly, the study sample consisted of patients who were diagnosed and treated in only 1 center, so the observed postoperative outcomes may not be applicable to other centers across Turkey. Thirdly, the severity and type of LMCA stenosis was determined by coronary angiography alone. Other imaging modalities such as intravascular ultrasound and fractional flow reserve were not utilized, which may have enabled us to obtain more clinical data. Finally, ostial lesions were not examined histologically because punch biopsies were not obtained from the ascending aortic wall intraoperatively. With this information, it would have been possible to better characterize the etiological factors that contributed to the formation of the ostial lesions.

Conclusion

Our results are consistent with previously published data regarding patient outcomes following operations to correct isolated LMCA stenosis. CABG is the standard of care and has a good prognosis and postoperative outcome. The duration of time free of coronary events and long-term survival for patients with isolated ostial LMCA stenosis did not significantly differ from that of patients without ostial stenosis. Our results are comparable with those in other large series such as Allones et al.'s study.

Conflict-of-interest issues regarding the authorship or article: None declared

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Keywords: Coronary angiography; isolated LMCA stenosis; surgical revascularization; long-term survival.

Anahtar sözcükler: Koroner anjiyografi; izole LMCA darlığı; cerrahi revaskülarizasyon; uzun dönem sağkalım.