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The Intramyocardial Left Anterior Descending Artery: Prevalence, Early and Mid-Term Surgical Outcomes After Coronary Artery Bypass Procedures: A Retrospective Single-Center Study

İntramiyokardiyal Sol Ön İnen Arter: Koroner Arter Baypas Prosedürlerinden Sonra Prevalans, Erken ve Orta Dönem Cerrahi Sonuçları: Retrospektif Tek Merkezli Çalışma

Sameh ALAGHA[a], Ferit ÇİÇEKÇİOĞLU[a]

[a]Department of Cardiovascular Surgery, Yozgat Bozok University Faculty of Medicine, Yozgat, Türkiye

ABSTRACT Objective: The aim of this study is to assess the prevalence of intramyocardial left anterior descending artery (IMLAD) and evaluate the early and mid-term outcomes in patients undergoing coronary artery bypass graft (CABG) procedures. **Material and Methods:** A retrospective analysis of 349 surgical reports of consecutive CABG procedures performed between January 2014 and October 2022 was conducted. Patients with IMLAD were matched with patients with epicardial left anterior descending artery (LAD) according to age, gender, and date of operation. A comparison between two groups was performed and follow-up data were obtained. **Results:** IMLAD was detected in 40 patients out of 349. The prevalence was 11.5%, and the median age was 56.5 years. There were 28 (70%) males. There were no statistically significant differences between the groups in terms of preoperative comorbidities, postoperative morbidities, reoperation rate for bleeding, mortality rates, and length of stay in the intensive care unit and the hospital. The cross-clamp and cardiopulmonary bypass times were comparable in both groups (p=0.350 and 0.765, respectively). The median follow-up time was 42 months (range 7-92 months) in the IMLAD group and 42.5 months (range 5-94 months) in the matched control group. Survival rates and freedom from reintervention rates were similar between the groups (p=0.368 and p=0.465, respectively). **Conclusion:** This study highlights the feasibility of performing surgeries involving IMLAD. Patients with IMLAD exhibited comparable early and mid-term clinical outcomes following CABG procedures compared to those with epicardial LAD.

Keywords: Coronary artery bypass; myocardial bridging; coronary vessels; prevalence

ÖZET Amaç: Bu çalışmanın amacı, koroner arter baypas greft (KABG) uygulanan hastalarda intramiyokardiyal sol ön inen arter prevalansını ve erken ve orta dönem sonuçlarını değerlendirmektir. **Gereç ve Yöntemler:** Ocak 2014-Ekim 2022 arasında KABG operasyonu gerçekleştirilen 349 hasta retrospektif olarak analiz edildi. İntramiyokardiyal seyreden sol ön inen arteri olan hastalar, yaş, cinsiyet ve operasyon tarihine göre epikardiyal seyreden sol ön inen arteri olan hastalarla eşleştirildi. İki grup karşılaştırıldı ve takip verileri elde edildi. **Bulgular:** Üç yüz kırk dokuz hastanın 40'ında intramiyokardiyal sol ön inen arter tespit edildi. Prevalansı %11,5 idi, medyan yaş değeri 56,5 yıl idi. Yirmi sekizi (%70) erkek idi. İki grup arasında ameliyat öncesi komorbiditeler, ameliyat sonrası morbiditeler, kanama nedeniyle reoperasyon oranı, mortalite oranları ve yoğun bakım ve hastane yatış süreleri açısından istatistiksel olarak anlamlı fark bulunmadı. Her iki grupta kros klemp ve kardiyopulmoner baypas süreleri açısından istatistiksel olarak fark bulunamadı (sırasıyla p=0,350 ve 0,765). İntramiyokardiyal sol ön inen arter grubunda medyan takip süresi 42 ay (7-92 ay) iken, eşleştirilmiş kontrol grubunda 42,5 ay (5-94 ay) idi. Gruplar arasında sağkalım ve yeniden koroner anjiyografi oranları açısından istatistiksel olarak fark bulunmadı (sırasıyla p=0,368 ve p=0,465). **Sonuç:** Bu çalışma, intramiyokardiyal seyreden sol ön inen arter vakalarında, cerrahi uygulanabilirliğini vurgulamaktadır. İntramiyokardiyal seyreden sol ön inen arteri olan hastalar, epikardiyal seyreden sol ön inen arteri olan hastalara göre KABG sonrasında benzer erken ve orta dönem klinik sonuçlar göstermiştir.

Anahtar Kelimeler: Koroner arter baypas; miyokardiyal köprüleme; koroner damarlar; prevalans

Correspondence: Sameh ALAGHA
Department of Cardiovascular Surgery, Yozgat Bozok University Faculty of Medicine, Yozgat, Türkiye
E-mail: samehalagha@gmail.com

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The intramyocardial bridge is considered a congenital coronary anomaly, it is described as a segment of a major epicardial coronary artery that passes deeply into the myocardium.[1] It was first recognised by Reyman et al. in an autopsy and then described in angiography images by Portman et al.[2,3] Although it can be observed in any epicardial artery, it is most commonly reported in the mid-section of the left anterior descending artery (LAD).[4]

The revascularisation of the LAD affects both the early and late postoperative outcomes of coronary artery bypass grafting (CABG). Intramyocardial LAD (IMLAD) has always been a challenging situation during CABG procedures due to difficulties in localizing and exposing the artery which may result in intraoperative complications such as prolonged cross-clamp time, ventricular and coronary vessel injury and subsequent intraoperative bleeding.[2,5] All of these factors have the potential to increase operative morbidity and mortality. In addition, low-quality anastomosis might increase the likelihood of suboptimal blood flow in the long term.

To date, few studies have investigated the outcomes and prevalence of IMLAD in surgical procedures.[2,6] The purpose of this study is to compare the short and mid-term clinical outcomes of patients with IMLAD to those of matched controls with epicardial LAD.

MATERIAL AND METHODS

STUDY DESIGN AND PATIENT POPULATION

Following the institutional review board approval, a retrospective review of medical records was performed to collect data from patients who underwent CABG between January 2014, and November 30, 2022. Three hundred forty nine patients who underwent primary on-pump and off-pump CABG procedures with or without concomitant cardiac procedures were identified. A total of 40 consecutive patients who had IMLADs were included in the study. Using the same database, those patients were matched with 40 other patients without IMLADs. The matching variables were age, gender, and date of operation. Collected data were patients' demographic variables, comorbidity factors including diabetes, hypertension, chronic pulmonary obstructive disease, intraoperative details such as the number of grafts, cross-clamp and cardiopulmonary bypass (CPB) times, postoperative hospital morbidities, survival, and coronary reinterventions. The recent follow-up of patients was obtained either by telephone communication or clinical visit.

The IMLAD was identified intraoperatively by not being visualized on the surface of the heart in any part of its entire course in which LAD was overlapped by a muscular layer, or via coronary angiography, which revealed systolic compression of a short segment of the vessel (Figure 1) (Figure 2).

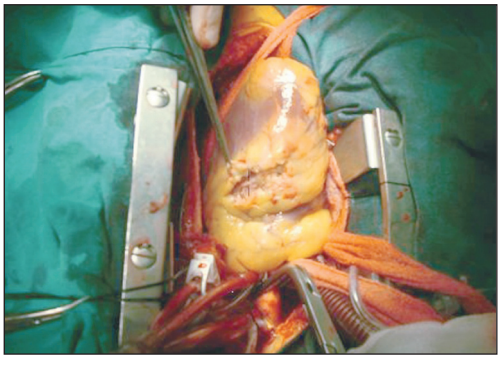

FIGURE 1: The intramyocardial left anterior descending artery (between the black lines) is seen after overlying muscle bands were excised.

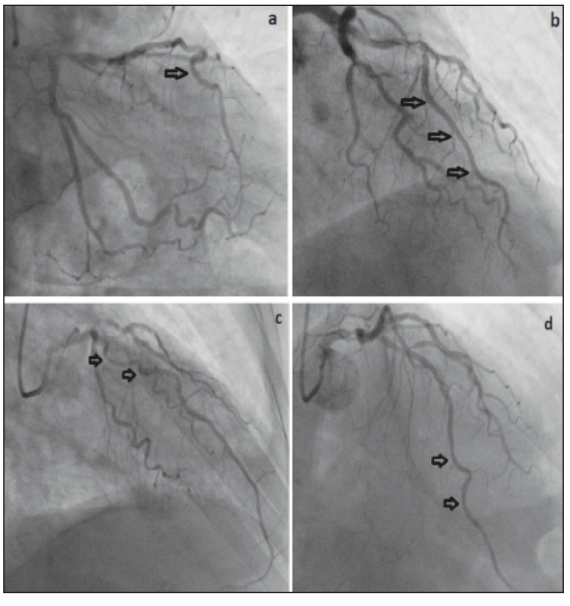

FIGURE 2: Coronary angiographic views of the left anterior descending artery depression and "wide-U" sign (arrowheads) (**a.** Right caudal, **b.** Right cranial oblique, **c.** Right cranial oblique, **d.** Anterior-posterior cranial).

SURGICAL TECHNIQUE

All the procedures were performed with a standard technique of median sternotomy and graft harvesting. In on-pump procedures, cold blood or del Nido cardioplegia was used. In off-pump procedures, a tissue stabilizer (Octopus Tissue Stabilization System, Medtronic, USA) was applied to immobilize the target site of coronary anastomosis.

A blind dissection was attempted to localise the IMLAD during the operations. This was achieved by dissecting down to the epicardial tissue over the interventricular groove with a 15-no surgical blade. To facilitate dissection, epicardial fat was separated on both sides using a fat spreader or 5-0 pledged stay sutures (Figure 3A). If this failed, the vein sign technique was applied, in which the anterior cardiac vein was used to locate the LAD, which usually lies below the vein.

Dissection was extended at least 2 cm proximally beyond the potential anastomosis site to prevent graft kinking and restriction of blood flow due to landing on the LAD with a sharp angle. In case of venous bleeding, minimal electrocautery was used during the LAD exposure. After completion of the LAD anastomosis, the dissected epicardium was sutured in two layers (continuous mattress suture with a second continuous layer) on each side of the anastomotic site using a 5-0 pledgeted Prolene suture in some cases (Figure 3B).

STATISTICAL ANALYSIS

Descriptive statistics are presented as mean with standard deviation or median with inter quantile range for numerical variables, while frequencies and percentages are used for the categorical variables. The distribution of variables was assessed by Kolmogorov-Smirnov and Shapiro-Wilk's tests. For analytical statistics, the independent samples t-test and Mann-Whitney test were used to compare 2 numerical variables based on the normality assumption, while Pearson chi-square test or Fisher's exact test were used to compare two categorical variables. The log-rank test was used to evaluate survival between both groups and demonstrated by Kaplan- Meier's curve. Reverse Kaplan Meier analysis was used in which "being alive" was the event in freedom from all-cause mortality analysis and "no reintervention" was the event in freedom from reintervention analysis. The data were analyzed using IBM SPSS statistics (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) predictive analytics software. p value <0.05 was considered statistically significant.

ETHICAL APPROVAL

This study was approved by the Clinical Research Ethical Committee (date: November 24, 2022, no: 2017-KAEK-189_2022.11.24_03) and conforms to the provisions of the Declaration of Helsinki.

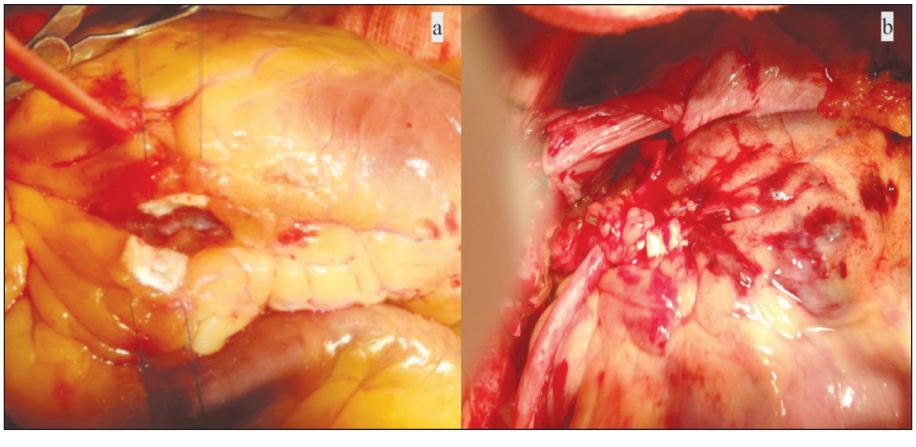

FIGURE 3: a) Operative image of dissected proximal left anterior descending artery with retracted overlying epicardial tissue, **b)** Operative picture following completion of left anterior descending artery anastomosis and saphenous vein graft to the diagonal branch. The surrounding epicardium is sewn on each side in a double-layer manner.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

A retrospective analysis of 349 surgical reports of consecutive CABG procedures performed over 7 years was conducted. IMLAD was presented in 40 (40/349, 11.5%) patients. The median age was 65.5 years. There were 28 (70%) males and 12 (30%) females.

Demographic and clinical data are summarized in Table 1. There was no statistically significant difference between both groups regarding body mass index, Euroscore II values and comorbidity factors. Carotid stenosis was higher in the non-intramyocardial group [13 (32.5%) vs. 5 (12.5%), p=0.032]. The median value of ejection fraction was higher in the non-intramyocardial group [(55%) vs. (50%), p=0.04].

INTRAOPERATIVE AND POSTOPERATIVE CHARACTERISTICS

Operative and postoperative data are demonstrated in Table 2. Concomitant operations were found as aortic valve replacement (n=1), and mitral valve replacement (n=1) in the IMLAD group, while there were no concomitant procedures in the matched control group, the cross-clamp and CPB times were comparable in both groups (p=0.350 vs. 0.765, respectively). Intra-aortic balloon pump was needed in 14 patients (35%) in the IMLAD group, while it was inserted in nine (22.5%) patients in the control group (p=0.217). Thirty day in-hospital mortality was four patients (10%) in the IMLAD group and two

TABLE 1: Preoperative patients' characteristics of the study groups.

	Total n=80	Intramyocardial group n=40	Matched controls n=40	p value
Age (y), median (IQR)	67 (12)	65.5 (13)	67.5 (12)	>0.999
Gender n (%)				
Male	56 (70)	28 (70)	28 (70)	>0.999
Female	24 (30)	12 (30)	12 (30)	
Euroscore II (%), median (IQR)	1.15 (0.6)	1.2 (0.5)	1.06 (0.5)	0.213
BMI (kg/m^2), mean (±SD)	28 (±4.7)	27.7 (±4.9)	28.5 (±4.5)	0.451
ACS, n (%)	19 (23.8)	9 (22.5)	10 (25)	0.793
HT, n (%)	27 (33.8)	14 (35)	13 (32.5)	0.813
DM, n (%)	30 (37.5)	17 (42.5)	13 (32.5)	0.356
HL, n (%)	21 (26.3)	12 (30)	9 (22.5)	0.449
Pulmonary disease, n (%)	8 (10)	3 (7.5)	5 (12.5)	0.712
Carotid stenosis, n (%)	18 (22.5)	5 (12.5)	13 (32.5)	**0.032**
EF (%), median (IQR)	55 (12)	50 (15)	55 (10)	**0.040**
EDD mm, median (IQR)	46 (6.75)	46 (9)	46 (6)	0.892
ESD mm, median (IQR)	30 (9.5)	28 (11)	30.5 (8)	0.667
Extent of coronary lesions, n (%)				
1 vessel	5 (6.3)	3 (7.5)	2 (5)	0.845
2 vessels	19 (24)	9 (22.5)	10 (25)	
3 vessels	37 (46)	20 (50)	17 (42.5)	
>3 vessels	19 (24)	8 (20)	11 (27.5)	
LMCA, n (%)	7 (9)	3 (7.5)	4 (10)	>0.999
Type of emergency, n (%)				
Elective	46 (57.5)	18 (45)	28 (70)	
Urgent	32 (40)	20 (50)	12 (30)	**0.038**
Emergent	2 (2.5)	2 (5)	0	

IQR: Inter quartile range; BMI: Body mass index; SD: Standard deviation; ACS: Acute coronary syndrome; HT: Hypertension; DM: Diabetes mellitus; HL: Hyperlipidemia; EF: Ejection fraction; EDD: End diastolic diameter; ESD: End systolic diameter; LMCA: Left main coronary artery.

TABLE 2: Operative and postoperative data.

	Total n=80	Intramyocardial group n=40	Matched controls n=40	p value
Type of procedure				
CABG	78 (97.5)	38 (95)	40	
CABG+AVR	1 (1.3)	1 (2.5)	0	0.494
CABG+MVR	1 (1.3)	1 (2.5)	0	
Use of LIMA	74 (92.5)	38 (95)	36 (90)	0.675
LAD patchplasty, n (%)	7 (9)	2 (5)	5 (12.5)	0.216
Graft numbers, median (IQR)	3 (1)	3 (1)	3 (2)	0.682
Cross clamp time (minimum), median (IQR)	68.5 (42)	71 (40)	64 (39)	0.350
CPB time, (minimum), median (IQR)	106 (62)	101 (65)	117 (56)	0.765
On-pump, n (%)	69 (86)	34 (85)	35 (87.5)	0.745
Off-pump, n (%)	11 (14)	6 (15)	5 (12.5)	
IABP, n (%)	23 (29)	14 (35)	9 (22.5)	0.217
Inotropic support >24 hours n (%)	31 (40)	17 (42.5)	14 (35)	0.491
ICU length of stay (day), median (IQR)	5 (2.75)	6 (3)	5 (3)	0.170
Hospital length of stay (day), mean (±SD)	10.74 (±3.8)	10.9 (±4.2)	10.6 (±3.3)	0.702
30-day mortality, n (%)	6 (7.5)	4 (10)	2 (5)	0.675

CABG: Coronary artery bypass graft; AVR: Aortic valve replacement; MVR: Mitral valve replacement; LIMA: Left internal mammary artery; LAD: Left anterior descending artery; IQR: Inter quartile range; CPB: Cardiopulmonary bypass; IABP: Intraaortic balloon pump; ICU: Intensive care unit: SD: Standard deviation.

TABLE 3: Postoperative morbidities.

	Total n=80	Intramyocardial group n=40	Matched controls n=40	p value
New-onset atrial fibrillation, n (%)	7 (9)	6 (15)	1 (2.5)	0.108
Renal failure, n (%)*	3 (4)	0	3 (7.5)	0.120
Stroke, n (%)	4 (5)	4 (10)	0	0.116
Reoperation for bleeding, n (%)	14 (17.5)	4 (10)	10 (25)	0.077
Sternal wound infection/mediastinitis, n (%)	8 (10)	1 (2.5)	7 (17.5)	0.057

*Creatinine level of >2 mg/dL

(5%) patients in the matched control group. The length of stay in the intensive care unit or hospital was not significantly different between the groups.

Postoperative comorbidities are presented in Table 3. A statistically significant difference was not observed between both groups regarding stroke, re-operation for bleeding, new onset renal failure, or atrial fibrillation.

FOLLOW-UP AND MID-TERM SURVIVAL ANALYSIS FOR BOTH GROUPS

Follow-up data were obtained from 31 (86%) patients in the intramyocardial group [median follow-up time was 42 (7-92) months postoperatively], and from 26 (68.4%) patients in the non-intramyocardial group [median follow-up time was 42.5 (5-94) months post-operatively].

In the intramyocardial group, death was not observed during follow-up. In the matched control group, two patients 2/38 (5.3%) died during follow-up.

Reverse survival analysis of the patients by the Kaplan-Meier method showed that the freedom from all-cause mortality rate in the intramyocardial group was 86% at two years and 28% at five years, the median survival time was 44 months. In the non-intramyocardial group, freedom from all-cause mortality rate was 97% in the first year and 22% at five years, the median survival time was 48 months. Log-rank test revealed no statistical significance between the groups, p=0.368 (Figure 4).

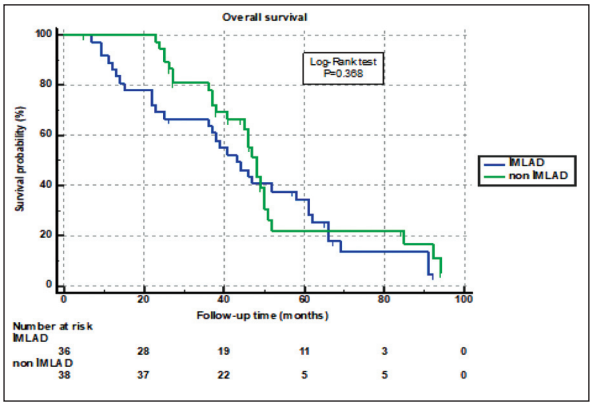

FIGURE 4: Kaplan-Meier curve for the freedom from all-cause death analysis in both groups.
IMLAD: Intramyocardial left anterior descending artery.

MID-TERM CORONARY REINTERVENTION ANALYSIS FOR BOTH GROUPS

One patient 1/36 (2.8%) had coronary reintervention during follow-up in the intramyocardial group (Figure 5). The freedom from coronary reintervention rate was 80% in the first year and 35% in five years. In the non-intramyocardial group, coronary reintervention was performed in two 2/38 (5.3%) patients during the follow-up period. Freedom from coronary reintervention rate was 94% at two years and 25% at five years. Log-rank test revealed no statistical significance between the groups p=0.465 (Figure 6).

DISCUSSION

In this retrospective single-center study, we evaluate IMLADs to determine the role of demographic, clinical and surgical features in the short and mid-term outcomes of these patients.

The reported prevalence of IMLAD ranges from 5% to 86% in autopsy and from 0.5% to 36% in angiographic series.[7,8] In the present study, the prevalence of IMLAD was found to be 11.5% among the study population. Vanker et al. observed IMLAD in 293 of 1,349 patients undergoing CABG and reported a prevalence of 21.7%, while other similar studies reported lower prevalence rates ranging between 1-2%.[2,6,9,10]

Our study demonstrates that patients with IMLADs have comparable early and mid-term outcomes to the matched control group. Cross-clamp and CPB times did not differ significantly between groups, despite the additional time required to locate the LAD which in turn reflects the comparable postoperative outcomes in both groups. Furthermore, the reoperation rate due to bleeding was also similar to the control group in spite of additional maneuvers performed to reveal the LAD.

Conventional coronary angiography remains the gold standard among imaging modalities for the diagnosis of coronary artery diseases due to its advantages in visualizing the features of coronary artery lesions.[11] In a previously published study, which investigated the angiographic characteristics of intramural coronary arteries, the authors state that

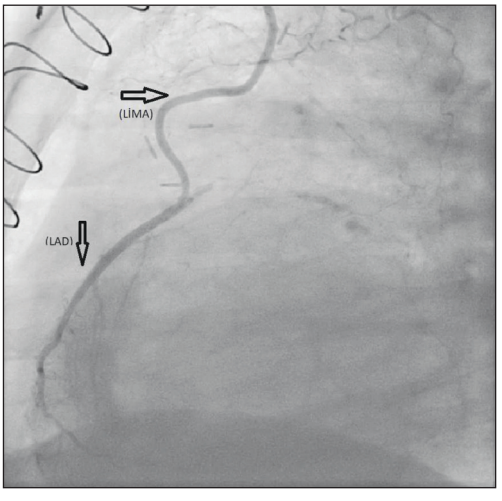

FIGURE 5: Postoperative coronary angiogram showing unrestricted blood flow from LIMA to intramyocardial LAD.
LIMA: Left internal mammary artery; LAD: Left anterior descending artery.

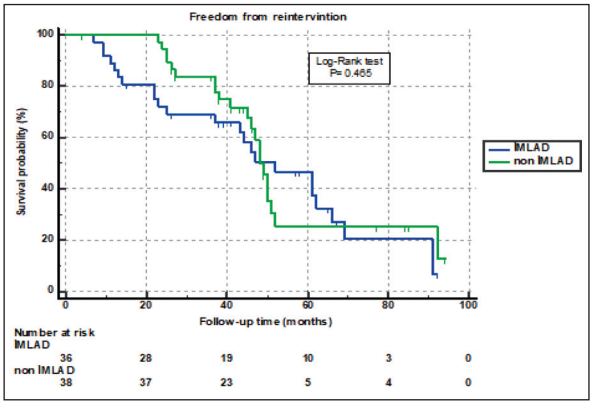

FIGURE 6: Kaplan-Meier analysis for freedom from coronary reintervention in both groups.
IMLAD: Intramyocardial left anterior descending artery.

intramyocardial parts of the LADs were less serpiginous and more straight than the usual epicardial vessels.[12] In angiographic images of our series, the IMLAD enters the myocardium at an acute angle and returns to the epicardial layer after a course of varying length, forming an image that we identified as a "wide-u" sign which is more visible in the right anterior oblique position (Figure 2).

In the case of an IMLAD as a target artery to be bypassed, there may be compelling situations for the surgeon regarding distal anastomosis. There are several maneuvers to localise the IMLAD. They include retrograde insertion of a probe by distal arteriotomy, using intraoperative Doppler ultrasound which is ineffective in a totally occluded artery, intraoperative cine angiography, and a blunt needle technique.[5,13-17] In our series, we prefer other alternatives which involve blind direct dissection of the visible portion of a distal LAD in the anterior interventricular groove, or retrograde dissection of a diagonal artery.[18,19] The other preferred technique is to use the great cardiac vein as a leading point to expose the vessel. Although there are many concerns about these maneuvers such as severe damage to the subepicardial myocardium resulting in perforation of the ventricles, or the arterial wall, we did not observe any of these complications in our series.[13,17-19]

Off-pump coronary artery bypass surgery in the presence of IMLAD is generally considered a relative contraindication.[20,21] In one study, color Doppler was used successfully, and LAD was localised in five cases during minimally invasive procedures without complications. The authors considered it unsafe to dissect the myocardium during a beating heart.[16] In our series we performed an off-pump procedure for six patients with IMLAD, however, we preferred to make the anastomosis as proximally as possible to avoid the unfavorable consequences of dissecting the myocardium and surrounding epicardial tissue.

During the procedures, we observed that the intramyocardial part of the LAD was free from atherosclerosis, which is consistent with previous observations in other studies.[10,12] We also noted that the arterial wall at this site was thinner, making it more vulnerable and requiring extreme caution during surgical anastomosis, this was explained previously by the significant biomechanical forces and increased wall shear stress in that part of the artery.[22] Risse et al. documented this fact histologically by showing a thinner intima in the intramural segment.[22] Ishii et al. also demonstrated the absence of synthetic-type smooth muscle cells which induced the production of collagen and elastic fibers which in turn play a role in accelerating the atherosclerosis process.[23] In addition, Masuda et al. observed a different expression of endothelin-1, which is involved in the pathogenesis of atherosclerosis in those patients.[24]

In the present study, the survival rates between the groups were comparable at five years. A previously published study reported short and late-term mortality of patients with IMLAD and revealed that morality rates at 5, 10, and 15 years were 4.3%, 7.6%, and 10.9% respectively, which were similar to mortality rates in non-IMLAD patients.[6]

During the follow-up, coronary angiography reintervention rates were comparable between groups in our study, suggesting that patients with IMLADs demonstrated high-quality anastomosis, as well as in patients with epicardial LADs. Moreover, this indicates that the tension and effects on healing from the double-layer suture we placed over the LAD anastomosis site did not affect graft flow to LAD. Based on our literature review, such analysis was not conducted in the previous studies, which limits our evaluation of these findings.

The main limitations were the retrospective design of the study and the small number of patients in our series, however, this study has several strengths. First, all patients with IMLAD were operated on by a single surgeon, Thus, the surgeon's learning curve had minimal impact on the overall series. Second, this study included a series of patients in whom IMLAD was a recognisable anatomic finding which made the selection bias improbable.

CONCLUSION

Patients with IMLAD have early and mid-term clinical outcomes following CABG comparable to those with epicardial left anterior descending arteries. The study suggests that despite the challenges posed by

IMLAD, including difficulties in localisation and the potential for intraoperative complications, these patients do not experience adverse outcomes in terms of postoperative morbidities, thus, our study underlines the benign nature of the myocardial bridge. By recognising the IMLAD preoperatively, surgeons would be able to avoid many intraoperative management complications. Further research, including prospective multi-center studies, may help confirm these findings and offer a more comprehensive understanding of the clinical implications of IMLAD in the context of CABG procedures.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sameh Alagha;* ***Design:*** *Sameh Alagha;* ***Control/Supervision:*** *Ferit Çiçekçioğlu;* ***Data Collection and/or Processing:*** *Sameh Alagha;* ***Analysis and/or Interpretation:*** *Sameh Alagha;* ***Literature Review:*** *Sameh Alagha;* ***Writing the Article:*** *Sameh Alagha, Ferit Çiçekçioğlu;* ***Critical Review:*** *Ferit Çiçekçioğlu;* ***References and Fundings:*** *Sameh Alagha;* ***Materials:*** *Ferit Çiçekçioğlu.*

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