Evaluation of the Predictive Value of Left Anterior Fascicular Block on Determination of Left Main and/or Proximal Left Anterior Descending Coronary Artery Disease in Patients with Stable Angina: A Propensity Score Matching Analysis

Sol Anterior Fasiküler Bloğun Stabil Anginalı Hastalarda Sol Ana ve/veya Proksimal Sol Ön İnen Koroner Arter Hastalığının Belirlenmesinde Öngördürücü Değerinin Araştırılması: Bir Eğilim Skoru Eşleştirme Analizi

Ömer Faruk Çırakoğlu[1], Sinan Şahin[1], Ahmet Seyda Yılmaz[2]

[1]Trabzon Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Cardiology, Trabzon, Turkey
[2]Recep Tayyip Erdoğan University Faculty of Medicine, Department of Cardiology, Rize, Turkey

ABSTRACT

Introduction: Successful revascularization of lesions located in the left main and/or proximal left anterior descending (LM and/or pLAD) coronary artery improves survival than medical therapy only. Therefore, accurate identification of high-risk patients with suspected stable angina pectoris is critical for outpatient clinics. Since the septal perforators of the left anterior descending coronary artery are the main source of blood supply of the left anterior fascicle, we hypothesized that the presence of left anterior fascicular block (LAFB) can predict obstructive stenoses of LM and/or pLAD coronary arteries in patients with suspected stable angina pectoris.

Methods: We consecutively enrolled 790 patients referred for invasive coronary angiography due to suspected stable angina pectoris.

Results: The number of patients with LAFBs was 68 (8.6%). Furthermore, 218 patients (27.6%) had obstructive coronary artery disease (CAD). The prevalence of obstructive CAD, revascularization with coronary artery bypass graft surgery, and obstructive LM and/or pLAD coronary artery lesions was higher in patients with LAFB. From univariate analysis, the presence of LAFB was significantly associated with predicting obstructive LM and/or pLAD lesions (odds ratio: 3,587; 95% confidence interval: 1,465-5,785; p=0.005). However, this association disappeared after adjustment for other cardiovascular risk factors.

Conclusion: In patients with suspected stable angina pectoris, LAFB is not frequently a "normal variant" and is associated with known cardiovascular risk factors. It acts as a marker rather than a determinant of obstructive LM and/or pLAD coronary artery lesions.

Keywords: Left anterior fascicular block, obstructive left main coronary artery lesion, obstructive proximal left anterior descending coronary artery lesion, stable angina pectoris

ÖZ

Amaç: Sol ana ve/veya proksimal sol ön inen (LM ve/veya pLAD) koroner arterde yer alan lezyonların başarılı revaskülarizasyonu, yalnızca medikal tedaviye kıyasla sağkalımı artırmaktadır. Bu nedenle, stabil angina pektoris şüphesi olan hastalarda bu bölgelerdeki kritik darlıklar için yüksek riskli hastaların saptanması önemlidir. Sol ön inen koroner arterin septal perforatörleri, sol anterior fasikülün ana kan besleme kaynağı olduğundan, stabil angina pektoris şüphesi olan hastalarda sol anterior fasiküler blok (LAFB) varlığının, LM ve/veya pLAD koroner arterlerinin obstrüktif stenozlarını öngörebileceği hipotez olarak düşünüldü.

Yöntemler: Stabil anjina pektoris şüphesi nedeniyle invaziv koroner anjiyografi için sevk edilen ardışık 790 hasta çalışmaya alındı.

Bulgular: LAFB'li hasta sayısı 68 (%8,6) idi. Ayrıca 218 hastada (%27,6) obstrüktif koroner arter hastalığı saptandı. LAFB'li hastalarda; obstrüktif koroner arter hastalığı, koroner arter by pass greft cerrahisi ile revaskülarizasyon tedavisi ve obstrüktif LM ve/veya pLAD koroner arter lezyonu prevalansı daha yüksekti. LAFB'nin varlığı, tek değişkenli analizde obstrüktif LM ve/veya pLAD lezyonlarını öngörmede istatiksel olarak önemli bir değişkendi (odds ratio: 3.587; %95 güven aralığı: 1.465-5.785; p=0,005). Ancak bu ilişki, diğer kardiyovasküler risk faktörleri için düzeltme yapıldıktan sonra ortadan kalktı.

Sonuç: Stabil anjina pektoris şüphesi olan hastalarda LAFB "normal bir variant" değildir ve bilinen kardiyovasküler risk faktörleri ile ilişkilidir, ancak obstrüktif LM ve/veya pLAD koroner arter lezyonunun bağımsız bir yordayıcısı olmaktan çok bir belirteç görevi görmektedir.

Anahtar Kelimeler: Sol anterior fasiküler blok, obstrüktif sol ana koroner arter lezyonu, obstrüktif proksimal sol ön inen koroner arter lezyonu, stabil angina pektoris

Introduction

Coronary artery disease (CAD) is the primary source of disability and even death worldwide (1). The World Health Organization estimates that CAD mortality will reach 23.4 million in 2030 (2). The most frequent presentation of ischemic heart disease is chronic stable angina (3). Diagnostic algorithms based on history, physical examinations, and electrocardiograms are well established. While invasive coronary angiography (ICA) has been considered the "gold standard" test for the detection of CAD, it is invasive and has also potential disadvantages such as predisposure to cerebrovascular events, bleeding, and even death (4). In patients without unstable conditions, current guidelines stipulate the first-line use of non-invasive tests to define the need for invasive tests such as coronary angiography, especially in patients with intermediate pre-test probability (5). Depending on patient selection, the predictive values of current pre-test probability models are still not optimal. In addition, obstructive coronary lesions are found in 41% of patients with positive results from non-invasive tests (6). Since successful revascularization of lesions in the left main and/or proximal left anterior descending (LM and/or pLAD) coronary artery improves survival when compared with medical therapy only, the accurate identification of high-risk patients with stable angina pectoris is crucial. Using cost-effective, easy obtainable, and non-invasive methods that can detect an obstructive LM and/or pLAD coronary arteries may be beneficial in clinical practice. Electrocardiography (ECG) is still an important part of the initial evaluation of patients presenting with cardiac complaints, despite its existence that spans out more than a century. Left anterior fascicular block (LAFB), an ECG pattern representing failure or delay of conduction in the left anterior fascicle, was initially defined as left anterior hemiblock by Rosenbaum et al. (7,8). Although there are conflicting results in different study populations regarding the clinical importance of LAFB (9-14), CAD remains one of the most common causes of LAFB (15). The His bundle splits into the two bundle branches at the fibrous and muscular boundaries joint of the interventricular septum. Then, the left bundle branch gives an anterior, posterior, and, in some cases, septal fascicles. The left anterior fascicle is nourished by the septal perforators from the LAD coronary artery mainly and therefore, is more sensitive to ischemia. Since the septal perforators of the LAD coronary artery are the main source of blood supply for the left anterior fascicle, we hypothesized that the presence of LAFB can predict obstructive stenoses of the LM and/or pLAD coronary arteries in patients with stable angina pectoris.

Methods

Study Population

We included 790 consecutively enrolled patients with stable angina pectoris and referred to ICA between September 2016 and January 2020. Each patient was included doing a coronary angiography. Those with angina pectoris and complaints equivalent to angina were considered eligible for the study. Afterward, a detailed medical history and at least one non-invasive diagnostic test was performed by an experienced cardiologist to determine CAD. Patients with acute coronary syndrome, history of CAD and cardiovascular consequence, malignancy, congenital heart disease, moderate-to-severe liver and/or renal diseases, acute or chronic inflammatory diseases, moderate-to-severe valvular heart disease, and cardiomyopathies were excluded from the study as well as those with preexisting right bundle branch block (RBBB), left bundle branch block (LBBB), pace rhythm, pre-excitation syndromes, and associated ischemic ST-T abnormalities. Sociodemographic and medical history parameters were recorded. Included patients were separated into two groups depending on the occurrence of LAFB. Patients were also grouped according to the presence of obstructive LM and/or pLAD lesions.

Informed consent was granted by all patients before enrollment. The approval form the Clinical Research Ethics Committee of University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital was obtained (approval number: 2020/62, date: 12.11.2020).

Electrocardiographic Evaluation

A standard surface 12-lead electrocardiogram ECG, with a paper speed of 25 mm/s and a voltage of 10 mm/mV was employed for investigations (Nihon Kohden, cardiofax GEM, ECG-9020K, Japan). All ECGs were recorded and analyzed by one experienced cardiologist blinded to the clinical data of the participants. LAFB was defined according to specified criteria: 1) QRS axis on frontal plan between -45 and -90 degrees, 2) qR pattern in lead aVL 3) R-peak time in lead aVL of 45 ms or more 4) QRS duration less than 120 ms (16).

Coronary Angiography and Echocardiography

Trans-radial or trans-femoral Judkins techniques were used to explore the coronary arteries in all patients. Obtained fluoroscopic images were judged by an experienced interventional cardiologist. Patients were categorized as individuals without CAD, with mild CAD, with significant CAD, and with obstructive CAD. Mild CAD was considered if lumen-diameter narrowing was less than 50% within any epicardial coronaries. In addition, significant CAD was accepted as lumen-diameter narrowing of more than 50% within any epicardial coronaries. Lastly, obstructive CAD was described as a lumen-diameter narrowing of more than 50% of the LM coronary artery or narrowing ≥70% within any epicardial coronaries. SYNTAX scores (version 2.28) were calculated in arteries with ≥1.5 mm diameter and have luminal obstruction ≥50%. Decisions related to revascularization strategies were made based on the preference of the attending physicians.

Transthoracic echocardiography (Philips Epiq 7 systems, Andover, MA) was performed on all participants at the time of their first examination. The left ventricular ejection fraction (LVEF) was obtained using the modified Simpson's method (17). Left ventricular hypertrophy (LVH) was equally detected by calculating the left ventricular mass (LVM) according to the Devereux formula (18). The LVM index (LVMI) was then derived by correcting the LVM for body surface area.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 (SPSS Inc. Chicago, Illinois, USA). Continuous variables were evaluated for normality distribution using the Kolmogorov-Smirnov test. If variables were normally distributed, they were expressed as the means ± standard deviation. Whereas, if the distribution was not normal, variables were expressed as median and inter-quartile ranges. However, categorical variables were expressed as numbers and percentages and

were compared using the chi-square test. An Independent sample t-test was employed for parametric variables, whiel the Mann-Whitney U test was employed for non-parametric variables. Propensity scores for all individuals were estimated using a logistic regression model including age, sex, occurrence of diabetes mellitus (DM), hypertension and dyslipidemia, current smoking, and family history of CAD. A 1:1 nearest neighbor matching was performed with a caliper width of 0.2. The score-matched pairs were reanalyzed. A logistic regression analysis was performed to predict the presence of obstructive LM and/or pLAD lesions. First, we separately analyzed the relationships between the dependent variable and risk factors for CAD and LAFB. The variables that have p-value of <0.1 in a univariate regression analysis were included in the multivariate logistic regression analysis (forced entry method). A p-value <0.05 (2-tailed) was considered statistically significant.

Results

We observed that 750 patients (94.9%) undertook at least one non-invasive test, and 40 patients (5.1%) were referredfor ICA directly (Table 1). The median age was 58 years old and 532 (67.3%) of them were males. The number of patients with LAFB was 68 (8.6%). Furthermore, 218 patients (27.6%) had obstructive CAD and had been treated with PCI, coronary artery bypass graft, or optimal medical therapy alone (18.5%, 7.6%, and 1.5%, respectively). The prevalence of obstructive CAD and CABG use was significantly different across LAFB and non-LAFB. Also, the prevalence of obstructive LM and/or pLAD lesions was higher in patients with LAFB. Patients with LAFB had a significantly higher LVMI. The prevalence of LAFB increased with increasing LVH grades (19) (Figure 1). Patients with obstructive LM and/or pLAD lesions were older and had a higher prevalence of hypertension, DM, dyslipidemia, family history of CAD, and LAFB (Table 2).

After propensity score matching (68 vs 68 patients), the age, sex, DM, smoking status, hypertension, dyslipidemia, family history of CAD were similar between groups (Table 3). The obstructive LM and/or pLAD lesion rate remained significantly higher in patients with LAFB [8 (11.8%) vs 22 (32.2%), p=0.004].

In univariate analyses, the presence of LAFB was a significant predictor of obstructive LM and/or pLAD lesions (odds ratio: 3,587; 95% confidence interval: 1,465-5,785; p=0.005). Multivariate logistic regression analysis,

using significant parameters obtained from univariate analysis, was conducted to reveal independent predictors of obstructive LM and/or pLAD lesions. A history of hypertension and DM were found to be independent predictors of obstructive LM and/or pLAD lesions. Although there was a significant relationship between the presence of LAFB and dependent variable in univariate logistic regression models, only known cardiovascular risk factors showed a direct significant association after adjusting for confounders. Thus, the presence of LAFB was not an independent predictor of obstructive LM and/or pLAD lesions (Table 4).

Discussion

We aimed at assessing the relationship between LAFB and obstructive LM and/or pLAD lesions in patients referred to ICA with stable angina pectoris. The cross-sectional analysis of our study revealed an association between the presence of LAFB and obstructive LM and/or pLAD lesions, advanced age, prevalence of dyslipidemia, and LVMI. Even though LAFB had a significant predictive value from univariate analysis, this
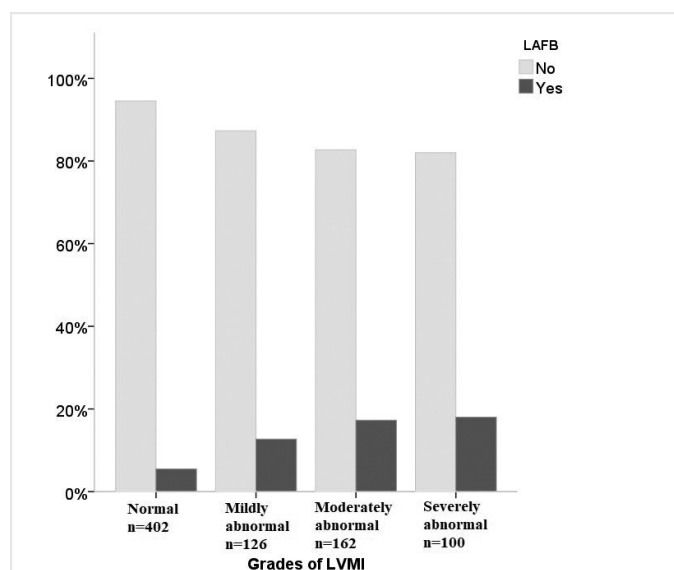

Figure 1. The plots show an upward trend in LAFB presence in line with increasing LVMI grades

LAFB: Left anterior fascicular block, LVMI: Left ventricular mass index

Table 1. Characteristics of symptoms and diagnostic tests of study population

	All patients (n=790)	Female (n=258)	Male (n=532)
Initial diagnostic test			
Exercise ECG	206 (26.1%)	52 (20.2%)	154 (28.9%)
CCTA	378 (47.8%)	128 (49.6%)	250 (47%)
MPI	166 (21%)	66 (25.6%)	100 (18.8%)
ICA	40 (5.1%)	12 (4.6%)	28 (5.3%)
Result of non-invasive testing			
Positive	258 (32.7%)	66 (25.6%)	192 (36.1%)
Negative	466 (59%)	174 (67.4%)	292 (54.9%)
Inconclusive	66 (8.4%)	18 (7%)	48 (9%)
Obstructive CAD	218 (27.6%)	54 (20.9%)	164 (31%)

CAD: Coronary artery disesae; CCTA: Coronary computed tomography angiography; ECG: Electrocardiogram; ICA: Invasive coronary angiography; MPI: Myocardial perfusion imaging

Table 2. Baseline characteristics and laboratory findings of study population according to the presence of obstructive LM and/or pLAD lesion

Baseline characteristics	All patients (n=790)	Obstructive LM and/or pLAD lesion − (n=652)	Obstructive LM and/or pLAD lesion + (n=138)	p
Age (years)	58 (50-65)	58 (48-64)	63 (57-65)	<0.001
Male gender, (n, %)	532 (67.3)	219 (67.2)	47 (68.1)	0.831
Diabetes mellitus, (n, %)	256 (32.4)	102 (31.3)	29 (42)	<0.001
Current smoking, (n, %)	310 (39.2)	132 (40.5)	27 (39.1)	0.680
Hypertension, (n, %)	240 (30.4)	164 (50.3)	55 (79.7)	0.001
Dyslipidemia, (n, %)*	452 (57.2)	91 (27.9)	29 (42)	<0.001*
Family history of CAD, (n, %)	240 (30.4)	87 (26.7)	34 (49.3)	<0.001
BMI (kg/m²)	29.4 (27-33.7)	29.4 (26.6-34.2)	30.4 (27.7-31.6)	0.306
BSA (m²)†	1.96 (1.85-2.07)	1.96 (1.86-2.07)†	1.92 (1.84-2.06)	0.118
LAFB, (n, %)	68 (8.6)	46 (7.1)	22 (15.9)	0.001
Laboratory parameters and echocardiography				
Hemoglobin (g/dL)	14.8 (13.5-15.8)	14.9 (13.5-16)	14.7 (13.2-15.3)	0.079
WBC (10³/µL)	7.7 (6.4-9.2)	7.6 (6.4-9.1)	8.9 (6.5-10.1)	<0.001
Neutrophil, (10³/µL)	4.2 (3.5-5.1)	4.1 (3.4-4.8)	5.1 (3.8-5.2)	<0.001
Lymphocyte, (10³/µL)	2.1 (1.9-2.7)	2.2 (2.0-2.7)	2.1 (1.9-2.2)	0.025
Platelets, (10³/µL)	240 (200-286)	241 (203-287)	232 (195-273)	0.065
Total cholesterol (mg/dL)	205 (182-240)	205 (179-235)	216 (187-252)	0.084
LDL-C (mg/dL)	149 (125-174)	144 (121-172)	157 (131-193)	<0.001
HDL-C (mg/dL)	40 (34-44)	40 (35-44)	35 (32-40)	<0.001
Triglyceride (mg/dL)	167 (128-202)	165 (127-206)	170 (151-199)	0.051
Serum creatinine (mg/dL)	0.81 (0.71-0.94)	0.80 (0.67-0.91)	0.9 (0.8-1.0)	<0.001
Urea (mg/dL)	32 (28-36)	32 (28-36)	36 (34-39)	<0.001
Sodium (mEq/L)	137 (133-142)	137 (133-142)	137 (135-141)	0.678
Potassium (mEq/L)	4.4 (3.8-5.0)	4.4 (3.9-5.0)	4.4 (3.8-4.9)	0.225
LVEF (%)	63 (60-65)	63 (60-65)	64 (60-65)	0.528
LV mass (g)	192 (169-227)	192 (169-220)	220 (175-241)	<0.001
LVMI (g/m²)	97 (85-116)	95 (83-113)	112 (97-120)	<0.001

BMI: Body mass index, BSA: Body surface area, CAD: Coronary artery disease, HDL-C: High-density lipoprotein cholesterol, LAFB: Left anterior fascicular block, LDL-C: Low-density lipoprotein cholesterol, LM and/or pLAD: Left main coronary artery and/or proximal left anterior descending coronary artery, LVEF: Left ventricular ejection fraction, LVMI: Left ventricular mass index, WBC: White blood cell, *: The presence of dyslipidemia was defined according to age- and gender-adjusted percentiles from National Health and Nutrition Examination Survey III data, †: Calculated according to the DuBois method

association disappeared after adjustment for other cardiovascular risk factors. We found that the presence of LAFB has no independent role in predicting obstructive LM and/or pLAD lesions. Therefore, it should be considered a marker rather than a determinant of LM and/or pLAD lesions in patients with suspected stable angina pectoris.

In previous studies, the presence of LAFB differed when evaluated in different groups. In the general population, the prognostic implications of LAFB have been examined in studies with inconsistent results. Miller et al. (14) demonstrated that patients with LAFB had the poorest outcome among patients with uncomplicated ventricular conduction blocks, and emphasized that LAFB is a significant predictor of mortality. Conversely, other epidemiological studies suggested that isolated LAFB may not have adverse prognostic implications (12,20,21). Biagini et al. (13) concluded that LAFB is associated with an increased risk of cardiac death in patients with suspected CAD referred for dobutamine stress echocardiography. Similarly, as a recent study revealed that the presence of LAFB is related to an increased risk of all-cause death when compared

with isolated RBBB in patients without apparent ischemic heart disease (22). In another study conducted in patients with no evidence of cardiac disease, investigators found a significant association between LAFB, and hypertension orcardiac disease (11).

Although LAFB has many etiologies, one of the most important causes is CAD (15). Previous studies have shown that high-grade narrowing of the LAD coronary artery can induce the development of LAFB (23-26). Assali et al. (23) reported that patients in whom LAFB develops during inferior wall acute myocardial infarction have a higher prevalence of stenosis in the LAD coronary artery. Lévy et al. (24) found that LAFB is associated with significant stenosis of the LAD coronary artery in patients with significant CAD at ICA. In another study, the same clinicians also showed that transient LAFB during an attack of angina pectoris may be indicative of a severe obstruction of the LAD coronary artery in the vicinity of the first perforator (25). It has been shown that selective opacification of the left coronary artery can cause transient left anterior hemiblock (26).

Table 3. Demographic, clinical, laboratory, and angiographic characteristics of study patients according to the presence of LAFB

Baseline characteristics	All patients (n=790)	Before matching			After matching		
		LAFB − (n=722)	LAFB + (n=68)	p	LAFB − (n=68)	LAFB + (n=68)	p
Age (years)	58 (50-65)	58 (50-64)	62 (56-69)	0.002	61 (51-68)	62 (56-69)	0.433
Male gender, n (%)	532 (67.3)	480 (66.5)	52 (76.5)	0.093	54 (79.4)	52 (76.5)	0.679
Diabetes mellitus, n (%)	256 (32.4)	228 (31.6)	30 (44.1)	0.076	21 (30.9)	30 (44.1)	0.111
Current smoking, n (%)	310 (39.2)	278 (38.5)	32 (47.1)	0.167	38 (55.9)	32 (47.1)	0.303
Hypertension, n (%)	240 (30.4)	214 (29.6)	24 (35.3)	0.141	19 (27.9)	24 (35.3)	0.356
Dyslipidemia, n (%)*	452 (57.2)	404 (56)	48 (70.6)	0.020	43 (63.2)	48 (70.6)	0.380
Family history of CAD, n (%)	240 (30.4)	212 (29.4)	28 (41.2)	0.043	18 (26.5)	28 (41.2)	0.120
BMI (kg/m^2)	29.4 (27-33.7)	29.4 (26.6-33.8)	29.8 (27.8-33.2)	0.244	28.7 (25.4-30.4)	29.8 (27.8-33.2)	0.002
BSA (m^2)†	1.96 (1.85-2.07)	1.95±0.15	1.96 (1.87-2.10)	0.500	1.97 (1.83-2.07)	1.96 (1.87-2.10)	0.449
Laboratory parameters and echocardiography							
Hemoglobin (g/dL)	14.8 (13.5-15.8)	14.8 (13.5-16)	14.7 (13.8-15.4)	0.435	15.1 (13.5-16.1)	14.7 (13.8-15.4)	0.146
WBC (10^3/µL)	7.7 (6.4-9.2)	7.8 (6.5-9.2)	7.65 (6-9)	0.762	8.1 (7.6-10.4)	7.65 (6-9)	0.052
Neutrophil, (10^3/µL)	4.2 (3.5-5.1)	4.2 (3.5-5.1)	4.3 (3.4-5.2)	0.715	4.95 (3.7-6.0)	4.3 (3.4-5.2)	0.008
Lymphocyte, (10^3/µL)	2.1 (1.9-2.7)	2.1 (1.9-2.7)	2.0 (1.7-2.5)	0.021	2.2 (2.1-3.0)	2.0 (1.7-2.5)	0.055
Platelets, (10^3/µL)	240 (200-286)	240 (200-286)	251 (198-294)	0.636	271 (232-299)	251 (198-294)	0.011
Total cholesterol (mg/dL)	205 (182-240)	205 (184-236)	217 (166-249)	0.080	212 (182-240)	217 (166-249)	0.670
LDL-C (mg/dL)	149 (125-174)	149 (125-174)	156 (133-183)	0.110	133 (128-167)	156 (133-183)	0.356
HDL-C (mg/dL)	40 (34-44)	40 (34-44)	37 (33-40)	0.056	36 (32-44)	37 (33-40)	0.807
Triglyseride (mg/dL)	167 (128-202)	167 (131-202)	171±76	0.557	154 (138-203)	171±76	0.848
Serum creatinine (mg/dL)	0.81 (0.71-0.94)	0.81 (0.70-0.94)	0.84 (0.72-0.95)	0.249	0.9 (0.7-1.0)	0.84 (0.72-0.95)	0.454
Urea (mg/dL)	32 (28-36)	32 (28-36)	32 (28-37)	0.541	32 (28-35)	32 (28-37)	0.190
Sodium (mEq/L)	137 (133-142)	137 (133-142)	137 (132-141)	0.101	136 (132-140)	137 (132-141)	0.958
Potassium (mEq/L)	4.4 (3.8-5.0)	4.4 (3.8-5.0)	4.4 (3.9-4.9)	0.657	4.4 (3.9-4.9)	4.4 (3.9-4.9)	0.944
LVEF (%)	63 (60-65)	63 (60-65)	65 (62-66)	0.070	65 (60-68)	65 (62-66)	0.840
LV mass (g)	192 (169-227)	187 (166-227)	227 (210-248)	<0.001	192 (170-241)	227 (210-248)	0.001
LVMI (g/m^2)	97 (85-116)	95 (83-113)	112 (104-129)	<0.001	97 (85-114)	112 (104-129)	<0.001
Angiographic characteristics							
Normal, n (%)	184 (23.3)	168 (23.3)	16 (23.5)	0.961	4 (5.9)	16 (23.5)	0.110
Mild CAD, n (%)	288 (36.5)	268 (37.1)	20 (29.4)	0.207	40 (58.8)	20 (29.4)	0.001
Significant CAD, n (%)	318 (40.3)	286 (39.6)	32 (47.1)	0.231	24 (35.3)	32 (47.1)	0.163
- LAD, n (%)	216 (27.3)	186 (25.8)	30 (44.1)	0.001	16 (23.5)	30 (44.1)	0.011
- CX, n (%)	130 (16.5)	114 (15.8)	16 (23.5)	0.100	18 (26.5)	16 (23.5)	0.692
- RCA, n (%)	190 (24.1)	168 (23.3)	22 (32.4)	0.094	16 (23.5)	22 (32.4)	0.252
- Single vessel disease, n (%)	136 (17.2)	126 (17.5)	10 (14.7)	0.566	6 (8.8)	10 (14.7)	0.287
- Three-vessel disease, n (%)	70 (8.9)	60 (8.3)	10 (14.7)	0.076	8 (11.8)	10 (14.7)	0.613
Obstructive CAD, n (%)	218 (27.6)	188 (26)	30 (44.1)	0.001	20 (29.4)	30 (44.1)	0.075
- PCI, n (%)	146 (18.5)	130 (18)	16 (23.5)	0.262	16 (23.5)	16 (23.5)	1.000
- CABG, n (%)	60 (7.6)	46 (6.4)	14 (20.6)	<0.001	4 (5.9)	14 (20.6)	0.011
- OMT alone, n (%)	12 (1.5)	12 (1.7)	0	0.284	2 (2.9)	0	0.154
Obstructive LM and/or pLAD lesion, n (%)	138 (17.5)	116 (16.1)	22 (32.2)	0.001	8 (11.8)	22 (32.2)	0.004
SYNTAX score	0 (0-8)	0 (0-7)	3 (0-21)	0.053	0 (0-4)	3 (0-21)	0.073
- Low (0-22), n (%)	682 (86.3)	630 (87.3)	52 (85.3)	0.013	60 (88.2)	52 (85.3)	0.072
- Intermediate (23-32), n (%)	66 (8.4)	56 (7.8)	6 (8.8)	0.048	4 (5.9)	6 (8.8)	0.090
- High (>32), n (%)	42 (5.3)	36 (5)	8 (9.5)	0.178	4 (5.9)	8 (9.5)	0.511

BMI: Body mass index, BSA: Body surface area, CABG: Coronary artery bypass graft, CAD: Coronary artery disesae, CX; Circumflex coronary artery, HDL-C: High-density lipoprotein cholesterol, LAD: Left anterior descending coronary artery, LAFB: Left anterior fascicular block, LDCC: Left dominant coronary circulation, LDL-C: Low-density lipoprotein cholesterol, LM and/or pLAD: Left main coronary artery and/or proximal left anterior descending coronary artery, LVEF: Left ventricular ejection fraction, LVMI: Left ventricular mass index, OMT: Optimal medical therapy, PCI: Percutaneous coronary intervention, WBC: White blood cell, *: The presence of dyslipidemia was defined according to age- and gender-adjusted percentiles from National Health and Nutrition Examination Survey III data, †: Calculated according to the DuBois method

Table 4. Predictors of patients with obstructive coronary artery disease and LM and/or pLAD lesion

	Predictors of patients with obstructive LM and/or pLAD lesion			
	Univariate analysis		Multivariate analysis †	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.037 (0.993-1.083)	0.094	-	-
Male gender	0.465 (0.189-1.046)	0.096	-	-
Hypertension	5.902 (2.470-8.098)	<0.001	4.907 (2.064-7.192)	<0.001
Diabetes mellitus	4.839 (2.034-7.513)	<0.001	4.154 (1.225-6.210)	0.022
Dyslipidemia	1.061 (0.677-1.662)	0.796	-	-
Current smoking	0.552 (0.242-1.258)	0.157	-	-
Family history of CAD	1.412 (0.612-3.259)	0.419	-	-
LAFB	3.587 (1.465-5.785)	0.005	2.554 (0.894-3.298)	0.160
LVMI	1.997 (0.981-1.014)	0.763	-	-

CAD: Coronary artery disease, LAFB: Left anterior fascicular block, LM and/or pLAD: Left main coronary artery and/or proximal left anterior descending coronary artery, LVMI: Left ventricular mass index, OR: Odds ratio, CI: Confidence interval, †: The variables included in multivariable analysis were age, male gender, hypertension, diabetes mellitus, and LAFB

It is difficult to distinguish between a left axis deviation caused by LAFB and that caused by LVH. In general, LVH does not shift the axis more leftward than -30 degrees. However, these two situations may overlap. Our results indicate that LVMI was higher in the LAFB group. In addition, LAFB prevalence was highest in patients with severely abnormal LVMI. LVH is associated with coronary heart disease mortality and hypertension (27). Moreover, as LVH advances, the deterioration in coronary microvascular circulation (28) can cause conduction abnormality in the left anterior fascicle, which is very sensitive to ischemia. Hypertension is an important cause of increased LVMI and the presence of LAFB. These two clinical parameters, which have a significant but not an independent predictive value in our study, are indirect markers that reflect the role of hypertension in CAD. However, the left conduction system structure is more complex and variable than the simplified trifascicular structure. This may be why an obstructive LM and/or pLAD lesions were not directly and independently associated to LAFB.

DM is a major risk factor for CAD with increasing prevalence. It is also associated with increased LVM and interstitial and perivascular fibrosis (29). Therefore, cardiomyopathy and LVH are two other DM-associated abnormalities in cardiovascular function. There is paucity of data on the relationship between DM and cardiac conduction system disorders. Jeong et al. studied 14,540 patients and found that DM is independently associated with RBBB, but not LBBB (30). In another study, García Rubí and Baduí Dergal (31). detected a high prevalence of bifascicular block among patients with diabetes. Although the increased prevalence of LBBB in patients with DM was not reported, the presence of LBBB in DM indicates advanced cardiovascular involvement and CAD complexity (32,33). In our study, DM was more prevalent in the group with LAFB. This could reveal the direct effect of diabetes on atherosclerosis or LVH. Another possible theory suggests that autonomic neuropathy is another complication in patients with diabetes associated with the emergence of LAFB in this group. However, the evidence for such an association is lacking; therefore, more research is necessary to ascertain this relationship.

Study Limitations

Our study has several limitations. The study was conducted with a relatively small sample. In addition, CAD was only evaluated through visual interpretation.

Conclusion

LAFB is associated with known cardiovascular risk factors, but it acts as a marker rather than a determinant of obstructive LM and/or pLAD lesions in patients with stable angina pectoris. The significantly increased prevalence of obstructive LM and/or pLAD lesions in patients with LAFB might be due to an increased prevalence in hypertension and DM, but there is a need larger studies to ascertain this finding. Nevertheless, LAFB is not frequently a "normal variant," and the presence of LAFB might help to identify obstructive LM and/or pLAD lesions in patients with suspected stable angina pectoris. Thus, physicians should have a low threshold for further cardiac evaluation if symptoms suggesting CAD are present.

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