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Original Article

# Left anterior descending myocardial bridge: Angiographic prevalence and its association to atherosclerosis



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#### ABSTRACT

*Objective:* Left anterior descending Myocardial Bridge (LADMB) is considered a benign condition and actually becomes a forgotten cause of serious cardiac events. This study was conducted to estimate the prevalence of LADMB and its association to atherosclerosis.

*Methods:* An observational retrospective study was conducted on patients referred for coronary angiography between June 2012 and June 2020. Coronary angiography database was revised and studied population was divided into 2 groups: LADMB group versus Non-LADMB group.

*Results:* LADMB was detected in 510 patients out of 35813 included in the study resulting in a prevalence at 1.42%. The mean age was 66.5 years. Male gender was more common than female (70vs30%). The prevalence of significant atherosclerotic LAD disease was more than two times higher in the non-LADMB group compared to the LADMB group. Statistical analysis revealed a significant negative association between LADMB and atherosclerosis (p < 0.001). A significant greater rate of MINOCA cases was observed in acute coronary syndrome LADMB patients.

*Conclusions:* LADMB is an inborn anatomic variation associated to atherosclerotic risk reduction in LAD. Physicians must be aware about the potential complications and pay attention to those classified at high risk for cardiovascular events.

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## 1. Introduction

Because myocardial bridge (MB) is usually benign, silent and incidentally discovered; it currently becomes a forgotten cause of hot topics in cardiovascular field like myocardial infarction and non-obstructive coronary artery disease (MINOCA). Firstly, described at autopsy by Reyman in 1737, MB is an anatomical congenital variant characterized by an intra-myocardial pathway of an epicardial coronary artery.<sup>1</sup> Until now, there are no available standard of care regardless that MB is a very old angiographic feature recognized by Portsmann in 1960.<sup>2</sup>

Previous studies have been attributed a wide spectrum of clinical presentation to MB such as acute coronary syndromes (ACS)

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including myocardial infarction,<sup>3</sup> silent ischemia,<sup>4</sup> arrhythmias<sup>3</sup> and sudden death.<sup>5</sup> The location, depth and length of MB on top of the degree of systolic compression were the determinant factors for clinical relevance.<sup>6</sup> Since angiography, the pathophysiological consequences and ischemia-inducing mechanisms of MB become more understood in parallel to the evolution of diagnostic imaging modalities like IVUS (intravascular ultrasound) and OCT (optical coherence tomography) whereas the therapeutic options remain limited.

The reported rates of MB with angiographic documented systolic compression varies between 0.5 and 12% and the middle part of left anterior descending (LAD) coronary artery is most commonly involved.<sup>7</sup> Usually, the Schwarz classification is used to guide the management of MB that was mainly based on beta blockers, calcium channel blockers and surgical intervention for refractory cases.<sup>8</sup> This study was conducted on one of the largest populations in the literature in order to estimate a recent prevalence of

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angiographic Left Anterior Descending Myocardial Bridge (LADMB) with systolic compression, its clinical presentation and its association to cardiovascular risk factors and coronary atherosclerosis. (Fig. 1).

# 2. Materials and methods

# 2.1. Study design and population

An observational retrospective single center study was conducted on all patients referred to coronary angiography in our interventional cardiology department between June 2012 and June 2020. Then, the studied population was divided into 2 groups: those with angiographic left anterior descending myocardial bridge and systolic narrowing versus others.

# 2.2. Data collection and end points

Data concerning the clinical indication for coronary angiography, cardiovascular risk factors (systemic hypertension, diabetes mellitus, dyslipidemia, smoking, familial history of coronary artery disease, body mass index, creatinine clearance), presence of previous significant cardiovascular disease, baseline characteristics (sex and age) and coronary angiography results were collected from the Hemolia® database. The study has been conducted according to the principles outlined in the Declaration of Helsinki and approved by the local ethics committee. In this study, we primarily aim to estimate the prevalence of angiographic LADMB and the related potential clinical presentation. The secondary end point is to investigate the correlation between LADMB and atherosclerotic coronary artery disease. A significant atherosclerotic left anterior descending coronary artery disease was visually assessed by 50% and more lumen diameter reduction on coronary angiogram.

#### 2.3. Statistical analysis

Quantitative data were summarized as means and standard deviations whereas qualitative data were summarized as count and percentage. Bivariate associations between continuous and categorical variables were studied with Student *t*-test while bivariate associations between categorical variables were studied with Chi square test. Then, variables found significantly associated with LADMB were introduced into multivariate logistic regression analysis investigating the association of LADMB and LAD atherosclerosis. A p value < 0.05 was considered significant. All statistical analysis was carried out using SPSS version 20.

# 3. Results

A total of 35813 patients were included in this observational descriptive study. LADMB were observed in 1.42% (510/35813) of cases. The mean age of studied population was  $66.5 \pm 13.4$  years. Out of 35813, 30% (10728) were females and 70% (25085) were males. The indication for coronary angiography referral was ACS (cardiac arrest, unstable angina, STEMI, and NSTEMI) in 33.6% (12037/35813), stable angina or atypical chest pain with silent ischemia in 27.2% (9740/35813), arrhythmia in 2.7% (965/35813), newly diagnosed or decompensated heart failure in 14.2% (5079/ 35813) and others (pre-surgical or valvular heart disease work-up) in 22.3% (7991/35813). A significant angiographic atherosclerotic disease reducing >50% the lumen of LAD was detected in 46.7% of the whole population (16724/35813). Regarding the prevalence of cardiovascular risk factors among the studied population: 50.5% had systemic hypertension, 24.3% had diabetes mellitus, 38.3% had dyslipidemia, 22.2% were smokers, 61.4% were overweight (BMI  $\geq$ 25) and 45.6% had chronic kidney disease (CrCl <60 ml/min) (Table 1).

Taking the group with LADMB from the whole studied population (510/35813), the mean of age was 66.3  $\pm$  13.6 years and 30%



Fig. 1. Left coronary angiogram with myocardial bridge. Left coronary angiogram showing non-significant coronary artery disease and LADMB (a) with severe systolic compression (b). LADMB: Left anterior descending myocardial bridge.

#### Table 1

Patients demographic data and bivariate association test between 2 groups.

	Whole population	LAD MB		P-value
	N = 53615 (%)	$\operatorname{Fes}(N=S10)\operatorname{No}(N=S10)$		
Mean age	$66.5 \pm 13.4$	66.3 ± 13.6	$66.5 \pm 13.4$	0.8
Sex				0.9
Male	25085(70)	357(60)	24728(70)	
Female	10728(30)	153(30)	10575(30)	
LAD disease	16724(46.7)	114(22.4)	16610(47)	< 0.001
Clinical situation				
ACS	12037(33.6)	175(34.3)	11862(33.6)	
Angina	9740(27.2)	168(32.9)	9572(27.1)	
Arrhythmias	965(2.7)	16(3.1)	949(2.7)	
Heart failure	5079(14.2)	26(5.1)	5053(14.3)	
Asymptomatic	7991(22.3)	125(24.5)	7866(22.3)	
Main CVRF				
Diabetes mellitus	8718(24.3)	58(11.4)	8660(24.5)	< 0.001
Systemic hypertension	18098(50.5)	202(39.6)	17896(50.7)	0.02
Dyslipidemia	13714(38.3)	171(33.5)	13543(38.3)	0.41
Smoking	7963(22.2)	121(23.7)	7842(22.2)	0.0003
$BMI \ge 25$	21988(61.4)	273(53.5)	21715(61.5)	< 0.001
CKD	13892(45.6)	159(36)	13733(45.7)	< 0.001

\*LADMB: Left anterior descending myocardial bridge. ACS: acute coronary syndrome. LAD: left anterior descending coronary artery. CVRF: cardiovascular risk factors. BMI: body mass index. CKD: chronic kidney disease.

were females. A significant angiographic atherosclerotic LAD lesion was identified in 22.4% (114/510) of the LADMB group and this proportion was two times higher in the non LADMB group (47% or 16610/35303). Moreover, 24.5% (125/510) of LADMB were incidentally discovered without related clinical relevance while 3.1% (16/510) may were related to arrhythmia, 5.1% (26/510) to heart failure, 32.9% (168/510) to angina and 34.3% (175/510) to ACS which were respectively the clinical indication to undergo for coronary angiography. Out of those presenting for ACS, 44% (77/175) were diagnosed with MINOCA whereas a significant coronary artery disease was detected in others (56%). Regarding cardiovascular risk factors: systemic hypertension (39.7 vs. 50.7%), diabetes mellitus (11.4 vs. 24.5%), dyslipidemia (33.5 vs. 38.3%), overweight (53.5 vs. 61.5%) and chronic kidney disease (36 vs. 45.7%) were less common in the LADMB group compared to others except for smokers (23.7 vs. 22.2%) (Table 1).

The first statistical analysis studying the bivariate association between the presence of LADMB and cardiovascular risk factors, demographic characteristics and LAD atherosclerotic disease showed a significant negative association with diabetes mellitus (p < 0.001), dyslipidemia (0.02), systemic hypertension (p < 0.001), body mass index (p < 0.0003), chronic kidney disease (p < 0.001) and LAD atherosclerosis (p < 0.001) while no significant association was observed with age (p = 0.8), sex (p = 0.9), and smoking (p = 0.41) (Table 1). Furthermore, a significant difference between the two groups (LAD-MB vs No LAD-MB) in terms of distribution of MINOCA was observed which was more common in LAD-MB group (44% vs 19%; p < 0.001) (Fig. 2). Then, a multivariate logistic regression investigating the association between LAD atherosclerosis and LADMB adjusted on the previous statistically significant variables confirmed the significant inverse relationship (OR = 0.3995% CI [0.30; 0.49]) (Table 2).



**Fig. 2.** Prevalence of MINOCA in acute coronary syndrome patients. Prevalence of MINOCA in acute coronary syndrome patients stratified by groups (LADMB vs. No LADMB). Black boxes (significant CAD); Grey boxes (MINOCA); P < 0.001 LADMB: Left anterior descending myocardial bridge. CAD: coronary artery disease. MINOCA: Myocardial infarction and non-obstructive coronary artery disease.

#### Table 2

Multivariate logistic regression investigating the association between LADMB and atherosclerotic LAD adjusted on previously significant variables.

Variables	P -value	O.R	95% CI
LAD atherosclerosis	<0.001	0.39	[0.30; 0.49]
Diabetes mellitus	< 0.001	0.47	[0.35; 0.64]
Dyslipidemia	0.67	1.04	[0.86; 1.25]
Systemic hypertension	0.058	0.81	[0.65; 1.07]
BMI	0.02	0.79	[0.65; 0.97]
CKD	<0.001	0.65	[0.51; 0.81]

\*LADMB: left anterior descending myocardial bridge. LAD: left anterior descending. BMI: body mass index. CKD: chronic kidney disease.

#### 4. Discussion

This study is interested in angiographic MB confined to the LAD coronary artery and showed a prevalence of angiographic LADMB at 1.42%. The global prevalence of angiographic MB reported in literature varies widely from 0.5 to 12%, but all previously published studies showed that LAD is the most involved coronary artery.<sup>9–15</sup> A recent published study by Çay et al performed on 25982 patients revealed an angiographic LADMB prevalence at 1.17%.<sup>16</sup> Indeed, it is worthy to mention that the prevalence of MB differs with the used diagnostic modalities. For example, it was estimated at 80% with autopsy series<sup>17</sup> and at 22.5% with CT-scan based studies.<sup>18</sup> Until now, the clinical significance of MB is debated and it is traditionally considered as benign inherited abnormality. In this study, onequarter of LADMB was detected incidentally while performing coronary angiography for pre-operative work-up (extra-cardiac surgery, valvular heart disease, aortic or peripheral vascular disease). Otherwise, the three-quarter were diagnosed in symptomatic patients presenting respectively for acute coronary syndromes, chest pain (typical or atypical angina), acute/chronic heart failure and arrhythmias. The causal relationship between LADMB and clinical presentation could not be investigated view the retrospective observational study type limited to coronary angiography database. Instead, the study findings emphasize on a potential role that could be attributed to MB in MINOCA cases. The mechanical compression or systolic milking effect of MB is the main mechanism predisposing to an adjacent plaque rupture<sup>3</sup> or spontaneous coronary dissection<sup>19</sup> resulting in acute coronary syndromes. Also, vascular compression enhances myocardial ischemia causing angina especially when systolic compression lead to a more than 50% reduction in vascular lumen.<sup>20</sup> Moreover, MB segment had a predilection for coronary spasm<sup>21</sup> and Kim et al showed a hyperreactivity to vasoconstrictive agents in the tunneled segments.<sup>22</sup>

In this study, the percentage of significant LAD atherosclerotic disease is more than two times higher in the non-LADMB group compared to LADMB group. In fact, a part of this difference could be due to the lower prevalence of cardiovascular risk factors in the LADMB group. However, this study showed a significant negative correlation between the presence of LADMB and the coexistence of atherosclerotic LAD coronary artery disease. The protective role of MB against atherosclerosis was explained by the prominent biomechanical forces and the increased wall shear stress in the tunneled segment.<sup>6</sup> This protective role was documented at histological level by Risse et  $al^{23}$  via showing a thinner intima in the bridged segment and Ishii et  $al^{24}$  by showing an absence of synthetic-type smooth muscle cells that promote collagen and elastic fibers production enhancing the progression of atherosclerosis. In addition, Masuda et al documented an alteration in the expression of endothelin-1 and other vasoactive agents that participate in the pathogenesis of atherosclerosis in patients with MB.<sup>25</sup> Instead, few published data suggest that a mid-LADMB contributes in the pathogenesis of atherosclerosis especially in the proximal adjacent coronary segment. For example, Nakaura et al<sup>26</sup> reported a positive correlation with mid-LADMB and atherosclerosis irrespective to atherosclerotic plaque localization, while Hong et al<sup>27</sup> reported a higher prevalence of coronary stenosis located proximally to the MB. In fact, we conventionally agree with the anti-atherosclerotic role of MB in the bridging segment whereas the proximal pro-atherogenic effect remains controversial and depending on the coexisting cardiovascular risk factors.<sup>6,27</sup>

Lastly, the management of MB is not well standardized. Both invasive and non-invasive strategies are reported with no available data from randomized clinical trials defining the optimal therapeutic approach.<sup>28</sup> Pharmacological management including betablockers<sup>29</sup> and non-dihydropyridine calcium-channel blockers were frequently used as first line therapy for symptomatic MB while the invasive strategies like percutaneous coronary intervention and surgical approach are recommended for refractory unresponsive cases.<sup>30</sup> In general, using beta-blockers are preferred over calcium channel blockers despite the absence of head to head comparison studies.<sup>31</sup> Indeed, the resulting beneficial symptomatic outcomes were explained by the mechanisms of action of these substances that reduce myocardial contractility and subsequently the burden of compression on the tunneled coronary segment, diminish the hemodynamic disturbances triggered by MB and decrease the heart rate prolonging the diastolic filling period.<sup>29</sup> Data from previous studies supported the symptomatic improvement associated with the use of beta-blockers especially for  $esmolol^{29}$  and  $nebivolol^{29-32}$  in cases of MB whereas no benefits regarding morbidity and mortality have been documented.<sup>33</sup> In parallel, the results from using percutaneous coronary stenting as a therapeutic approach for recalcitrant MB cases are controversial. Regardless the improvement of symptoms and hemodynamic abnormalities noted by numerous studies after performing percutaneous coronary intervention,<sup>34</sup> multiple deleterious outcomes such as stent fracture,<sup>35</sup> stent thrombosis<sup>36</sup> and in-stent restenosis<sup>37</sup> were commonly observed constituting a limitation for stent implantation in MB condition. In opposition, coronary artery bypass graft (CABG) and myotomy (unroofing) are the preferred therapeutic approach for MB cases refractory to medical therapy. We preferentially proceed with surgical unroofing which relieve the myocardial ischemia via correcting the anatomic abnormality and improving blood flow<sup>31</sup> while CABG is preferred for extensive MB (>25 mm), deep MB (>5 mm), persistent diastolic compression and coexisting significant coronary artery disease.<sup>38–40</sup>

The limitation of this study is the retrospective nature. Only the written reports were reviewed while coronary angiograms weren't. Some physicians may miss to note the presence of myocardial bridge which subsequently leads to an underestimation to the prevalence of LADMB. Indeed, it is worthy to mention that reports on Hemolia® database could not be validated by operators if the required parameters had not completed leading to attenuate the potential missing values.

In conclusion, this study conducted on one of the largest populations in literature estimates the prevalence of LADMB at 1.42% which was closer to previous published data. Myocardial bridge which is an inborn congenital abnormality may result in lifethreatening complications. Physicians must be aware about the potential consequences and the available therapeutic strategies. Future prospective studies targeting MB pathophysiological pathway, ischemia mechanisms, clinical significance and atherosclerotic pathogenesis are required in order to select high risk patients, establish an appropriate direct therapy and prevent the cardiovascular events. **Key messages:** 

It is well known that myocardial bridge is a common silent inborn coronary abnormality. This study provides an up-to-date A. Matta, R. Canitrot, V. Nader et al.

review about the angiographic prevalence of LAD-MB (Left anterior descending myocardial bridge) and the potential corresponding clinical relevance. This study shows a negative association between the presence of LAD-MB and development of significant atherosclerotic disease. Furthermore, we introduce the hypothesis of correlation between myocardial bridge and MINOCA (myocardial infarction with no obstructive coronary artery) in order to put into question a probable contributing role of MB to this clinical entity which could be the purpose for future studies.

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## **Declaration of competing interest**

The authors declare that there are no conflicts of interest.

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