EXPLORING MYOCARDIAL BRIDGES CHARACTERISTICS IN NORTH-EASTERN ROMANIA. A RETROSPECTIVE ANALYSIS

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EXPLORING MYOCARDIAL BRIDGES CHARACTERISTICS IN NORTH-EASTERN ROMANIA: A RETROSPECTIVE ANALYSIS (Abstract): Myocardial bridges are defined by a segment of the coronary artery taking an intramuscular route, diverging from its usual superficial path over the myocardial tissue and, instead, traversing through the myocardium itself. Currently, their true prevalence remains uncertain and challenging to estimate accurately. Their dynamic presentation shapes the diversity of clinical manifestations, resulting in highly variable expressions among individuals. **Materials and methods:** We conducted a retrospective analysis of myocardial bridge characteristics in patients undergoing coronary computed tomography angiography (CCTA) at the "Prof. Dr. George I.M. Georgescu" Institute of Cardiovascular Diseases in Iasi, Romania, from 2012 to 2022. Additionally, we sought to investigate any potential correlation between the presence of myocardial bridges and the development of atherosclerosis and coronary artery disease. **Results:** Out of the 66 patients with myocardial bridges, 44 were males, accounting for 66.7% of the total cases. The average age was of 59.42 years (± 11.84 years). In 97% of cases, the left anterior descending artery (LAD) was affected, primarily at its middle segment (60.6%). The mean width measured 3.02±1.22 mm and the mean length was 20.33±9.25 mm. A significant elevation in the average calcium score level was observed among males (p=0.025). Individuals with myocardial bridge thickness over 5 mm showed significantly higher average calcium scores (p=0.025). **Conclusions:** Using CCTA improves the detection of clinically significant myocardial bridges, with the middle segment of the left anterior descending artery being the primary site in most cases. The study suggests a potential link between myocardial bridges thickness and higher coronary artery calcium scores, prompting further exploration. Correlations with atherosclerosis and hypertension require deeper investigation for a comprehensive understanding of myocardial bridges clinical impact. **Keywords:** MYOCARDIAL BRIDGES, CORONARY ARTERY ANOMALIES, ROMANIAN POPULATION, CARDIAC IMAGING.

INTRODUCTION

Initially documented by Reymann in 1737, myocardial bridging represents a congenital cardiac anomaly wherein a layer of cardiac muscle overlays a section of a coronary artery passing through the myocardium, forming a bridge-like configuration. This intramural portion of the artery, referred to as the "tunneled" artery, is surrounded by cardiac muscle tissue (1, 2). The prevalence of myocardial bridges varies depending on the diagnostic method employed. Post-mortem investigations yield the highest detection rate for myocardial bridges, ranging up to 86%, with an average of 25% (1). Invasive procedures like conventional coronary angiography can detect approximately 12% of myocardial bridges. Given the current inclination towards non-invasive approaches for identification, coronary computed tomography angiography (CCTA) emerges as the most accurate for assessing myocardial bridges. It provides superior capabilities in delineating the bridge's dimensions, as well as evaluating the degree of the induced compression (1). With various methods available to detect these anomalies, each differing in accuracy and specificity, the true prevalence of myocardial bridges remains uncertain and challenging to estimate accurately. However, there is a high likelihood that the actual prevalence of myocardial bridges exceeds current estimates (1). The predominant localization of myocardial bridges is typically within the left anterior descending artery (LAD), particularly evident in its mid-segment (3). When assessed using CCTA, myocardial bridges are categorized based on their depth: superficial (≥1 mm), deep (≥2 mm), and very deep (≥5 mm). Additionally, myocardial bridges are classified as short if their length is <25 mm and long if their length is ≥25 mm. This classification criterion aids in distinguishing between benign and clinically significant myocardial bridges based on their depth and length within the cardiac muscle (4). While the superficial and short myocardial bridges might usually be asymptomatic, those with a depth ≥2 mm and a length ≥25mm can have clinical manifestation that might vary from angina, heart block to acute coronary syndrome, syncope and even rarely sudden death (5). At the same time, recent studies aim to discern whether the presence of myocardial bridges exhibits a potential protective or detrimental effect on various cardiac conditions. Researchers analyzed the values of Ki-67 marker, assessing artery inflammation and atherosclerosis, and macrophages among the bridged segment of the coronary arteries (6). This study revealed their lower levels in the segments with myocardial bridges, compared to the other areas of the artery. Nevertheless, there are authors who contradict this hypothesis, suggesting that the existence of myocardial bridges could be a factor in determining coronary artery disease and therefore, ischemia (1). The diverse array of clinical expressions associated with myocardial bridges are significant given the absence of standardized guidelines for their identification, monitoring and treatment (7).

AIMS. Our study aimed to explore the characteristics of myocardial bridges observed in patients seeking care at "Prof. Dr. George I.M. Georgescu" Institute of Cardiovascular Diseases, over a decade within the North Eastern region of Romania. Additionally, we sought to investigate any potential correlation between the presence of myocardial bridges and the development of atherosclerosis and coronary artery disease. The motivation for our investigation started from the limited existing research on

the prevalence and attributes of myocardial bridges within the Romanian population. This gap in knowledge highlights the importance of our study in contributing to a deeper understanding of cardiovascular anomalies within this specific demographic.

MATERIALS AND METHODS

Study design and patients

Our research investigated a cohort of 12,758 patients with cardiovascular diseases who underwent coronary computed tomography angiography (CCTA) from 2012 to 2022 at "Prof. Dr. George I.M. Georgescu" Institute of Cardiovascular Diseases from Iasi, Romania. The information employed in this study was obtained from the medical files of the patients. The acquired data facilitated the categorization of the enrolled cohort into various groups based on anomalies of the coronary arteries, with a primary focus on myocardial bridges. Our database included demographic variables including the age and gender (female/male) of the patients, all of whom were adults. Simultaneously, we documented the presence of coronary artery disease, chronic cardiac failure, dyslipidemia, hypertension and coronary angioplasty with stents. The study design and protocol were approved by the Ethics Committee of "Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania (no. 115/15.10.2021).

CCTA Assessments (Myocardial Bridges and Agatston score)

In this investigation, we initially incorporated data concerning the affected coronary artery by myocardial bridges, along with detailed characteristics regarding the depth and length of these structures. All measurements pertaining to these parameters were recorded in millimeters (mm). Subsequently, our classification scheme stratified myocardial bridges into three distinct categories based on depth: superficial (<2mm), deep (≥2 and <5), and very deep (≥5 mm). Regarding length, we defined two categories relative to a threshold of 25 mm: those falling below this threshold were categorized as short, whereas those equal to or exceeding it were classified as long. Concurrently, we documented the presence of atherosclerosis and consecutively assessed the degree of stenosis in the affected coronary artery with myocardial bridge, classifying stenosis in non-critical if the diameter of the coronary artery was <70% and critical if it was ≥70%.Furthermore, we integrated the Agatston calcium score into our database, categorizing it into four different groups: 0. no atherosclerosis (0 Agatston units), 1. mild (1-100Agatston units), 2. moderate (101-400Agatston units) and 3. severe (>400Agatston units).

Statistical analysis

Data were collected and subjected to analysis using the *Statistical Package for Social Sciences version 27.0* (IBM Corp., Armonk, NY, USA). Specifically, the analysis utilized the ANOVA test, a widely recognized method for examining variance across multiple groups. Primary indicators such as the minimum and maximum values, along with frequency distributions, were examined to gain insights into the range and distribution of the data. Indicators of central tendency including the simple arithmetic mean and median were calculated to understand the average or typical value of the dataset. Indicators of dispersion, such as the standard deviation and standard error, were computed to assess the spread or variability of the data points around the mean. Additionally, confidence intervals of the mean were determined to quantify the precision of the estimated

population parameters. Qualitative significance tests were conducted to examine the significance of categorical variables within the dataset. All analyses maintained a significance level of $p < 0.05$.

RESULTS

Among the examined patients, 350 (2.74%) exhibited coronary artery anomalies, and among them, 66 were diagnosed with myocardial bridges (18.9%). Out of the total cohort, 44 were males, constituting 66.7% of the patients, while 22 were females, accounting for 33.3% (fig. 1).

The age ranged from 22 to 84 years, with an average level of 59.42 years ± 11.84 years, which is relatively close to the median value (60.50 years) (fig. 2).

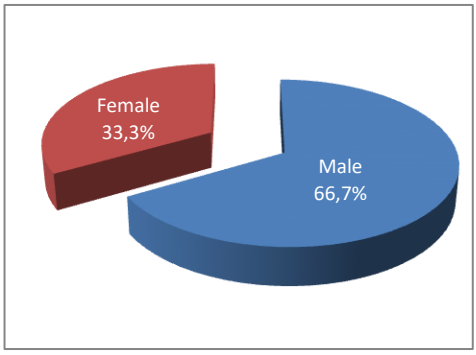

Fig. 1. Gender distribution among patients with myocardial bridges

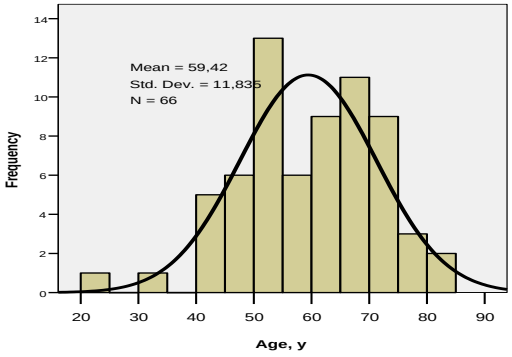

Fig. 2. Diagnostic age histogram for patients with myocardial bridges

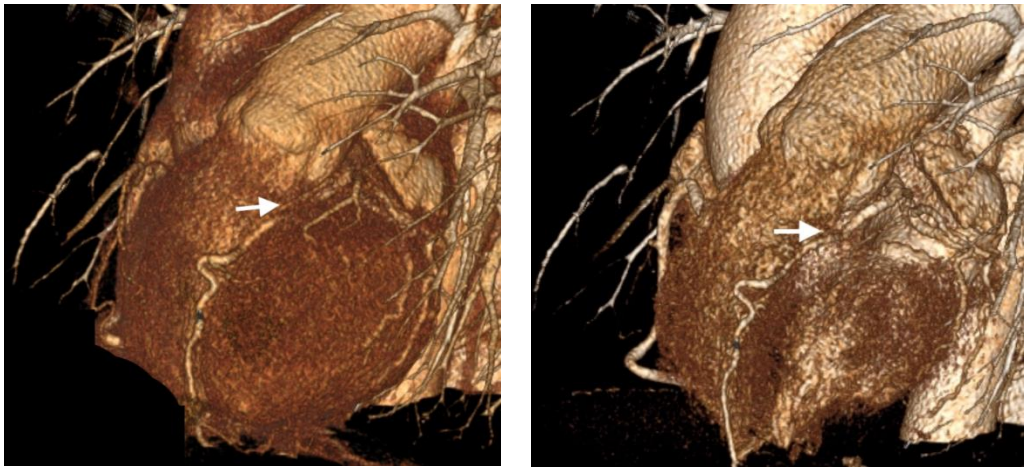

Fig. 3. 3-dimensional volume-rendered images obtained from coronary computed tomography angiography of a myocardial bridge in the middle segment of the left anterior descending artery in a female patient

In 97% of cases, the primary coronary artery affected was the left anterior descending artery (LAD) (fig. 3). Only one instance of myocardial bridge was observed

on the right coronary artery (RCA) and another one on the left main (LM).

The middle segment of the LAD was the most common site of myocardial bridges localization, accounting for 62.5% of total bridges found (tab. I).

TABLE I.

Localization of myocardial on the left anterior descending artery (LAD), left main (LM) and right coronary artery (RCA)

Characteristics	Coronary		
	LAD (n=64)	LM (n=1)	RCA (n=1)
Location			
proximal	11 (17.2%)	1 (100%)	1 (100%)
medial	40 (62.5%)	0 (0%)	0 (0%)
distal	12 (18.8%)	1 (100%)	0 (0%)

Furthermore, our investigation explored the primary characteristics of myocardial bridges, examining their morphology concerning length and width, as well as the presence of stenosis (tab. II). Analysis of myocardial bridge depth revealed that the majority of patients (69.7%) exhibited deep myocardial bridges, with a smaller proportion presenting very deep myocardial bridges (16.7%), and a further subset displaying superficial myocardial bridges (13.6%) (tab. II). In terms of length, data indicated that a significant portion of patients (74.2%) had short myocardial bridges, while the remaining 25.8% presented long ones.

TABLE II.

Characteristics of myocardial bridges

Myocardial bridges Coronary Artery	N	%
LAD	64	97.0
LM	1	1.5
RCA	1	1.5
Location on the coronary artery		
Proximal	13	19.7
Medial	40	60.6
Distal	13	19.7
Width (mm)		
Mean ± SD	3.02±1.22	
median/limits	2.50/1.3-6.0	
Thickness (mm)		
< 2	9	13.6
2-5	46	69.7
≥ 5	11	16.7
Length (mm)		
Mean ± SD	20.33±9.25	
median/limits	18/8-50	
Dimensions		
Short	49	74.2
Long	17	25.8

The mean width measured 3.02 ± 1.22 mm, indicating a relatively consistent range. Conversely, the mean length was 20.33 ± 9.25 mm, demonstrating a wider dispersion of values. Simultaneously, 24 patients exhibited stenosis on the LAD, with only one case showing involvement of the RCA (tab. 3). When evaluating the degree of the stenosis of the affected coronary arteries, the results revealed a mean value of 13.26±21.13. There were 12 patients (18%) who presented stenosis ≥50%, and just one patient with stenosis >70%. Nevertheless, in our study, only 3 male patients (5%) underwent stent placement.

TABLE III.

Morphological aspects of myocardial bridges

Characteristics	Coronary		
	LAD (n=64)	LM (n=1)	RCA (n=1)
Stenosis	24 (37.5%)	0 (0%)	1 (100%)
Thickness			
< 2 mm	9 (14.1%)	0 (0%)	0 (0%)
2-5 mm	44 (68.8%)	1 (100%)	1 (100%)
≥ 5 mm	11 (17.2%)	0 (0%)	0 (0%)
Length			
Long	17 (26.6%)	0 (0%)	0 (0%)
Short	47 (73.4%)	1 (100%)	1 (100%)

Our analysis of the coronary artery calcium score revealed a heterogeneous distribution among patients. While a substantial portion (42.4%) exhibited a mild score, a significant proportion (40.9%) presented zero scores, indicating absence of calcification. Additionally, a smaller percentage (9.1%) exhibited severe scores, while moderate scores were observed in just 7.6% of cases (fig.4). This spectrum of findings underscores the differences of calcium deposition within the coronary arteries with myocardial bridges, suggesting varying degrees of cardiovascular risk among the studied population.

Our observations revealed a significant elevation in the average calcium score level among males (p=0.025) (fig.5).

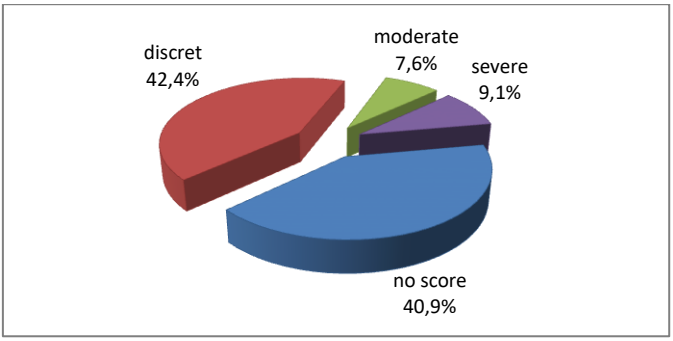

Fig. 4. Coronary Artery Calcium Score in patients with myocardial bridges

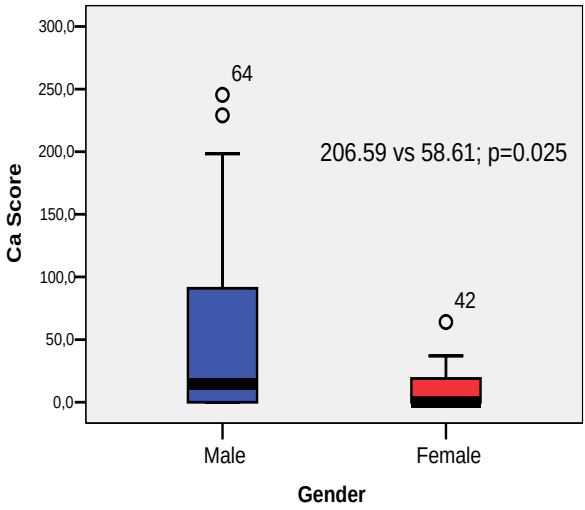

Fig. 5. Average calcium score levels by gender

Simultaneously, the average calcium score level was significantly higher in individuals with a myocardial bridges thickness exceeding 5 mm (p=0.025) (fig. 6).

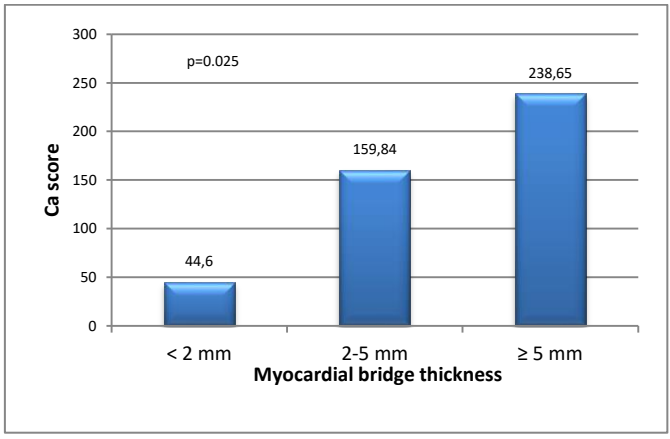

Fig. 6. Comparison of Average Calcium Score Levels between Myocardial Bridge Thickness Groups

Our investigation into the prevalence of hypertension, dyslipidemia, coronary artery disease (CAD), and chronic heart failure among these patients offered promising insights, observing a predominant occurrence of these conditions in males. Hypertension manifested in 29 patients (44%), with a noteworthy observation that half of the male cohort was affected by this condition. Dyslipidemia was observed in 9 male individuals and 6 female patients. Furthermore, CAD was identified in 25 patients (38%), while chronic heart failure was diagnosed in 17 individuals (26%) (tab. IV).

TABLE IV.
Associated conditions by gender in patients with myocardial bridges

Comorbidities	Male (n=44)		Female (n=22)		Chi² Test p	RR	IC95%
	n	%	n	%			
Hypertension	22	50.0	7	31.8	0.157	1.68	0.79-3.57
Dyslipidemia	9	20.5	6	27.3	0.537	1.14	0.73-1.80
Coronary artery disease	18	40.9	7	31.8	0.470	1.31	0.62-2.76
Chronic cardiac failure	14	31.8	3	13.6	0.098	2.20	0.74-6.51

DISCUSSION

The large spectrum of coronary artery anomalies comprises of a variety of rare congenital conditions, exhibiting diverse morphologies, clinical presentations, and potential hemodynamic implications (8).

Myocardial bridges, included within this category, are distinguished by a segment of the coronary artery taking an intramuscular route, diverging from its usual superficial path over the myocardial tissue and, instead, traversing through the myocardium itself. Therefore, this anomaly may impact not only the anatomy of the coronary arteries, but also the blood flow distribution among the myocardium(9).The extent of this effect fluctuates depending on the degree of compression in the bridged region during contraction, creating a 'milking' action that reduces blood flow and could predispose to ischemia. This dynamic presentation not only influences myocardial perfusion, but also shapes the occurrence and diversity of clinical manifestations in patients with myocardial bridges, resulting in highly variable expressions among individuals (10).

Their identification is now achievable through both invasive methods, such as Intravascular Ultrasound (IVUS) or coronary angiography, and non-invasive approaches like echocardiography, CCTA and Cardiac Magnetic Resonance Imaging (CMRI) (5). Echocardiography serves as a valuable tool for detecting myocardial bridges, although its specificity is limited-it may reveal irregularities in the septal wall motion from end-systole to early-diastole, alongside preserved heart function in the apex(4).Non-invasive imaging techniques, particularly CCTA, offer the highest accuracy and specificity in detecting myocardial bridges. CCTA alone can detect up to 86% of cases, emphasizing its efficacy. In contrast, the prevalence of myocardial bridges detected via coronary angiography is a mere 1.7%. This discrepancy underscores the superiority of non-invasive methods in identifying these anomalies (5). At the same time, CMRI, due to the lack of contrast administration or radiation exposure, is preferable for younger athletes and patients with kidney failure. Recent studies show its superiority over MDCT in detecting calcified coronary artery lesions, but its use in detecting myocardial bridges is still limited due to the poor spatial resolution (11, 12). Our study revealed a detection rate of myocardial bridges at 0.51% among all patients scanned (12758). Remarkably, among all coronary artery anomalies observed, myocardial bridges ranked as the third most common, accounting for up to 18.9% of cases (13).

In our study, we included patients aged 22 to 84 years, with a mean age of 59.42 years ± 11.84, reflecting the diverse age range at which myocardial bridges are

identified. Furthermore, we noted a predominant presence of male patients with myocardial bridges (66.7%), consistent with findings from prior studies, thereby underscoring their heightened prevalence among men (2).

While myocardial bridges may occur across any of the primary coronary arteries, prevailing research underscores their most common occurrence along the left anterior descending artery (LAD), especially within its middle segment (10). Our study corroborates this notion, particularly evident in the predominant presence of myocardial bridges in the LAD in 97% of cases. Additionally, a small minority of cases (3%) featured myocardial bridges on the right coronary artery (RCA) and left main coronary artery (LM). However, our findings reveal a distribution pattern within the myocardial bridges localization: the middle portion was most frequently affected, observed in 40 patients, followed by the distal and proximal segments, each exhibiting nearly comparable prevalence rates (18.8% and 17.2%, respectively).

Debates persist over the role of myocardial bridges within the structure of the coronary artery, with discussions focusing on their potential protective or detrimental impacts. Coronary atherosclerosis involves the formation of plaques into the main arteries of the heart, predisposing to the development of thrombotic events triggered by their rupture (14). Though some theories propose that myocardial bridges may offer protection against atherosclerosis development, additional research is necessary to validate this hypothesis. Several studies revealed that the vascular segments with myocardial bridges exhibit a notable reduction in the occurrence of atherosclerotic lesions compared to those without it (6).

In our study, 38% of the patients exhibited stenosis on the coronary artery affected by the myocardial bridge, with a majority of 24 cases involving the LAD. Simultaneously, we examined the calcium score, also referred to as the Agatston Calcium Score, to assess the presence and extent of calcium buildup within the coronary arteries while utilizing CCTA. This score serves as a predictive instrument for imminent cardiovascular disease progression and helps in shaping therapeutic strategies. At the same time, it is an important non-invasive tool that could not only be used in evaluating the patients with clinical manifestations, but also in asymptomatic individuals with low to moderate risk of developing CAD (14). The observation that 41% of patients in our study recorded a zero-calcium score, indicating a reduced likelihood of developing CAD in the near term, alongside 42% displaying mild scores, could further highlight the potentially protective function of myocardial bridges in the coronary arteries. At the same time, only a small percentage of patients (18%) presented stenosis ≥50%. Despite only 17% of patients exhibiting moderate and severe calcium scores, careful consideration is warranted. Concurrently, our study revealed a noteworthy increase in the average calcium score level among males ($p=0.025$). These findings underscore the necessity for ongoing surveillance of the patients, given the unpredictability of myocardial bridge manifestations and clinical outcomes.

Two primary characteristics of myocardial bridges are their length, spanning between four and forty millimeters, and their depth, ranging from one to ten millimeters (15).A meta-analysis study indicated that, through angiography and CCTA, the average length of myocardial bridges was 21

millimeters, with a depth of 3 millimeters. Autopsy findings revealed a mean length of 19.3 millimeters and a depth of 3.2 millimeters for myocardial bridges. Nevertheless, it is evident that even subtle variations may arise, influenced by the method of investigation-whether invasive (angiography) or non-invasive (CCTA), as well as through autopsy (1). Despite these differences, the dimensions remain remarkably similar across the various modalities. In our study implying the evaluation of myocardial bridges through CCTA the mean length was 20.33±9.25, while the width was 3.02±1.22.

Based on their depth, we classified myocardial bridges as superficial (1-2mm), deep (≥2 and <5mm), and very deep (≥5 mm). The majority of myocardial bridges were deep, with 44 individuals presenting it on the LAD and two patients on the RCA, respectively on the LM. Superficial and very deep myocardial bridges were present in almost the same proportions, with just two more patients presenting superficial compared to very deep. Simultaneously, regarding their length, myocardial bridges were categorized as short (<25mm) and long (≥25 mm), with only 25.8% presenting long myocardial bridges. Clinical significance in myocardial bridges is typically defined by a depth of≥2 mm and a length of≥25 mm (4). In our study, we found that 26% of the patients met this criterion, with 6 individuals exhibiting long and deep myocardial bridges (9%) and 11 individuals displaying long and very deep myocardial bridges (17%). At the same time, a higher value of the depth is associated with increased chance for the development of cardiovascular events (4). This theory is further supported by one of our findings, which indicated a higher average calcium score level in individuals with a myocardial bridge thickness exceeding 5 mm (p=0.025). This suggests an elevated risk of potential rupture of atherosclerotic plaques, thereby predisposing individuals to acute coronary syndromes.

Typically, most myocardial bridges are benign and asymptomatic, particularly when their depth is less than one millimeter. However, they can occasionally become clinically significant. Their initial presentation may manifest as angina (stable, unstable or vasospastic), often occurring during systole when the myocardial bridge is compressed (5, 11).Unstable angina was more frequently identified in patients affected by this anomaly than troponin-positive myocardial infarction (5). Nevertheless, there are no correlation between the severity of the angina and the dimensions of the myocardial bridge (1).More severe manifestations include Takotsubo syndrome, heart blocks, or, in extremely rare cases, sudden death (5). Research indicates that male patients affected by this anomaly are at elevated risk of experiencing ventricular tachycardia or premature ventricular contractions during physical exertion. This heightened risk is attributed to the occlusion of the coronary artery, potentially leading even to sudden death, scenario also observed in high-performance athletes with myocardial bridges (1, 16).

Currently, there are several hypotheses regarding the development of myocardial ischemia in these patients. In healthy individuals, 80% of coronary flow occurs during diastole, but in those with myocardial bridges, systolic compression disrupts this normal flow pattern. Concurrent tachycardia can further reduce diastole, exacerbating myocardial bridge manifestations and

increasing oxygen consumption, potentially leading to ischemia. Another phenomenon is the “branch steal" in myocardial bridges, resulting in lower diastolic pressures in the affected segment and more local ischemia in mild-moderate bridges compared to distal myocardium. Additionally, the continuous milking effect of the anomaly exposes sub-endothelial tissue and activates the coagulation system, thereby increasing the risk of intracoronary thrombogenesis and raising questions about the true extent of their contribution to cardiovascular mortality (11, 16).

In our research, we explored the presence of hypertension as a potential accelerator of atherosclerosis and, consequently, CAD. Our findings revealed that hypertension was prevalent in 44% of the patients, notably affecting 50% of male participants. Similarly, when investigating the presence of CAD, we observed its occurrence in 38% of the patients, predominantly affecting 18 male patients compared to only 7 female patients. Additionally, fewer patients exhibited chronic cardiac failure, with a majority of affected individuals being male. These observations underscore a gender disparity in the prevalence of cardiovascular conditions among individuals with myocardial bridges, with men exhibiting a higher frequency of hypertension, CAD, and chronic cardiac failure compared to women. Nevertheless, in our study, dyslipidemia was present only in 15 patients (23%).

In such clinical scenarios, pharmacological treatment is necessary to alleviate symptoms arising from concurrent disorders such as arrhythmias, hypertension, or hypertrophy (5). In the therapeutic management of myocardial bridges, beta-blockers are prioritized to optimize hemodynamic function, followed by non-dihydropyridine calcium channel blockers, which have a vasodilator effect and are able to improve symptomatology. Additionally, antiplatelet therapy should be considered to prevent and mitigate acute events in hypertensive patients with coronary artery disease (CAD) (5, 1).

In cases where pharmacological interventions prove inefficient and the affected coronary artery exhibits significant stenosis, stent implantation may emerge as the preferred solution. Prior studies have demonstrated enhanced clinical outcomes following coronary stenting in patients with myocardial bridges. However, in situations where neither medical treatment nor coronary stenting are feasible, surgical myotomy may be considered. Alternatively, another surgical option entails the anastomosis of the internal mammary artery (IMA) to the LAD (2). Finally, coronary artery bypass grafting may be considered in severe cases of myocardial bridges with significant hemodynamic impact and dimensions exceeding 25 millimeters (1). In our study we observed that only three male patients needed coronary angioplasty with stents, comprising just 5% of the total patient population, suggesting that only in certain situations myocardial bridges may lead to severe enough hemodynamic compromise to necessitate invasive interventions.

CONCLUSIONS

Utilizing a sensitive and precise investigative technique such as CCTA improves the detection of clinically significant myocardial bridges, with the middle segment of the left anterior descending artery being the primary site in most cases. The study suggests a potential link between myocardial bridges thickness and higher coronary artery

calcium scores, prompting further exploration. Correlations with atherosclerosis and hypertension require deeper investigation for a comprehensive understanding of myocardial bridges clinical impact.

CONFLICT OF INTEREST AND FUNDING

The authors declare no conflicts of interest. This research received no external funding.

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